

**IRON DEFICIENCY ANEMIA ASSOCIATION WITH FEBRILE SEIZURE**Dr. Abdul Qayum\*<sup>1</sup>, Dr. Inam Ur Rehman<sup>2</sup>, Dr. Ammad Akbar<sup>3</sup><sup>1</sup>Nishtar Medical University and Hospital Multan.<sup>3</sup>Nishtar Medical University and Hospital Multan.<sup>3</sup>University, Guangzhou China.**\*Corresponding Author: Dr. Abdul Qayum**

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**ABSTRACT**

**Background:** There is controversy regarding association of Iron deficiency anemia and febrile seizures. Febrile seizures is one of the most common neurological disorder in children, which mostly encounters 3% to 5% of children between the 3 to 60 months of age. Similarly Iron deficiency is known cause of neurological symptoms like behavioural changes, attention and learning deficits in children. Some studies supports the idea that anemia is more common in children with febrile seizures, whereas others have reported that iron deficiency raises the seizure threshold. There are some other studies that doesn't support this hypothesis. Purpose of this study was to find association between iron deficiency anemia and febrile seizures in children. **Methods:** It was a case control study done at pediatrics department Nishtar Hospital Multan from September 2017 to February 2018. We evaluated 100 children aged between 5 months to 6 years. We enrolled 52 patients who presented with febrile convulsions as Cases and remaining 48 children who presented with febrile illness without convulsions as Controls. Detailed history and examination was done. All the patients were evaluated for iron deficiency anemia by measuring by measuring haemoglobin level, serum ferritin level, Total iron binding capacity (TIBC), Red Cell Distribution, Mean Corpuscular Haemoglobin Concentration (MCHC), Mean Corpuscular Volume (MCV) and peripheral blood film. Patients with iron deficiency anemia amongst controls and cases were documented. Percentages and Odds ratio were derived from the collected data. **Results:** We found that 34.61% of cases (18 out of 52) were having iron deficiency anemia whereas, 22.91% of controls (11 out of 48) had iron deficiency anemia as revealed by low levels of haemoglobin level, serum ferritin level, Mean Corpuscular Haemoglobin Concentration and Mean Corpuscular Volume. Odds ratio was 1.78. **Conclusion:** Patients with febrile seizures are 1.93 times more likely to have iron deficiency anemia compared to febrile patients without seizures.

**KEYWORDS:** Iron Deficiency Anemia, Febrile Seizures, Serum Ferritin, Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin Concentration (MCHC).

**INTRODUCTION**

Iron deficiency is the most common nutritional deficiency of infancy and childhood. In developing countries almost 50% of preschool children suffer from anemia that is mainly caused by iron deficiency.<sup>[1]</sup> Iron is an essential element needed for the haemoglobin synthesis, important role in neurotransmitters production and function, hormonal function and DNA duplication.<sup>[2,3]</sup>

Febrile seizures (FS) refer to the benign convulsions that affects 2-5% of children between the ages of 6 months to five years, with body temperature of 38°C or higher not resulting from Central Nervous System infection or any metabolic imbalance. This condition occurs in 2-5% of the children who are neurologically healthy.<sup>[4-5]</sup> FS causes emotional, physical, and mental damages, which

are stressful for parents, and affects families' quality of life.<sup>[6]</sup>

The exact cause of FC is unknown, but several genetic and environmental factors have been implicated.<sup>[7]</sup> Some recent studies have shown that iron-deficiency anemia could be a risk factor for febrile seizures, because the age for peak incidence of febrile seizures is 14 to 18 months which overlaps with that of iron deficiency anemia which is from 6 to 24.<sup>[8-10]</sup> As IDA is preventable cause, incidence of febrile seizures can be reduced by treating iron deficiency anemia with diet and iron supplements.<sup>[11]</sup> In Pakistan, studies showed iron deficiency anemia as predisposing factor of increase in febrile fits.<sup>[12-13]</sup> Neurological symptoms like poor attention, learning deficiency, weak memory, delayed motor development and behavioural disturbances caused by iron deficiency are well known.<sup>[14]</sup> Thus it is possible

that iron deficiency may predispose to other neurological disturbances like febrile seizures. On the contrary, some studies have reported that iron deficiency can be a protective mechanism against convulsions by increasing the convulsion threshold, and thus iron supplements should be given with caution to the children.<sup>[15-16]</sup> However, the studies carried out so far have showed conflicting results. This current study was done to see association of anemia with febrile fits in our hospital.

## METHODOLOGY

It was a case control study done at pediatrics department Nishtar Hospital Multan from September 2017 to February 2018. We evaluated 100 children aged between 5 months to 6 years. We enrolled 52 patients who presented with febrile convulsions as Cases and remaining 48 children who presented with febrile illness without convulsions as Controls. Detailed history and examination was done. All the patients were evaluated for iron deficiency anemia by measuring by measuring haemoglobin level, serum ferritin level, Total iron binding capacity (TIBC), Red Cell Distribution, Mean Corpuscular Haemoglobin Concentration (MCHC), Mean Corpuscular Volume (MCV) and peripheral blood film. Patients with iron deficiency anemia amongst controls and cases were documented. Percentages and Odds ratio were derived from the collected data. Simple Febrile convulsion was defined as a convulsion associated with raised temperature more than 38 °C in a child without any central nervous system infection or inflammation and acute systemic metabolic abnormality lasting less than 15 minutes and not reoccurring within 24 hours. Cases were defined as children with minor febrile illnesses, who were hospitalized with a convulsion that fulfilled criteria for febrile seizure.

