

COMPARISON OF SERUM ZINC LEVEL IN FEBRILE CHILDREN WITH AND WITHOUT CONVULSIONS

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Article Received on 13/03/2022

Article Revised on 02/04/2022

Article Accepted on 23/04/2022

ABSTRACT

Introduction: The pathophysiology of febrile seizure remains unknown, genetic factors or electrolyte disturbance may have a role in its occurrence or recurrence. Zn²⁺ is needed for synthesis of GABA. When a patient develops low levels of zinc, the N-methyl-D-aspartate receptors become activated and induce an epileptic discharge in children with high fever. The main objective of the study is to estimate serum zinc level in febrile children with and without convulsions and to evaluate the association of serum zinc level in febrile convulsions. **Methods:** A comparative study was done on 80 children during 1¹/₂-year period in hospitals attached to Aarupadai Veedu Medical College from November 2019 to May 2021. 80 children were divided into two groups of 40 each of children with febrile convulsions and 40 children with fever without convulsions, Serum zinc levels were investigated in both the groups. The laboratory reference range is 65-130µg/dl. The serum Zinc levels in both the groups are compared using Chi square test and Independent T test. **Results:** Majority of patients were in the age group below 2 years, comprising of 40% in children with febrile convulsions and 42.5% in children with fever. Among 40 febrile convulsions female: male ratio was 1.35:1 and among 40 febrile children male; female ratio was 1: 1. Upper Respiratory tract infection constituted the major trigger factor in groups, 67.5% in cases and 62.5% in controls. Serum zinc levels were low in 72.5% of febrile children as compared to only 45% of children with fever (P-0.041). Febrile children with convulsion had a low mean serum zinc level of 52.52µg/dl as compared to mean of normal serum zinc value of 79.1 µg/dl in children with fever. Mean serum zinc level were significantly low in children with febrile convulsions with (P-0.001). **Conclusions:** This study shows that serum zinc levels are decreased in children with febrile convulsions when compared to children with fever alone without convulsions, thus indicating that zinc deprivation plays significant role in the pathogenesis of febrile convulsions. The role of zinc in febrile convulsions should be investigated by further studies and if the results are reproducible, zinc supplementation can be given in febrile convulsions.

KEYWORDS: 6months-6years, Febrile seizures, Fever, Low serum zinc level.**INTRODUCTION**

A seizure is defined as a transient occurrence of signs and symptoms as a result of abnormal excess or synchronous activity of neurons in the brain.^[1] At least 10% of pediatric age group experience seizures. Febrile seizures are the most common convulsive event in childhood, occurring in 2% to 5% of children.^[2] High fever, syncope, infection, head trauma, toxins, or hypoxia could be some of the causes that provoke seizures in children.^[3,4]

The most common type of seizures observed in children is febrile seizures.^[5] They are defined as an "event in infancy or childhood occurring usually between age group of six months of age to six years^[6] of age, associated with fever without any evidence of intracranial (CNS)

infection or any defined cause".^[7] Upper respiratory tract infection (URTI), lower respiratory tract infection (LRTI), otitis media, acute gastroenteritis (AGE), are some of common childhood illness that predispose to febrile convulsions and children respond to these infections with comparably higher temperatures.^[7] Multiple trace elements are responsible for pathogenesis of convulsions by their virtue of activity of co-enzyme or by influencing ion channels and receptors. Zinc stimulates the activity of pyridoxal kinase, involved in pyridoxal phosphate synthesis from pyridoxal. Pyridoxal phosphate stimulates the activity of glutamic acid decarboxylase that catalyzes GABA synthesis. So, decrease in zinc levels lowers GABA level that precipitate seizures.^[8]

Zinc levels in children with febrile seizure were significantly lower than those in children with afebrile seizure.^[10] To regard the importance of febrile seizure and its possible contributing factors including serum zinc level this study is been conducted to compare the serum zinc levels in febrile children with and without convulsions during 18 months in Aarupadai Veedu Medical college and Research institute. The objectives of the study are to estimate serum zinc level in febrile children with and without convulsions and to evaluate the association of serum zinc level in febrile convulsions.

