

Original research article

The association between iron deficiency anemia and febrile seizures in children of age group 1 to 5 years in a tertiary care hospital, Guntur

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Abstract

Introduction: Febrile seizures are seizures that occur in children between 6 months and 60 months of age, with body temperature of 38°C or higher not resulting from Central Nervous System (CNS) infection or any metabolic imbalance without any prior afebrile seizures. Among many risk factors identified for febrile seizures, iron deficiency is hypothesized to be one of the risk factor for occurrence of febrile seizures. Our study has also reported that IDA could be a risk factor for febrile seizures and can be considered as one of the modifiable risk factors that predisposes to febrile seizures in children.

Methods: A total of 100 children aged between 1 to 5 years were included in the present study and were further divided into 2 groups of 50 each, as cases and controls. A detailed history was taken and clinical examination was done in both cases and controls with particular attention to development delay and family history of seizure. Complete haemogram, iron profile and other appropriate investigations were done in both the groups and results were compared.

Results: The mean age of onset of febrile seizures was 24 months. There was slightly male predominance, with male: female ratio of 1.7:1. Majority of children with febrile seizures were found to have iron deficiency anemia as opposed to children in control group which was statistically significant. (76% vs 20%), p-value<0.001. All the indices of iron deficiency anemia, like haemoglobin, MCV, MCH, serum iron, serum ferritin were low in febrile seizures group compared to control group. The difference was found to be statistically significant (p-value<0.001).

Conclusions: Iron deficiency anemia (IDA) was more frequent among children with febrile seizures. The result suggests that IDA may be a risk factor for febrile seizures. Early detection and timely correction of iron deficiency may be of help for prevention of recurrence of febrile seizures in children of this age group.

Keywords: Febrile seizure, Ferritin level, Hemoglobin, IDA-iron deficiency anemia

Introduction

Febrile seizures (FS) are seizures that occur in children between the ages of 6 months and 60 months, with body temperature of 38 °C or higher not resulting from Central Nervous System (CNS) infection or any metabolic imbalance without any prior afebrile seizures. This condition occurs in 2-5% of the children who are neurologically healthy ^[1].

A simple febrile seizure is a primary generalized, usually tonic-clonic attack associated with fever, not recurrent within a 24-hour period and lasting for a maximum of 15 min. A complex febrile seizure is more prolonged (>15 min), is focal, and /or reoccurs within 24 hour.

The precise cause of febrile seizure is not known, but several genetic and environmental factors have been implicated. The maximum age of febrile seizure occurrence is 14-18 months, which overlaps with the maximum prevalence of Iron Deficiency Anaemia (IDA).

IDA is the most common nutritional deficiency in the world ^[2]. Iron is used as cofactor for metabolism of many neurotransmitters, monoamine and aldehyde oxidase in the brain. The metabolism of these neurotransmitters, monoamine and aldehyde oxidase will be affected in the patient with iron deficiency leading to decrease in these neurotransmitters, which may decrease the threshold for seizure. Fever can worsen the negative effects of low serum ferritin on the brain and trigger seizure.

Different factors have been considered for febrile seizures, including familial (genetic) factors, prenatal factors, present acute illness, the highest degree of fever and finally anemia. Iron deficiency anemia (IDA), as the most common type of anemia during infancy and childhood, occurs usually between 9-24 months of age and this period coincides with the peak incidence of FS. Considering the age of prevalence of IDA and FS which are the same, the role of iron in the metabolism of neurotransmitter (such as GABA and serotonin) and some enzymes (such as monoaminoxidase and aldehydase), a relationship between IDA and FS is probable. With respect to the high prevalence of febrile seizures and IDA in children and considering the fact that IDA is a probable risk factor for febrile seizure occurrence, this

study was conducted to determine the association between iron deficiency anemia and febrile seizures^[3, 4].

Methods

The study was a hospital based case control study which was conducted in the Department of Pediatrics, government general hospital, Guntur, a tertiary care Center in Andhra Pradesh, India, from January 2020 to June 2021. A total of 50 Children in the age group from 6 months to 5 years admitted with first episode of simple febrile seizure were taken as cases. The control group included 50 children in the same age group admitted with acute febrile illness without seizures. Children with epilepsy and developmental delay were excluded from the study. Children on iron therapy were also excluded.

