

## ORIGINAL ARTICLE

## IRON DEFICIENCY ANAEMIA —A RISK FACTOR FOR FEBRILE SEIZURES IN CHILDREN

Ahmad Sherjil, Zaheer us Saeed\*, Sohail Shehzad\*\*, Rabia Amjad\*\*\*

Department of Paediatrics, \*Department of Pathology, HIT Hospital, Taxila, \*\*Department of Paediatrics, CMH Mangla, \*\*\*Department of Paediatrics, POF Hospital, Wah Cantt

**Background:** Iron deficiency anaemia and febrile seizures are two common diseases in children worldwide as well as in our country. Iron insufficiency is known to cause neurological symptoms like behavioural changes, poor attention span and learning deficits in children. Therefore, it may also be associated with other neurological disturbances like febrile seizures in children. Objective of our case-control study was to find association between iron deficiency anaemia and febrile seizures in children. **Methods:** This multicentre study was conducted in Department of Paediatrics HIT Hospital Taxila Cantt, Department of Paediatrics CMH Mangla and Department of Paediatrics POF Hospital Wah Cantt, from June 2008 to June 2010. Three hundred and ten children aged between 6 months to 6 years were included in the study. One hundred and fifty-seven children who presented with febrile seizures were our cases, while, 153 children who presented with febrile illnesses without seizures were recruited as controls. All patients were assessed for iron deficiency anaemia by measuring haemoglobin level, serum ferritin level, Mean Corpuscular Haemoglobin Concentration (MCHC) and Mean Corpuscular Volume (MCV). Patients with iron deficiency anaemia amongst controls and cases were documented. Percentages and Odds ratio were derived from the collected data. **Results:** 31.85% of cases (50 out of 157) had iron deficiency anaemia whereas, 19.6% of controls (30 out of 153) were found to have iron deficiency anaemia as revealed by low levels of haemoglobin level, serum ferritin level, Mean Corpuscular Haemoglobin Concentration and Mean Corpuscular Volume. Odds ratio was 1.93. **Conclusion:** Patients with febrile seizures are 1.93 times more likely to have iron deficiency anaemia compared to febrile patients without seizures.

**Keywords:** Iron Deficiency Anaemia, Febrile Seizures, Serum Ferritin, Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin Concentration (MCHC)

## INTRODUCTION

The World Health Organization estimates that anaemia, largely caused by iron deficiency, affects between 500 million and two billion people worldwide.<sup>1,2</sup> In some developing countries, up to 50 percent of preschool children have anaemia that principally is caused by iron deficiency.<sup>1</sup> It is the most common nutritional deficiency and haematological disease of infancy and childhood.<sup>3</sup> Iron is a nutritional element not only needed for the synthesis of haemoglobin, but is also essential for enzymes involved in neurochemical reactions.<sup>4</sup> Neurological symptoms like poor attention span, learning deficits, weak memory, delayed motor development and behavioural disturbances caused by iron deficiency are well known.<sup>2-4</sup> Thus it is possible that iron deficiency may predispose to other neurological disturbances like febrile seizures. Febrile seizures occur in 2 to 4% of all children with a recurrence rate of 30 to 40%.<sup>5</sup> Age for peak incidence of febrile seizures is 14 to 18 months which overlaps with that of iron deficiency anaemia which is from 6 to 24 months.<sup>6,7</sup>

There is a need to explore relation between febrile seizures and iron deficiency anaemia. Despite these facts, only a handful of international<sup>11-13</sup> and a single local researcher<sup>10</sup> have tried to establish

association between iron deficiency anaemia and febrile seizures. Ironically, results of these studies are completely conflicting. While most studies have suggested iron insufficiency as a predisposing factor for febrile seizures, some have even described iron deficiency anaemia to be less frequent in children with febrile seizures.<sup>9</sup> Keeping in view the prevalence of these two clinical entities as well as difference of opinion in available studies, we conducted a case-control study to evaluate iron deficiency anaemia as a risk factor for febrile seizures.

