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Correlation of serum level and selective blood indices in children with feberile seizures in Chittoor district, India

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ABSTRACT

Background: A seizure or convulsion is a paroxysmal, time-limited change in motor activity and/or behavior that result from abnormal electrical activity in the brain. Seizures are common in the pediatric age group and occur in approximately 10% of children. Most seizures in children are provoked by somatic disorders originating outside the brain, such as high fever, infection, syncope, head-trauma, hypoxia, toxins, or cardiac arrhythmias. To study the association between iron deficiency and the first febrile seizure.

Methods: The present study is a retrospective study conducted at the teaching hospital, Chittoor district from August 2019 to December 2019. In this study to detect low iron status as a possible risk factor for first febrile seizures, 63 cases, and 63 age and sex-matched controls are studied and analyzed.

Results: In this study family history of febrile seizures is seen only in 28.5% of cases. The mean serum ferritin level in this study is 14.5ng/ml. Thus the mean serum ferritin, HB, and MCV are found to be signed on the lower side among children with febrile seizures.

Conclusions: Plasma ferritin level and blood indices are significantly lower in children with febrile seizures as compared to children without febrile seizures suggesting that iron-deficient children are more prone to febrile seizures.

Keywords: Febrile seizures, Iron deficiency anemia, Mean corpascular volume, Serum ferritin

INTRODUCTION

A seizure or convulsion is a paroxysmal, time-limited change in motor activity and/or behavior that result from abnormal electrical activity in the brain. Seizures are common in the pediatric age group and occur in approximately 10% of children.¹ Most seizures in children are provoked by somatic disorders originating outside the brain, such as high fever, infection, syncope, head-trauma, hypoxia, toxins, or cardiac arrhythmias.² Other events, such as breath-holding spells and gastroesophageal reflux, can cause events that simulate seizures. A few children also exhibit psychogenic seizures of psychiatric origin. Less than one-third of seizures in children are caused by epilepsy, a condition in which seizures are triggered recurrently from within the brain.³

For epidemiological classification purposes, epilepsy is considered to be present when two or more unprovoked seizures occur at an interval greater than 24 hr apart.⁴ The cumulative lifetime incidence of epilepsy is 3% and more than half of cases begin in childhood. However, the annual prevalence of epilepsy is lower (10.5-0.8%) because many children outgrow epilepsy.⁵ Although the outlook for most children with symptomatic seizures or those associated with epilepsy is generally good, the seizures may signal a potentially serious underlying systemic or central nervous system (CNS) disorder that requires thorough investigation and management.⁶ For children with epilepsy, the prognosis is generally good, but 10-20% have. persistent seizures refractory to drugs, and those cases pose a diagnostic and management challenge.⁷ Seizures have been recognized since ancient

times and although improvement has been made in management over this century compared to the previous 2000 years, there are still far too many children whose lives are crippled by poorly controlled seizures.⁸ Infants and children are more prone to have seizures than adults. This appears to reflect greater neuronal excitability at certain ages as the excitatory glutamate system and inhibitory gamma aminobenzoic acid (GABA) system do not always balance each other. This also results in the tendency to exhibit symptomatic seizures related to high fever, virus infection, minor asphyxia, medication, bacterial toxins, and biochemical upsets such as hypo- or hypernatremia and hypocalcemia. Childhood seizure differs from adult seizure since the brain is a developing organ.⁹ The clinical picture is not static and the pattern of fits may change with age, e.g. infantile spasms can evolve into Lennox-Gastaut syndrome. Also, many types of seizures are restricted to childhood.¹⁰

METHODS

The present case-control study is a retrospective study conducted at the teaching hospital, Chittoor district from August 2019 to December 2019. In this study to detect low iron status as a possible risk factor for first febrile seizures, 63 cases, and 63 age and sex-matched controls are studied and analyzed.

Exclusion criteria

Children with Iron supplementation/therapy, Hematological disorders chronic illness Neurological deficit, previous history of seizures.

After getting informed consent from the parents of cases and controls, they are subjected to a detailed history and clinical examination, and the findings are entered in the proforma. Blood samples are collected and measures of serum ferritin (the single most sensitive tool for evaluating the iron status) Hemoglobin (HB), Mean corpuscular volume (MCV), and Mean corpuscular hemoglobin (MCH) are measured and compared. Serum ferritin estimation: Chemiluminescence immunoassay for the quantitative determination of serum ferritin. For this 2ml of blood was collected into vacutainers through venipuncture under strict aseptic precautions.