A detailed history was taken in cases regarding duration of fever, time interval between onset of fever and convulsion, duration for which convulsion lasted, history of developmental delay and family history of epilepsy^[5, 6]. Detailed examination was done in cases to rule out possible central nervous system infection, developmental delay and any other co-morbidities. Control group was also examined to rule out any associated significant comorbidities.

Complete haemogram, red cell indices, iron profile were done in both the groups. Other necessary investigations were carried out wherever it was necessary. Diagnosis of iron deficiency anemia was made in a child with low haemoglobin (microcytic hypochromic anemia with reduced RBC count and increased red cell distribution width (RDW>15%).

At the end of the study, the data were collected and analyzed statistically using Student's t-test (unpaired) and Chi-square test. $p < 0.05$ was considered statistically significant^[7, 8].

Results

The study group consisted of total 100 children. Among them, 50 were cases and 50 controls. Majority of the children were in age group of 12-36 months in both the groups. (45% in cases, 40% in controls) Figure1. The mean age group of children with febrile seizure was 24 months. Majority of children were males (64% and 56% in case and control group respectively) Figure2. Male to female ratio was 1.7:1 among cases. Majority of children belonged to lower socioeconomic class in both the study groups. (70%, 60% among cases and controls respectively). Majority of children in both the groups were exclusively breastfed (80% and 70% in cases and control respectively). Initiation of complementary feeding at 6 months of age was poor in children with febrile seizure group compared controls (20% versus 50%).

Mean Hb level among cases was 9.7g/dl whereas in controls it was 12.7g/dl, which was statistically significant (p -value<0.001). Mean MCV and MCH levels in the cases were 66.6fl, 23.04pg and in controls, these values were 85.9fl, 28.5pg, respectively which was statistically significant. Mean RDW among cases was 15.08% compared to controls (12.22%) which was statistically significant. Mean serum iron level was found to be low among cases compared to controls (44.46 mg/dl and 120.4mg/dl respectively). Mean TIBC was 452.6microgram/dl in cases and 401.2 mcg/dl in control, which was statistically significant (p value<0.001).Transferrin saturation was less among case group (12.08%) compared to controls (39%), the difference was statistically significant. Mean serum ferritin level was 13.7 mcg/l in the cases and 43.4 mcg/l in controls which was statistically significant. Table1. Iron deficiency anemia was found in 38 children in the case group (76%) and 10(20%) in control group.

Mean Hb level among cases with simple febrile seizures was 9.6g/dl±1.7 whereas in complex febrile seizures it was 10.7g/dl±1.2 which was statistically not significant (p -value<0.27). Mean MCV and MCH levels in the cases with simple febrile seizures were 65.8fl, 22.8pg and in, complex febrile seizures these values were 70.9fl, 23.9pg, respectively which was statistically not significant. Mean serum ferritin level was 13.0±7.9 mcg/l in the cases with simple febrile seizures and 17.4±8.3 mcg/l in complex febrile seizures which was statistically not significant.

