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# Prospective Observational Study to Determine the Correlation between Iron Deficiency Anemia and Simple Febrile Seizures in Children

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**Abstract:** ***Introduction: Iron deficiency anemia and simple febrile seizures are two most common conditions occurring in children aged between 6months to 60 months of age. It is postulated thatiron deficiency reduces the metabolism of some neurotransmitters such as monamine and aldehyde oxidase and this alters the seizure threshold of a child. Hence this study was conducted to correlate between iron deficiency anemia and simple febrile seizures. Methodology: It was prospective observational study. A total of 33 children were included in the study. All the children between the age group of 6months to 5 years presenting with simple febrile seizures were included in the study. Their iron status was determined by various parameters (Hemoglobin, MCV, MCH, MCHC, Hematocrit, RDW, serum iron and serum ferritin). And the iron status was correlated with the occurrence of febrile seizures. Results: A total of 33 children were included in the study. The prevalence of iron deficiency anemia in children with simple febrile seizures was found to be 69.7%. It was found that all the parameters. There was statistical significant difference in all the parameters between children with IDA and without IDA presenting with simple febrile seizures. Conclusion: Iron deficiency anemia is an important risk factor which predisposes children to develop simple febrile seizures. It is a treatable cause, improving the iron deficiency anemia not helps in the overall well being of the child but also raises the seizure threshold in children prone to develop simple febrile seizures.***

**Keyword:** Iron Deficiency anemia, Simple febrile seizures, Iron status

## 1. Introduction

Febrile seizures and iron deficiency anemia are two common conditions occurring in children between 6 months and 60months[1].

Febrile seizure is one of the most common convulsive event in children younger than 5 years of age. It occurs in 2-5% of all the children worldwide. Peak incidence is around 18 months of age.

It is defined as seizures occurring in infants and children with fever between 6 – 60 months of age without any evidence of CNS infection or other identified causes[1, 2].

There are many postulations put forward to explain the mechanism of febrile seizures[3]-

- Rise in temperature- It has been observed that magnitude of temperature does not affect the occurrences of febrile seizures. Hyperthermia decreases gamma aminobutyric acid receptor mediated inhibition and shifts the balance towards excitation. This is mediated by reducing GABA release from the presynaptic terminals[3].
- Various inflammatory mediators like TNF alpha, IL 1 beta acts by increasing the release of glutamate from glia and neurons and by decreasing GABA receptor mediated currents and increased excitation[3].
- Another postulation is that children with fever have an increase in respiratory rate which leads to respiratory alkalosis resulting in increased neuronal excitation[3].
- Genetic susceptibility: The genetics of febrile seizure is complex and not very well understood. 25-40% of the children with febrile seizures have a positive family history[3].
- Trace elements: Low levels of zinc have been reported in children presenting with febrile seizures[3].

Several morphological and biochemical changes at the tissue level has been shown to be the result of iron deficiency. Iron deficiency anemia leads to functional impairment at various tissues such as the myocardium, peripheral cortex, liver, jejunum and kidney[4].

Iron deficiency anemia leads to long term impairment of mental and psychological development in children[4]. Cognitive dysfunction, psychomotor retardation, behavioural impairment, Pica, breath holding spells, restless leg syndrome are conditions that are associated with iron deficiency anemia[1, 5]

The effect of iron deficiency anemia on the young developing brain and also mechanisms such as altered development of hippocampus neurons, slowed visual and auditory evoked potentials, alteration in synaptic neurotransmitter systems like norepinephrine, dopamine, glutamate, delayed maturation of myelin are hypothesized to be responsible for the various symptoms stated above[4, 5, 6].

IDA has been proposed as a risk factor for febrile seizures but not other types of seizures. As stated above, it has been associated with restless leg syndrome and ADHD[6].

Many studies have been conducted on the correlation between iron deficiency anemia and febrile seizures and iron deficiency anemia has been postulated as a risk factor for febrile seizures.

Iron deficiency reduces the metabolism of some neurotransmitters such as monamine and aldehyde oxidase and this alters the seizure threshold of a child[5].

## 2. Materials and Methods

**Source of data:** All children with simple febrile seizures between the age group of 6 months to 5 years were included in the study.

**Study design:** A prospective observational study**.**

**Study period:** November 2019 – January2020

**Ethical Clearance:** Ethical clearance has been obtained by the Institutional Ethics Committee of Sri Devaraj URS Medical College, Tamaka, Kolar. Number: SDUMC/KLR/IEC/111/2019-2020

**Inclusion Criteria:** All Children with simple febrile seizures aged between 6 months to 5 years of age. Generalised seizures associated with fever, lasting less than 15 minutes, not recurring within the febrile period without any postictal neurological abnormalities.

**Exclusion Criteria:** Children with complex febrile seizures, Head injury, acute encephalitis, neuroinfection, children with cerebral palsy, child who is a known case of epilepsy, patients previously diagnosed with hematologic problems like haemolytic anemias, bleeding or coagulation disorders, haematologic malignancy; those who were on iron supplementation were excluded from this study.

