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ROLE OF ZINC IN FEBRILE SEIZURES IN CHILDREN

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ABSTRACT
Background: Febrile convulsion is the most common type of seizures in childhood. Zinc has been studied in the context of pathophysiology of febrile seizure. The objective of the present study was to compare the serum zinc levels in children with febrile seizure from healthy children. **Methods:** The present study was a cross sectional study. A total of 40 children aged between 6 months to 5 years fulfilling the inclusion criteria were included. The study comprised of 2 groups, one with febrile seizures (40 cases) and another group of similar sex and age matched healthy children (40 cases). Serum zinc was measured by colorimetric method and compared among the groups using statistical methods. **Results:** There was no significant difference in sex, age, weight, height and head circumference between the two groups (P >0.05). Mean serum zinc level was48.89 ± 17.17 µgm/dl and 95.80 ± 18.76 µgm/dl in febrile seizure group and healthy children group respectively. It was significantly lower in first group compared to other. **Conclusions:** Serum zinc level was lower in children with simple febrile seizures as compared to healthy children which were found to be statistically significant.

KEYWORDS: Febrile seizure, Serum zinc level, healthy children.

INTRODUCTION
Febrile Seizure (FS) is one of the most common neurological conditions in childhood. Although febrile seizure are generally of a benign nature, they remain a serious condition currently due to the recurrence rates seen in some cases and the slight risk they carry of developing into epileptic attacks.

The etiology of febrile seizure is still not clear. Various factors have been described in the pathophysiology of febrile seizures like bacterial and viral infections, susceptibility of the immature brain to temperature, association with interleukins, circulating toxins, trace element deficiency and iron deficiency[1]. Role of trace elements like selenium, magnesium, copper and zinc have been described in association with febrile seizures. Trace elements appear to play a role by their ability to modulate neurotransmission by acting on ion channels and their coenzyme activity.[2-5]

Zinc is an important element in growth, development and normal brain function. It is also an important cofactor for different enzymes, and is involved in cellular growth and differentiation, enzymatic activity of different organs, proteins and cellular metabolism. In brain, zinc is present in synaptic vesicles in subgroup of glutaminergic neurons. In this form it can be released by electrical stimulation and may serve to modulate responses at receptors for number of different neurotransmitters. These include both excitatory and inhibiting receptors particularly NMDA (N-methyl-D aspartate) and GABA (Gamma aminobutyric acid) receptors respectively.[6,7]

Decreased zinc levels modulate the activity of glutamic acid decarboxylase, the rate limiting enzyme in the synthesis of GABA, which is a major inhibitory neurotransmitter.7 Any abnormalities of GABAergic function, including synthesis, synaptic release, receptor composition, trafficking or binding, and metabolism, can each lead to a hyperexcitable, epileptic state.[8] Zinc has an inhibitory effect on NMDA receptors which is responsible for excitatory phenomenon after binding with glutamate.[9] Thus decreased zinc levels may play a role in pathogenesis of febrile seizures.

This study aims to determine zinc levels in children who have febrile convulsions and thus help to reveal possible associations between zinc deficiency and febrile convulsions.

MATERIAL AND METHODS
The present study was a cross sectional study conducted for0ne year during 2014 to 2015. A total of 40 children aged between 6 months to 5 years fulfilling the inclusion criteria were included. Inclusion criteria were children with simple febrile seizure and and normal development. Febrile seizures were defined as seizures accompanied with fever (≥38°C) without Central Nervous System