The serum is separated from cells by centrifugation. The assay is based on microplates coated with highly specific anti-ferritin-human antibodies. During the procedure, the binding of the analyte, as well as the formation of the sandwich complex and enzymatic color reaction take place during three different reaction phases. Calibrators, controls, and undiluted patient samples are pipetted together with sample buffer into the wells of the microplate. Any present ferritin molecules bind to the inner surface of the wells. After 30 minutes of incubation, the microplate is washed with a buffer for removing non-reactive serum components.

Statistical analysis

The effect of iron status on first febrile seizure with odds ratio (OR) and 95% confidence limit was arrived by univariant analysis. An odds ratio was considered statistically valid and meaningful if the upper and lower limits of confidence interval do not include unity. The value of OR was considered significant if the probability (p) was <0.05. All continuous data were analyzed by the use of a t-test or Mann Whitney U test. All proportionate data were analyzed with chi-square or Fischer exact test.

RESULTS

Table 1 shows A maximum incidence of febrile seizures is found in the age group of 1year- 2year (58.7%), followed by 2-3years (22.2%) and 6months-1year (19.1%). The mean age is 18 months. The incidence of febrile seizures is found to be higher in males (58.7%) with a male: female ratio of 1.4:1. Eighteen children (28.5%) in the febrile seizures group have a positive family history of febrile seizures when compared to none among controls.

Table 1: Incidence of febrile seizures concerning age and gender.

Ago	Male		Female		Total	
Age	N	%	N	%	N	%
6 months-1year	7	1.1	5	8	12	19.1
1 year-2year	20	31.7	7	27	37	58.7
2 year-3year	10	15.9	4	6.3	14	22.2
Total	37	58.7	26	41.3	63	100

Table 2: Mean value of serum ferritin and blood indices among those who had febrile seizures and controls.

Variables	Cases		Contro	Controls		
	Mean	SD	Mean	SD	p-value	
Sr. Ferritin (ng/ml)	14.5	10.6	34.9	23.3	0.00	
HB (gm%)	9.8	1.2	11.3	1.1	0.00	
MCV (fl)	76.0	8.5	79.5	7.5	0.02	
MCH (pg)	27.7	3.1	28.7	3.6	0.11	

The mean ferritin level among febrile seizures group is found to be 14.5±10.6ng/ml whereas in controls it is 34.9±23.3ng/ml, (p=0.00). The mean Hemoglobin (HB) for cases is 9.8±1.2gm/dl, whereas in controls it is 11.3±1.1gm/dl (p=0.00). The Mean Corpuscular Volume (MCV) for cases is 76±8.5fl and for controls, it is 79.5±7.5fl, (p=0.02). The Mean Corpuscular Hemoglobin (MCH) for cases is 27.7±3.1pg and for controls it is 28.7±3.6pg (p= 0.11).Thus the mean serum ferritin, HB, and MCV are found to be signed on the lower side among children with febrile seizures when compared to the children who did not have febrile seizures, which is statistically significant. Even though the MCH is less

among children with febrile seizures it did not achieve statistical significance (Table 2).

Forty one children (65.1%) with febrile seizures have serum ferritin level <10ng/ml whereas only 15 children (23.8%) in the control group have ferritin level <10ng/ml with a (p=0.00). The number of children with hemoglobin <11gm/dl is 51 (80.9%) in febrile seizures group whereas among controls it is only 19 (30%) (p=0.00). The Mean Corpuscular Volume <70fl is seen in 23 (36.5%) cases, whereas in controls it is only 8 (12.7%) (p=0.003).10 children (15.9%) in cases and 9 children (14.3%) in controls have Mean Corpuscular Hemoglobin <24pg (p=1). Thus a significant proportion of children with febrile seizures have low serum ferritin, Hemoglobin, and Mean Corpuscular Volume than did the controls. However, the proportion of children with low Mean Corpuscular Hemoglobin among those with febrile seizures and controls did not achieve statistical significance (Table 3).

Table 3: Proportion of children with low serum ferritin/blood indices among cases and controls.

