



Assessing Iron Deficiency As A Risk Factor For Febrile Seizures In Children Between 9 Months – 5 Years By Using Multiple Parameters

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Abstract

Introduction: Iron deficiency (ID), preventable and treatable nutritional deficiency occurs during infancy and childhood, usually between 9-24 months of age and this period coincides with the high incidence of febrile convulsions. Most of the CNS enzymes are iron-dependent for their appropriate function. Iron deficiency causes dysregulation of normal cellular and organ function. The most obvious result of ID is anemia that affects all the organs in the body resulting in cognitive changes and behavioral disturbances, physical growth impairment, and immune dysfunction. It is well-formed fact that iron supplementation can reduce breath-holding spells. Neurological symptoms like learning deficits, memory disturbances, delayed motor development, poor attention span and behavioral disturbances caused by iron deficiency are well known. Thus an association between febrile convulsions and iron deficiency anemia may exist.

Aim Of The Study: To determine the association between iron deficiency and febrile seizures.

Materials And Methods: This prospective study was conducted in Government virudhunagar Medical College & Hospital, virudhunagar, from August to October 2021 over 3 months. blood samples were taken for evaluating Hb%, Ferritin, Iron, TIBC, and other necessary laboratory tests. Lumbar puncture was done for children < 12 months of age and in children with suspicion of acute CNS infection. All necessary information was noted in the previously prepared proforma sheet.

Results: The total number of cases analyzed was 60, out of which 35 (58.3%) were males and 25 (41.7%) were females. Simple febrile seizures were seen in 38(63.33%) cases and complex type was seen in 22(36.67%) 7. Respiratory tract infection was seen in 30 (50%) of cases, Urinary tract infections in 13 (21.7%), Acute Gastroenteritis in 7 (11.7%), Nonspecific illnesses like viral fever in 10 (16.7%) of cases as a cause of fever. 8. Clinical pallor was noted in 18 (30%) of cases as against 12(20%)of the control group. It was noted that pallor was 1.714 times more in cases than that seen in the control group. 9. There was a significantly higher rate of IDA (Hb% - < 11gm) among children with febrile convulsions than in controls (40% vs. 15%) with a p-value of 0.002. IDA was seen 3.778 times greater in a child with febrile seizures than in a febrile child without seizures. 10. Children with febrile seizures had significant hemoglobin levels with a mean of 11.06 with a p-value of 0.022. Mild anemia was noted in 15 (25%), moderate anemia was seen in 9 (15%) out of 60 cases. None of the cases had severe anemia.

Conclusion: The present study showed that hemoglobin, serum ferritin, and serum iron levels are significantly lower in children suffering from febrile seizures than febrile children in the control group, suggesting that a low iron status has an important role in children with febrile seizures. Consequently measuring serum ferritin is a specific, sensitive, and reliable test for detecting iron depletion in the early stages of the disease itself and the

best standard for determining the total body iron stores. Therefore, complete blood count and screening for ID with serum iron studies are recommended in the workup of children with the first febrile convulsion itself

Keywords: Seziures, Iron Defiency, Chronic Infections , behavioral disturbances

Introduction

Iron deficiency (ID), preventable and treatable nutritional deficiency occurs during infancy and childhood, usually, between 9-24 months of age, and this period coincides with the high incidence of febrile convulsions. Most of the CNS enzymes are iron-dependent for their appropriate function.^[1] Iron deficiency causes dysregulation of normal cellular and organ function. Iron requirements on a bodyweight basis are proportional to growth velocity. Hence iron deficiency is most common in the preschool years and during puberty. As fetal red blood cells undergo destruction soon after birth, full-term infants are normally born with adequate iron stores in the liver and hematopoietic tissue.^[2] This leads to iron deposition in these tissues, especially if the cord is ligated. Iron deficiency commonly arises after six months of age, if complementary foods do not provide enough absorbable iron, even for exclusively breastfed babies. The most obvious result of ID is anemia that affects all the organs in the body resulting in cognitive changes and behavioral disturbances, physical growth impairment, and immune dysfunction. It is well-formed fact that iron supplementation can reduce breath-holding spells.^[3] Neurological symptoms like learning deficits, memory disturbances, delayed motor development, poor attention span and behavioral disturbances caused by iron deficiency are well known. Thus an association between febrile convulsions and iron deficiency anemia may exist.^[4] The age range of occurrence of IDA and febrile convulsion is common to both conditions. Iron has a significant role in the production, function, metabolism of neurotransmitters, hormonal function, DNA replication, and certain enzymes like monoamine oxidase and aldehyde oxides at the cellular level.¹⁶ IDA is associated with neurologic dysfunction in children, including delayed development, breath-holding spells, and benign idiopathic intracranial hypertension.^[5] Considering the role played by Hb in carrying O₂ to body tissues such as the brain and the

