

## Original Research

### Role of Zinc in Febrile Seizure

Gaurav Kumar Sharma<sup>1</sup>, Anil Kumar Chaudhary<sup>2</sup>, Upendra Prasad Sahu<sup>3</sup>

<sup>1</sup>Junior Resident, <sup>2</sup>Professor and HOD, <sup>3</sup>Associate Professor

Department Of Pediatrics and Neonatology, Rajendra Institute Of Medical Sciences (RIMS), Ranchi, Jharkhand.

#### ABSTRACT:

**Background:** 3 to 5% of children below 5 yrs experience febrile seizure. Zinc has been studied in pathophysiology of febrile seizure. The objective of this study was to compare the serum zinc levels in children with febrile seizure, fever without seizure and in healthy children. **Methods:** The present study was a cross sectional study in which a total of 75 children aged 6 months to 5 years meeting the inclusion criteria were included. The study comprised of 3 groups - Group A: Children with febrile seizures (25 cases), Group B: Children with fever, but no seizures (25 cases) and Group C: Healthy children (25 cases). Serum zinc was determined and compared statistically among these groups. **Results:** There was no significant difference in sex, age, weight, height, temperature at admission and head circumference in the three groups ( $P > 0.05$ ). Mean serum zinc level was  $48.58 \pm 14.86$   $\mu\text{gm/dl}$  in group A,  $62.64 \pm 16.79$   $\mu\text{gm/dl}$  in group B and  $84.90 \pm 19.86$  in Group C. Zinc level was least in febrile seizure group than group B and maximum in group C. **Conclusions:** This study shows that serum zinc levels are decreased in children with febrile seizures which were found to be statistically significant. The level of zinc plays a vital role in the pathogenesis of febrile seizures

**Key words:** Febrile seizure, Serum zinc level, Fever.

Received: 2 December, 2019

Accepted: 28 January, 2020

**Corresponding Author:** Dr. Gaurav Kumar Sharma, Junior Resident, Department Of Pediatrics and Neonatology, Rajendra Institute Of Medical Sciences (RIMS), Ranchi, Jharkhand, India

**This article may be cited as:** Sharma GK, Chaudhary AK, Sahu UP. Role of Zinc in Febrile Seizure. J Adv Med Dent Scie Res 2020;8(4):25-27.

#### INTRODUCTION

Febrile seizures are seizures that occur between ages of 6 to 60 months of age (peak 12-18 months) associated with temperature of 38 degree Celsius or more in the absence of central nervous system infections or metabolic imbalance without previous afebrile seizures. FS is divided into simple (benign) and complex types. Simple febrile seizure is a primary generalized usually tonic clonic type associated with fever lasting for a maximum of 15 minutes not recurring within a 24 hour period. Complex FS is a seizure that lasts longer than 15 min, recurring within 24 h. Parents of these children are concerned about risk of recurrence. Risk factors for recurrence of febrile seizure are :- age less than 1 year, duration of fever in less than 24 h and 38 to 39C (100.4-102.2F) fever as major risk factors. Minor risk factors are a positive family history of FS, family history of epilepsy, Complex FS, day care, male sex, and lower serum sodium at the time of presentation.

The etiology of febrile seizure is not fully clear. Genes implicated are SCN1A, SCN1B, SCN9A and CPA6. Various factors have been described in the pathophysiology of febrile seizures like dysregulation between the proinflammatory IL-1,  $1\beta$ , IL-6 and IL-8 cytokines and anti-inflammatory ILR1-A cytokines in various bacterial and viral infections, susceptibility of the immature brain to temperature, associated circulating toxins, iron deficiency deficiency of trace elements like selenium, magnesium, copper and zinc have been studied in association with febrile seizures. Trace elements may modulate neurotransmission by acting on ion channels and their coenzyme activity. Role of Zinc is an important in growth, development and normal brain functions as it is a co-factor for different enzymes, involved in cellular growth and differentiation, affecting proteins and cellular metabolism. In our brain, zinc is present in synaptic vesicles in a subgroup of glutaminergic neurons released by electrical stimulation and hence may modulate responses at receptors for different

neurotransmitters. These include both excitatory and inhibiting receptors particularly NMDA and GABA receptors respectively. In case of decreased zinc levels the activity of glutamic acid decarboxylase, the rate limiting enzyme in the synthesis of GABA is affected. Any abnormalities of GABAergic function namely synthesis, synaptic release, receptor composition, trafficking or binding, and metabolism, may lead to a hyper-excitability, epileptic state.

The aim of this study is to determine zinc levels in children with febrile seizures and also find an association between zinc deficiency and febrile seizures.

