



SIMPLE FEBRILE SEIZURE AND IRON DEFICIENCY ANAEMIA- IS THERE ANY ASSOCIATION

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Abstract

Background: Febrile seizures occurs mostly in children 14–18 months of age, which overlaps with the maximum prevalence age of iron-deficiency anemia, which is between 1 and 2 years of age. It is well established that iron deficiency may cause some behavioral and developmental problems. The relationship between iron deficiency and febrile seizure is not yet well determined, the present study was conducted to see the association between iron deficiency anaemia and simple febrile seizures. **Methods:** This prospective case control study was conducted in SMGS Hospital, GMC Jammu from January 2018 to December 2020 after taking approval from institutional ethical committee. Cases included children of age group 6 months to 5 years presenting with simple febrile seizure to the casualty or OPD of this hospital. For each case, a control was selected with similar age group and same sex who came for short duration fever (less than 3 days) but without seizures. deficiency was defined as per WHO criteria After proper consent of parents of the study children, blood samples of the study children were sent for the above mentioned investigations in hospital's central laboratory. Samples were taken during afebrile period. **Results:** Total 200 subjects were included in the study, 100 in each group. Iron deficiency anaemia was seen in 46 subjects (46%) in case group and in 13(13%) subjects in control group. The results were statistically significant { $p < 0.0001$, odds ratio (95% CI) 5.70(2.82 TO 11.51)}. **Conclusion:** Iron deficiency anaemia can be considered as a risk factor for febrile seizures and treatment of iron deficiency anaemia may prevent occurrence of febrile seizures.

Keywords: Simple febrile seizure, Iron deficiency anaemia, Complete blood count, Serum ferritin.

INTRODUCTION

Febrile Seizures are the most common cause of convulsions in children and a frequent cause of emergency hospital admissions. Between 2% and 5% of children (more common in boys) in Europe and the United States experience at least one febrile seizures before the age of 5 years (Hackett *et al.*, 2007; Gourie-Devi *et al.*, 2004; Berg, 2013). Although earlier Indian studies suggested that up to 10% of children experience a febrile seizure, recent data indicate that the incidence rate in India is similar to western figures (Rantala *et al.*, 2005; Berg *et al.*, 1995). Febrile seizures occurs mostly in children 14–18 months of age, which overlaps with the maximum prevalence age of iron-deficiency anemia, which is between 1 and 2 years of age (Hartfield *et al.*, 2009). Iron deficiency is the most common trace element deficiency that leads to a decrease in the production of hemoglobin, causing IDA. Iron is also essential for the metabolism of the brain and neurotransmitters and in the production of myelin, which is crucial for nerve cell function and can lower the amplitude and threshold of neuron excitation (Kumari *et al.*, 2012). It is also well understood that iron is a cofactor that is necessary in several enzymes and plays an important role in neurotransmitter production and function, hormonal function, and DNA duplication. In this way, iron deficiency can affect the function of the nervous system and thereafter increases the risk of convulsions (Heydarian and Vatankhah, 2012). Iron is an essential element for the metabolism of the body and the proper function of many enzymes depends on its presence at an adequate level. Iron is involved in the metabolism of neurotransmitters and enzymes such as monoaminoxidase, cytochrome, peroxidase, and catalase. Also, it is well established that iron deficiency may cause some behavioral and developmental problems (Nasehi *et al.*, 2013).

However, the studies carried out so far have reported conflicting results. Some studies have reported that in the patients with iron deficiency, febrile convulsion is significantly higher than that in the control group (Hartfield *et al.*, 2009; Ur-Rehman and Billoo, 2005; Daoud *et al.*, 2002). On the contrary, some authors have concluded that the risk of febrile seizure in anemic children seems to be less than that in children with no febrile seizure (Talebian and Momtazmanesh, 2007) and that iron deficiency can be a protective mechanism against convulsions by increasing the convulsion threshold. Other studies have shown that iron deficiency plays no role in pediatric febrile seizures (Salehi Omran *et al.*, 2009; Amirsalari *et al.*, 2010). Since the relationship between iron deficiency and febrile seizure is not yet determined, chance or other unknown factors can be considered as causes (Bidabadi and Mashouf, 2009). Considering the above results, the present study was conducted to see the association between iron deficiency anaemia and simple febrile seizures.

METHODS

This prospective case control study was conducted in SMGS Hospital, GMC Jammu from January 2018 to December 2020 after taking approval from institutional ethical committee. Cases included children of age group 6 months to 5 years presenting with simple febrile seizure to the casualty or OPD of this hospital. Diagnostic criteria for simple febrile seizures, based on AAP Clinical Practice Guidelines (American Academy of Pediatrics, 2008), included seizure associated with fever (≥ 100.4 deg F) and seizure was generalized, short duration (less than 15 minutes), no recurrence of seizures within 24 hours, child is otherwise neurologically healthy and without any neurological abnormality before and after the episode of seizure, with age group between 6 months to 5 years.

