

A Study of Serum Zinc Levels in Children with Febrile Seizures in a Referral Hospital

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ABSTRACT

BACKGROUND

Several trace elements are found to play a significant role in the evolution of febrile convulsions by co-enzyme activity. The aim of the study is to estimate the serum zinc levels in children with simple and complex febrile seizures and compare them with serum zinc levels in febrile children without seizures.

METHODS

This prospective comparative study was designed to have three groups – children with simple febrile seizures, complex febrile seizures and febrile children without seizures.

RESULTS

About 46% of children with simple febrile seizures were in the age group of 1 to 2 years. Complex febrile seizures were common (40%) between 6 months to 1 year of age. The mean serum zinc levels in the simple febrile seizures group, complex febrile seizures group and no seizures group were 57.69 mcg/dL, 60.66 mcg/dL and 73.12 mcg/dL respectively ($p=0.002$). About 66% and 80% of children with simple febrile seizures and complex febrile seizures respectively had low serum zinc levels compared to only 20% in no seizures group. The multivariate analysis of serum zinc levels with various age groups ($P=0.441$) and gender ($P=0.462$) did not demonstrate any significant association.

CONCLUSIONS

The present study has demonstrated significantly lower levels of serum zinc in children with simple and complex febrile seizures. Further research should be directed to test the hypothesis as to whether correction of zinc deficiency prevents febrile seizures in children.

KEYWORDS

Febrile Seizures, Zinc, Children

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BACKGROUND

Infants and children are more prone to have seizures than adults due to the greater neuronal excitability at certain ages as the excitatory glutamate system and inhibitory Gamma Amino Butyric Acid (GABA) system do not always balance each other.¹ This result in symptomatic seizures related to fever, infections, drug intake, bacterial sepsis and electrolyte disturbances like hyponatremia and hypernatremia.² Febrile seizure is usually defined as an episode in infancy or childhood usually occurring between the ages of six months to 6 years accompanied along with fever but without evidence of any intracranial infection or other defined cause.³ A simple febrile seizure is generalized, tonic-clonic in nature lasts for a few seconds and rarely up to 15 minutes, is followed by a brief period of post ictal drowsiness and occurs only once in 24 hours.⁴ A febrile convulsion is described as a complex or complicated type when the duration is more than 15 minutes, when repeated convulsions occur within 24 hours or when focal seizure activity or focal findings are present during the post ictal period.⁵ Febrile seizures occur in young children at a time in their development when seizure threshold is low. These seizures occur early in a disease during the sudden rise of temperature. Febrile seizures are seen with childhood infections such as respiratory infections, otitis media and gastroenteritis.

About 94% occur within the first three years of age and 6% after three years of age.⁴ About one half appears during second year of life with peak incidence between 18 to 22 months. Febrile seizures that are seen before 6 months of age should raise the high degree of suspicion of infections like acute bacterial meningitis. Genetics have a definite contribution in febrile seizures.⁶ The chance after one child is affected is 10%; it rises to almost 50% if one parent had febrile convulsion.⁷ The exact mode of inheritance is not clearly understood. Most studies suggest an autosomal dominant inheritance with reduced penetrance. Linkage studies in chromosomes have mapped the gene to chromosome 19p and 8q 13-21.

The incidence in India varies between 3-5% and many studies show a slight male preponderance.⁸ A number of trace elements are found to play a significant role in the evolution of febrile convulsions by co-enzyme activity. Studies have also shown that many trace elements like iron, zinc, copper, selenium and magnesium play a major role in febrile convulsions. Zinc is an important co-factor of glutamate decarboxylase which is the enzyme needed for gamma amino butyric acid synthesis in central nervous system and the reduced zinc levels in cerebrospinal fluid have also been associated with febrile convulsions.⁹ Zinc deficiency plays an important role in febrile seizures as zinc increases the storage capacity of glutamate and reciprocally pyridoxine increases the activity of glutamate decarboxylase which results in gamma amino butyric acid syntheses. Thus, decreased serum zinc levels lead to decreased GABA synthesis which would precipitate seizures.¹⁰ The aim of this study is to estimate the serum zinc levels in children with

simple and complex febrile seizures and to compare them with serum zinc levels in febrile children without seizures.

