

Original Research Article

Serum zinc levels in children with simple febrile seizures

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ABSTRACT

Background: Febrile seizures are the most common seizures in childhood and are often associated with nutritional deficiencies. The present study was done to find any correlation of serum zinc levels in children with simple febrile seizures.

Methods: This study was a hospital based prospective case control study, involving 60 children (30 cases and 30 controls) aged between 6 months to 60 months. Serum zinc level was measured in all subjects by atomic absorption spectrophotometer. Data was analysed by using frequency, percentage and Pearson's chi square test.

Results: Most cases (80%) had serum zinc levels <90 mcg/dl, in comparison with children in the control group where only 30% had serum zinc levels <90 mcg/dl. The mean serum zinc level was 78.9 ± 14.26 mcg/dl in cases with simple febrile seizures and 96.7 ± 12.12 mcg/dl in the control group.

Conclusions: The mean serum zinc level was significantly lower in children with simple febrile seizures in comparison with controls.

Keywords: Children, Febrile, Seizures, Zinc

INTRODUCTION

Febrile seizures are the most common provoked seizures affecting children. Incidence varies between 3-10%, whereas studies from the developed world report 2-5% of all children between the ages of 6 months to 5 years being affected.¹

Febrile seizures are defined as seizures that occur in children between the age of 6 to 60 months with a temperature of 38°C (100.4°F) or higher, not as a result of central nervous system infection or any metabolic imbalance, which occur in the absence of a history of prior afebrile seizures. Simple febrile seizures (SFS) are febrile seizures which are primary generalized, lasting less than 15 min, and not recurrent within a 24 hour period.²

Zinc is the second most common trace mineral in the body and is present in every living cell. Zinc is present in nucleic acids, gene regulating proteins and more than 200 metalloenzymes. Zinc is also a cofactor of glutamate decarboxylase, an enzyme needed for the synthesis of Gamma-amino butyric acid (GABA), which is an important inhibitory neurotransmitter responsible for seizures. Hence it is postulated that zinc deficiency might have a role in the pathogenesis of febrile convulsion. This study was an attempt to evaluate the association between serum zinc levels and simple febrile seizures.

METHODS

This study was a case control study, conducted in 60 children in the age group of 6 months to 5 years admitted to the paediatric ward and PICU (Paediatric Intensive

care Unit) of a tertiary care medical college hospital between 1st November 2015 and 31st May 2017. After taking an informed written consent, 30 children with simple febrile seizures were enrolled as cases. For every case included in the study, the next child aged between 6 months to 5 years, admitted to the paediatric ward with any febrile illness without seizures was taken as control without matching of age or gender. The age, gender, nature of febrile illness, the seizure type and duration and family history of febrile seizures/epilepsy was recorded. Physical examination findings including temperature at admission, anthropometry, nutritional status was recorded in a prevalidated proforma. Serum zinc level was estimated along with other investigations at the time of admission. Data was analyzed by using frequency, percentage and Pearson's chi square test. The study protocol was approved by the ethical committee of the institution.

RESULTS

All 60 subjects included in the study had serum zinc levels in the normal range of 60-120 mcg/dl.

The serum zinc levels were between 60-90 mcg/dl in 24 cases (80%) and remaining 6 cases (20%) had serum zinc levels between 90-120 mcg/dl (Table 1). The mean serum zinc level in cases with simple febrile seizures was 78.9 ± 14.26 mcg/dl (Figure 1A).

Table 1: Comparison of serum zinc levels in cases and controls.

Serum zinc levels	Cases	Controls
60-90 mcg/dl	24 (80%)	9 (30%)
90-120 mcg/dl	6 (20%)	21 (70%)
Total	30 (100%)	30 (100%)

This finding had a p value of 0.000434, which is statistically highly significant. Odds ratio - 8.5, 95% C.I - 30.46

In the control group, the serum zinc levels were between 60-90 mcg/dl in only 9 children (30%) and 21 children (70%) had between 90-120 mcg/dl (Table 1). The mean serum zinc level in the control group was 96.7 ± 12.12 mcg/dl (Figure 1B).

