

Association of Indicators of Iron Deficiency with Febrile Seizure in Children Admitted in Tertiary Center in Rajasthan

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Abstract

Objectives: Febrile Seizure is the most common form of seizure in childhood. There is conflicting evidence regarding the association between iron deficiency and febrile seizure. Hence, this study was undertaken to find out the association between different indicators of iron deficiency with febrile seizure in children admitted in the Pediatric wards of a Hospital in Udaipur, Rajasthan.

Methodology: A total of 159 children were selected by the complete enumeration method. Parameters of iron deficiency were estimated in them and age, sex-matched controls. Mann-Whitney U test and Spearman's rank-order correlation coefficient were used to find out the association between indicators of iron deficiency with febrile seizure. The binary logistic regression method was used to find out the adjusted odds ratio. $P < 0.01$ was considered statistically significant.

Results: About 53.5% of the study population (mean age: 3.01 ± 1.37 years) was male. Mean hemoglobin, serum iron, serum ferritin, mean corpuscular volume, and mean corpuscular hemoglobin concentration were significantly higher in the control group, while the reverse is true for serum total iron-binding capacity. Serum ferritin became the most significant parameter, responsible for 57.3%–76.4% variability of febrile seizure. Overall, our model correctly predicted 50% variance of the dependent/outcome variable.

Conclusion: Iron deficiency is more common among children with febrile seizure. Hence, iron prophylaxis may be given to children with febrile seizure.

Keywords: Febrile Seizures, Ferritin, Iron Deficiency.

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Introduction

The most common type of seizure occurring in childhood is febrile seizure, which occurs in 2%–5% of children with normal neurological function.[1] Approximately five lakhs cases of febrile seizures occur every year in the US.[2] Two percent–4% cases of febrile seizures may develop epilepsy in future. [1,3] Hence, identification of the risk factors of febrile seizure is important. Iron deficiency is the most common form of micronutrient deficiency in the world, affecting almost one-third population of the world. Anemia is the most common manifestation of iron deficiency. However, it also affects other organ systems, including the central nervous system (CNS) where it causes the behavioral problem, cognitive dysfunction, psychomotor retardation, etc., Iron deficiency is associated with altered development of hippocampal neurons, delayed maturation of myelin, and alteration of levels of different neurotransmitters, including serotonin, dopamine, etc.[4,5] Iron deficiency also inhibits degradation of some neurotransmitters.[6] Moreover, iron deficiency is also aggravated by

fever.[7] There is conflicting evidence on the association between iron deficiency and febrile seizure. Some studies identified iron deficiency as a potential risk factor of febrile seizure,[8,9] while some found it as protective.[10] Some authors found no association between febrile seizure and iron deficiency.[11] Since results are conflicting, and studies are scarce in the Indian context, this study was undertaken to find out the association between different indicators of iron deficiency and febrile seizure among the children admitted with febrile seizure in the Pediatric department of Pacific Institute of Medical Sciences, Udaipur, Rajasthan

Methodology

A hospital-based prospective study was conducted among the children admitted with febrile seizure in between May 2025 and February 2025 in the Pediatric department of Pacific Institute of Medical Sciences, Udaipur, Rajasthan. Total of 159 cases were selected by complete enumeration method. Age- and sex-matched controls were selected from febrile patients without any seizure. Some

parameters such as hemoglobin, serum iron, serum ferritin, total iron-binding capacity (TIBC), mean corpuscular volume (MCV), and mean corpuscular hemoglobin concentration (MCHC) were checked for both cases and controls. Blood samples were collected within 24 h of admission. For quality control, all the tests were done in the same laboratory of our college. Each report was double-checked by two different laboratory technicians. They were not informed about the purpose of the study. The same thermometer was used to check the axillary temperature of the participants.

Collected data were entered into Microsoft Excel Worksheet. Categorical data were coded. Mean and standard deviation was calculated for each variable. Significantly associated variables in the table were further considered for Spearman's rank-order correlation to find out the strength and association of the relationship, which is measured by Spearman's coefficient. Serum ferritin, iron, MCV, MCHC, TIBC, and hemoglobin were entered in step 1–6, respectively. The adjusted odds ratio was determined with 95% confidence interval. $P < 0.01$ was considered statistically significant. All the statistical analysis was done to by SPSS software version 23. The febrile seizure was defined as a seizure occurring in childhood after 1 month of age, associated with a febrile illness not caused by an infection of the CNS, without previous neonatal seizures or a previous unprovoked seizure, and not meeting criteria for other acute symptomatic seizure.[12]

Results

Table 1: Value of different iron status indicators among cases and controls (n=318)

Parameter	Cases (n=159)	Control (n=159)	Z & P value
Hemoglobin (mg/dl)	9.4 (1.3)	13.1 (2.1)	13.24, <0.01
Ferritin (ng/ml)	53.2 (10.8)	81.9 (10.5)	13.97, <0.01
Serum iron (μ g/dl)	67.4 (20.9)	141.4 (35.9)	13.56, <0.01
Serum TIBC (μ g/dl)	366.2 (80.2)	296.8 (37.9)	7.54, <0.01
MCV (fl)	80.5 (6.2)	90.8 (3.2)	12.74, <0.01
MCHC (g/dl)	29.4 (2.3)	32.4 (1.8)	10.33, <0.01