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Table 1. Comparison of hematological parameters between cases and controls

Parameters	Cases(n=100)	Controls(n=100)	P value
Hb	10.02 ± 1	11.5 ± 1.5	<0.0001 [†]
MCV	70 ± 7.5	85 ± 5.1	<0.0001 [†]
MCH	19 ± 2.1	28 ± 2.6	<0.0001 [†]
MCHC	26 ± 4.2	33 ± 3.3	<0.0001 [†]
RDW	17 ± 1.2	13.2 ± 2.1	<0.0001 [†]
TIBC	340 ± 34	230 ± 20	<0.0001 [†]
Transferrin saturation (%)	12.1 ± 1.1	16 ± 1.2	<0.0001 [†]
Serum ferritin	36 ± 10	44 ± 12	<0.0001 [†]

[†]Independent t test

Table 2. Comparison of iron deficiency anemia between cases and controls

Iron deficiency anemia	Present	Absent	Total	P value	Odds ratio(95% CI)
Cases(n=100)	46(46.00%)	54(54%)	100(100.00%)	<0.0001*	5.70(2.82 to 11.51)
Controls(n=100)	13(13%)	87(87%)	100(100.00%)		
Total	59(29.50%)	141(70.50%)	200(100.00%)		

* Chi square test

For each case, a control was selected with similar age group and same sex who came for short duration fever (less than 3 days) but without seizures. Children with signs of CNS infections, electrolyte imbalance, neurodevelopmental delay, hepatosplenomegaly, those with chronic liver, renal, cardiac, gastrointestinal, endocrinal or any other chronic disorder disorders were excluded from the study. Iron deficiency was defined as per WHO criteria (World Health Organization, 2001): hemoglobin less than 11g/dl, mean corpuscular volume (MCV) less than 72fl, mean corpuscular hemoglobin (MCH) less than 24pg, mean corpuscular hemoglobin concentration (MCHC) less than 30g/dl, total iron binding capacity (TIBC) less than 210µg/dl, transferrin saturation less than 15%, red cell distribution width(RDW) more than 15% and serum ferritin less than 30µg/l. After proper consent of parents of the study children, blood samples of the study children were sent for the above mentioned investigations in hospital's central laboratory. Samples were taken during afebrile period.

RESULTS

Total 200 subjects were included in the study, 100 in each group. In each group there were 58(58%) males and 42(42%) females. Mean age of cases was 3.5±1.3 years and that of controls was 3.2±1.1 years. Comparison of hematological parameters between cases and controls is statistically significant [Table 1]. Iron deficiency anaemia was seen in 46 subjects(46%) in case group and in 13 subjects in control group(13%) [Table 2]. The results were statistically significant {p<0.0001, odds ratio(95% CI) 5.70(2.82 TO 11.51)}.

DISCUSSION

In the present study, maximum cases of febrile seizures were reported in males as compared to females. In study conducted by Pathan HG in 2017, preponderance of males was observed over females among cases of febrile seizures (Pisacane *et al.*, 1996). Mean age of cases was 3.5±1.3 years and that of controls was 3.2±1.1 years. Kumari *et al.*, Pisacane *et al.*, Vaswani *et al.*, and found similar result in their study (Kumari *et al.*, 2012; Vaswani *et al.*, 2009; Bhat *et al.*, 2020). Prevalence of anaemia is approximately four times higher in children who had simple febrile seizures than in children without febrile seizure in our study. Our study also revealed that iron deficiency anaemia has a significant association with simple febrile seizures.

Thus, iron deficiency anaemia can be considered a significant risk factor for the occurrence of febrile seizures. Kumari *et al* in their study showed 63.6% of children with simple febrile seizure had iron deficiency anaemia with crude odds ratio of 5.34(3.27-8.73) (Kumari *et al.*, 2012). Pisacane *et al.* found similar results with odds ratio of 3.3 (1.7-6.5) (Vaswani *et al.*, 2009). Study conducted by Jehangir *et al.* also showed similar results with odds ratio of 5.17 Sherjil *et al.* (2010) in their study have shown that 31.85% of subjects who presented with febrile seizures had iron deficiency anaemia with odds ratio of 1.93 (Sharma, 2018). All hematological parameters in present study were significantly abnormal in those who presented with seizures that those who didn't. Similar results were seen in study conducted by Sharma *et al.* who revealed that mean serum ferritin levels, values of hemoglobin and MCV were significantly low in children who had simple febrile seizures vs those who had not. Similar results were shown by Jehangir *et al* and Sherjil *et al.* (2010).

Conclusion

There is association between iron deficiency anaemia and simple febrile seizures. Thus iron deficiency anaemia can be considered as a risk factor for febrile seizures and treatment of iron deficiency anaemia may prevent occurrence of febrile seizures. Also patients with simple febrile seizures should be screened for iron deficiency anaemia to prevent its recurrence.

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