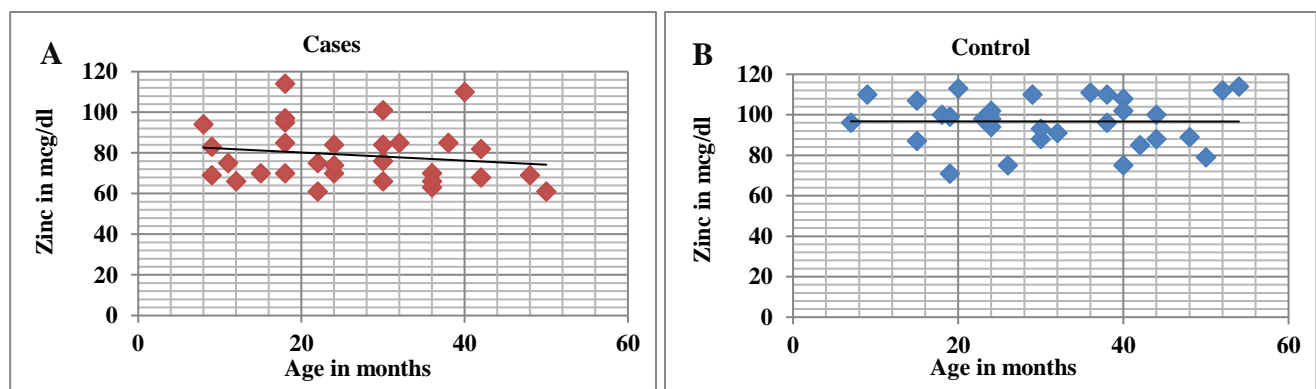


Figure 1: (A and B) Scatter Plot showing serum zinc levels in cases and controls.

Serum zinc levels based on age group

A total of 16 cases and 12 controls were in the age group of 6 months to 2 years, while 14 cases and 18 controls were in the 2 to 5 years age group. The mean age was 27.3 ± 12.14 months in case group and 30.03 ± 12.99 in control group.

Out of 16 cases below 2 years, 12 children (75%) had serum zinc levels between 60-90 mcg/dl and 4 children (25%) had serum zinc level more than 90 mcg/dl. In the control group, only 2 out of 12 children (16.66%) below 2 years had a serum zinc level less than 90 mcg/dl (Table 2). The mean serum zinc levels were 80.1 ± 13.64 and 97.9 ± 10.5 in cases and controls between 6 months to 2 years respectively.

Among 14 cases between the age group of 2 years to 5 years, 12 cases (85.7%) had serum zinc levels <90 mcg/dl in comparison with 7 controls (38.8%). Only 2 cases (14.3%) in this age group had serum zinc levels >90 mcg/dl, against 11 controls (61.2%) (Table 3). The mean serum zinc levels were 77.2 ± 12.9 and 96.1 ± 11.8 in cases and controls between 2-5 years respectively.

Table 2: Serum zinc levels in children between 6 months to 2 years.

Serum zinc	Cases	Controls
60-90 mcg/dl	12 (75%)	2 (16.7%)
90-120 mcg/dl	4 (25%)	10 (83.3%)
Total	16 (100%)	12 (100%)

Table 3: Serum zinc levels in children between 2-5 years.

Serum zinc	Cases	Controls
60-90 mcg/dl	12 (85.7%)	7 (38.8%)
90-120 mcg/dl	2 (14.3%)	11 (61.2%)
Total	14 (100%)	18 (100%)

Serum zinc levels in cases based on gender

Out of 20 male children, 17 children (85%) had serum zinc levels between 60-90 mcg/dl and 3 (15%) had serum zinc levels more than 90 mcg/dl. Among 10 females, 7 cases (70%) had serum zinc levels between 60-90 mcg/dl and 3 cases (30%) had zinc levels more than 90 mcg/dl. Among cases, the mean serum zinc levels were 75.6 ± 12.6 in males and 85.5 ± 13.9 in females. In the control group, the mean serum zinc levels were 92.8 ± 12.8 in males and 101.6 ± 8.1 in females (Tables 4 and 5).

Table 4: Serum zinc levels in male children.

Serum zinc level	Cases	Controls
60-90 mcg/dl	17 (85%)	7 (60%)
90-120 mcg/dl	3 (15%)	10 (40%)
Total	20 (100%)	17 (100%)

Table 5: Serum zinc levels in female children.

