Iron Deficiency as a Risk Factor for Simple Febrile Seizures

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Abstract

Objectives: To determine the association between iron status and febrile seizure.

Patients and Methods: This case-control study was conducted among 120 children of age group 6 months to 3 years and hospitalized for the first episode of Febrile Seizures (FS). The case group was compared to a group of 80 age- and sex-matched controls admitted with the same diagnosis of infection but without seizure. The control and case groups were matched based on family history of FS, age, sex and temperature.

Venous blood samples were examined for erythrocyte sedimentation rate (ESR), serum iron, serum ferritin, total iron-binding capacity and complete blood count (CBC). The CBC included measurements of red blood cell (RBC), hemoglobin (Hb), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), WBC, and platelets.

Results: Non significant differences between the cases and the control group in terms of age, temperature, sex, ESR, WBC, RBC, MCV, MCHC and platelets. The mean Hb, HCT, serum ferritin, serum iron, and MCH were significantly low in children with first febrile seizures as compared to controls.

Conclusions: Low levels of serum ferritin and iron might play a role in the pathogenesis of simple febrile seizure.

Key Words: Iron deficiency — Febrile seizures.

Introduction

THE World Health Organization estimates that anaemia, largely caused by iron deficiency, affects between 500 million and two billion people worldwide [1,2]. In some developing countries, up to 50 percent of preschool children have anaemia that principally is caused by iron deficiency [11]. It is the most common nutritional deficiency and haematological disease of infancy and childhood [3]. Iron is a nutritional element not only needed for the synthesis of haemoglobin, but is also essential for enzymes involved in neurochemical reactions [4]. Neurological symptoms like poor attention span, learning deficits, weak memory, delayed motor development and behavioural disturbances caused by iron deficiency are well known, [2-4]. Thus it is possible that iron deficiency may predispose to other neurological disturbances like febrile seizures.

Febrile seizures are the commonest cause of seizures in children, occuring in 2-5% of children [1]. Complications like aspiration can occur during each episode of seizures [6-7]. Febrile seizure episodes are agonizing to the parent and child and can cause psychological trauma to both [8]. Iron deficiency is postulated as a risk factor for febrile seizures in children and it is an easily correctable condition [9,10]. We, therefore, studied the association between iron deficiency and simple febrile seizures.

Patients and Methods

We performed a prospective case-control study of children with first simple febrile seizure admitted to the Pediatrics Ward of a tertiary Hospital from April 2010 to December 2010. Approval from the ethical committee and informed consent from the parents of the children were obtained. We enrolled 120 children of the age group 6 months to 3 years with a diagnosis of first febrile seizure. A control group (80 patients) was selected randomly from patients between 6 months and 3 years of age who were admitted with the same diagnosis of infection (respiratory and gastrointestinal) but without seizure. Diagnostic criteria for simple febrile seizures 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. Children who were admitted to the Hospital with a history of fever and convulsions were included in the study.
Exclusion criteria:

Children presenting with atypical febrile seizures, afibrile seizures, those having any signs of central nervous system infection, those with any chronic neurodevelopment problems, those who were previously diagnosed cases of other hematologic problems, bleeding or coagulation disorders, haematologic malignancy, those who were on iron supplementation, and very sick children were excluded from the study.

The control and case groups were matched based on family history of FS, age, sex, temperature and cause of illness. Within admission, venous blood samples were obtained for complete blood count (CBC), erythrocyte sedimentation rate (ESR), and platelets (PLT) Count.

Serum iron (SI), serum ferritin (SF), TIBC and CBC (including RBC, Hb, HCT, MCV, MCH, MCHC) were measured. The ferritin assay was performed using a Stat Fax 2100 ELISA plate reader (Awareness Technology Inc., USA). Serum iron concentration and TIBC were measured by direct spectrophotometry using an RA 1000 autoanalyzer (Technicon Instruments Corporation, USA).

Statistical analysis:

Data were entered and analyzed using the Statistical Package for Social Science (SPSS). Nominal data were expressed as frequency and percentage. Numerical data were expressed as means and standard deviations and were compared using student’s t-test. Associations were tested using Pearson’s correlations. p-value less than 0.05 were considered significant.

Results

Of the 200 children studied, 120 with FS were enrolled in the case group, and (80) were considered as controls. Non significance differences between the studied groups in terms of age, sex and temperature (Table 1).

There were no significance differences in terms of ESR, WBC, and platelets, RBC, MCHC, and TIBC levels between the cases and the control group (Table 2).

HB, HCT, MCH, mean serum ferritin and serum iron, were significantly low in the febrile convulsion group as compared to control group (Table 2).

The mean levels of MCV in the FS group was lower than that in the control group, but the differences were non significant.

It is shown from Table (2) that hemoglobin (HB), hematocrit (HCT), mean corpuscular hemoglobin (MCH), serum ferritin (SF), serum iron (SI) were significantly low in cases as compared to control.

Table (1): Variable with simple febrile seizures in children between 6 months and 3 years of age.

<table>
<thead>
<tr>
<th></th>
<th>Cases (n=120)</th>
<th>Control (n=80)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE (months)</td>
<td>23.9±3.3</td>
<td>24.1±3.9</td>
<td>0.69</td>
</tr>
<tr>
<td>Mean±SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temperature, °C</td>
<td>39.2±0.8</td>
<td>39.4±1.0</td>
<td>0.11</td>
</tr>
<tr>
<td>Mean±SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female*</td>
<td>54 (45%)</td>
<td>40 (50%)</td>
<td>0.48</td>
</tr>
<tr>
<td>Family history of febrile seizure*</td>
<td>30 (25%)</td>
<td>8 (10%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Family history of epilepsy*</td>
<td>31 (25.8%)</td>
<td>7 (8.8%)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*Number (%).