METHODS

This prospective comparative study was conducted in the Department of Paediatrics at our hospital in hospitalized children between the age groups from six months to six years during the period from April' 2019 to December' 2019. The study was designed to have three groups – children with simple febrile seizures, children with complex febrile seizures and febrile children without seizures. The sample size for children with seizures was derived after an analysis of previous years admission rate of febrile seizures in our hospital. The sample size for febrile children without seizures was targeted to be double that of children with seizures to allow more freedom of comparison between the groups. Thus about 30 consecutive children with simple febrile seizures from 6 months to 6 years of age, 20 consecutive children with complex febrile seizures and 100 consecutive children with fever but without seizures in the same age group formed the study population. Children with cerebral palsy, mental retardation, developmental delay, seizure disorder, children with features of intracranial infection, children on zinc supplementation and children on anti-epileptic drugs were excluded from the study.

A detailed history of presenting complaints including duration of fever, type and duration of convulsions, family history of febrile seizures and history suggestive of the fever aetiology was taken. Vital signs including temperature, heart rate, respiratory rate, capillary refilling time, blood pressure, temperature and anthropometry were recorded. General examination and systemic examination of the central nervous system were done. Complete blood count, urinalysis and chest x-ray were done to identify the aetiology of fever. Cerebro Spinal Fluid (CSF) analysis was done in all children of febrile seizures less than one year of age and in all children with complex febrile seizures. Computed Tomogram (CT) brain and Electro Encephalo Gram (EEG) were done in cases of complex febrile seizures. Two ml of whole blood was collected by venepuncture under strict aseptic precautions for assessment of serum zinc levels by calorimetric method. The normal serum zinc level was taken as 60–120 mcg/dL. Informed consent was obtained from the parents of all the participants. Institutional ethical committee clearance was obtained. The observations were statistically analysed by Chi square test to study the statistical difference between the parameters.

RESULTS

The results are tabulated in tables 1 - 3. About 46% of children with simple febrile seizures were in the age group of 1 to 2 years. Complex febrile seizures were common (40%) between 6 months to 1 year of age. On analysis of gender distribution, a male preponderance was observed in

	Age												Total
	6 Mon-1 Year		1-2 Years		2-3 Years		3-4 Years		4-5 Years		5-6 Years		
	n	%	n	%	n	%	n	%	n	%	N	%	
Simple Febrile Seizure	4	13	14	46	6	20	2	7	2	7	2	7	30
Complex Febrile Seizure	8	40	6	30	4	20	0	0	0	0	2	10	20
Fever with No Seizure	20	20	28	28	20	20	10	10	12	12	10	10	100

	Gender Distribution												Total	
	6 Mon-1 Year		1-2 Year		2-3 Year		3-4 Year		4-5 Year		5-6 Year			
	M	F	M	F	M	F	M	F	M	F	M	F		
Simple Febrile Seizure	4	0	6	8	4	2	0	2	1	1	1	1	16	14
Complex Febrile Seizure	6	2	2	4	2	2	0	0	0	0	0	2	10	10
Fever with No Seizure	12	8	14	14	8	12	6	4	6	6	4	6	50	50

	Family History of Febrile Seizures						Total
	Present			Absent			
	n	%		n	%		
Simple Febrile Seizure	8	26		22	74		30
Complex Febrile Seizure	4	20		16	80		20
Fever with No Seizure	2	2		98	98		100
P Value	0.042						

Table 1. Demographic Profile of the Study Group

	Gastroenteritis	Otitis	Enteric Fever	Lower Respiratory Tract Infections	Pharyngitis	Upper Respiratory Tract Infections	Urinary Tract Infections	Viral Fever	Total
	No (%)	No (%)	No (%)	No (%)	No (%)	No (%)	No (%)	No (%)	
	Simple Febrile Seizure	4(13)	2(7)	0(0)	2(7)	0(0)	12(40)	4(13)	6(20)
Complex Febrile Seizure	0(0)	2(10)	0(0)	4(20)	0(0)	8(40)	2(10)	4(20)	20
Fever with No Seizure	0(0)	0(0)	16(16)	20(20)	8(8)	12(12)	14(14)	30(30)	100
P Value	0.015	0.203	0.015	0.109	0.045	0.009	0.702	0.479	150

Table 2. Analysis of Aetiology of Fever

Zinc	Serum Zinc Levels						Total	Mean Serum Zinc level ±SD
	Low		Normal		n	%		
	n	%	n	%				
Simple Febrile Seizure	20	66	10	34	30	100	57.69 ± 9.46	
Complex Febrile Seizure	15	80	5	20	20	100	60.66 ± 11.33	
Fever with No Seizure	20	20	80	80	100	100	73.12 ± 15.15	
P value	0.002							