MCV=Mean corpuscular volume; TIBC=Total iron binding capacity; MCHC=Mean corpuscular hemoglobin concentration

Table 2: The seven variable correlation matrix showing relationship between the dependent and independent variables with help of Spearman's Coefficient (n=318)

Variables	Febrile seizure	Hemoglobin	Ferritin	Iron	TIBC	MCV	MCHC
Febrile seizure	1.000	-0.744*	-0.785*	-0.762*	0.424*	-0.717*	-0.581*
Hemoglobin		1.000	0.574*	0.566*	-0.334*	0.521*	0.413*
Ferritin			1.000	0.602*	-0.346*	0.536*	0.449*
Iron				1.000	-0.568*	0.514*	0.484*
TIBC					1.000	-0.326*	-0.279*
MCV						1.000	0.392*
MCHC							1.000

D*Value is statistically significant at the level of 0.01. MCV=Mean corpuscular volume; TIBC=Total iron binding capacity; MCHC=Mean corpuscular hemoglobin concentration

The mean age of the study population was 3.01 ± 1.37 years. 53.5% of them were male. Maximum of them were from the rural population (53.0%) and belonged to middle socioeconomic status (41.2%) according to the modified BG Prasad scale. Mean hemoglobin level (9.40 ± 1.25 mg/dl vs. 13.12 ± 2.05 mg/dl), mean serum ferritin (53.15 ± 10.87 ng/ml vs. 81.88 ± 10.56 ng/ml), mean serum iron (67.46 ± 20.97 mcg/dl vs. 141.37 ± 35.89 mcg/dl), mean MCV (80.57 ± 6.14 fl vs. 90.79 ± 3.25 fl), and mean MCHC (29.42 ± 2.36 g/dl vs. 32.44 ± 1.89 g/dl) level were significantly higher in control group. On the other hand, mean TIBC level was significantly higher among cases (366.20 ± 80.25 mcg/ dl) than controls (296.85 ± 37.92 mcg/dl) [Table 1]. Hence, there was a relative iron deficiency state among the cases.

In our model, we found that higher level of serum ferritin, serum iron, MCV, and MCHC were protective for febrile seizure having an adjusted odds ratio of 0.757 (95% confidence interval: 0.640–0.895), 0.920 (95% confidence interval: 0.871–0.972), 0.527 (95% confidence interval: 0.331–0.839), and 0.386 (95% confidence interval: 0.156–0.951), respectively. Serum ferritin, serum iron, MCV, and MCHC can explain 73.6%–98.1% variance of febrile seizure. Serum ferritin alone can explain 57.3%–76.4% variance of febrile seizure. Overall, our model can correctly predict 50% of the outcome variable [Table 2]. Although serum iron and serum TIBC had a significant correlation with the dependent variable in the correlation matrix, they became insignificant in our regression model.

Discussion

Similar to the findings of our study, Modaresi et al. also found that mean hemoglobin, ferritin, iron, and MCH were lower in children with febrile seizures than the control group.[13] Akbayram et al. also found that serum iron level is lower in children with febrile seizure than healthy children.[14] Rehman and Billoo[9] also reported hemoglobin and serum ferritin level were significantly lower among children with febrile seizure than children without seizure. Similar to our finding Vaswani et al. [15] also noted that the mean serum ferritin level is significantly lower in cases of febrile seizure than controls. Choudhury [16] et al. also found that hemoglobin, MCH, and serum ferritin level were significantly lower in febrile seizure cases than controls. Fallah [17] et al. also noticed that serum hemoglobin, serum iron, and serum ferritin level were lower among children with febrile seizures than controls.

Contrary to our finding, Derakhshanfar[18] et al. reported that hemoglobin, serum iron, serum ferritin, and MCV level were higher and TIBC was lower among children with febrile seizure than febrile children without seizure. Similar to the findings of Derakhshanfar and et al., Kobrinsky [19] et al. also noted that hemoglobin, hematocrit, and MCV were higher in children with febrile seizure.

In different studies, Kumari [20] et al, Sherjil [21] et al. and Sadeghzadeh [22] et al. found that the frequency of iron deficiency anemia was higher among the children with febrile seizure than their healthy counterparts/control group. On the other hand, Kobrinsky [19] et al. Talebian and Momtazmanesh,[23] and. Abaskhanian[24] et al. reported a higher prevalence of iron deficiency anemia among the control group than the children with febrile seizure. Amirsalari[11] et al. and Momen and Hakimzadeh[25] found no association between iron deficiency and febrile seizure.

These discrepancies may be due to differences in selection criteria, criteria of selection of controls, nutritional status of the participants, and different geographic areas of the studies (for example, if the study area is a malaria-endemic area, iron deficiency may be more prevalent in the control group too).

Conclusion

Indicators of iron deficiency should be checked in all children with febrile seizure, and iron prophylaxis should be given to those who have iron deficiency. Further studies have (preferably multicentric) to be undertaken to find out the other risk factors of febrile seizure as our model can predict only 50% of the dependent variable.

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