## METHODS

The present study was a cross sectional study conducted at Rajendra Institute of Medical Sciences, Ranchi during the period December 2018 to January 2019. The sample size of 75 children between ages 6 months to 5 years fulfilling the inclusion criteria were included in this study. There were 3 groups - Group A: Children having febrile convulsions (25 cases), Group B: Children with only fever, but no seizures (25 cases) and Group C: Healthy children (25 cases). Inclusion criteria were:- children having simple febrile seizures, acute febrile illness without seizures and normal development. Children with CNS infections, diarrhea, pneumonia, PEM, developmental delay and or neurological deficit and children on zinc therapy were excluded from this study.

Informed and written consent was obtained from parents of all the children in this study. Socio-demographic profile data, details of seizure, pattern of febrile illness, family history of epilepsy/febrile seizures, temperature at admission, nutritional status and vitals like heart rate, respiratory rate blood pressure etc were measured. The axillary temperature was recorded with mercury thermometer placed in axilla for three minutes, following which general and systemic examination were done in detail. 2 ml of blood using sterile needle, was collected aseptically in morning, non-fasting state within 24 hours patients appearing in all the 3 groups. The sample was centrifuged for 4 minutes at 3000-4000 rpm and serum collected via this was preserved at 2-8°C in sterile deionized plain vials. Estimation of serum zinc

was done using colorimetric test kit within 6 hours of collection. The reagent used was 2-(5-bromo-2-pyridylazo)-5-(Npropyl-N-sulphopropylamino)-phenol. Zinc forms a red chelate with it. The mechanism is that there is increase in the absorbance of wavelength at 560 nm which is proportional to the concentration of zinc.

A cut off level of serum zinc at 65 µgm/dl was taken in this present study for zinc deficiency. Zinc levels were compared in the three groups. Various statistical methods used were contingency table analysis, descriptive statistics, independent sample t test, 2 way ANOVA. All the statistical calculations were done through SPSS 16.0 software for windows. **RESULTS** There was no significant difference regarding sex, age, weight, height, head circumference temperature at admission between the 3 groups. :

Baseline characteristics, anthropometric parameters, temperature at admission and mean serum zinc levels in 3 groups. [Table 1]

The mean serum zinc was compared in different groups. It was found to be significantly decreased in febrile seizure group compared to febrile illness group and normal children ( $P < 0.01$ ). No statistically significant difference in the serum zinc levels in relation to age and sex parameters were found in these groups. 66% of Group A and 34% of Group B had serum zinc  $< 65$  µgm/dl. There was a statistically significant difference in serum zinc between the groups ( $P < 0.005$ ).

## DISCUSSION

The results obtained in this study reflect that the mean serum zinc level in children with febrile seizure is lower than children in febrile group and normal healthy children and the difference being statistically significant.

Other studies that have been conducted regarding the role of zinc in febrile seizures like Burhanoglu M et al. had found a similar correlation. Ehsani F et al. study which was carried out study on 34 children with febrile seizure and 58 healthy children had also found lower serum zinc levels in children with febrile seizure was than those in control group and the difference was significant, statistically.

**Table 1:** Baseline characteristics, anthropometric parameters, temperature at admission and mean serum zinc levels in 3 groups

Variables	Febrile seizure group n=25	Febrile group n=25	Normal children n=25
SEX : male female	16(64%) 9(36%)	15(60%) 10(40%)	14(56%) 11(44%)
AGE IN MONTHS	26.14 ± 14.83	27.58 ± 15.81	29.72 ± 15.41
MEAN WEIGHT (kg)	11.84 ± 2.32	12.62 ± 1.44	13.54 ± 2.67
MEAN HEIGHT(cm)	82.84 ± 11.22	84.92 ± 15.09	85.89 ± 15.26
MEAN HEAD CIRCUMFERENCE (cm)	48.5 ± 2.33	48.28 ± 2.21	48.78 ± 2.49
Mean temperature at admission (°C)	38.67	38.64	
MEAN SERUM ZINC(mcg/dl)	48.58 ± 14.86	62.64 ± 16.79	84.90 ± 19.86

Tütüncüoğlu S et al. reported that the serum zinc level among children with febrile seizure was considerably lower than those in control group. 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. 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. Contrary to our study, Kafadar I et al. had 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.

There is a vital role of zinc in nervous system function too. Brain contains an abundant value of zinc, especially in hippocampus region. Upto 15 percent of zinc may be stored in synaptic vesicles in glutamatergic synapses thus acts as a neurotransmitter and potentiates the communicating and locomotive function, and may have some role in evolution. Zinc deficiency diminishes hippocampal zinc and that may lead to seizure discharges. But the complete mechanism of this has been poorly understood. Further studies are required to for better analysis.

#### LIMITATIONS OF THIS STUDY

Limitations of the study were zinc estimation in the present study was done by colorimetric method.

Atomic Absorption Spectrometry (AAS) is a more accurate method to measure serum zinc level. Though AAS was not done, there is a good correlation between AAS and colorimetric method which is used in the present study. The 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 shows that serum zinc levels are decreased in children with febrile seizures. The level of zinc plays a vital role in the pathogenesis of febrile seizures. So further studies need to be done to establish the efficacy and safety profile of zinc as a drug to prevent recurrences of febrile seizures.