fact that a rise in body temperature may exaggerate the symptoms of anemia. Fever can worsen the negative effects of anemia on the brain and thus trigger seizure attacks. Low ferritin in serum may decrease the seizure threshold^[6]. After considering the conflicting evidence of the previous studies regarding the positive or negative association of iron on the occurrence of febrile convulsions as illustrated in the review of literature, we designed this study to determine the association between iron deficiency anemia and febrile convulsions in 9 months to 5-year-old children, which is the common age for the occurrence of febrile seizures.^[7]

Materials And Methods

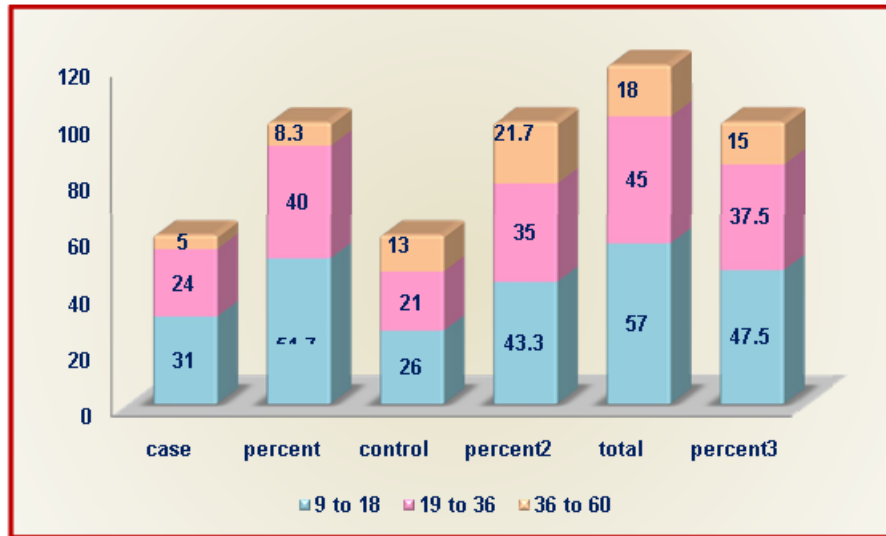
This prospective study was conducted in Government virudhunagar Medical College & Hospital, virudhunagar, from August to October 2021 over 3 months. Lumbar puncture was done for children < 12 months of age and in children with suspicion of acute CNS infection. All necessary information was noted in the previously prepared proforma sheet. Children admitted in general medical wards for febrile seizures in the age group of 9 months – 5 years. Inclusion criteria: Cases- Children with febrile seizures in the age group of 9 months – 5 years. Control-Children with febrile illness without seizures. Exclusion Criteria: Children with neurological infections, patients known for other causes of anemia, developmental delay, those on iron supplements, convulsions due to electrolyte imbalance (or) drug toxicity, family history of epilepsy. Upon arrival to the general medical ward after initial stabilization, the history regarding seizure type and further details, nature of febrile sickness and associated complaints, family history of seizure disorder / febrile seizures, any history of drug intake were taken. Controls were group matched to cases on age (9-18 months; 19- 36 months; 37-60 months). The groups were not matched on gender, because there are no gender differences seen in ID in children of this age or febrile seizures. The 3 age groups were broad in range to enable data collection and

matching. WHO - weight for age classification was used to determine the grading of nutritional status as normal, underweight, and severely underweight. A physical examination was performed. Following parents' consent, blood samples were taken for evaluating Hb%, Ferritin, Iron, TIBC, and other

necessary laboratory tests. Lumbar puncture was done for children < 12 months of age and in children with suspicion of acute CNS infection. All necessary information was noted in the previously prepared proforma sheet.

