



To Study the Association between Iron Deficiency Anemia and Febrile Convulsion in Children in a Tertiary Care Center- A Case Control Study.

Dr Brajesh Kumar Senior Resident, Dept. of Pediatrics, JLNMC, Bhagalpur, Bihar.

Dr Sushil Bhushan Associate Professor, Dept. of Pediatrics, JLNMC, Bhagalpur, Bihar.

Dr Anil Kumar Junior Resident, Dept. of Pediatrics, JLNMC, Bhagalpur, Bihar.

ABSTRACT **Objective:** This study was conducted with the objective of finding the effects of iron deficiency anemia on febrile convulsion.

Material and methods: A case control study was done in a tertiary care center, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar from February 2015 to January 2017, to evaluate the relationship between iron deficiency anemia and febrile convulsions. 140 cases and 140 controls were included in the study. Cases were children of age group 6 months to 6 years presenting with febrile convulsion. Controls were children of same age group presenting with febrile illness but without any convulsions. A detailed history and clinical examination was done in both cases and controls matched for age and sex and blood investigations were done to diagnose iron deficiency anemia. In all children hemoglobin (Hb) levels, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), red cell distribution width (RDW) and plasma ferritin (PF) were determined and the data collected were analyzed statistically.

Results: The mean plasma ferritin (PF) was significantly lower in cases compared to controls ($p=0.001$) and RDW was significantly higher in cases compared to controls ($p=0.001$). The mean Hb%, MCV were lower in cases compared to controls.

Conclusion: Iron deficiency is a significant risk factor for febrile seizures in children of age group six months to six years. Early detection and timely correction of iron deficiency may be helpful for prevention of febrile seizures in children.

KEYWORDS : Iron Deficiency Anemia, Febrile Convulsion, Children, Hemoglobin, S.Ferritin.

INTRODUCTION

Introduction: Simple febrile convulsion is the most common disease of the nervous system in children. There are hypotheses that iron deficiency may affect febrile convulsion and the threshold of neuron excitation. WHO estimates that anemia largely caused by iron deficiency, affecting between 500 million and two billion people worldwide. [1,2] It is the most common nutritional deficiency and haematological disease of infancy and childhood.[3] Iron is a nutritional element not only needed for the synthesis of haemoglobin, but it is also essential for enzymes involved in neurochemical reactions. [4] The exact pathophysiology of febrile seizure is unknown. [5] Age for peak incidence of febrile seizure is 12 to 18 months, which overlaps with that of iron deficiency anemia which is from 6 to 24 months. [6,7]

Considering the age prevalence of iron deficiency anemia and febrile convulsion which are the same, the role of iron in the metabolism of neurotransmitter (such as GABA and serotonin) and some enzymes (such as monoamine and aldehyde oxidase), the function of hemoglobin in conveying oxygen to the brain and since fever can exacerbate symptoms that result from anemia, a relationship between iron deficiency anemia and febrile convulsions is probable. [8,9,10]. Some studies have suggested iron deficiency as a predisposing factor for febrile seizures, some described iron deficiency anemia is less frequent in children with febrile seizures. [11] Considering the conflicting results of the previous studies, we designed this case control study to evaluate the relationship between iron deficiency anemia and febrile convulsions.

MATERIAL AND METHODS

A case control study was conducted in a tertiary care Centre, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar from February 2015 to January 2017 involving 140 children aged between 6 months to 6 years with febrile seizures were enrolled as cases. Febrile seizures were defined as a seizure occurring in association with a febrile illness, in the absence of CNS infection or any other defined causes of seizures. [12] Children with a history of epilepsy, central nervous system (CNS) infections, developmental delay and neurological deficits, on iron therapy were excluded from the study. A control group of 140 children were selected from among children hospitalized for a febrile illness (such as upper and lower respiratory tract infections and gastroenteritis) but without seizures. Controls were group matched to cases on age and sex. An informed consent was obtained from parents or the guardian. Demographic data, seizure details, nature of febrile illness, the family history of epilepsy/febrile seizures, temperature at admission and nutritional

status were recorded. Blood samples were collected from all participants for measurement of haemoglobin (Hb), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), red cell distribution width (RDW) and serum ferritin was done. Iron deficiency anemia was defined as Hb <11g/dl, MCV <70 fl, MCH <27 pg, RDW >15%, serum ferritin <12 ng/ml (WHO). [13] In presence of fever, a higher cutoff value of serum ferritin (25-50ng/ml) was considered. [14] Cases and controls were compared with respect to blood indices and serum ferritin. Chi-square, ANOVA, unpaired t-tests were used for statistical analysis.

RESULTS

140 cases (80 male, 60 female) and 140 controls (80 male, 60 female) were enrolled. The mean ages of children in the febrile seizure and control groups were 1.7 ± 1.2 and 1.8 ± 1.5 year respectively. Respiratory tract infections were the most common cause of fever in the study followed by GIT infections. In this study we observed significantly low serum ferritin and significantly higher RDW in febrile seizure cases compared to controls.

Table 1: Haematological parameters of cases and controls.

Parameters	Cases (n=140) [Mean±SD]	Control (n=140) [Mean±SD]	p- value
Hb%	9.2 ± 1.3	9.6 ± 1.0	0.50
MCV (fl)	72.3 ± 5.3	75.0 ± 4.9	0.36
MCH (pg)	25.5 ± 3.1	25.9 ± 3.3	0.16
RDW%	16.3 ± 1.5	12.9 ± 1.5	0.000
Serum ferritin(ng/ml)	28.5 ± 20.5	54.3 ± 35.6	0.000

Table 2: Underlying causes of fever among cases and controls.

