

# ASSOCIATION BETWEEN IRON DEFICIENCY ANEMIA AND FEBRILE SEIZURES

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## ABSTRACT

**Objective:** To find out the association between iron deficiency anemia and the frequency of first febrile seizure.

**Methodology:** It was a comparative study conducted at Pediatric Medicine, Kuwait Teaching Hospital Peshawar and Hayatabad Medical Complex Peshawar from January 2015 to December 2015 in which a total of 160 patients were observed by taking 80 participants each in group A and group B respectively. Children in Group A were having febrile seizures while those in Group B were febrile but not having seizures.

**Results:** The mean age of group A was  $25 \pm 1.28$  months while that of group B was  $24 \pm 1.26$  months. Frequency of Iron deficiency in group A was 38% while that in group B was 20% with a p value of 0.003.

**Conclusion:** Febrile seizures were twice as common in children having iron deficiency anemia as compared to those who did not have iron deficiency anemia.

**Key Words:** Iron deficiency anemia, Febrile seizures

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## INTRODUCTION

The commonest neurological symptom in children is seizures and most frequent seizures are febrile seizures. All the children and infants have experienced at least a single episode of simple febrile seizure; between 2% and 5% of infants and children under the age of five, with majority of them between 12-18 months of age. Recurrence of febrile seizures occur in 30% of those children having first episode of febrile seizures and 50% of those having two or more episodes.

The febrile seizure is quite common in childhood but still it is extremely frightening, anxiety provoking and emotionally disturbing in those parents who witness the episode<sup>1</sup>. Recent studies have shown that some micronutrients may play role in febrile seizures. Iron is essential part of enzymes that are involved in neurochemical reactions<sup>2</sup>. Symptoms like poor attention span, learning deficit, behavioral disturbances, delayed motor development and weak memory have well established relationship with iron deficiency anemia<sup>3</sup>. The most prevalent nutrition problem in the world today is iron deficiency anemia and it is estimated to effect 5 million children in developing countries<sup>3</sup>.

Iron has numerous biological effects and play very important role in neurological functioning<sup>3,4</sup>. Such neu-

rological functions include myelin formation, brain energy metabolism and neurotransmitter metabolism. The metabolism of numerous neurotransmitters, aldehyde oxidases and monoamines is reported to be reduced among the children having iron deficiency anemia<sup>4</sup>. The children having iron deficiency anemia not only show lower threshold for febrile seizure but also influence type, duration, and recurrence of seizure<sup>5</sup>. Some of previous studies showed that deficiency of iron play an important part in febrile seizures pathogenesis in children<sup>4-6</sup>. While in contrast some of the studies concluded that iron deficiency raises the threshold for febrile seizures<sup>7</sup>. Moreover, some studies have shown that iron deficiency anemia is not a frequent occurrence with febrile seizures<sup>8</sup>. Hence, it is the need of time to explore the association of iron deficiency anemia and febrile seizures.

The association between iron deficiency anemia and febrile seizures has been studied in the region before as both are common problems in this region<sup>9,10</sup>. Efforts have been made to scrutinize the association of febrile seizures and iron deficiency anemia through worldwide studies. Some of the studies have established the role of iron deficiency anemia as a leading risk factor to cause febrile seizures<sup>9,10</sup> whereas other have found no association of iron deficiency anemia as a precursor for the

acute seizures<sup>11</sup>. Therefore, our study was designed to find the relationship between iron deficiency anemia and febrile seizures among children under the age of 5 years.

## METHODOLOGY

The study was conducted at Kuwait teaching hospital Peshawar and Hayatabad Medical Complex Peshawar. Study design was comparative study and the duration of the study was one year (January 2015 to December 2015) in which 160 children were included. These children were divided into two groups. Group A having 80 participants and group B having 80 participants. Children in group A were having febrile seizures while those in Group B were febrile but did not have seizures. Children from the age of six months to five years of either gender presenting with first episode of febrile seizures were included in the study. Children diagnosed as having neurological deficits such as cerebral palsy, birth history of asphyxia, epilepsy and developmental delay, those having meningitis or those having afebrile seizures or metabolic seizures were excluded from study.

Eligible patients approaching through Pediatric Medicine Out Patient Department as well as those admitted in Pediatric Ward was registered in the study trial by taking informed consent. Group A with and group B without having febrile seizures. Both groups had equal number of children matched for age and gender. Work up for seizures and iron deficiency anemia was done by complete history, physical examination, lab investigation including blood CP and serum ferritin. All the required data of the both groups was obtained and recorded as per designed format on the prescribed per-forma by the investigator.

Ethical issues were addressed as; informed consent was taken from guardians or parents. Data obtained during study was kept confidential. Bias in study was controlled by strictly following exclusion and inclusion criteria. All the data obtained was entered on SPSS and was analyzed by using version 16. Mean SD was expressed for continuous variable like age. Frequency/percentages were calculated for categorical variables; gender, diagnosis, treatment provided, and complications developed. Stratified analysis (analysis within the different age groups) was performed to control any effect modification due to age, gender, duration of dis-

ease and diagnosed condition of disease on complications that patients develop. Chi square test was applied in which statistical significance was given to p value of <0.05.

## RESULTS

The mean age of group A was  $25 \pm 1.28$  months while that of group B was  $24 \pm 1.26$  months. Both groups had majority of male children. The details are given in table 1.

As per the status of Hb level, it was  $10.48 \pm 1.16$ g for group A and  $12 \pm 2.31$  g for group B with a p value of 0.004. MCV and ferum ferritin levels for both groups are given in table 2.

Table 3 gives detail of iron deficiency anemia in both groups. The rate of iron deficiency anemia in Group A was 38% while that in group B was 20% with a p value of 0.003.