#### REFERENCES

1. Margaretha L, Masloman N. Correlation between serum zinc level and simple febrile seizure in children. *Pediatric Indonesia*. 2010;50: 326-330.
2. Ehsanipour F, Talebi-Taher M, Harandi NV, Kani K. Serum zinc level in children with febrile convulsion and its comparison with that of control group. *Iran J Pediatr*. 2009;19:65-68.
3. Vestergaard M, Obel C, Henriksen TB, Christensen J, Madsen KM, Ostergaard JR. The Danish National Hospital Register is a valuable study base for epidemiologic research in febrile seizures. *J Clin Epidemiol*. 2006;59:61-66.
4. Daoud AS, Batiha A, Abu-Ekteish F, Gharaibeh N, Ajlouni S, Hijazi S. (2002): Iron status: a possible risk factor for the first febrile seizure. *Epilepsia*. Jul; 43(7):740-743.

5. American Academy of Pediatrics. American Academy of Pediatrics Steering Committee on Quality Improvement and Management Subcommittee on Febrile Seizures. *Febrile Seizures: clinical practice guideline for the longterm management of the child with simple febrile seizures*. *Pediatrics* 2008;121:1281-6
6. Millichap JG, Millichap JJ Role of viral infections in the etiology of febrile seizures *Pediatr Neurol* 2006;35(3): 165-72
7. Holtzman ft Obana K, Olson J. Hyperthermia-induced seizures in the pup:a model for febrile convulsions in children. *Science* 1981;213(4511):1034-6
8. Tsai FJ Hsieh YY, Chang CC. Polymorphisms for interleukin I beta exon 5 and interleukin 1 recepto antagonist in Taiwanese children with febrile convulsions. *Arch Pediatr Adolesc Med* 2002;156(6):545-8.
9. Virta M, Hueme M. Increased plasma levels of pro-and anti-inflammatory cytokines in patients with febrile seizures. *Epilepsia* 2002;43(8):920-3.
10. Amiri M, Farzin L, Moassesi ME, Sajadi F. Serum Trace Element Levels in Febrile Convulsion *Biol Tr Elem Res* 2010;135(1):38-44
11. Kumari PL, Nair MK, Nair SM, Kailas L, Geetha S. Iron deficiency as a risk factor br simple febrile seizures – a case control study *Indian Padiatr* 2011;49(1):17-9
12. Ehsoni F, Vahid-Harandi M, Kany K. Determination of serum Zinc in children affected by febrile convulsion and comparison with control group. *The journal of Iranian Medical sciences University* 2006;12:219-76
13. Margaretha L, Masloman N. Correlation between serum Zinc level and simple febrile seizure in children. *Pediatr Indones* 2010;50(6):326-30.
14. Iman Abd El Rehim Mohamed Aly, Howyda Mohamed Kmal, Doaa Refaey Soliman and Mona Hassan Mohamed. Iron profile parameters and serum zinc and copper levels in children with febrile convulsions in Banha. *Journal of American Science* 2014;10(7): 320-7.
15. Siddarth S. Joshi and Sumanth Shetty. Zinc levels in Febrile Seizures. *International Journal of Biomedical Research* 2014;5(10):85-89
16. Ganesh R, Janakiraman L. Serum Zinc levels in children with simple febrile seizure. *Clin Pediatr (Phila)* 2008;47(2):164-66.
17. Heydarian F, Ashrafzadeh F, Ghasemian A. Serum Zinc level in patients with simple febrile seizure. *Iran J Child Neurology* 2010;4(2):41-4.
18. Mahyar A, Pahlavan A, Varasteh-Nijad A. Serum Zinc level in children with febrile seizure. *Acta Medica Iranica* 2008;46(6):67-9.
19. Kafadar I, Akini AB, Pekun F, Ada E. The Role of Serum Zinc Level in Febrile Convulsion Etiology. *J Pediatr Inf* 2012;6:90-3.
20. Talebian A, Vakili Z, Talar SA, Kazerni M, Mousavi GA. Assessment of the relation between serum Zinc and magnesium levels in children with febrile convulsion. *Iranian Journal of Pathology* 2009;4:157-60.
21. Gündüz Z, Yavuz I, Kopardal M, Kurnanda S, Saraymen R. Serum and cerebrospinal fluid Zinc levels in children with febrile convulsions. *Acta Paediatr Jpn* 1996;38(3):273-41.
22. World Health Organization and United Nations Children Fund. Clinical management of acute diarrhoea. WHO/UNICEF Joint Statement; 2004. 8(3):237-41
23. Barhanoglu M, Tutuncuoglu S, Coker C, Tekgul H, Ozgur T. HypoZincaemia in febrile convulsion. *Eur J Pediatr* 1996;155(6):498-501.