(CNS) infection. Children with diarrhea, pneumonia, protein energy malnutrition, developmental delay and or neurological deficit and children on zinc therapy were excluded from the study. Socio-demographic data, seizure details, nature of febrile illness, family history of epilepsy/febrile seizures, temperature at admission, nutritional status and vital signs namely heart rate, respiratory rate and blood pressure were measured. The axillary temperature was recorded in all children with mercury thermometer placed in axilla for three minutes, followed by general examination and systemic examination in detail. Another group of similar sex and age matched healthy children (40 cases) was also taken . Taking aseptic precaution, 2 ml of blood from venipuncture using 22 gauge sterile needle, was collected in morning, non-fasting state within 24 hours of contact of patient in children in both the groups. The sample was centrifuged for 3-4 minutes at 3000-4000 rpm; serum thus obtained is collected and preserved at 2-8°C in sterile deionized plain vials. Estimation of serum zinc was done within 4 hours of collection. Method used was based on colorimetric test kit, reagent used was 2-(5-bromo-2-pyridylazo)-5-(N-propyl-N-sulphopropylamino)-phenol. Zinc forms a red chelate with it. Increase in the absorbance of wavelength 560 nm can be measured and is proportional to concentration of the zinc.

In the present study serum zinc level less than 65 µgm/dl was taken as cut off for zinc deficiency.11 The three groups included in the study were compared with respect to serum zinc level.

Statistical methods used were descriptive statistics, contingency table analysis, independent sample t test, 2 way ANOVA. All the statistical calculations were done through SPSS 16.0 for windows.

RESULTS

There was no significant difference regarding sex, age, weight, height, head circumference temperature at admission between the 2 groups. The mean serum zinc was significantly decreased in febrile seizure group compared to normal children (P <0.01). Mean serum zinc level was 48.89 ± 17.17 µgm/dl and 95.80 ± 18.76 µgm/dl in febrile seizure group and healthy children group respectively. [Table 1] There was a statistically significant difference in serum zinc between two groups (P <0.001).

Table 1: Comparison of baseline anthropometric parameters, and mean serum zinc levels between two groups.

Variables	Febrile Seizure group(N 40)	Healthy children group(N 40)
Sex Male/Female	25/15	23/17
Age (months)	22.15± 14.85	25.86±16.89
Mean weight (kg)	12.62± 3.69	12.54±3.78
Mean height (cm)	80.96±11.98	81.92±12.68
Mean head circumference (cm)	47.6 ± 3.56	47.80± 3.59
Mean serum zinc (µgm/dl)	48.89 ± 17.17	95.80±18.76

DISCUSSION

The results of this study revealed that the mean serum zinc level in children affected with febrile seizure is lower than normal healthy children and the difference is statistically significant.

Limited numbers of studies have been conducted regarding the role of zinc in occurrence of febrile seizures. Burhanoðlu M et al. reported that the average level of serum zinc in children affected with febrile seizure was less than control group.[10] Ehsani F et al. carried out study on 34 children with febrile seizure and 58 healthy children revealed that the serum zinc level in children with febrile seizure was lower than those in control group and the difference was significant, statistically.[11] Tütüncüoðlu S et al. reported that the serum zinc level among children with febrile seizure was considerably lower than those in control group.[12] In a study by Hamed SA et al., it was shown that the trace elements such as zinc have crucial role in pathogenesis of seizures.[13] The study of Gündüz Z et al. on 102 children with febrile seizures indicated that the serum zinc level in the group affected with febrile seizures was significantly lower than those in control group.[14] In a very latest study by Mishra OP et al. on 20 children with febrile seizures and 48 children as control group, it was reported that the serum zinc level in children affected with febrile seizure was lower than those in control group, and the difference was significant.[15] In contrast to our study, Kafadar I et al. found no significant difference in serum Zinc concentration in children with febrile convulsion and other two control groups. This may be due to the smaller sample size in their study.[16]

The reason for reduction of serum zinc level in patients affected with febrile seizure is not clear. However, fever and acute infection may have some roles in developing such condition.[17] It is believed that the release of Tumor Necrosis Factor (TNF) and interleukin (IL) during fever or tissue injury may result in reduction of serum zinc level. Izumi Y et al. proposed that the hypozincemia during fever trigger the NMDA receptor, one of the members of glutamate family of receptors, which may play an important role in the initiation of epileptic discharge during febrile seizures.[18]

Limitations of the study was that same children in simple febrile seizure group should have had a follow up serum

zinc estimation when healthy, which would have shown the baseline serum zinc status. Further studies are required in this aspect.

CONCLUSION

This study showed that Serum zinc level was lower in children with simple febrile seizures as compared to healthy children.

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