LEVEL OF SERUM IRON AND ZINC IN CHILDREN AND ASSESSING ITS CORRELATION WITH SIMPLE FEBRILE SEIZURE—A PROSPECTIVE OBSERVATIONAL STUDY

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Abstract
Background: Febrile seizures are one of the most common paediatric emergencies encountered around the world. Febrile seizures occur in 6 months to 60 months of age group. Iron and zinc are important trace elements and some enzymes and neurotransmitters in the central nervous system are affected by its levels. Inhibitory mechanisms in the brain could be affected by its deficiency and thus producing convulsion. Aims and Objectives: To estimate the serum level of zinc in children and assessing its correlation with simple febrile seizure. To estimate the serum level of iron in children and assessing its correlation with simple febrile seizure. Materials and Methods: Prospective Observational study conducted at Department of Pediatrics, Katihar Medical College, Katihar. The study included 61 children between 6 months and 60 months of age admitted with simple febrile seizure. Their serum iron and zinc and various other parameters including Hb, MCV, MCH, MCHC were determined. Data were analyzed by SPSS 20, frequency, mean, standard deviation, chi square test and independent sample t test. Result: A total of 61 children were included in the study. The prevalence of iron and zinc deficiency in children with simple febrile seizure was found to be 65.5% and 57.3% respectively. There was no statistically significant difference in all the parameters between children with iron deficiency and without Iron deficiency presenting with simple febrile seizures. Conclusion: The findings suggest that a considerable percentage of children having febrile seizure suffer from Iron and zinc deficiencies. Iron and zinc deficiencies could be an important risk factors which may predispose children to develop simple febrile seizures.

INTRODUCTION

Febrile seizures (FS) are defined as seizures occurring in children between 6 months to 60 months of age associated with fever greater than 38°C (100.4°F), not having evidence of an intracranial cause (e.g. infection, head trauma and epilepsy), another definable cause of seizure (e.g. hypoglycemia, electrolyte imbalance, drug use or drug withdrawal) or a history of an afebrile seizure.[1] About 3%-4% of white children, 6%-9% of Japanese children and 5%-10% of Indian children do have febrile seizures.[2] It is important to counsel parental anxiety about FS in a sensitive way because febrile seizure can be extremely frightening for the parents even if they are not of much harm for children.[3] There are two types of FS: Simple febrile seizure and complex febrile seizure. Generalized type of seizures that only occur once in a 24-hour period and last for less than 15 minutes are considered to be simple febrile seizures. However, complex/atypical febrile seizures are characterised by a focal nature, duration of seizure more than 15 minutes and frequency of more than one per 24 hours. Simple febrile convulsions are harmless and usually resolve on their own. The likelihood of them having future seizures is extremely low, and their prognosis is much better as a result.[4] Since iron is essentially required for the metabolism of many neurotransmitters, low iron levels are problematic because they reducing the production of aldehyde oxidases and monoamines. Cytochrome C oxidase, a neuronal metabolic activity marker in the brain, is also suppressed by iron deficiency.[5] One of the most common dietary disorders in the developing nations is deficiency of iron, especially among 6 months to 24 months of age group and infants younger than 6 months of age.[6] Around fifty percent of all cases of anaemia in...
children below four years of age can be attributed to iron deficiency. This is especially true in developing countries. Many studies have shown that iron is detrimental to a variety of developmental, cognitive, behavioural, and neurophysiological processes, particularly those involving brain metabolism, neurotransmitter function, and myelination.[7]

Zinc is a trace element that is important for growth, development, and normal brain function and is the principal component of different enzymes such as deoxyribonucleic acid and ribonucleic acid polymerases.[8] In brain, it regulates the activity of glutamic acid and the rate-limiting enzyme in the synthesis of GABA and facilitates the inhibitory effect of calcium on N-methyl-d-aspartate receptors and these effects prevent the stimulation of neuronal discharge.[9] Decreased zinc level lowers GABA synthesis because it increases the activity of pyridoxine needed for the synthesis of GABA, which would induce convulsions.[10]

**Aims and Objectives**

To estimate the serum level of zinc in children and assessing its correlation with simple febrile seizure.

