

Iron Deficiency as a Risk Factor for First Febrile Seizure

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We conducted this study to determine the role of iron deficiency as a risk factor for first febrile seizure in children. Fifty children between 6 months to 6 years with first febrile seizure (Cases) and 50 children with febrile illness but without convulsions (Controls) were enrolled from the pediatric ward of a tertiary care hospital. Iron deficiency was determined by estimation of hemoglobin, red blood cell indices and serum ferritin. The mean serum ferritin level ($\mu\text{g/L}$) was significantly low in Cases (31.9 ± 31.0) as compared to Controls (53.9 ± 56.5) with $P = 0.003$. Iron deficiency could be a potential risk factor for febrile seizure in children.

Key words: *Febrile seizure, Serum ferritin, Iron deficiency.*

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Febrile seizures are the most common type of seizures, occurring in 3 to 4 % of children(1). Owing to their association with epilepsy in future, various studies have attempted to identify the risk factors associated with them *viz*, family history of febrile seizures, epilepsy, perinatal factors and temperature peak. Pisacane, *et al.*(2) reported that low iron level is associated with febrile seizure, whereas Kobrinsky, *et al.*(3) reported that iron deficiency raises the threshold for seizures. As iron is important for function of neurotransmitters and various enzymes, low level of serum ferritin may lower the seizure threshold(4). Fever can worsen the negative effects of low serum ferritin on the brain and trigger seizure(2). We conducted this study to determine any association between iron deficiency and first febrile seizure.

METHODS

A case-control study was conducted from August 2005 to July 2006 following approval from Institutional Ethics Committee. Fifty consecutive children aged 6 months to 6 years, admitted to the Pediatric ward with first episode of febrile seizure were enrolled as cases. Febrile seizure was defined as a seizure occurring in association with a febrile

illness, in the absence of CNS infection or any other defined causes of seizure(1). Children with previous febrile/afebrile seizures, neurological infections, developmental delay, or on iron therapy were excluded. A control group was selected from age and sex matched children admitted with febrile illness including respiratory infections or acute gastroenteritis but without seizures and without iron supplements.

Demographic data, seizure details, nature of febrile illness, family history of epilepsy / febrile seizures, temperature at admission, and nutritional status were recorded. IAP weight for age classification was used to grade protein energy malnutrition(5). Estimation of hemoglobin, red blood cell indices (MCV and MCH) and serum ferritin (Microwell Elisa) was done.

Iron deficiency anemia was defined as hemoglobin $<11\text{g/dL}$, MCV $<70\text{fl}$, MCH $<27\text{pg}$ and serum ferritin $<12\text{ }\mu\text{g/dL}$ (6). In presence of fever, a higher cut-off value of serum ferritin (25-50 $\mu\text{g/L}$) was considered(7). Cases and Controls were compared with respect to blood indices and serum ferritin. Chi-square and ANOVA tests for discontinuous variables and unpaired *t* test for

WHAT THIS STUDY ADDS?

- Serum ferritin level is significantly low in children with first episode of febrile seizure.

continuous variable at 5% significance ($P < 0.05$) level were used for statistical analysis.

RESULTS

Fifty Cases and 50 Controls were enrolled. Their demographic characteristics and hematological parameters are depicted (**Table I**). The proportion of children with low ferritin ($<25\mu\text{g/L}$) was significantly higher ($P < 0.0001$) in Cases (34, 68%) than in Controls (15, 30%). With serum ferritin $<12\mu\text{g/L}$, the proportion of children with low ferritin was comparable in Cases (6,12%) vs Controls (2,4%) ($P=0.14$). Thirty four cases and 15 controls had a low ferritin value ($\leq 25\mu\text{g/L}$). It was observed that amongst Cases, 77% had no PEM, 15% grade I PEM and 8% grade II PEM whereas within Controls, 60% had no PEM and 40% had grade I PEM.

DISCUSSION

We observed significantly low serum ferritin levels in children with first febrile seizure than in controls. Similar results were observed by Pisacane, *et al.*(2). Daoud, *et al.*(8) reported that mean serum ferritin was significantly low in children with first febrile seizure and also proportion of children with low ferritin was significantly higher in febrile seizure

group than in controls. Previous studies have reported an association between iron deficiency and breath holding spells and improvement with iron therapy(9).

The study does have some limitations. Serum ferritin, a nonspecific acute phase reactant can rise in any inflammatory disease. Iron deficiency and convulsions may be seen in lead poisoning but lead levels could not be determined in our subjects. Larger studies are needed to confirm our findings.

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TABLE I DEMOGRAPHIC DATA AND HEMATOLOGICAL PARAMETERS OF CASES AND CONTROLS

Parameters	Cases (n = 50)	Controls (n = 50)	P value
Age (years)	1.73 ± 0.94	1.75 ± 0.91	0.91
Temperature at admission (°C)	38.6 ± 0.36	38.5 ± 0.29	0.13
Height (cm)	80.9 ± 9.3	81.3 ± 9.1	0.85
Weight (Kg)	9.9 ± 2.1	10.0 ± 2.1	0.88
Hemoglobin (g/dL)	9.4 ± 1.2	9.5 ± 1.0	0.70
MCV (fL)	73.4 ± 9.5	73.6 ± 8.3	0.89
MCH (pg)	21.4 ± 3.1	21.7 ± 2.9	0.71
Serum ferritin (μg/L)	31.9 ± 31.0	53.9 ± 50.5	0.003

REFERENCES

1. 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. p. 1994-1995.
2. 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.
3. Kobrinsky NL, Yager JY, Cheang MS, Yatscoff RW, Tenenbein M. Does iron deficiency raise the seizure threshold? *J Child Neurol* 1995; 10: 105-109.

4. Oski FA, Honig AS. The effects of therapy on the developmental scores of iron deficient infants. *Pediatrics* 1978; 92: 21-25
 5. Gupta P, Shah D. Protein Energy Malnutrition. In: Ghai OP, Gupta P, Paul VK, editors. *Ghai Essential Pediatrics*. 6th ed. New Delhi: CBS Publishers & Distributors; 2004.p. 101-118.
 6. De Gruchy GC. *Clinical Hematology in Medical Practice*, 5th ed. Victoria: Blackwell Science Ltd; 2004.
 7. Dallman PR, Yip R, Oski FA. Iron deficiency and related nutritional anemias. In: Nathan DG, Oski FA, editors. *Hematology of Infancy and Childhood*. 4th ed. Mexico: Saunders; 1993. p. 413- 450.
 8. Daoud AS, Batieha A, Abu Etiesh F, Gharaibeh N, Ajlouni S, Hijazi S. Iron status: a possible risk factor for first febrile seizure. *Epilepsia* 2002; 43: 740-743.
 9. Daoud AS, Batieha A, AL- Sheyyab M, Abuekteish F, Hijazi S. Effectiveness of iron therapy on breath holding spells. *J Pediatr* 1997; 130: 547-550.
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