	Age Wise Mean Serum Zinc Levels in µg/dL				
	6 Mon - 1 Year	1-2 Years	2-3 Years	3-4 Years	4-5 Years
	Simple Febrile Seizure	51.5	60.6	58.7	52.8
Complex Febrile Seizure	63.5	62.7	59.7	54.1	50.7
Fever with No Seizure	64.9	71.6	75.7	72.0	87.1
P value	0.441				

Parameter	Gender Wise Mean Serum Zinc Levels in µg/dL	
	Male	Female
	Simple Febrile Seizure	59.25
Complex Febrile Seizure	59.96	62.05
Fever with No Seizure	71.72	74.61
P value	0.462	

Table 3. Analysis of Serum Zinc Levels

simple febrile seizures with a male: female ratio of 1.14:1. But no gender preponderance was observed in complex febrile seizures. A significantly higher proportion of children in the febrile seizures group had a positive family history of febrile seizures than the children in the no seizures group - 26% for simple febrile seizures, 20% for complex febrile seizures and 2% for no seizures group (P=0.042). On analysis of the aetiology for the fever upper respiratory tract infections (40%) and viral fever (20%) were common in the simple febrile seizures group. On analysis of the aetiology of the fever in the no seizure group, viral fever (30%) and lower respiratory tract infections(20%) were commonly observed. The statistical analysis of the aetiology of fever showed a significantly higher number of children with simple febrile seizures had gastroenteritis (p=0.015) and upper respiratory tract infections (p=0.009). The children in the no seizure group showed a significantly higher number of enteric fever (P=0.015) and pharyngitis (P=0.045).

The mean serum zinc levels in the simple febrile seizures group, complex febrile seizures group and no seizures group were 57.69 mcg/dL, 60.66 mcg/dL and 73.12 mcg/dL respectively (Table 2). About 66% and 80% of children with simple febrile seizures and complex febrile seizures respectively had low serum zinc levels compared to only 20% in no seizures group. This association was statistically significant with a P value of 0.002. The multivariate analysis of serum zinc levels with various age groups (P=0.441) and gender (P=0.462) did not demonstrate any significant association (Table 3).

DISCUSSION

In the present study, the complex febrile seizures were common in less than 1-year age group and simple febrile seizures were common in 1 to 2 years age group. In studies

conducted by Samir S et al, Lynette et al and Hartfield et al the mean age for febrile seizures were 15 months, 18 months and 17.9 months respectively.¹¹⁻¹³ In the present study a male preponderance was observed in simple febrile seizures with a male: female ratio of 1.14:1. Studies by Leelakumari et al and Samir S Shah et al also demonstrated a male preponderance in their studies.¹⁴ In the present study about 26% and 20% of the children with simple and complex febrile seizures had positive family history of febrile seizures. Studies by Siddique et al, Saidalhaque et al and Farwell et al reported positive family history in 30%, 20% and 29% of children with febrile seizures respectively.^{15,16} In the present study upper respiratory tract infections (40%) and viral fever (20%) were significantly associated with simple febrile seizures. Similar observations were made by Rantala et al, Mahyaret al and Srinivasa et al.^{17,18,19} In the present study the mean serum zinc levels in the simple febrile seizures group, complex febrile seizures group and no seizures group were 57.69 mcg/dL, 60.66 mcg/dL and 73.12 mcg/dL respectively. Children in the simple and complex febrile seizures group had a significantly lower level of serum zinc than the no seizures group. Kumar L et al in his study demonstrated that zinc values were significantly lower in cases when compared to controls.²⁰ Other studies have also demonstrated significantly lower levels of serum zinc in children with febrile seizures.^{21,22,23} The serum zinc levels did not show any significant correlation with age and gender in the present study. Also, no significant difference in serum levels between children with simple and complex febrile seizures was observed in the present study.

In the recent years zinc has been associated with many childhood illnesses like infections, hypogonadism, weight loss, delayed wound healing, emotional disturbance, dermatitis, night blindness, alopecia and poor appetite.²⁴ The demonstration of its deficiency being associated with febrile seizures makes febrile seizures as one of the preventable diseases in children. Further research should be directed to test the hypothesis of whether correction of zinc deficiency prevents febrile seizures in children.

CONCLUSIONS

The present study has demonstrated significantly lower levels of serum zinc in children with simple and complex febrile seizures when compared to children with fever and no seizures. Further research should be directed to test the hypothesis as to whether correction of zinc deficiency prevents febrile seizures in children.

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