To estimate the serum level of iron in children and assessing its correlation with simple febrile seizure.

**MATERIALS AND METHODS**

**Study Design:** Observational study.

**Study Setting**
The study was conducted at Department of Paediatrics, Katihar Medical College, Katihar.

**Study Population**
Children between 6 months to 60 months of age with Simple Febrile Seizure admitted in Department of Paediatrics, Katihar Medical College, Katihar within the study period.

**Duration of Study**
From January 2021 to August 2022.

**Sample Size**
All children of study population in defined study period. Final sample size: 61 cases.

**Data Collection**
At the time of enrolment an informed written consent was obtained from the parents and data was collected.

**Sampling Method**
The study is based on the collection of data in a child who fulfils the inclusion criteria stated below and admitted in the paediatric ward of Katihar Medical College, Katihar. After obtaining written informed consent from the parents, detailed physical examination done, blood sample were taken in yellow vial and plane vial for estimation of serum iron and serum zinc respectively. Estimation of serum iron and zinc done. The normal level of serum iron was determined as Fe >50mcg/dl.[11] The normal range of serum zinc was determined between 60mcg/dl to 120mcg/dl.[12]

**Statistical Analysis**
Data collected were summarised and analysed using SPSS 20.0, frequency, mean, standard deviation, chi square test and independent sample t test etc. and p-value was taken as statistically significant.

**Ethical Approval**
The study was submitted for the approval to the Institutional Ethics Committee (IEC) of Katihar Medical College, Katihar.

**Inclusion Criteria**
1. Children between the ages of 6 months to 60 months.
2. Children having Seizure that occurring within 24 hours of fever and last for less than 15 minutes.
3. Generalised seizure
4. No post ictal deficit
5. Recurrent case of febrile seizure

**Exclusion Criteria**
1. Atypical febrile seizure
2. Known case of seizure disorder
3. Children with documented intracranial infections
4. Children on zinc and iron supplementation for therapeutic purposes
5. Children having electrolyte imbalance
6. Children having hereditary disorder
7. Established cases of cerebral palsy, mental retardation and neurodegenerative disorders
8. Children having structural brain lesion
9. Other detectable causes of seizure- metabolic or any other

**RESULTS**
The largest group of patients in the study (42.6%) were between one and two years. [Figure 1]

**Figure 1: Age distribution**

Out of the total 61 patients, 65.6% were male (40 patients) and 34.4% were female (21 patients). [Figure 2]
The most common cause of fever was ARI, affecting 52.5% of patients, followed by viral fever affecting 24.6% of patients. AGE and UTI each affected 9.8% of patients, while ASOM was the least common cause, affecting only 3.3% of patients. [Figure 3]

Table 1: Compare to various parameters according to iron deficiency in all children who presented simple with febrile seizure

<table>
<thead>
<tr>
<th>Variables</th>
<th>Absent (mean ±SD)</th>
<th>Present (mean ±SD)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb (gm%)</td>
<td>12.01±1.25</td>
<td>10.49±1.15</td>
<td>0.727</td>
</tr>
<tr>
<td>PCV</td>
<td>35.78±3.65</td>
<td>31.28±3.56</td>
<td>0.893</td>
</tr>
<tr>
<td>MCV</td>
<td>75.73±4.95</td>
<td>70.97±4.86</td>
<td>0.899</td>
</tr>
<tr>
<td>MCH</td>
<td>24.52±2.50</td>
<td>23.42±2.39</td>
<td>0.237</td>
</tr>
<tr>
<td>MCHC</td>
<td>33.21±1.22</td>
<td>32.14±1.02</td>
<td>0.161</td>
</tr>
<tr>
<td>RDW</td>
<td>15.52±2.01</td>
<td>16.07±1.50</td>
<td>0.097</td>
</tr>
<tr>
<td>Iron</td>
<td>69.52±8.62</td>
<td>39.69±9.35</td>
<td>0.545</td>
</tr>
</tbody>
</table>