## DISCUSSION

Clinical presentation of iron deficiency anemia includes neurological symptoms like poor memory, behavioral changes, delayed motor mile stones, poor attention span, learning deficit<sup>11</sup>. The Italian study observed and published the association of febrile seizures with iron deficiency anemia in mid-90s<sup>12</sup>. The same findings were observed in other international studies in same era.

Hartfield and colleagues in a retrospective study from the University of Alberta, Canada reported that the febrile seizures were more common in children having iron deficiency anemia as compared to those who have febrile illness but does not have iron deficiency anemia<sup>13</sup>. However, the role of iron deficiency in febrile seizures was denied by some international studies. In a study from Iran, Bidabadi and Moushaf from the University of Guilan reported that iron deficiency was less common in children having first febrile seizure<sup>14</sup>. In 2005, the study conducted by Naveed-ur-Rehman and his colleagues at Agha Khan University Hospital had concluded that the iron deficiency anemia was the risk factor in etiology of the febrile seizures<sup>15</sup>. Significantly low serum ferritin level was reported among the children having first episode of febrile seizures<sup>15</sup>. The same association has

**Table 1: Age and gender distribution of the sample**

Variables		Group A (With Febrile Seizure) n=80 Mean $\pm$ SD	Group B (Without Febrile Seizure) n=80 Mean $\pm$ SD
Age (in months)		25 $\pm$ 1.28	24 $\pm$ 1.26
Gender	Male	46(58%)	47(59%)
	Female	34(42%)	33(41%)

**Table 2: Hb status, MCV level and serum ferritin**

Investigations	Group A (With Febrile Seizures) n=80 Mean ± SD	Group B (Without Febrile Seizures) n=80 Mean ± SD	p value	Significance
Hb Level g/dl	10.48 ± 1.16	12 ± 2.31	0.004	Yes
MCV Level fu/l	71 ± 6.63	77 ± 6.00	0.002	Yes
Serum Ferritin µg/g	10 ± 1.82	15 ± 2.12	0.002	Yes

**Table 3: Iron deficiency**

Iron Deficiency Anemia	Group A (With Febrile Seizures)	Group B (Without Febrile Seizures)	P value
Yes	30(38%)	16(20%)	0.003
No	50(62%)	64(80%)	

been found in our study. The advantages of our study were period of long study, large sample size and of being conducted in two different tertiary hospitals.

The relationship between iron deficiency anemia and convulsions in malarial patients had been reported in the previous studies<sup>16</sup>. Developmental delay and behavior disturbances were also reported to be associated with iron deficiency anemia in early life and treating anemia early may reverse these processes<sup>13,15</sup>. Kobrinsky et al suggested the high threshold of febrile seizures among children having iron deficiency anemia<sup>16</sup>.

Children in his study who were having febrile seizures were not found to be iron deficient as defined by hemoglobin concentration with  $P < .03$ <sup>16</sup>. Another study reported that thalassemic patients were having low incidence of febrile seizures as compared to general population<sup>17</sup>. This suggests that brain metabolism have effects due to iron overload that prevents febrile seizures in these children.

Another study conducted by Daoud et al<sup>18</sup> showed that children having febrile convulsions had low serum ferritin level when compared to those having febrile illness without convulsions. Pisacane et al<sup>19</sup> suggested a significant relationship among febrile convulsions and iron deficiency anemia. They further reported that febrile seizures were significantly more common among those children having iron deficiency anemia, these children were having low serum iron level along with low hemoglobin level. Iron deficiency anemia was reported in 30% of the patients with febrile seizures as compared to 14% of the children of control group. Serum ferritin level was however not measured in the study.

However, the findings of a study conducted in Iran by Omen et al<sup>20</sup>, are contradicting and showing no relationship between first episode of febrile seizures and iron deficiency anemia. Another study conducted in

Holy Family Hospital Rawalpindi also shows positive association of iron deficiency with febrile seizures<sup>9</sup>.

In our study the difference in MCV was not significant in group A and group B between ages of six months to two years while it was significant in age group of 2 years to 5 years. A study conducted by Kobrinsky in Fargo<sup>16</sup> reported high level of hemoglobin and MCV among the children having febrile seizures. Our study showed significantly low level of hemoglobin, MCV and serum ferritin level in children with febrile convulsions than in control group. The same findings were reported in a study done by Daoud et al<sup>18</sup>. A study published in European journal reported significantly high level of plasma iron and ferritin level and low level of TIBC in those children having first febrile seizures as compared to control. In our study serum ferritin was measured after 72 hours of onset of febrile seizures. On presentation none of the patient in either group treated with therapeutic dose of iron but at some occasions some of them had used non therapeutic doses of iron supplements.

Evidences have proven the role of iron in proper neurological functioning that's how its deficiency would lead to the initiation of febrile convulsions.

### LIMITATION

The deficiency of the study was we were unable to account for some of the confounding factor like lead poisoning leading to iron deficiency anemia. We also didn't assess the recurrence of febrile convulsions after iron supplementations.

### CONCLUSION

Febrile seizures were twice as common in children having iron deficiency anemia as compared to those who did not have iron deficiency anemia. Those children having febrile seizures have significantly low se-

rum ferritin level as compared to those who did not have seizures. to the initiation of febrile convulsions.

## RECOMMENDATION

It is proposed that every child with febrile seizures should be given therapeutic iron supplementation. It is also suggested that screening and treatment of iron deficiency anemia in children should be done at an early stage.

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## CONTRIBUTORS

SAK conceived the idea, planned the study and critically reviewed the manuscript. AS helped in the analysis of data and write up of the article. MAN helped acquisition of data and did statistical analysis. All authors contributed significantly to the submitted manuscript.