METHODS

A comparative Cross-sectional study was done after getting institutional ethical clearance for 1¹/₂-year period in hospitals attached to Aarupadai Veedu Medical College from November 2019 to May 2021.

The study included Children who are Febrile (Temperature > 38°C), febrile convulsions children aging 6 months to 6 years not associated with any neurodevelopmental delay or CNS infection and whose Parents are willing to give informed consent. Children who are already on zinc supplementation, antiepileptic medication, diarrheal diseases, undernourished children are excluded from the study. Informed written consent was obtained.

Comparative study was done on 80 children fulfilling the criteria who were divided into two groups, 40 children with febrile seizures and 40 febrile children who were matched for age and sex, following which blood sample was taken and the serum zinc level was estimated.

Serum Zinc levels were measured by Inductively Coupled Plasma Mass Spectrometry technique. The laboratory reference range was 65-130mcg/dl which was considered as normal. Data entry was done in MS Excel

and analyzed by SPSS Software (v20). The serum Zinc levels in both the group are compared using Chi square test and Independent T test.

RESULTS

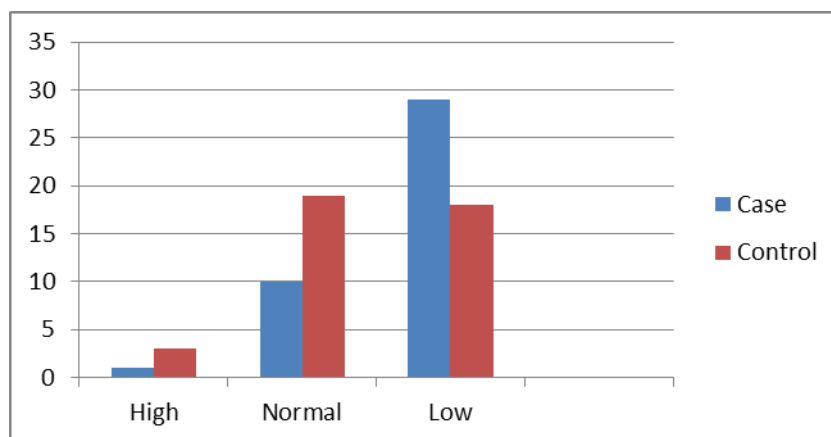
In children with febrile convulsions (Cases) 40% (16) of children were below 2 years of age, 22.50% (9) between 2.1 to 3 years, 22.50% (9) between 3.1 to 4 years and 15% (6) between 4.1 to 5 years of age. In children with fever (Controls) 42.50% (17) were below 2 years of age, 22.50% (9) were between 2.1 to 3 years, 5% (2) were between 3.1 to 4 years of age and 30% (12) were between 4.1 to 5 years of age.

In the cases 42.50% (17) were males and 57.50% (23) were females. In the controls 50% (20) were females and 50% (20) were males. Upper respiratory tract infection (URTI) was found to be the most common triggering factor in both case group with 67.50% (27) and control group with 62.50% (25). Family history of febrile convulsions were positive in 12.5% (5) of cases and 10% (4) of controls. Average temperature in children with febrile convulsion was 101.87F and in children with fever was 101.42F. P-value is 0.057 (>0.05: statistically not significant).

Among 40 children with febrile convulsions, 29 (72.50%) had low serum zinc level (<65mcg/dl) as compared to 18(45%) out of 40 in children with fever, mean serum zinc level were significantly low in children with febrile convulsions with p value of 0.041 (<0.05) - statistically significant (Table 1 & Figure 1). Children with febrile convulsions had a mean serum zinc value of 52.52 mg/dl (low) as compared to mean of 79.87mg/dl (normal) in children with fever. Children with febrile convulsions had a mean fever seizure interval of 10.48hrs and mean duration of seizure in the group was 33.25 sec.

Table 1: Zinc levels in children with febrile convulsions and fever.