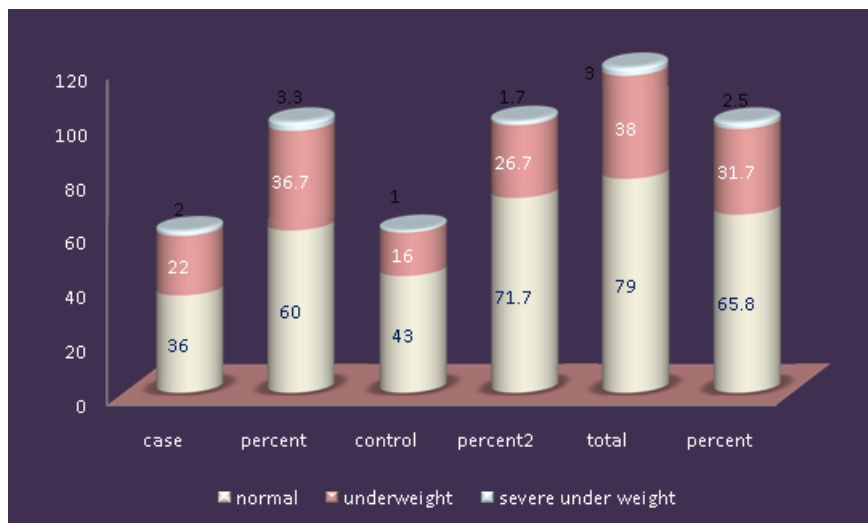
Results

Graph: 1 Frequency Distribution Of Patients Based On Age In Months



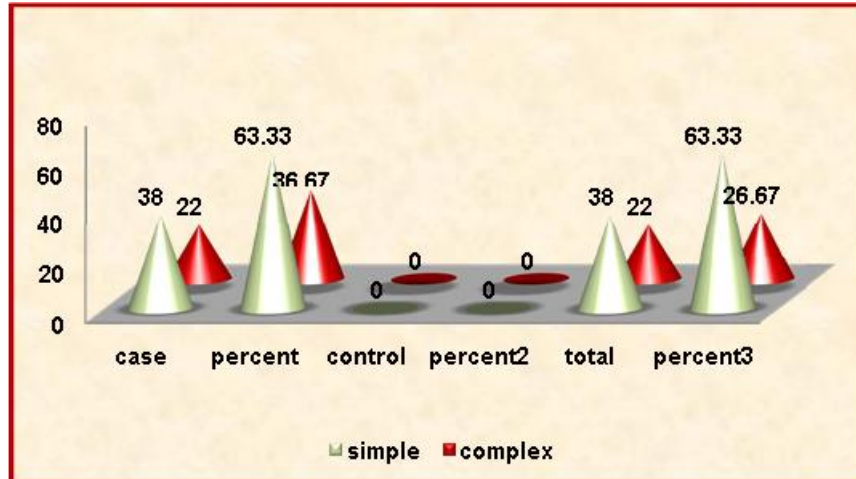
Graph:1 (51.7%) were seen in the age group of 9-18 months, 24 (40%) were seen in the age group of 19- 36 months, 5 (8.3%) were seen in the age group of 37-60 months. Maximum cases were seen in the age group of 9-18 months. The mean age in months for the cases group was 20.53 as against 25.85 in the control group. In the study group of 60 cases, 58.33% were males, 41.67% were females,

Graph 2: Nutritional Status Between The Groups



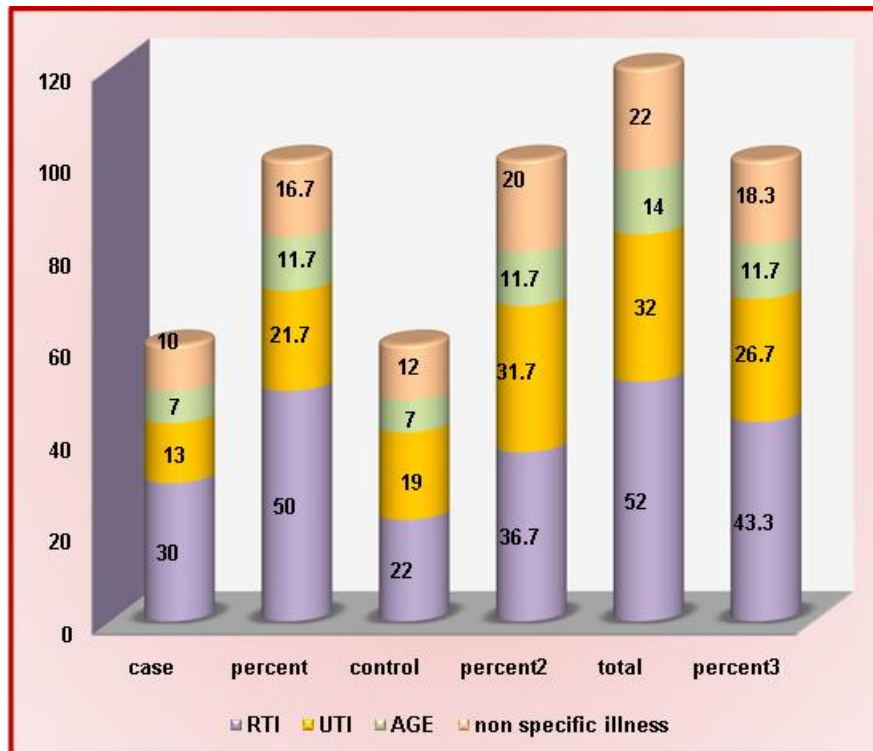
Graph:2 Nutritional status was normal in 60% of cases as against 71.7% of controls. Underweight was seen in 36.7% of cases as against 26.7% of the control group. Severe underweight was seen in 3.3% of cases as against 1.7% of the control group.