## PATIENTS AND METHODS

This multicentre study was conducted in Department of Paediatrics HIT Hospital Taxila Cantt, Department of Paediatrics CMH Mangla and Department of Paediatrics POF Hospital Wah Cantt. Three hundred and ten children of age 6 months to 6 years were included in the study over a period of 2 years, from June 2008 to June 2010. One hundred and fifty-seven children who presented with febrile seizures were the cases, while, 153 children who presented with febrile illness without seizures were taken as controls. Febrile seizure was defined as a convulsion associated with an elevated temperature greater than 38 °C in a child between 6 months to 6 years of age without central nervous system infection or inflammation, acute systemic metabolic

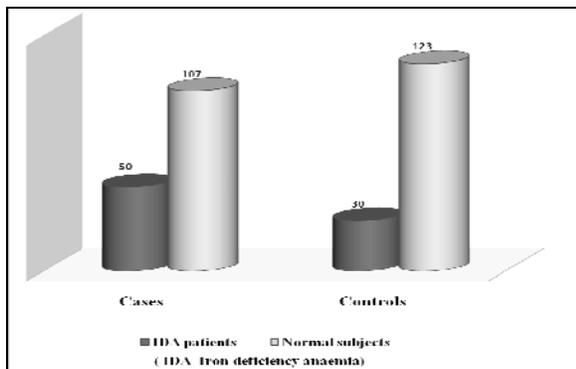
abnormality that may produce convulsions and history of previous afebrile seizures. Cases were defined as children with minor febrile illnesses, who were hospitalised with a convulsion that fulfilled criteria for febrile seizure. Minor febrile illnesses accepted were pharyngitis, adenitis and otitis media. Controls were defined as age and gender matched children, with minor febrile illness but without any kind of seizures. Exclusion criteria for all subjects included co-morbid conditions like epilepsy, major febrile sicknesses like enteric fever and severe pneumonia, patients already on iron therapy, patients with delayed development, and patients known for other causes of anaemia. Iron deficiency anaemia was defined as haemoglobin level below 9.0 gm/dL, Serum ferritin level below 7 µg/L, Mean Corpuscular Volume (MCV) below 65 fL and Mean Corpuscular Haemoglobin Concentration (MCHC) below 28 gm/dL. Blood samples were collected in the Paediatric wards of HIT Hospital, POF Hospital and CMH Mangla, and sent to Pathology Departments of respective hospitals for measurements of these four parameters. Equipment used was Sysmax KX-21 Haematology Counter and Access II Immunoassay Analyser (Beckman Coulter) in these hospitals. A proforma was used to endorse every patient's particulars and laboratory results. SPSS-17 was used for statistical analysis for this data.

**RESULTS**

Over a period of 2 years, 310 children, between the ages of 6 months to 6 years, fulfilling the inclusion criteria, were recruited. 153 were controls and 157 were cases.

Fifty out of 157 (31.85%) cases had iron deficiency anaemia whereas, 30 out of 153 (19.6%) controls were found to have iron deficiency anaemia, (Figure-1). Chi-Square test confirmed statistical significance of the difference observed in the two groups ( $p < 0.05$ ).

Odds ratio\* derived from these results was 1.93, as shown in Table -1.



**Figure-1: Iron deficiency Anaemia patients amongst cases and controls**

**Table-1: Odds Ratio Iron Deficiency Anaemia**

	Present	Absent
Cases (n=157)	50 (A)	107 (B)
Controls (n=153)	30 (C)	123 (D)

\*Odds Ratio=A/B×D/C=50/107×123/30=1.93

**DISCUSSION**

Iron is an essential element in the metabolism and functioning of enzymes required in neurochemical reactions. These include monoamineoxidase, cytochrome, peroxidase and catalase.<sup>2,8</sup> Clinically neurological symptoms like poor attention span, learning deficits, poor memory, delayed motor development and behavioural changes caused by iron deficiency are well known.<sup>2-4</sup> Its association with febrile seizures was first observed and published in mid 90's in an Italian study.<sup>8</sup> This was followed by few more international studies.<sup>11-15</sup> In 2009, Hartfield and colleagues, from University of Alberta, Canada reported in a retrospective study that children with febrile seizures were twice as likely to have iron deficiency as those with febrile illness alone. Some international studies denied any role of iron insufficiency in febrile seizures. In fact, in an Iranian study, Bidabadi and Moushaf from University of Guilan, concluded that iron deficiency is less frequent in children with first febrile seizure.<sup>9</sup> In 2001, Naveed-ur-Rehman and colleagues conducted the only local study at Aga Khan University Hospital which convincingly associated iron deficiency anaemia, as a risk factor, with febrile seizures.<sup>10</sup> These handfuls of studies are too few and bear conflicting results. Our study has the advantages of large sample size, a long period of study, and of being conducted in three different hospitals. It is deficient in not being able to account for some confounding factors leading to iron deficiency anaemia like lead poisoning.<sup>14</sup> Secondly, we considered iron deficiency anaemia synonymous with iron insufficiency whereas it is not impossible that fits may have been related to iron insufficiency and not to iron deficiency anaemia.