Zinc levels	Children with febrile convulsions		Children with fever		Total		p value
	n	%	n	%	n	%	
High	1	2.50%	3	7.50%	4	5%	0.041
Low	29	72.50%	18	45%	47	58.75%	
Normal	10	25%	19	47.50%	29	36.25%	
Total	40	100%	40	100%	80	100%	



NORMAL REFERENCE VALUE OF ZINC. Serum zinc levels: 65-130 µg/dl.
(Low levels < 65 µg/dl; High level > 130 µg/dl)

Figure 1-ZINC levels in children studied.

DISCUSSION

Febrile seizure is a neurologic problem occurring in children aged between 6 months to 6 years. The etiology of febrile seizure remains unknown but genetic factors or electrolyte disturbances may have a role in its occurrence or recurrence. To date it is understood that febrile seizures can be induced by several factors. It is believed that Febrile seizure is an age-dependent response of the immature brain to fever. The postulation made so is supported by the fact that (80 -85%) febrile seizures have occurrence between 6 months and 3 years of age, with the peak incidence being 18 months. Although the mechanism of this increased susceptibility is unclear, animal models suggest that there is increased neuronal excitability during the normal brain maturation. Gamma amino butyric acid is an important inhibitory neurotransmitter. Element zinc has a regulatory effect on glutamic acid decarboxylase and the synthesis of GABA. Various studies have been made to identify predisposing risk factor like family history, metabolic disturbance (especially serum zinc, magnesium, glucose, calcium).

The mean serum zinc levels in the present study in children with febrile convulsion was 52.52 (normal serum zinc level 65-130 µg/dl) and the mean serum zinc value in children with fever was 79.87, Children with febrile convulsions had statistically significant low serum zinc levels when compared to children with fever alone without convulsions.

Children with fever alone did not show decrease in serum zinc level compared to other groups which is similar to findings of other studies. Ganesh R et al^[11] compared serum zinc levels in 38 cases of simple febrile seizure with 38 age matched controls with statistically significant results ($p < .001$). The mean serum zinc level obtained in cases was 32.17 µg/dl.

Other AmiriM et al^[12], Modarresi MR et al^[13], Lee J and Kim JH^[14], and also gave similar results which are comparable with our study with serum zinc level values of 66.13 +/- 18 µg/dl, 13.8 µg/dl, 60.5 µg/dl respectively.

In a study conducted by Talebian A et al^[15], the mean serum zinc levels were noted to be normal with 116.8 µg/dl. However, Garty BZ et al^[16] had their findings which did not support the hypothesis that febrile convulsions are related to the reduced zinc concentration. But there was no significant difference in serum zinc levels between simple and complex febrile convulsions.

The serum zinc levels did not show any significant correlation with age of onset, sex, axillary temperature or fever seizure interval in our study.

As serum zinc concentration in any population is influenced by factors such as dietary pattern, vitamin A, vitamin D deficiency, zinc levels in the soil and water, further studies are needed in this aspect to identify the probable cause for this finding.

This study shows that serum zinc levels are decreased in children with febrile convulsions when compared to children with fever without convulsions, indicating that zinc deprivation plays significant role in the pathogenesis of febrile convulsions. Zinc deficiency could be the potential risk factor for occurrence of febrile convulsions.

The role of zinc in febrile convulsions should be investigated by further studies and if the results are reproducible, zinc supplementation can be given in febrile convulsions. Our study has a limitation of not correlating the serum zinc level in complex febrile convulsions. Study does not take into account other trace element deficiency. The study fails to investigate the reduction in occurrence of febrile convulsions with zinc supplementation on follow up of cases and controls.

CONCLUSION

This study shows that serum zinc levels are decreased in children with febrile convulsions when compared to children with fever alone without convulsions, thus indicating that zinc deprivation plays significant role in the pathogenesis of febrile convulsions. The role of zinc

in febrile convulsions should be investigated by further studies and if the results are reproducible, zinc supplementation can be given in febrile convulsions.

ACKNOWLEDGEMENT

Conflict of interest: None.

Funding: Self funding.

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