Graph 3: Distribution Of Type Of Febrile Seizures In Cases:



GRAPH :3 Simple febrile seizures were seen in 63.33% of cases and complex type was seen in 36.67% of cases. Febrile seizures 1st, 2nd, 3rd episodes were seen in 60%, 31.7%, and 8.3% of cases respectively.

Graph: 4 Causes Of Febrile Illness Between Both Groups



Graph:4 In our study, Respiratory tract infection was seen in 50% of cases. Urinary tract infections in 21.7%, Acute Gastroenteritis in 11.7%, Nonspecific illnesses like a viral fever in 16.7% of cases as a cause of fever respectively.

Table :1 Clinical Pallor Between The Groups

			Group		Total
			Case	Control	
Pallor	Present	Count	18	12	30
		% within pallor	60.0%	40.0%	100.0%
		% within group	30.0%	20.0%	25.0%
	Absent	Count	42	48	90
		% within pallor	46.7%	53.3%	100.0%
		% within group	70.0%	80.0%	75.0%
Total	Count	60	60	120	
	% within pallor	50.0%	50.0%	100.0%	
	% within group	100.0%	100.0%	100.0%	

Table :1 Pearson Chi-Square P- Value= 0.206 NS In our study, Clinical pallor was noted in 30% of cases as against 20% of the control group. Clinical pallor was noted 1.714 times more in the cases group than that seen in the control group.

Table 2:Hemoglobin levels between cases and control

Hb%	CASE		CONTROL	
	NO	%	NO	%
<7 (severe anemia)	0	0	0	0
7 - 9.9 (moderate)	9	15	7	11.67

10 - 10.9 (mild)	15	25	2	3.33
>=11 (normal)	36	60	51	85
Total	60	100	60	100

Table:2 Mild anemia was noted in 15 (25%), moderate anemia was seen in 9 (15%) out of 60 cases. None of the cases had severe anemia. In our study, 60 patients when compared to 60 controls had significant hemoglobin levels with a mean of 11.06 in cases with a p-value of 0.022. Hemoglobin level <11gm% (IDA) was seen in 40% of children with febrile seizures as against 15% of febrile children without seizures. IDA was seen 3.778 times greater in a child with febrile seizures than in a febrile child without seizures.

Table 4:Serum ferritin levels between cases and control

Ferritin	CASE		CONTROL	
	NO	%	NO	%
<10	7	11.67	2	3.33
10- 19.9	11	18.33	9	15
20-29.9	10	16.67	2	3.33
>=30 (normal)	32	53.33	47	78.33
total	60	100	60	100

Table:4 Low serum ferritin was noted in 28 cases of which majority (11) belonged to the 10-19.9 µg/L. 7 children had values in the range of <10 µg/L. The mean serum ferritin level in the cases group was 53.17 as against 53.896 with a p-value of 0.000. Serum ferritin was significantly lower in 46.7% of cases compared to 21.7% of control with a p-value of 0.004 (significant). In our study, patients with febrile seizures are 3.163 times more likely to have iron deficiency (low serum ferritin level) compared to febrile patients without seizures.

