



IRON DEFICIENCY ANEMIA AND FEBRILE SEIZURES IN CHILDREN 6 MONTHS TO 6 YEARS IN CENTRAL INDIA

Pediatrics

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ABSTRACT

Background and Objectives: Pediatric Febrile seizure is very common occurrence in childhood and this study evaluates association between febrile seizures and iron deficiency anemia.

Materials and Methods: We conducted a hospital based case-control study on 120 children 6 months to 6 years old age hospitalized at a tertiary care hospital in central India from January 2018 to December 2018. Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH), Mean Corpuscular Haemoglobin Concentration (MCHC), Red Blood Count (RBC) and Red Cell Distribution Width values were collected and analysed statistically with SPSS Ver 20.0.

Results: There were no differences regarding age and sex between the groups. Respiratory tract infections were the most common cause of fever. There was significant difference in hemoglobin, hematocrit, MCHC, MCV, RDW in the two groups.

Conclusion: In children with febrile seizures, iron deficiency anemia was more common.

KEYWORDS

iron deficiency, Febrile seizure

INTRODUCTION

Pediatric febrile seizures, which represent the most common childhood seizure disorder, exist only in association with an elevated temperature. Evidence suggests, however, that they have little connection with cognitive function, so the prognosis for normal neurologic function is excellent in children with febrile seizures.(1) Epidemiologic studies have led to the division of febrile seizures into 3 groups, as follows:

- Simple febrile seizures
- Complex febrile seizures
- Symptomatic febrile seizures

This is a unique form of seizures that occurs in early childhood and only in association with an elevation of temperature. The underlying pathophysiology is unknown, but genetic predisposition clearly contributes to the occurrence of this disorder.(2)

No evidence suggests that any therapy administered after a first simple febrile seizure will reduce the risk of a subsequent afebrile seizure or the risk of recurrent afebrile seizures (ie, epilepsy).

Oral diazepam can reduce the risk of subsequent febrile seizures. Because it is intermittent, this therapy probably has the fewest adverse effects. If preventing subsequent febrile seizures is essential, this would be the treatment of choice.(3)

Although it has been felt that antipyretic therapy cannot prevent simple febrile seizures, it is desirable for other reasons, for instance comfort. A randomized controlled trial published in 2018 suggested that rectal acetaminophen 10 mg/kg given every 6 hours may prevent febrile seizure recurrence within the same febrile episode.(4, 5)

Weakening of the antioxidative defense mechanisms and increased levels of free radicals can result to seizures (6). Thereby, electrolyte imbalances and deficiency of micronutrients such as zinc, selenium, magnesium, copper and vitamin D seen in the malnutrition and failure to thrive can predispose children to the febrile seizures (7–10).

Iron plays an important role in the neural activity, enzymatic reactions and metabolism of neurotransmitters (11). In developing countries, iron deficiency is the most common nutritional problem. its peak incidence is in the ages between 6 to 24 months old, which overlaps with the peak incidence of febrile convulsion that is in the ages from 14 to 18 months old (11,12). In these countries, 46%-66% of children less than four years age have anemia that half of this prevalence is due to iron deficiency anemia(13).

Anemia- defined as hemoglobin level below two standard deviations from normal values for age- affects changes in synaptic neurotransmitter systems including norepinephrine, dopamine, glutamate, and gamma-aminobutyric acid (GABA) (14,15). The possibility of lowering seizure threshold and increasing the risk of febrile seizures by the anemia have been discussed in many studies (13,14). While others have concluded that anemia does not predispose to febrile seizures and may even have a protective effect (16–18).

We investigated the relationship between iron deficiency anemia and febrile seizures in this study.

MATERIALS AND METHODS

It was a case control study which was done on admitted patients in the department of Pediatrics in a tertiary teaching hospital in central India from January 2018 to December 2018. A total of 120 patients were selected of which 60 were cases and 60 were controls. The study was approved by institutional ethical committee. Cases with known epilepsy, complex seizures, CNS infection, mentally retarded and metabolic disorders were excluded. Age, sex and weight were documented. Diagnosis of simple febrile seizures was made after detailed history and examination. Control group of 60 febrile cases with same age and gender but without seizures were selected to compare with case group. Axillary temperature more than 37 degree C was considered as fever. seizures lasting less than 15 minutes and not recurring within 24 hour without CNS infection or metabolic imbalance were considered simple febrile seizures. Cases in both groups with haemoglobin <11.5 Gm/dl, haematocrit, Decreased Red Blood Cell (RBC), Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH), Mean Corpuscular Haemoglobin Concentration (MCHC) and increased Red Cell Distribution Width (RDW) were taken as diagnostic criteria for Iron Deficiency Anaemia. Other causes of anaemia were ruled out through clinical evaluation. Serum Ferritin Level could not be done as this facility was not available in hospital and patients were not able to afford it. SPSS version 20 was used to enter and analyse data. As the sample size was small, Fisher's exact test was applied for comparison. P value<0.05 was considered as significant.