**Procedure**:
All the children with simple febrile seizures (whose CSF analysis was normal, without any abnormalities in the serum elctrolytes, blood glucose and serum calcium) were included in the study.

Venousblood sample was drawn under aseptic precautions at the time of admission

All the children were assessed for serum Hb, MCV, MCH, Hematocrit, RDW, serum iron and serum ferritin.

Iron Deficiency Anemia was defined as [4]:
Hb<11g%
MCV< 80 fl
MCH < 27pg
MCHC< 33%
RDW >14.5%
Serum ferritin <12 ng/ml
Serum Iron <40 mcg/dl

**Statistical analysis:**
Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. **Chi-square test or Fischer's exact test** (for 2x2 tables only) was used as test of significance for qualitative data.

Continuous data was represented as mean and standard deviation. **Independent t test** was used as test of significance to identify the mean difference between two quantitative variables

**Graphical representation of data:** MS Excel and MS word was used to obtain various types of graphs

**P value** (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

**Statistical software:** MS Excel**,** SPSS version 22 **(**IBM SPSS Statistics, Somers NY, USA) was used to analyze data

## 3. Results

In our study prevalence of Iron deficiency anaemia among children with simple febrile seizures was 69.7%.

In our study 36.4% were female child and 63.6% were male child.

Majority of the subjects 42.4% belongs to 2-3yrs of age group followed by 30.3% of the subjects belongs to 1-2yr age group,
18.2% were in 3-4yrs age group and only 9.1% of subjects were in 4-5yr age group.

**Table 1:** Distribution of subjects according to gender and Iron deficiency anaemia

| Gender | Iron deficiency anaemia | | Total |
|---|---|---|---|
| | Absent | Present | |
| Female | 4 | 8 | 12 |
| Male | 6 | 15 | 21 |
| Total | 10 | 23 | 33 |

Among female child 8 out of 12 had Iron deficiency anaemia and 4 out of 12 did not had Iron deficiency anaemia. Among male child 15 out of 21 had Iron deficiency anaemia and 6 out of 21 did not had Iron deficiency anaemia. P value 0.775, there was no statistical significant difference found between gender and Iron deficiency anaemia

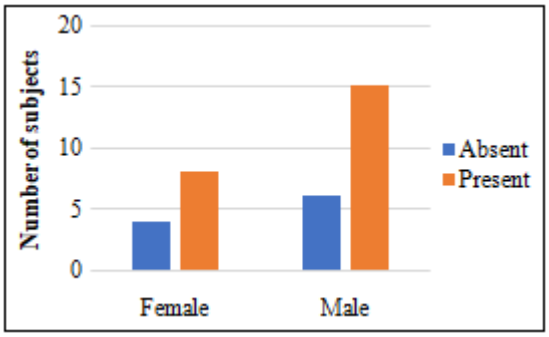


**Figure 1:** Graph showing Distribution of subjects according to gender and Iron deficiency anaemia

**Table 2:** Distribution of subjects according to age group and Iron deficiency anaemia

| Age group | Iron deficiency anaemia | | Total |
|---|---|---|---|
| | Absent | Present | |
| 1-2yrs | 1 | 9 | 10 |
| 2-3yrs | 5 | 9 | 14 |
| 3-4yrs | 3 | 3 | 6 |
| 4-5yrs | 1 | 2 | 3 |
| Total | 10 | 23 | 33 |

P value 0.353, there was no statistical significant difference found between age and Iron deficiency anaemia.

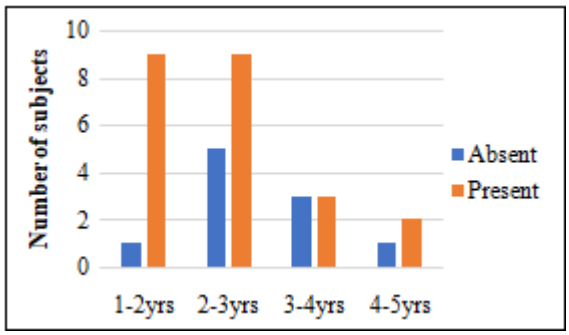


**Figure 2:** Graph showing Distribution of subjects according to age group and Iron deficiency anaemia

**Table3:** Distribution of subjects according to episode and Iron deficiency anaemia

| Number of Episode | Iron deficiency anaemia | | Total |
|---|---|---|---|
| | Absent | Present | |
| 1 | 4 | 11 | 15 |
| 2 | 3 | 9 | 12 |
| 3 | 3 | 2 | 5 |
| 4 | 0 | 1 | 1 |
| Total | 10 | 23 | 33 |

P value 0.427, there was no statistical significant difference found between episode and Iron deficiency anaemia.

