

Serum zinc level in children presenting with febrile seizures

Muhammad Waqar Rabbani¹, Ibad Ali², Hafiz Zahid Latif³
Abdul Basit⁴, Muhammad Ali Rabbani⁵

ABSTRACT

Objective: To determine the frequency of low serum zinc level in children presenting with febrile seizures at The Children's Hospital and the Institute of Child Health (CH/ICH) Multan.

Methods: This is an observational cross sectional study conducted at the Department of Pediatric Medicine, The Children's Hospital and the Institute of Child Health, Multan from September 2010 to March 2011. Children (6 months to 6 years of age) presenting with febrile seizures who satisfied inclusion and exclusion criteria were enrolled for the study. Cause of fever was determined after detailed history, physical examination and relevant investigations. Four milliliters centrifuged blood sample was preserved in acid washed test tube. Separated serum was used to measure serum zinc level by employing Randox kit on auto-analyzer in all cases. The outcome variable (serum zinc level) was recorded on a predesigned proforma.

Results: Out of 100 enrolled children, there were 66 (66%) male with male to female ratio of 1:0.52. Mean age of the children was 23.97±14.45 months. Upper respiratory tract infection was the most frequent cause of fever apparent in 24 children (24%) followed by tonsillitis 17 (17%), pneumonia 16 (16%), urinary tract infection 16 (16%), otitis media 15 (15%), and bronchiolitis 12 (12%). Frequency of low serum zinc level was 26% in children with febrile seizures.

Conclusion: Zinc deficiency could be a potential risk factor for febrile seizure in children.

KEY WORDS: Febrile Seizure, Convulsion, Serum zinc level, Epilepsy.

doi: <http://dx.doi.org/10.12669/pjms.294.3464>

How to cite this:

Rabbani MW, Ali I, Latif HZ, Basit A, Rabbani MA. Serum zinc level in children presenting with febrile seizures. *Pak J Med Sci* 2013;29(4):1008-1011. doi: <http://dx.doi.org/10.12669/pjms.294.3464>

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1. Dr. Muhammad Waqar Rabbani, DCH, FCPS,
 2. Dr. Ibad Ali, DCH, FCPS,
 3. Dr. Hafiz Zahid Latif, MBBS,
 4. Dr. Abdul Basit, MBBS,
 5. Muhammad Ali Rabbani,
Undergraduate MBBS student,
Nishtar Medical College,
Multan, Pakistan.
- 1-4: Department of Pediatric Medicine,
The Children Hospital & The Institute of Child Health,
Multan, Pakistan.

Correspondence:

Dr. Muhammad Waqar Rabbani, DCH, FCPS,
Associate Professor Pediatrics,
Department of Pediatric Medicine,
The Children Hospital & The Institute of Child Health,
Multan, Pakistan.
E-mail: w.rabbani@yahoo.com

* Received for Publication: February 4, 2013

* Accepted: June 1, 2013

INTRODUCTION

A seizure is a paroxysmal event caused by abnormal electrical discharge inside the brain.¹ Febrile convulsion; twice as common in boys as in girls, is one of the most common type of seizure occurring in children between 5 months and 6 years of age, accounting for 30% of all seizures in children.^{2,3} This is an age dependent response of the immature brain to fever in children,⁴ who do not have an intracranial infection, metabolic disturbance, or history of afebrile seizures.⁵ Eighty to eighty five percent febrile seizures occur between 6 months and 3 years of age, with peak incidence at 18 months.^{6,7} Children with a simple febrile seizure has potential for recurrence and 2-7% of children may develop epilepsy by adolescence.^{8,9} Contrary to

simple febrile seizure, complex febrile seizures are prolonged (>15 minutes), focal and occur more than once in 24 hours.¹⁰

Zinc is an important micronutrient that plays a significant role in growth and development, immune system response, enzymatic activity of different organs, proteins and cellular metabolism, neurological functions, nerve impulse transmission and hormone release.^{11,12} The possible role of zinc deficiency in provoking febrile seizures has been reported in different studies.^{13,14} Zinc stimulates the activity of pyridoxal kinase, the enzyme that modulates GABA level, a major inhibitory neurotransmitter.¹⁵ It also modifies the affinity of neurotransmitters and thus prevents the excitatory neuronal discharge.² In addition, zinc significantly reduces the severity of illness and the duration of fever in children with pneumonia and diarrhea by the activation of immune enhancing T-cells.^{11,16}

Earlier no such study has been done in this region to see the association between low serum zinc level and febrile fits. This study will provide a base line data and help in the formulation of guidelines for zinc supplementation as a part of management of febrile fits.

METHODS

This study was carried out from September 2010 to March 2011 at the department of Pediatric Medicine, the CH/ICH Multan, Pakistan. Patients, 6 months to 6 years of age presenting in Emergency department with fever ($\geq 38^{\circ}\text{C}$) and history of fits within last 6 hours, having normal cerebrospinal fluid examination and normal; serum glucose, sodium, potassium, calcium and magnesium levels were included. The patients who had any evidence of central nervous system infection, epilepsy, metabolic seizures or those who are already on zinc therapy for any other ailment like malnutrition, diarrhea, pneumonia or acrodermatitis enteropathica were excluded.

This cross sectional study was performed after permission from Institutional Ethical Committee.

Table-I: Low Serum Zinc Level in Febrile Seizure Patients in Relation to Age Groups.