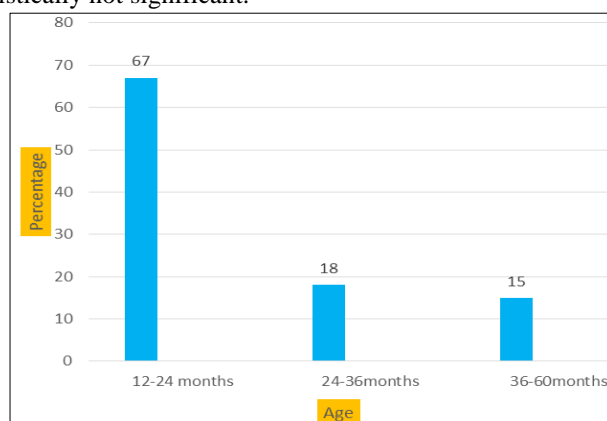


Fig 1: Age distribution among cases

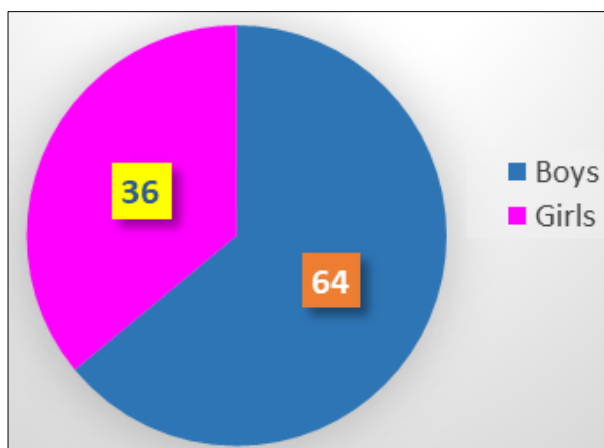


Fig 2: Gender distribution among case

Table 1: Various haematological parameters among cases and control groups

Lab parameters	Cases (n=50) Mean ± SD	Control(n=50) Mean ± SD	P- value
Hemoglobin (gm/dl)	9.7±1.6	12.7±0.7	<0.001
MCV(fl)	66.6±8	85.9±5.2	<0.001
MCH (pg)	23.0±4.3	28.5± 0.6	<0.001
RDW%	15.08±1.22	12.22±1.06	<0.001
TIBC (mcg/dl)	452.6±31.8	401.2±19.5	<0.001
S.Iron (mcg/dl)	44.46±2.67	120.54±29.08	<0.001
Serum ferritin (microgram per litre)	13.7±8.1	43.4± 7.7	<0.001

Table 2: Comparison of various laboratory parameters among different studies (mean values)

Study	Hb (gm/dl)	MCV (fl)	MCH (pg)	Serum ferritin (mcg/l)	Serum iron (mcg/dl)
Present study	9.7	66.6	23.0	13.7	44.46
Vaswani <i>et al.</i>	9.4	73.4	21.4	31.9	50.2
ParvizKarimi <i>et al.</i>	9.4	67	24.8	29.5	45.67
Khawaja Tahir Aziz <i>et al.</i>	10.5	70	25.3	15.5	42.10
Midhun Ramesh <i>et al.</i>	10	70	24	22	40
Zaineb A Hameed <i>et al.</i>	10.2	72	24	20	45.6

Discussion

The mean age of onset of febrile seizure in the present study was 24±12 months which was comparable to other studies. In present study, 72 percent of children in cases were in between the ages of 13 and 24, whereas 62% of controls were in between the ages of 13 and 24 months. Hartfield *et al.*,^[8] Found that the majority of cases were in the age category of less than 24 months, with a mean age of 17.9 months. Leela Kumara *et al.*,^[12] Discovered that 55.8 percent of cases and 56.5 percent of controls were under the age of 17 months in their research. A research by Alberto Romero Guzman *et al.*,^[15] Reported a 55 percent prevalence rate in children aged 6 to 24 months.

In present study among 50 cases with febrile seizure 32 (64%) were males and 18 (36%) were females, with a ratio of male to female 1.7:1. In study conducted by Radhika Vaghela *et al.* (2020)^[10] (there is a male predominance of 56% for simple febrile seizure. Similar findings were observed in studies done by Kumari *et al.*, Hartfield *et al.*, Azhar *et al.* and Alberto *et al.*^[14, 8, 15]. Regardless of the era of the study or particulars of the design; boys have consistently emerged with higher frequency of febrile seizures.

Family history of febrile seizures In present study, four (8 percent) cases out of 50 had a history of febrile seizures in the family and zero (0 percent) among 50 control group had family history of febrile seizures. In Azhar S Daoud *et al.*, (2002)^[11]. study 18 percent cases had family history of febrile seizures

Hematological analysis: In the study population of 100 children, the mean hemoglobin in cases was 9.7 and in controls was 12.7. The mean Hb is considerably lower in cases compared to controls ($p < 0.001$). This was in accordance with the results obtained by Radhika Vaghela *et al.*^[10] Among the 50 cases, the

mean hemoglobin in cases with simple febrile seizures is 9.6 and with complex febrile seizures is 10.3. In present study there is no statistically significant difference in mean Hb between cases with simple febrile seizures and complex febrile seizures ($p=0.27$)