INFECTIONS	FEBRILE SEIZURE CASES (n=140)	CONTROLS (n=140)	p- value
Respiratory tract infections	80	90	N.S
GIT infections	50	40	N.S
Enteric fever	6	4	N.S
Viral fever	4	6	N.S

DISCUSSION

Given the effects of anemia, and especially those of iron deficiency anemia that is the most common type, it is possible that anemia influences occurrences of convulsion in these patients. Numerous studies have addressed the association between IDA and febrile seizure in children. The results, however, have been controversial and even

primary researches with high number of cases have failed to provide unequivocal results. We observed significantly low serum ferritin levels in children with febrile seizures than in controls. Similar results were observed by Pisacane, et al. [15] But in contrast with these studies Mansouri et al reported mean ferritin was higher in the convulsive group with no statistically significant difference. [16] Kobrinsky et al deduced that iron deficiency might have a protective effect on febrile convulsion.[17] Iron has been found to act as a cofactor in a number of enzymatic reactions at the cellular level and effects neurotransmitter production, 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, stroke and breath-holding spells. Screening for IDA should be considered in children with febrile seizures. Fever can worsen the negative effect of anemia or for iron deficiency on the brain and a seizure can occur as a consequence. Alternatively, anemia can be associated with the severity of a febrile illness and more severe cases could be more likely to get seizures. [17] Iron deficiency anemia may reduce the seizure threshold in the infancy and childhood. Low PF level is associated with and may play a role in febrile seizures. As we know, ferritin is an acute phase reactor that nonspecifically increases in response to any febrile illness. Given that blood samples were taken to measure the levels of Fe, TIBC, and ferritin after the body temperature of the patients had been brought down to the normal level, the differences in ferritin levels between the two groups cannot be attributed to fever. The limitation of our study is that it is a hospital-based study, so the prevalence of exposure and outcome variables may be different from a community setting.

CONCLUSION

Early detection and timely correction of iron deficiency may be helpful for prevention as well as recurrence of febrile seizures in children of this age group. Furthermore, it is advisable to prescribe iron supplements earlier and more carefully to children who have important and well known risk factors for febrile convulsion, such as family history of febrile convulsion.

REFERENCES

- Lozoff B, Jimenez E, Smith JB. Double burden of iron deficiency in infancy and low socioeconomic status. *Arch Pediatr Adolesc Med*, 2006; 160: 1108–12.
- Mahoney DH. Iron-Deficiency Anemia in children. (Web document) www.UptoDate.com. Last Literature Review version, 2009; 17.2: May.
- Ohls RK, Christensen RD. Iron-Deficiency Anemia. *Nelson Text book of Pediatrics*. 18th Edition. Philadelphia: Saunders, 2008; 2014–7.
- Ambruso DR, Hays T, Goldenberg NA. Iron Deficiency Anemia. *Current Diagnosis and Treatment- Paediatrics*. 19th Edition. Denver USA: McGraw Hill, 2009; 810–11.
- Varma RR. Febrile seizures. *Indian J Pediatr*, 2002; 69(8): 697-700.
- Johnston VJ. Seizures in Childhood. *Nelson Text book of Pediatrics*. 18th Edition. Philadelphia: Saunders, 2009; 1994–5.
- Fishman MA. Febrile seizures. (Web document) www.UptoDate.com Last Literature Review version, 2010; 8.1.
- Harris RJ. Iron deficiency anemia: does it really matter? *Paediatr Child Health*, 2007; 17(4): 143.
- Parks YA, Wharton BA. Iron deficiency and the brain. *Acta Paediatr Scand*, 1989; S5(suppl 361):717.
- Weatherall DJ, Clegg JB. *The thalassaemia syndromes*. 4th ed. London: Blackwell Science, 2001; 192: 231.
- Bidabadi E, Mashouf M. Association between iron deficiency anemia and first febrile convulsion: A case-control study. *Seizure*, 2009; 18(5): 347–51.
- Johnston MV. Seizures in childhood: Febrile seizures. In: Behrman RE, Kliegman RM, Jenson HB, editors. *Nelson's Textbook of Pediatrics*. 17th ed. Pennsylvania: Saunders, 2004; 1994–1995.
- World Health Organization. *Iron Deficiency Anemia. Assessment, Prevention and Control. A Guide for Program Managers*. WHO/NHD/013; Geneva, 2001.
- Dallman PR, Yip R, Oski FA. Iron deficiency and related nutritional anemia's. In: Nathan DG, Oski FA, editors. *Hematology of Infancy and Childhood*. 4th ed. Mexico: Saunders, 1993; 413–450.
- Pisacane A, Sansone R, Impagliazzo N, Coppola A, Rolando P, D'Apuzzo A, et al. Iron deficiency anemia and febrile convulsion: Case control study in children under 2 years. *BMJ*, 1996; 313: 343.
- Mansouri M, Bidabadi E, Sobhani AR. Relation of Iron Deficiency Anemia with First Febrile Convulsion. In: Sreenivasa B et al. *Convulsion In 6 month to 5 year old Children*. *J Med Faculty Guilan Univ Med Sci.*, 2007; 60(15): 65-73.
- Kobrinsky N, Yager JY, Cheang Ms, Yatscoff RW, Tenenbein M. Does iron deficiency raise the seizure threshold? *J Child Neurol*, 1995; 10(2): 105-9.