Variables		Cas	Case		itrol	p-value	
Serum	<10	41	65.1	15	23.8		
ferritin (ng/ml)	>/-10	22	34.9	48	76.2	0.00	
HB	<11	51	80.9	19	30.1	0.00	
(gm%)	>/-11	12	19.1	44	69.9	0.00	
MCV	< 70	23	36.5	8	12.7	0.003	
(fl)	>/-70	40	63.5	55	87.3	0.003	
MCH	<24	10	15.9	9	14.3	1.00	
(Pg)	>/-24	53	84.1	54	85.7	1.00	

Table 4: Serum ferritin and blood indices among cases and controls.

Variables		Odds ratio	95% CI	p- value	
Serum ferritin	<10	6.0	2.7, 13.0	0.00	
(ng/ml)	>/-10	1.0	Reference	0.00	
HB (gm%)	<11	9.8	4.3, 22.5	0.00	
	>/-11	1.0	Reference	0.00	
MCV (fl)	< 70	4.0	1.6, 9.7	0.003	
	>/-70	1.0	Reference		
MCH (pg)	<24	1.1	0.4, 3.0	1.00	
	>/-24	1.0	Reference	1.00	

Odds of children with febrile seizures having low serum ferritin level is six when compared to those who did not have febrile seizures. OR (95% CI) = 6 (2.7-13.0). Odds of children with febrile seizures having low Hemoglobin level is 9.8 when compared to those who did not have febrile seizures. OR (95% CI) = 9.8 (4.3-22.5) Odds of children with febrile seizures having low Mean Corpuscular Volume is four when compared to those who did not have febrile seizures. OR (95% CI) = 4 (1.6-9.7) Odds of children with febrile seizures having low Mean

Corpuscular Hemoglobin is 1.1 when compared to those who did not have febrile seizures which is not statistically significant OR (95% CI) = 1.1 (0.4-3) (Table 4).

DISCUSSION

In this study to detect low iron status as a possible risk factor for first febrile seizures, 63 cases, and 63 age and sex-matched controls are studied and analyzed. In the present study, authors found that the peak incidence of febrile seizures occur during one to two years of age and the mean age is 18 months. This is comparable to previous studies. The present study depicts that the incidence of febrile seizures is slightly higher in boys than in girls and the male: female ratio 1.4:1. This is similar to the study by Gastaut H, Poirier et al, reported no gender difference in their study. In this study family history of febrile seizures is seen only in 28.5% of cases. But the Forfar textbook of pediatrics mentions that 50% will have a family history of convulsions and 80% of twins are concordant for monozygotic convulsions. The mean serum ferritin level in this study is 14.5ng/ml.¹¹

Whereas Gastaut H et al, in his study group from Jordan found that the mean ferritin level was 29.5ng/ml. It is probably because iron deficiency anemia is more prevalent in this country; the mean serum ferritin level of Indian children is also low when compared to Western standards. 12 Berg AT et al, in his study found that a significant proportion of children with febrile seizures had only low serum ferritin levels. The proportion of children with febrile seizures having low hemoglobin, Mean Corpuscular Volume, and Mean Corpuscular Hemoglobin were not statistically significant. Whereas this study demonstrates a statistically significant difference in the proportion of children with febrile seizures have not only low serum ferritin but also low hemoglobin and low Mean Corpuscular Volume. This is similar to the findings reported by Ellenberg JH et al.¹³

The children in Western countries if they are iron deficient are mostly in the early stage. So the study was done by Daoud AS et al, in Jordan has a significant proportion of children with low ferritin levels, without significant difference in HB, MCV, and MCH. Whereas Indian children/children of this neighboring country Pakistan are in the stages of latent or overt iron deficiency.¹⁴ So this study and the study done by Rehman N et al, had a significantly greater proportion of children with not only low serum ferritin but also low HB and MCV. 15 As similar to previous studies by Pisacane A et al, this study also demonstrates an association between iron deficiency and febrile seizures. Thus iron deficiency is one of the possible risk factors for febrile seizures. Developmental problems, risk of pediatric stroke, the occurrence of febrile seizures, and breath. Holding spells are perhaps the tip of the iceberg, of the neurological consequences of iron deficiency. With appropriate recognition, treatment or better yet, prevention the

neurological sequelae of iron deficiency are entirely preventable and perhaps reversible. 16,17

CONCLUSION

Plasma ferritin levels and blood indices are significantly lower in children with febrile seizures as compared to children without febrile seizures suggesting that iron-deficient children are more prone to febrile seizures. A follow-up study of patients found to be iron deficient at the time of a first febrile seizure to determine the incidence of subsequent febrile seizures after treatment for iron deficiency would be of great interest.

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Institutional Ethics Committee

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