RESULTS

A total of 60 cases of febrile seizures were studied and Control group had also 60 cases for comparison. Matching variables of both groups are shown in table-1. Both the groups were comparable at the base line as shown in the table-1. Causes of fever are shown in table 2. In case group 42 had Haemoglobin <11.0 gm% while in control group 26 cases had haemoglobin <11.0 gm% (Odd Ratio 3.0513 95% CI

1.0533–8.8390). Mean Haemoglobin, Haematocrit, Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH), Mean Corpuscular Haemoglobin Concentration (MCHC), Red cell Distribution Width (RDW) and Red Blood Cell (RBC) had statistically significant difference between the two groups P value as shown in table-3.

DISCUSSION

Febrile seizures are very common in pediatric age group of 6 months to 6 years.. First time, association of Iron Deficiency Anaemia with febrile seizures was studied by Piscane et al (23). In his study, Iron Deficiency Anaemia was significant in febrile seizures cases as compared to control cases. In a study done in Bhopal in 2015, done by Shreya Gupta et al, 70 children with Febrile Seizures showed significant low Hb (<11 Gm/dl) as compared to 100 children in control group. Fallah et al from Iran showed low Mean Hb (11.46±1.18 gm/dl) in case group as compared to control group (11.9 ± 0.89 gm/dl) which was significant.(19) Similarly in a Pakistani study done in Abbottabad in 2013 by Ambreen Sultan et al 68% had low Hemoglobin. 31 children with febrile seizures as compared to 32% in 31 children with fever but without febrile seizures. (20) Our study showed significant low haemoglobin in case group (42/60, 70%) as compared to control group (26/60, 43%) which was significant (p- value <0.05). It also showed low mean Hb (9.8 ± 1.5) in 60 children with febrile seizures as compared to mean Hb (11.1 ± 1.2) in 30 children in control group (p- value <0.05). It correlates closely with international and national studies. In our study, other haematological indicators mean Haematocrit, MCV, MCH, MCHC were significantly lower in case group than control group while RDW was higher in cases than controls, an indicator of iron deficiency anaemia. In Egyptian children, Boshra et al (21) showed mean haemoglobin, haematocrit and MCH significant low in simple febrile seizures case as compared to control group. Similarly, an Indian study done by Srinivasa et al (21) showed low Haemoglobin, MCV, MCHC in febrile seizures cases as compared to control (Odd ratio 1.84). In another Indian study done in 2015 by M.S. Raju et al (22) haemoglobin <11.0 in cases was 84% while in control groups 65% and this difference was significant.

CONCLUSION

These results show that iron deficiency anaemia predisposes to febrile seizures and if it is treated and prevented well in time, incidence of febrile seizures can be reduced.

Table 1: showing matching variable between cases and control groups:

Variable	Cases	Controls	P value
Age (months)	28.6 ± 14.60	25.86 ± 15.82	0.4
Sex	Male=34, female=26	Male=32, female=28	0.9
Urban/Rural	Rural=38, urban=22	Rural=42, urban=18	0.8
Family history of febrile seizures	Yes=4, no=56	Yes=6, no=54	0.9
Family history of epilepsy	Yes=2, no=58	Yes=8, no=52	0.35
Weight	11.2 ± 3.1	10.8 ± 3.2	0.51
Temperature	101.3 ± 1.5	101.2 ± 1.2	0.7
TLC count	13600 ± 5912	12900 ± 6004	0.39

Table 2: Showing causes of fever in cases and control groups:

Diseases	Cases (%)	Controls (%)	Total N (%)
Respiratory tract infection	31 (51.66)	21 (35)	52 (43.33)
Gastroenteritis	9 (15)	11 (18.33)	20 (16.66)
Otitis media	3 (5)	2 (3.33)	5 (4.17)
Sinusitis	-	4 (6.67)	4 (3.33)
Urinary tract infection	5 (8.33)	7 (11.67)	12 (10)
Fever without localizing sign-	-	7 (11.67)	7 (5.83)
Not known	12 (20)	8 (13.33)	20 (16.67)

Table 3: showing comparison between variables, cases and controls:

Variable	Cases means and SD	Controls Means and SD	P value
Hemoglobin (gm%)	9.8 ± 1.5	11.1 ± 1.2	<0.001
Hematocrit (%)	31.1 ± 4.1	33.65 ± 2.23	0.002
MCV (fl)	67.82 ± 13.36	73.9 ± 5.1	0.012

MCH (pg)	23.63 ± 3.17	25.32 ± 2.93	0.018
MCHC (gm/dl)	31.57 ± 2.73	32.9 ± 2.29	0.03
RDW	49.2 ± 8.1	41.1 ± 3.9	0.002
RBC count (Millions)	3.8 ± 0.5	4.1 ± 0.8	0.03

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