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Original Research Article

Determine the Association between Iron Deficiency Anemia and Febrile Seizures

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Abstract

Aim: This study was aimed at evaluating the association between iron deficiency anemia and febrile seizures.

Methods: This was a prospective hospital based study and Cases (n=50) were patients with typical febrile convulsions between 1 year to 5 years (AAP clinical practice guidelines) was conducted in the Department of Pediatrics, DMCH, Darbhanga, Bihar, India. A control group (n=50) was selected from age and sex matched children admitted with febrile illness but without a seizure.

Results: The result shows that 86% (n=43) children had Hb <11 gm/dl from the case group as compared to 24% (n=12) in control group with significant p-value (p <0.01). The proportion of cases with anemia was significantly higher as compared to that of controls (p=0.012). The result shows, mean hemoglobin level and MCV in cases were significantly lower as compared to that in controls (p <0.04). RDW value is significantly higher in cases as compared to control (p <0.04). No significant difference between the two groups was observed with respect to mean MCH levels (p >0.04). Serum ferritin and serum iron levels in cases were significantly lower as compared to that in controls (p <0.01). TIBC value is significantly higher in cases as compared to control (p <0.01).

Conclusion: The findings suggest that a considerable percentage of children having febrile seizures suffer from iron-deficiency anemia and low serum iron. This means the low serum iron and the presence of anemia can serve as a reinforcing factor for febrile seizures in children.

Keywords: Febrile convulsions, Iron-deficiency Anemia, Children

Introduction

Febrile seizure (FS) is the most common type of childhood seizure, which occurs in 2–5% of neurologically healthy children. FS is defined as a seizure associated with a febrile illness in the absence of central nervous system (CNS) infections or acute electrolyte abnormalities in 6-60month old children without previous afebrile seizures. [1] FS is further classified as simple and complex types. Complex FS is defined as a seizure lasting more than 15 min, and recurring within 24 h or focal seizure. Iron deficiency is one of the most frequent micronutrient deficiencies and affects at least one third of the population of the world. [2] Anemia is the most common clinical manifestation of iron deficiency, but other organs and systems may also be affected. Cognitive dysfunction, psychomotor retardation, behavioral impairments, pica, breath holding spells, restless leg syndrome, and thrombosis could be associated with iron deficiency. [3,4] Effect of iron deficiency in the developing brain and mechanisms such as altered development of hippocampus neurons, impairment of energy metabolism, delayed maturation of myelin, slowed visual and auditory evoked potentials and alterations in synaptic neurotransmitter systems including norepinephrine, dopamine, glutamate, γ-aminobutyric acid, and serotonin may be responsible for these symptoms. [5,6] On the other hand, fever may aggravate the negative effects of iron deficiency on the brain. [7]

Given the age prevalence of IDA and FS, which play the same role as iron in neurotransmitter synthesis (such as GABA dopamine and serotonin), [8] and certain enzymes, such as monoaminoxidase, the role of hemoglobin in carrying oxygen to the brain, and fever, that worsen symptoms induced by anemia, a relationship between IDA and FS is probable.

Anemia is the most common clinical manifestation of iron deficiency, but other organs and systems may also be affected. Cognitive dysfunction, psychomotor retardation, behavioral impairments, pica, breath holding spells, restless leg syndrome, and thrombosis could be associated with iron deficiency. [9,10] Effect of iron deficiency in the developing brain and mechanisms such as altered

development of hippocampus neurons, impairment of energy metabolism, delayed maturation of myelin, slowed visual and auditory evoked potentials and alterations in synaptic neurotransmitter systems including norepinephrine, dopamine, glutamate, γ- aminobutyric acid, and serotonin may be responsible for these symptoms. [11] On the other hand, fever may aggravate the negative effects of iron deficiency on the brain. [12] The relationship between iron deficiency anemia (IDA) and FS has been evaluated in several studies with conflicting results.

The aim of this case-control study was to evaluate the relation of Iron Deficiency Anemia with the first episode of Febrile Seizure. A family history of convulsions; maternal smoking; and alcohol consumption during pregnancy have been associated with febrile seizures, but the risk factors remain largely unknown. Iron is involved in the metabolism of several neurotransmitters, and monoamine and aldehyde oxidase are reduced in iron deficiency anemia, which is common during the second and the third year of life and has been associated with behavioral and developmental disturbances. Thus, it can be investigated that the association between iron deficiency anemia and febrile seizures by a case-control study.

Materials and Methods

This was a prospective hospital based study and Cases (n=50) were patients with typical febrile convulsions between 1 year to 5 years (AAP clinical practice guidelines) was conducted in the Department of Pediatrics, DMCH, Darbhanga, Bihar, India for one year. A control group (n=50) was selected from age and sex matched children admitted with febrile illness but without a seizure.

Hematological investigations include Haemoglobin, MCV, MCH, RDW, Serum Ferritin, Serum Iron, TIBC and Peripheral blood smear. Anthropometrical data collection includes weight, recorded on an electronic weighing scale; Measurement of length and height using infantometer and stadiometer respectively; Head circumference was measured using a plastic tape measure by cross tape method; IAP weight for age classification was used to grade protein-energy malnutrition.