We recommend follow up studies on the same subjects to establish iron deficiency anaemia as an etiological factor for febrile seizures. For this purpose we are conducting an interventional, prospective study on the same patients, which is under way at present. Another finding of interest was that in our study sample, prevalence of iron deficiency anaemia ranged from 20% to 32% whereas in most Western studies it is mentioned as 8% to 10%. Therefore, we also recommend emphasis on screening and treatment of iron insufficiency in children in general.

**CONCLUSION**

Children with febrile seizures are almost twice as likely to have iron deficiency anaemia as compared to children with a febrile illness without seizures.

Iron deficiency anaemia can be regarded as a risk factor that predisposes to febrile seizures in children.

## REFERENCES

1. 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.
2. Mahoney DH. Iron-Deficiency Anaemia in children. (Web document) [www.UptoDate.com](http://www.UptoDate.com). Last Literature Review version 17.2: May 2009.
3. Ohls RK, Christensen RD. Iron-Deficiency Anaemia. *Nelson Text book of Pediatrics*. 18<sup>th</sup> Edition. Philadelphia: Saunders; 2008. p. 2014–7.
4. Ambruso DR, Hays T, Goldenberg NA. Iron Deficiency Anaemia. *Current Diagnosis and Treatment- Paediatrics*. 19<sup>th</sup> Edition. Denver USA: McGraw Hill; 2009. p.810–11.
5. Habib Z, Akram S, Ibrahim S, Hasan B. Febrile seizures: Factors affecting risk of recurrence in Pakistani children presenting at The Agha Khan University Hospital. *J Pak Med Assoc* 2003;53:11–7.
6. Johnston VJ. Seizures in Childhood. *Nelson Text book of Pediatrics*. 18<sup>th</sup> Edition. Philadelphia: Saunders; 2009. p.1994–5.
7. Fishman MA. Febrile seizures. (Web document) [www.UptoDate.com](http://www.UptoDate.com) Last Literature Review version 8.1. January 2010.
8. Pisacane A, Sansone R, Impagliazzo N, Coppola A, Rolando P, D'Apuzzo A, *et al*. Iron deficiency anaemia and febrile convulsions: case-control study in children under 2 years. *BMJ* 1996;313(7053):343.
9. Bidabadi E, Mashouf M. Association between iron deficiency anemia and first febrile convulsion: A case-control study. *Seizure*. 2009;18(5):347–51.
10. Naveed-ur-Rehman, Billoo AG. Association between iron deficiency anemia and febrile seizures. *J Coll Physicians Surg Pak* 2005;15:338–40.
11. Hartfield DS, Tan J, Yager JY, Rosychuk RJ, Spady D, Haines C, *et al*. The association between iron deficiency and febrile seizures in childhood. *Clin Pediatr (Phila)* 2009;48:420–6.
12. Daoud AS, Batieha A, Abu-Ekteish F, Gharaibeh N, Ajlouni S, Hijazi S. Iron status: a possible risk factor for the first febrile seizure. *Epilepsia* 2002;43:740–3.
13. Macdonald CE, Playford RJ. Iron deficiency anaemia and febrile convulsions and coeliac disease. *BMJ* 1996;313(7066):1205.
14. Wike WM, Kiser WR. Iron deficiency anaemia and febrile convulsions. Possible confounding factors include lead toxicity. *BMJ* 1996;313(7066):1205.
15. Kobrinsky NL, Yager JY, Cheang MS, Yatscoff RW, Tenenbein M. Does iron deficiency raise the seizure threshold? *J Child Neurol*. 1995;10(2):105–9.

## Address for Correspondence:

**Maj. Dr. Ahmad Sherjil**, Classified Child Specialist, D-12, HIT Taxila Cantt, Pakistan. **Cell:** +92-321-2713728

**Email:** [drahmadsherjil@yahoo.com](mailto:drahmadsherjil@yahoo.com)