Iron Deficiency as a Risk Factor for Simple Febrile Seizures– A Case Control Study

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Abstract: Background: Febrile seizures are the most common seizures in children. Incidence is around 2-5% among children of age group 5-60 months. There is variable association between febrile convulsions and hematological parameters associated with iron deficiency anemia in children. Iron deficiency is also associated with many of the behavioural disorders in children.

Objective: To study the role of iron deficiency as a risk factor for simple febrile seizures.

Design: Prospective Case control study.

Setting: Pediatric department of a tertiary care teaching hospital.

Participants: 60 cases and 60 controls were included in the study. Consecutive cases and concurrent controls were selected. Cases were children of age group 6 months to 60 months presenting with 1st episode simple febrile seizures. Controls were children of same age group presenting with short febrile illness but without any seizures.

Methods: This is a case control study conducted over a period of one year in a tertiary care hospital. Consecutive sixty children with first prospective episode of febrile seizure in the age group of 5 months-60 months admitted in the institution were taken as cases and sixty children with fever due to other causes without seizures were taken as controls. Various blood parameters were compared among these two groups and statistically analysed for the outcome.

Results: Highly significant association was found between iron deficiency and simple febrile seizures in both univariate and multivariate analysis. Crude odds ratio was 3.27 (P<0.001).

Conclusions: Iron deficiency is a significant risk factor for simple febrile seizures in children of age group 6 months to 60 months.

I. Introduction

Febrile seizure is the most common neurologic disorder of children and the most frequent type of seizure in this age group. It occurs in 3%-4% of children under 5 years, most frequently from 14 to 18 months of age, although incidence rates as high as 14% have been reported. The recurrence rate of febrile seizure for the first time is 50% in children under 1 year of age and 28% for those older than 1. The simple febrile seizures are diffuse seizures lasting less than 15 minutes and occurring once over 24 hours. If focal seizure or focal symptoms following the seizure are multiple or lasting more than 15 minutes, the seizure will be termed complex febrile seizure. Febrile seizure is more common in boys, usually manifesting as tonic-clonic convolution. Febrile seizure episodes are agonizing to the parent and child and can cause psychological trauma to both. Simple febrile seizure reflects a genetic predisposition to convolution manifesting with abrupt elevation of body temperature. Otitis media, and upper respiratory tract infections (especially influenza) are among the most common clinical conditions resulting in febrile seizure in children. The pathophysiology of febrile seizure remains to be accurately described; different studies have reported various risk factors, including iron deficiency as iron is needed for brain energy metabolism, for metabolism of neurotransmitters and for myelination. On the other hand, there are studies that fail to corroborate such an association, as well as those which demonstrate the opposite. Therefore, since iron deficiency anemia is a common disorder of pediatrics and preliminary data have failed to demonstrate a definitive association, we undertook the present study to investigate the association between iron deficiency anemia and febrile seizure in children.
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II. Methods

This case control study was done in the Department of Pediatrics, Gauhati medical college, during August 2016 to February 2017. Ethical clearance was obtained for the study from the Ethical committee, Gauhati Medical College.

Cases were children of age group 6 months to 60 months presenting with 1st episode of simple febrile seizures to the Pediatrics Emergency Department and wards of the hospital during the study period.

Diagnostic criteria for simple febrile seizures (based on AAP Clinical Practice Guidelines) included seizures associated with fever and the seizures were 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 seizures, with age group between 6 months to 5 years. Consecutive cases were selected for the study and concurrent controls were selected from the same setting and included febrile children of age group 6 months to 5 years who presented with short duration fever (<3 days) but without seizures. Cases and controls were selected in 1:1 ratio. No matching was done.

Children presenting with atypical febrile seizures, afebrile seizures, h/o of neonatal or previous unproved seizures, h/o recent trauma or other causes of proved seizure, those having any signs & lab findings suggestive of central nervous system infection or any metabolic cause of provoked seizure, those with any chronic neurodevelopment problems, readmission for febrile seizure, those who were previously diagnosed cases of other hematologic problems like hemolytic anemias, bleeding or coagulation disorders, haematologic malignancy, those who were on iron supplementation, and very sick children were excluded from the study.

After informed consent, detailed history was elicited and physical examination was done. Hospital records were also examined for relevant data. The diagnosis of anemia was made by a paediatrician who studied the results of tests without knowing the groups to which each of the test results belonged.

For children aged 6 months to two years, IDA was defined as Hb<10.5 g/dl, hematocrit (Hct)<33%, MCV<70 fL, MCH<23 pg, MCHC<30 g/dL, and RBC<3.7×10⁶ cell/mm³. For 2-5-year-old children, IDA was defined as Hb<11.5 g/dL, Hct<34%, MCV<75 fL, MCH<24 pg, MCHC<31 g/dL and RBC<3.9×10⁶ cell/mm³. MCHC, MCH, MCV, and peripheral blood smear were used to rule out other causes of anemia.

III. Results

60 cases and 60 controls were included in the study. Among the 60 cases 16 were diagnosed to have Iron Deficiency anemia. Among the 60 controls 6 were having iron deficiency. Iron deficiency anemia was found to be a significant variable. Crude odds ratio was 3.27 (P<0.001).

<table>
<thead>
<tr>
<th>CASES (30)</th>
<th>CONTROLS(30)</th>
<th>ODDS RATIO</th>
<th>P-VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>IRON DEFICIENCY</td>
<td>16(26.6%)</td>
<td>6(10 %)</td>
<td>3.27</td>
</tr>
</tbody>
</table>

IV. Discussion

Iron deficiency was found as a significant risk factor for simple febrile seizures in children of age group 6 months to 5 years in our study. In the study done by Pisacane, et al., among children of the same age group, similar results were noted and the odds ratio was 3.3 (95% CI of 1.7-6.5). Iron status was measured by hemoglobin.

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MCV and serum iron in that study. Dawn, et al.27 also found similar results with children with febrile seizures almost twice likely to have iron deficiency compared to controls.

In the study by Daoud, et al.,28 the significance of iron status as a possible risk factor was evaluated. The mean serum ferritin level in the cases was 29.5 mcg/L, much lower than the values in the controls (53.5 mcg/L).

Similar observations were made in a study done by Vaswani, et al.29 from Mumbai. The mean serum ferritin level was significantly low in children with firstfebrile seizures (31.9±31.0 mcg/L) as compared to controls (53.9±56.5 mcg/L) (P=0.003). However, no significant difference was noted in the mean haemoglobin value of cases (9.4±1.2 g/dL) and controls (9.5±1.0 g/dL) (P=0.7), or in the mean value of blood indices.

Our study also adds & support the previous studies and prove that iron deficiency as a risk factor for febrile seizure.

The study does have some limitations. As the study involved only a small sample size and was a hospital-based study the prevalence of exposure and outcome variables may be different from a community setting. Serum ferritin, a nonspecific acute phase reactant can rise in any inflammatory conditions, although both cases and controls were having fever at the time of enrollment.

We report iron deficiency as a modifiable risk factor for simple febrile seizures in Indian children of age group 6 months to 60 months. Early detection and timely correction of iron deficiency may be helpful for prevention of simple febrile seizures in children of this age group.

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References

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