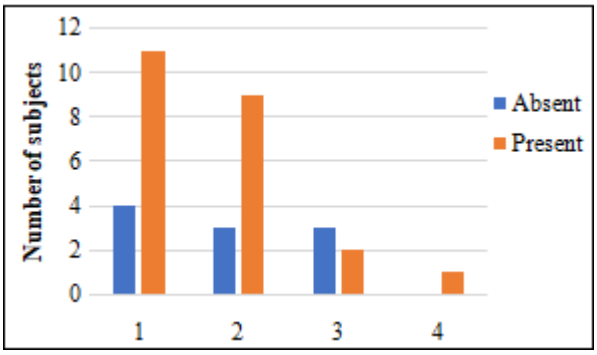


**Figure 3:** Graph showing Distribution of subjects according to episode and Iron deficiency anaemia

**Table 4:** Distribution of subjects according to the diagnosis

| Diagnosis | Number of cases | Percentage |
|---|---|---|
| URTI | 11 | 33% |
| Viral Fever | 6 | 18% |
| UTI | 6 | 18% |
| Acute GE | 4 | 12% |
| LRTI | 3 | 9% |

**Table 5:** Comparison of various parameters according to Iron deficiency anaemia in all children who presented with simple febrile seizures

| | Iron deficiency anaemia | | | | P value |
|---|---|---|---|---|---|
| | Absent | | Present | | |
| | Mean | SD | Mean | SD | |
| Haemoglobin | 13.05 | 0.89 | 8.70 | 1.60 | <0.001 |
| HCT | 0.34 | 0.03 | 0.25 | 0.04 | <0.001 |
| MCV | 83.70 | 7.30 | 67.20 | 5.27 | <0.001 |
| MCH | 28.72 | 3.02 | 20.27 | 3.43 | <0.001 |
| MCHC | 0.36 | 0.02 | 0.25 | 0.04 | <0.001 |
| RDW | 13.56 | 1.97 | 17.41 | 1.49 | <0.001 |
| Ferritin | 15.60 | 3.65 | 9.16 | 1.62 | <0.001 |
| Iron | 53.50 | 8.47 | 29.06 | 3.30 | <0.001 |

It can be seen that there is statistical significant difference with respect to all the parameters

## 4. Discussion

A total of 33 children were included in our study. It was a prospective observational study. In our study the prevalence of iron deficiency anemia among children with simple febrile sizures was 69.7%. 36.4% were female and 63.6% were males.

Majority of the patients (42.4%) belonged to the age group of 2-3 years. Out of the 33 children included in our study for 15 children this was the first episode of simple febrile seizures, 11 of them had iron deficiency anemia. For 12 children it was the second episode and 9 out of them had iron deficiency anemia. For 5 children this was the 3rd episode and 2 of them had iron deficiency anemia.

URTI (33%) was found to be the most common etiology for fever. 18% of the children had viral fever, 18% of the children had UTI, 12 % had acute GE and 9% of the children had LRTI.

The various parameters which were considered for diagnosing iron deficiency anemia were Hb, Hematocrit, MCV, MCH, MCHC, RDW, ferritin and serum iron. The mean values in children with iron deficiency anemia presenting with simple febrile seizures was Hb of 8.7g%, MCV of 67.2, MCH of 20.2, MCHC of 0.25, RDW of 17.4, serum iron of 29.06 and serum ferritin was 9.1.

There was statistical significant difference in all the parameters between children with IDA and without IDA presenting with simple febrile seizures.

Our study was prospective observational study when compared to various other studies conducted which were case control studies.

Krishnan et all conducted a prospective case control study over a period of 1 year in children presenting with first episode of simple febrile seizures. There was a significant difference of mean serum ferritin values between the 2 groups[6].

The mean ferritin was low in children with simple febrile seizures compared to the control group and the study concluded that significantly low serum ferritin in children with simple febrile seizures compared to the control group and IDA is a significant risk factor for simple febrile seizures.

Similar study was conducted by Abhishek Sharma and Radhika Sharma which was a prospective case control study which analysed Hb, MCV, MCH, MCHC and RDW in children with simple febrile seizures. They concluded that screening for IDA should be done in all children presenting with simple febrile seizures[5].

However another prospective case control study conducted by Rugmini Kamalanand and Balaji MD concluded that there was no significant difference in cases and controls with

respect to parameters used to determine Iron deficiency anemia. Iron deficiency anemia was not a significant risk factor for simple febrile seizures[7].

Yousefichaijan et all conducted a case control study to determine the effects of iron deficiency anemia on simple febrile seizures. A total of 382 children were included in the study. They observed that the prevalence of anemia in the group with simple febrile seizures was significantly less than that in the control group. This study reported that the probability of the occurrences of convulsions in children affected with anaemia not only does not increase but it apparently decreases significantly and that anemia may have a protective action against occurrence of febrile convulsiosn.[11]

Hence there is conflicting views and observation regarding the association between iron deficiency anemi and simple febrile seizures, however it has to be emphasised that iron deficiency anaemia leads to long term impairment in the mental and psychomotor development of the child. So identification and correction of iron deficiency anemia helps in the well being of the child and also helps in raising the seizure threshold in children prone to develop simple febrile seizures.

## 5. Conclusion

Hence there is need for further research to determine if iron deficiency anemia is a significant risk factor for simple febrile seizures. It is important because iron deficiency anemia is a treatable cause and its treatment not only improves the overall well being of the child but also increases the seizure threshold in children prone to develop simple febrile seizures.

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