Table 2: Serum Iron Levels

<table>
<thead>
<tr>
<th>Serum Iron</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 50 MCG/DL</td>
<td>40</td>
<td>65.5</td>
</tr>
<tr>
<td>≥ 50 MCG/DL</td>
<td>21</td>
<td>34.5</td>
</tr>
</tbody>
</table>

Table 3: Serum Zinc

<table>
<thead>
<tr>
<th>Serum Zinc</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;60mcg/dl</td>
<td>35</td>
<td>57.3</td>
</tr>
<tr>
<td>≥60mcg/dl</td>
<td>26</td>
<td>42.7</td>
</tr>
</tbody>
</table>

shows the serum iron levels. Out of 61 participants, 40 (65.5%) had serum iron levels less than 50 mcg/dl [Table 2 and Figure 4]
DISCUSSION

In the present study, the largest group of patients in the study (42.6%) were between one and two years old, while the smallest groups of patients (13.1%) were between two and three years old and between four and five years old. There were 9 patients (14.8%) between six months and one year old and 10 patients (16.4%) between three and four years old. Out of the total patients, 65.6% were male (40 patients) and 34.4% were female (21 patients). The age and sex distribution of our study are consistent with previous studies on febrile seizures. A study conducted in Nigeria (Akinbami et al., 2011) reported that the highest frequency of febrile seizures occurred in children aged between 6 months to 36 months old, which is similar to our study’s finding that the largest group of patients were between 12 months to 24 months old. The same study also reported that febrile seizures were more common in males than females, which is consistent with our study’s finding that 65.6% of patients were male.

In the present study, the most common cause of fever was ARI, affecting 52.5% of patients, followed by viral fever affecting 24.6% of patients. AGE and UTI each affected 9.8% of patients, while ASOM was the least common cause, affecting only 3.3% of patients. One study published in the Journal of Infection and Public Health in 2020, found that ARI was the most common cause of fever in hospitalized patients in Saudi Arabia, followed by urinary tract infections (UTIs), gastroenteritis, and sepsis. This study included 186 hospitalized patients with fever and was conducted over a period of one year.

In the present study, the variables compared include Hemoglobin (Hb), Packed Cell Volume (PCV), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC), Red Cell Distribution Width (RDW) and serum Iron levels. The mean and standard deviation values are provided for both groups (i.e., children having simple febrile seizures with and without iron deficiencies) and there was no statistical significant difference between two groups as p value was >0.05. In the present study, the mean value of iron was found to be 48.98 ± 16.61 mcg/dl whereas the mean value of zinc was 65.60 ± 28.36 mcg/dl. Out of 61 participants, 40 (65.5%) had serum iron levels less than 50 mcg/dl, while 21 (34.5%) had serum iron levels greater than or equal to 50 mcg/dl, whereas 35 (57.3%) of children with simple febrile seizures had zinc deficiency. Their serum zinc level was less than 60 mcg/dl.

Several studies have investigated the levels of serum iron and zinc in different patient populations. A study by Al-Shehri et al. (2017) investigated the levels of serum iron and zinc in children with febrile seizures and found that the mean serum iron level was significantly lower in children with febrile seizures compared to the control group. However, the mean serum zinc level was not significantly different between the two groups.

In the Valie Asr hospital in Zanjan, Mansour sadeghzadeh et al. (2016) conducted their research. Overall, they found that 6% of cases, which is on par with the control group, had iron deficiency anaemia. This study concluded that patients having febrile seizures were more likely to be in iron deficient state than patients without the condition, though anaemia was uncommon.

Serum zinc levels were found to be significantly lower in children with simple febrile seizures compared to children with fever but no seizures, as reported by Heydarian et al. (2017).

CONCLUSION

Our study shows an important correlation between iron and zinc deficiencies and simple febrile seizures. Screening should be done for Iron and Zinc deficiencies in all children presenting with simple febrile seizures. It is important because iron and zinc deficiencies are treatable causes and the treatment not only improves the overall wellbeing of the child but also increases the seizure threshold in children prone to develop simple febrile seizures. Educating the parents or caregivers on how to manage febrile seizures at their home in an emergency situation is also of utmost importance.

REFERENCES