The mean MCV in the cases group is considerably lower than in the control group ($p<0.001$), similar to the results obtained by kamalammal and Balaji *et al.*,^[16]. And Radhika Vaghela *et al.*^[10]. Among the 50 cases, mean MCV in cases with simple febrile seizures was 65.8 and with complex febrile seizures was 70.9. In present study there is no statistically significant difference in mean MCV between cases with simple febrile seizures and complex febrile seizures ($p=0.09$)

The mean MCH in cases was 23.0 and in controls was 28.5. The mean MCH in the cases group is significantly lower than the control group ($p<0.001$), similar to the results obtained by kamalammal and Balaji *et al.*,^[16]. Radhika Vaghela *et al.*^[10] and Karimi *et al.*,^[12]. Among the 50 cases, the mean MCH in cases with simple febrile seizures was 22.8 and with complex febrile seizures was 23.9. In present study there is no statistically significant difference in mean MCH between cases with simple febrile seizures and complex febrile seizures groups ($P=0.49$).

The mean serum ferritin in cases was 13.7 pg/dl and in controls was 43.4pg/dl. The mean serum ferritin in the cases group is considerably lower than the control group ($p<0.001$), similar to the results obtained by Radhika Vaghela *et al.*,^[10]. Among the 50 cases with febrile seizures, the mean serum ferritin in cases with simple febrile seizures was 13.0 and with complex febrile seizures was 17.4. In present study there is no statistically significant difference in mean serum ferritin between cases with simple febrile seizures and complex febrile seizures ($p=0.16$). The mean TIBC in cases was 452.6 and in controls was 401.2. The mean TIBC in the cases group is significantly higher than in the control group ($p<0.001$). Among the 50 cases with febrile seizures, the mean TIBC in cases with simple febrile seizures was 454.0 and with complex febrile seizures was 444.9. In present study there is no statistically significant difference of mean TIBC between cases with simple febrile seizures and complex febrile seizures ($p=0.46$). From the above hematological parameters, the incidence of IDA was higher in cases compared to controls. The incidence of IDA was similar in cases with both simple and complex febrile seizures.

Vaswani *et al.*^[9]. Did a study in which the mean serum ferritin level was considerably low in cases with first febrile seizures (31.9 $\mu\text{g/l}$) as compared to controls (53.9 $\mu\text{g/l}$) ($P=0.003$). However, no significant difference was noted in the mean hemoglobin values of cases (9.4 ± 1.2 g/dL) and controls (9.5 ± 1.0 g/dL) or in the mean value of MCV ($P=0.89$) and MCH ($P=0.71$).

Khawaja Tahir Aziz *et al.*,^[17]. (2017) conducted a case-control study, in this study mean hematocrit, MCV, MCH, MCHC had statistically significant low levels in the cases group than control groups with $p\text{-value} < 0.05$.

Midhun Ramesh *et al.* (2015)^[18] conducted a study in Chennai to ascertain the association between serum ferritin and simple febrile seizures. In this study Serum ferritin ($p=0.012$), Hb ($p=0.042$), and hematocrit ($p=0.029$) were lower in cases group significantly compared to controls.

Zaineb A Hameed *et al.* (2019)^[19] conducted a study to evaluate the relationship between iron deficiency and zinc deficiency in febrile seizures. In this study mean Hb, MCV, MCH, MCHC, serum ferritin of the case group was statistically significantly lower than control groups but the mean TIBC of the case group was higher compared to controls but not statistically significant.

Rahul Majumdar *et al.* (2013)^[20] did a study with 50 cases with febrile seizures and 50 cases without febrile seizures concluded that 58% of cases were having IDA compared to 18% in control groups, suggesting iron deficiency a risk factor for febrile seizures.

Comparable to various studies, Table 2 hematological parameters suggestive of iron deficiency was predominant in febrile seizures group than in control group.

Conclusion

Iron deficiency anemia was more frequent among children with febrile seizure. Strong association was found between various parameters of iron deficiency anemia and occurrence of febrile seizure. Screening for IDA should be considered in children with febrile seizure. Early detection and timely correction of iron deficiency may be of help for prevention of recurrence of febrile seizures in children of this age group.

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