Controls were defined as children with minor febrile illness but without any kind of seizures. Iron deficiency anemia 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.

**Inclusion criteria:** Cases with typical febrile convulsions between 5 months to 6 years.

**Exclusion criteria:** Patients with known conditions like epilepsy, complex seizures, CNS infection, mentally retarded, metabolic disorders, major febrile sicknesses like enteric fever and severe pneumonia, patients already on iron supplements and patients known for other causes of anemia.

Samples with electrolyte imbalance, hypoglycemia, meningitis, encephalitis and shigellosis etc.

A proforma was used to endorse every patient's particulars and laboratory results. SPSS-17 was used for statistical analysis for this data.

SPSS version 20 was used to enter and analyze data.

## RESULTS

We found that 34.61% of cases (18 out of 52) were having iron deficiency anemia whereas, 22.91% of controls (11 out of 48) had iron deficiency anemia as revealed by low levels of haemoglobin level, serum ferritin level, Mean Corpuscular Haemoglobin Concentration and Mean Corpuscular Volume. Odds ratio was 1.78.

**Table 1: Iron deficiency Anemia patients amongst cases and controls.**

	IDA subjects		Normal subjects	
	Frequency	Percentage	Frequency	Percentage
Cases (n=52)	18	34.61%	34	65.3%
Controls (n=48)	11	22.91%	37	77.09%

**Table 2: Odds Ratio Iron Deficiency Anemia.**

	Present	Absent
Cases	18	34
Controls	11	37

\*Odds Ratio=A/B×D/C=18/34×37/11=1.78

## DISCUSSION

Iron is required for proper functioning of enzymes like monoamine oxidase, cytochrome, peroxidase and catalase.<sup>[17-18]</sup> These enzymes are necessary for neurochemical reactions. Iron deficiency is well known cause of neurological symptoms like attention deficit, learning deficits, poor memory, delayed motor development and behavioural changes.<sup>[17]</sup> The effects of iron deficiency on the developing brain have been

studied on different animal models. Abnormalities in brain iron metabolism, myelination, and disruption of normal neurotransmitter activity may predisposes febrile seizure in patient with iron deficiency.<sup>[19]</sup> Further work is required in this area using an animal model of febrile seizure and iron deficiency to illuminate the mechanism is warranted.

Association between iron deficiency and febrile seizures was first reported and published in mid-90's in an Italian study.<sup>[20]</sup> This was followed by few more international studies.<sup>[21]</sup> In 2009, Hartfield and colleagues reported in a retrospective study that children with febrile seizures were more likely to have iron deficiency as those with febrile illness alone. A local study conducted at Aga Khan University Hospital in 2001 by Naveed-ur-Rehman and colleagues reported that febrile convulsions are

convincingly associated with ID.<sup>[22]</sup> In a study (Pisacane *et al.*, 1996) it was reported that anemia in the case group (30%) was higher than in the hospital control group (14%) and the healthy group (12%).

Vaswani *et al.* also reported that 68% cases of febrile seizures were iron deficient compared to 30% of the controls. A meta-analysis of eight case-control studies that have tested the relationship between febrile seizures and iron deficiency suggested that iron deficiency may be associated with an increased risk of febrile seizures in children (Idro *et al.*, 2010).

In a study conducted in Thailand showed that thalassemic is 4.4 times protected from febrile convulsions than normal population. The researchers suggested that it might be due to high iron level in thalassemia patients and the role of iron in brain metabolism, which leads to less occurrence of febrile convulsion in those children (Auvichayapat *et al.*, 2004).

Some international studies denied the fact that there is association between iron deficiency and febrile convulsions. A study done in Iran by Bidabadi concluded that iron deficiency is less frequent in children with first febrile seizure.<sup>[23]</sup> Again, in the study of Kobrinsky *et al.*, the febrile convulsion group suffered less from iron deficiency. These are few studies that denied this fact and bear conflicting results.

According to the findings of the present study, the incidence of febrile seizures in children suffering iron deficiency anemia was observed to be more than that control group. In conclusion, iron deficiency can be added to the list of risk factors for febrile convulsions. Accordingly, children with febrile seizures are suggested to be monitored for diagnosis and treatment of iron-deficiency anemia. Therefore, it is recommended that screening and treatment of iron insufficiency should be in general.

## LIMITATIONS

There was no proper criteria selected to diagnose ID.

Parameters such as ferritin, serum iron, TIBC, transferrin saturation, and FEP were not properly discussed.

These traditional measures of iron profile are influenced by infection and, therefore, they are not reliable indicators of iron status in the setting of acute infection.

## CONCLUSION

Patients with febrile seizures are 1.93 times more likely to have iron deficiency anemia compared to febrile patients without seizures.

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