Family history of febrile seizures and epilepsy were significantly high in cases as compared to control with p (0.001).

Table (2): Laboratory data between cases and controls.

<table>
<thead>
<tr>
<th></th>
<th>Cases (n=120)</th>
<th>Control (n=80)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESR mm/hr</td>
<td>14.3±2.5</td>
<td>14.8±2.6</td>
<td>0.17</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PLT/mm 3</td>
<td>333.3±49.57</td>
<td>318.3±58.359</td>
<td>0.06</td>
</tr>
<tr>
<td>WBC imm 3</td>
<td>12.5±3.20</td>
<td>12.3±2.12</td>
<td>0.56</td>
</tr>
<tr>
<td>RBC mL/ mm</td>
<td>4.0±239.44</td>
<td>4.0±239.44</td>
<td>0.26</td>
</tr>
<tr>
<td>Cu mm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HB g/dL</td>
<td>10.4±1.30</td>
<td>11.5±1.71</td>
<td>0.001</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCT %</td>
<td>33.2±1.60</td>
<td>34.1±1.49</td>
<td>0.001</td>
</tr>
<tr>
<td>MCV fL</td>
<td>79.3±2.07</td>
<td>79.5±1.25</td>
<td>0.29</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCH pg</td>
<td>26.9±1.39</td>
<td>27.9±1.40</td>
<td>0.001</td>
</tr>
<tr>
<td>MCHC g/L</td>
<td>33.0±1.44</td>
<td>33.3±1.30</td>
<td>0.07</td>
</tr>
<tr>
<td>Serum Ferritin ng/mL</td>
<td>52.7±17.93</td>
<td>79.4±2.36</td>
<td>0.001</td>
</tr>
<tr>
<td>Serum Iron tig/dL</td>
<td>60.17±1.72</td>
<td>87.97±1.43</td>
<td>0.001</td>
</tr>
<tr>
<td>TIBC ug/dL</td>
<td>378.0±5.18</td>
<td>377.0±5.33</td>
<td>0.21</td>
</tr>
</tbody>
</table>

ESR : (Erythrocyte sedimentation rate).
PLT : (Platelet).
WBC : (White blood corpuscle).
HB : (Hemoglobin).
HCT : (Hematocrit).
RBC : (Red blood cell).
MCH : (Mean corpuscular hemoglobin).
MCHC : (Mean corpuscular hemoglobin concentration).
MCV : (Mean corpuscular volume).
SF : (Serum ferritin).
SI : (Serum iron).
TIBC : (Total iron-binding capacity).
Discussion

Febrile seizures occur in 2 to 4% of all children with a recurrence rate of 30 to 40% [iii. Age for peak incidence of febrile seizures is 14 to 18 months which overlaps with that of iron deficiency anaemia which is from 6 to 24 months [12,13].

Iron deficiency is the commonest micronutrient deficiency worldwide, and is a preventable and treatable condition [14]. Iron is needed for brain energy metabolism, for metabolism of neurotransmitters and for myelination. Thus, iron deficiency may alter the seizure threshold of a child [15,16]. Iron deficiency is postulated as a risk factor for febrile seizures in children and it is an easily correctable condition [9,10]. We, therefore, studied the association between iron deficiency and simple febrile seizures.

Increasing peak temperature has been reported to increase the risk of FS progressively [17], but our data showed no marked differences in mean peak temperature at admission between cases and controls.

We have found that family history of FS, which most likely represents a genetic susceptibility to seizures with fever [17], and family history of epilepsy were significantly higher among cases than controls.

This agree with KUMARI, et al. [18] who found that family history of FSs, and family history of epilepsy were significantly higher among cases than control. The genetic and familial component has been recognized in other studies [19,20].

In our study we measured iron status components (serum iron, ferritin, RBC, Hb, HCT, MCV, MCH, MCHC, and TIBC) among cases and controls. In the present study, we found that the mean serum ferritin level, serum iron level, HB, HCT, and MCH in the FS group were significantly low in cases as compared to control group.

There were non significant differences in other measures of iron components, such as RBC, MCV, MCHC, and TIBC, between cases and controls. Because the serum ferritin level is higher in males than in females [21] and increases in response to fever and inflammation [22], we matched the case and control groups by age, sex, ESR, and underlying illness. Plasma ferritin provides a sensitive, specific, and reliable measurement for determining iron deficiency at an early stage, and it may be the best indicator of total body iron status [23]. Fever, however, was present in all patients in the two groups.

Daoud et al., reported that the mean level of ferritin in cases with first febrile seizure is significantly low as compared to reference group, but the mean levels of HB, MCV, and MCH were lower in children with first febrile seizure than in children in a control group, although the differences were non significant [24].

Pisacane et al., compared the levels of HB, MCV, and serum iron among controls and patients with FS, and they reported that iron deficiency is significantly more frequent among the cases than controls [25].

Rajwanti et al. [26] found that the mean serum ferritin level was significantly low in children with first febrile seizures as compared to controls. However, non significant difference was noted in the mean hemoglobin value of cases and controls, or in the mean value of blood indices.

Naveed et al., found that the proportions of cases with low levels of HB, HCT, MCV, MCH, and ferritin were higher among children with FS than among controls and the differences were statistically significant [27].

Conclusion:

We report iron deficiency as a risk factor for simple febrile seizures in children. Low level of plasma ferritin may lower the seizure threshold, as iron is important for the function of various enzymes and neurotransmitters present in the central nervous system [28]. Fever may worsen the negative effects of low plasma ferritin level on the brain, and therefore seizures can be triggered [25].

Early detection and timely correction of iron deficiency may be helpful for prevention of simple febrile seizures in children of this age group.

References

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