Inclusion Criteria

- Age between 1 year to 5 years
- The temperature of 38 degree Celsius (100.4 o F) or higher
- Not the result of central nervous system infection or any Metabolic imbalance.
- Occur in the absence of a history of prior afebrile seizure.
- Primarily generalized, usually tonic-clonic.
- Lasting for a maximum of 15 min.
- Not recurrent within a 24 hrs period.

Exclusion Criteria

- Children with neurological infection
- Children with developmental delay
- Children on iron therapy
- Children with previous febrile/afebrile seizure

Statistical Methods: Statistical analysis was done using appropriate statistical software.

Results

Table 1: Distribution of cases according to hemoglobin levels

Haemoglobin Level(gm/dl)	Cases	Controls
No anemia (≥11gm/dl)	6 (12)	37 (74)
Anemia		
Mild anemia (10-10.9gm/dl)	12 (24%)	5 (10%)
Moderate anemia (7-7.9gm/dl)	30 (60%)	5 (10%)
Severe anemia (<7gm/dl)	2 (4%)	3 (6%)

Table 1 shows that 86% (n=43) children had Hb <11 gm/dl from the case group as compared to 24% (n=12) in control group with significant p-value (p <0.01). The proportion of cases with anemia was significantly higher as compared to that of controls (p=0.012).

Table 2: Hematological parameters

Parameters	Cases		Controls		P-Value
	Mean	SD	Mean	SD	
Hb(gm/dl)	9.10	1.65	10.06	1.66	<0.01
MCV(fl)	67.89	15.32	17.65	9.96	<0.04
MCH(pg)	21.98	5.11	24.80	5.77	0.063
RDW	17.99	6.78	16.19	2.34	<0.04

Table 2 shows, mean hemoglobin level and MCV in cases were significantly lower as compared to that in controls ($p < 0.04$). RDW value is significantly higher in cases as compared to control ($p < 0.04$). No significant difference between the two groups was observed with respect to mean MCH levels ($p > 0.04$).

Table 3: Mean level of iron metabolic markers in cases and controls

Iron metabolic markers	Case (Mean)	Control (Mean)
Serum ferritin	44.89	60.9
Iron	52.34	64.55
TIBC	389.67	331.33

Serum ferritin and serum iron levels in cases were significantly lower as compared to that in controls ($p < 0.01$). TIBC value is significantly higher in cases as compared to control ($p < 0.01$).

Discussion

Febrile seizures are the most common type of seizures, occurring in 3 to 4 % of children. [13] Owing to their association with epilepsy in future, various studies have attempted to identify the risk factors associated with them viz, family history of febrile seizures, epilepsy, perinatal factors and temperature peak. Pisacane, et al. [14] reported that low iron level is associated with febrile seizure, whereas Kobrinsky, et al. [15] reported that iron deficiency raises the threshold for seizures. As iron is important for function of neurotransmitters and various enzymes, low level of serum ferritin may lower the seizure threshol. [16] Fever can worsen the negative effects of low serum ferritin on the brain and trigger seizure. [14]

In the present study, the majority of subjects in both groups were males. Sex analysis reveals that 68% were males and 32% females in the case group. Leela Kumari et al [17] also reported 53% of male children in their study. In the present study, characteristics studied were temperature, weight (Kg), height (Cm), nutritional status among which mean temperature was found to have a difference between cases and control but was not statistically significant (p-value = 0.412). This is in accordance to study by Modaresi M et al [18], Vaswani et al [19] and Daoud et al [20] who although reported a higher incidence of high temperature in case group but it was not statically significant. The incidence of anemia was higher among cases as compared to controls. This difference was statistically significant ($p<0.01$).

Other workers of the field as Derakhshanfar et al [21] and Modaresi M et al [18] also reported a statistically significant difference from the control group. The iron status components were measured (Hb, MCV, MCH, RDW, serum iron, ferritin, and TIBC) among cases and controls. In the present study, it was found that the mean ferritin and serum iron levels in the FS group were significantly lower than the corresponding levels in the control group ($p < 0.01$). Daoud et al [20] reported that the mean level of ferritin in cases with first febrile seizure is significantly lower than that in a control group. Pisacane et al [14] compared the levels of serum iron among controls and patients with FS, and they reported that iron deficiency anemia is significantly more frequent among the cases than among the controls.

Conclusion

The findings suggest that a considerable percentage of children having febrile seizures suffer from iron deficiency anemia and low serum iron. The association between iron deficiency anaemia and febrile seizures was previously investigated without any definitive results and more data was presented for this study. All the less, the preference bias as well as the confusing social status appear unusual in this analysis. IDA was more frequent in children with Febrile Seizures than children with febrile illness alone. The findings indicate that IDA may be a risk factor for FFS. IDA monitoring should be done in children with FFS. Fever can worsen the negative effects of anaemia or iron deficiency on the brain, which can lead to seizures. Conversely, anaemia can be correlated with the frequency of a febrile disorder, and more serious patients may be more prone to cause epilepsy.

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