Age in years	No. of Patients	No. of Patients with Low Serum Zinc	Percentage (%)
0.6 - 3	63	15	23.8
>3 - 6	37	11	29.7
Total	100	26	

Key: Age is rounded to the nearest year.

All the details of the study were explained to the parents/guardians and informed consent was taken. Cause of fever was determined by detailed history, complete physical examination and relevant investigations (complete blood count, complete urine examination, malarial parasite, and typhidot test). CSF examination was done in all patients younger than 1.5 years of age and selective older patients who had any clinical suspicion of central nervous system infection. Serum zinc level was assessed in all patients within 6 hours of febrile seizure. Four milliliters centrifuged blood sample was preserved in acid washed test tube. Separated serum was used to measure serum zinc level by employing Randox kit UK on auto-analyzer in the chemical pathology laboratory of the hospital. Normal values of serum zinc level were defined from 70–120 $\mu\text{g}/\text{dl}$ in pediatric age group (5 months to 6 years).

The data was analyzed using computer program SPSS-10. Descriptive statistics were applied. Quantitative variable like age was analyzed by mean and standard deviation. Qualitative variables like gender and serum zinc level which is an outcome variable (normal/abnormal) were analyzed by taking frequencies and percentages.

RESULTS

Hundred children (6 months to 6 years of age) with febrile seizure were included in the study. Mean age of the children was 23.97 ± 14.45 months. Frequency of low serum zinc level was 26% in children with febrile seizures. Sixty three (63%) children were between 6 months to 3 years of age while rest of the 37(37%) were between >3 years to 6 years of age. Low serum zinc level in different age groups is given in Table-I. There were 66 (66%) male children with a male to female ratio of 1:0.52, frequency of low serum zinc level with reference to male and female patients has been described in Table-II.

Upper respiratory tract infection was the most frequent cause of fever evident in 24 children (24%)

Table-II: Low Serum Zinc Level in Febrile Seizure Patients in Relation to Gender.

Sex	Total No. of Patients	No. of Patients with Low Serum Zinc	Percentage (%)
Male	66	19	28.8
Female	34	7	20.6
Total	100	26	

Key: Age is rounded to the nearest year.

Table-III: Low Serum Zinc Level in Febrile Seizure Patients with Relation to Causes of Fever.

<i>Causes</i>	<i>Total No. of Patients</i>	<i>No. of Patients with Low Serum Zinc</i>	<i>Percentage (%)</i>
Upper respiratory tract infection	24	6	25.0
Tonsillitis	17	5	29.4
Pneumonia	16	5	31.3
Urinary tract infection	16	5	31.3
Otitis media	15	3	20.0
Bronchiolitis	12	2	16.7
Total	100	26	

followed by tonsillitis 17 (17%), pneumonia 16 (16%), urinary tract infection 16 (16%), otitis media 15 (15%), and bronchiolitis 12 (12%) in children having febrile seizures. Rate of low serum zinc level in various causes of fever is mentioned in Table-III.

DISCUSSION

Febrile seizure is a commonly occurring problem in young children. Although its pathogenesis is debatable, studies have revealed that the genetic factors, family background, immunologic disorders, iron deficiency and zinc deficiency may play a role in febrile seizure. The infection state exhibits non-specific host responses, including immune responses such as changes in the concentrations of certain plasma proteins, cytokines (tumor necrosis factor, interleukin-1, interleukin-6) and interferon which may result in reduction of serum zinc level. Hypozincemia has been suggested as a possible change during the rising phase of body temperature in febrile patients.¹⁷

This study was conducted at the CH/ICH Multan. Age of presentation in majority of children (63%) was 6 months to 3 years. Frequency of low serum zinc level was found in 26% children with febrile seizures in this study, which is comparable with several international studies in children with febrile seizure. Mollah MA et al¹⁴ in 2008 published a study comparing serum and CSF Zinc levels of febrile seizure children to their matched non-seizure febrile peers. Mean Zn concentration in both serum and CSF was less in febrile seizure children than in their matched non-seizure febrile peers ($p < 0.001$). Kumar L et al¹⁸ in a recent case control study found that mean serum zinc level was significantly lower in cases as compared to control

($p < 0.05$) in children having febrile seizure. Ganesh R et al¹³ compared serum zinc levels in 38 cases of simple febrile seizure with 38 age matched controls with statistically significant results ($p < .001$). Amiri M et al,¹⁹ Modarresi MR et al,²⁰ Hydarian F et al,²¹ Lee J and Kim JH,²² and Talebian A et al,²³ also gave similar results which are comparable with our study. However Garty BZ et al²⁴ had their findings which did not support the hypothesis that febrile convulsions are related to the reduced zinc concentration.

One limitation of our study is the lack of a control group. Furthermore, it was done in small number of patients. As the base line zinc level was lacking in these febrile seizure patients, which prevented us from reaching a definite conclusion whether infectious diseases were responsible for low zinc levels or there was pre-existing hypozincemia. More prospectively designed, multi center studies involving larger sample sizes are needed to answer these questions.

CONCLUSION

In conclusion, this study revealed that the low serum zinc levels (26%) in our study are fairly sufficient to support the hypothesis that Zinc deficiency could be a potential risk factor for febrile seizure in children.

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Authors Contribution:

Rabbani MW, Ali I, Latif HZ and Basit A: Conceived, designed, manuscript writing, editing and review of manuscript. Rabbani MA: Editing and review of manuscript.