Table 5:Serum TIBC levels in cases and control

TIPS	CASE		CONTROL	
	NO	%	NO	%
<400(normal)	52	86.67	54	90
400-500	6	10	6	10
>500	2	3.33	0	0
Total	60	100	60	100

Table:5 out of 60 cases had high TIBC levels in the range of 400-500 µg/dl. In our study, there was no significant difference in serum TIBC levels in each group with a p-value of 0.570.

Discussion

The total number of cases analyzed was 60, out of which 35 (58.3%) were males and 25 (41.7%) were females. Our study was demonstrating an increased occurrence of febrile seizures in boys as compared to girls. In the group of 60 cases, 31 (51.7%) were seen in the age group of 9-18 months, 24 (40%) were seen in the age group of 19-36 months, 5 (8.3%) were seen in the age group of 37-60 months. The peak incidence of FS was noted between 14 to 18 months as per Aicardi's epilepsy febrile convulsions guidelines^[8]. In our study also, the maximum incidence was seen in the age group of 9-18 months. Mean age was 20 (SD 9.89) months for cases (p-value 0.025), 25 (SD 15.11) months for controls. Nutritional status was normal in 36 (60%) of cases as against 43 (71.7%) of controls. Underweight was seen in 22 (36.7%) of cases as against 16 (26.7%) of the control group. Severe underweight was seen in 2 (3.3%) of cases as against 1 (1.7%) of the control group. Family history of febrile seizures was seen in 21 (35%) of cases as against 10 (16.7%) of the control group. (p=0.022). Patients with febrile seizures were 2.69 times more likely to have a positive family history of febrile seizures compared to a febrile child without seizures.^[9] Febrile seizures 1st, 2nd, 3rd episodes were seen in 60%, 31.7%, and 8.3% of cases respectively. Simple febrile seizures were seen in 38 (63.33%) of cases and complex type was seen in 22 (36.67%). Respiratory tract infection was seen in 30 (50%) of cases, Urinary tract infections in 13 (21.7%), Acute Gastroenteritis in 7 (11.7%), Nonspecific illness like a viral fever in 10 (16.7%) of cases as a cause of fever. Clinical pallor was noted in 18 (30%) of cases as against 12 (20%) of the control group. It was noted that pallor was 1.714 times more in cases than that seen in the control group.^[10] There was a significantly higher rate of IDA (Hb% < 11 gm) among children with febrile convulsions than in controls (40% vs. 15%) with a p-value of 0.002. IDA was seen 3.778 times greater in a child with febrile seizures than in a febrile child without seizures. Children with febrile seizures had significant hemoglobin levels with a mean of 11.06 with a p-value of 0.022. Mild anemia was noted in 15 (25%), moderate anemia was seen in 9 (15%) out of 60 cases.^[11] None of the cases had severe anemia. Serum ferritin was significantly lower in 28 (46.7%) cases compared to 13 (21.7%) of control with a p-

value of 0.004 (significant). In our study, patients with febrile seizures are 3.163 times more likely to have iron deficiency (low serum ferritin level) compared to febrile patients without seizures. This study showed that low serum ferritin was noted in 28 cases of which the majority^[12] belonged to the 10-19.9 µg/L. Persons had values in the range of <10 µg/L. In our study, it was found that 10 children (16.7%) with febrile seizures had low levels of serum iron (<22) which was found to be statistically significant with a p-value of 0.004, relative risk was 11.8. There was a significant difference in serum iron with the mean being 53.79 in the cases group which was found to be statistically significant with a p-value of 0.002^[13]. It was noted that 11 children out of 60 cases had low levels of Iron in the range of 10-21.9 µg/dl but none of the individuals had a value less than 10 µg/dl. TIBC level was high in 8 (13.3%) of cases as against 6 (10%) in the control group, but there was no significant difference in serum TIBC levels in each group. There was no statistically significant difference noted in serum TIBC level with a mean value of 351.70 (p-value 0.312). 6 out of 60 cases had high TIBC levels in the range of 400-500 µg/dl. The Mean Values for Serum ferritin, Iron, TIBC levels in the control group studied were within the normal range.^[14,15]

Conclusion

The present study showed that hemoglobin, serum ferritin, and serum iron levels are significantly lower in children suffering from febrile seizures than febrile children in the control group, suggesting that a low iron status has an important role in children with febrile seizures. Consequently measuring serum ferritin is a specific, sensitive, and reliable test for detecting iron depletion in the early stages of the disease itself and the best standard for determining the total body iron stores. Therefore, complete blood count and screening for ID with serum iron studies are recommended in the workup of children with the first febrile convulsion itself.

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