Serum zinc level	Cases	Controls
60-90 mcg/dl	7 (70%)	2 (15.39%)
90-120 mcg/dl	3 (30%)	11 (84.61%)
Total	10 (100%)	13 (100%)

Serum zinc levels based on duration of seizures

Out of 17 children who had seizure duration of less than 5 minutes, 8 children had serum zinc levels between 60-90 mcg/dl and 9 children had zinc levels more than 90 mcg/dl. Among 7 children who had seizure duration of 5 to 10 minutes, 4 had zinc levels between 60-90 mcg/dl and 3 had serum zinc levels more than 90 mcg/dl. In 6 children who had seizure duration of 10 to 15 minutes, 5 children had zinc levels between 60-90 mcg/dl and only one child had zinc levels more than 90 mcg/dl. The mean serum zinc level was 79.3 ± 13.3 , 82 ± 18.3 and 74.1 ± 5.8 in children with seizure duration lasting <5 minutes, 5-10 minutes and 10-15 minutes respectively.

Serum zinc levels based on past history of seizures

Out of 7 children who had past history of febrile convulsion, 3 children had serum zinc levels in the range of 60-90 mcg/dl and 4 children had zinc levels more than 90 mcg/dl. Among 21 children who did not have past history of seizures, 14 children had zinc levels between 60-90 mcg/dl and 7 children had serum zinc levels more than 90 mcg/dl. The mean serum zinc level was 80.2 ± 13.8 in children with past history of febrile seizures

and 78.5 ± 13.8 in children with no febrile seizures in the past.

Serum zinc levels based on nutrition status

In this study, 5 children had grade I malnutrition, out of which 2 children had serum zinc levels between <90 mcg/dl and 3 had zinc levels >90 mcg/dl. Among 25 children without malnutrition, 15 had serum zinc levels <90 mcg/dl and 10 children had serum zinc levels >90 mcg/dl. The mean serum zinc level was 85.8 ± 15.3 in children with febrile seizures and malnutrition and 77.5 ± 13.1 in children with febrile seizures and no malnutrition.

DISCUSSION

In this prospective case control study, we have tried to compare serum zinc levels in febrile children with and without seizures and also correlate with age, gender, nutritional status, duration of seizures and past history of febrile seizures. The present study included 30 children with simple febrile seizures (SFS) as cases and 30 children with febrile illness without seizures as controls.

Serum Zinc levels in Cases vs Controls

The serum zinc level was in the normal range of 60-120 mcg/dl in all cases and controls but 80% of cases (24 out of 30) had serum zinc levels <90 mcg/dl, whereas only 30% children in the control group (9 out of 30) had serum zinc levels <90 mcg/dl. The mean serum zinc level in the SFS group (cases) and the control group was 78.9 ± 14.26 mcg/dl and 96.7 ± 12.12 mcg/dl respectively. This finding had a p value of <0.001, which was statistically highly significant.

The results of the studies by Gayathri D et al, Karthikeyan P et al Mohammad Reza et al and Heydarian F et al were very similar to findings of this study. They found significantly lower mean serum zinc levels in children with SFS in comparison to febrile controls without seizures.³⁻⁶

Studies by Ganesh R et al, and Mahyar A et al, compared serum zinc levels in children with simple febrile seizures and age-matched healthy controls. The serum zinc level was significantly lower in children with simple febrile seizures.⁷⁻⁸

Ganesh R et al, also compared serum zinc levels in children with simple febrile seizures, epileptic seizures and healthy controls and concluded that serum zinc levels were lower in children with febrile seizures than in those with epileptic seizures and normal children.⁹

Lee et al, and Ehsanipour et al, found that the serum zinc level was significantly lower in children with febrile seizures (case group) when compared to controls (children with fever without seizures and children with non-febrile seizures).^{10,11}

Similarly, Sampath Kumar et al, concluded that children with febrile convulsions both simple and complex have significantly lower serum zinc levels when compared to children with fever alone without convulsions.¹²

Contrary to findings of this study, Cho WJ et al, from Korea did not find any significant difference between serum zinc levels in children with febrile seizure from the control group.¹³

Papierkowski A et al, Mollah MA et al and Gunduz et al, showed significant decrease in values of serum and CSF zinc levels in children with febrile seizures in comparison with febrile children without seizures.¹⁴⁻¹⁶ On the contrary, Garty et al found no reduction in CSF Zinc concentration in children with febrile convulsions.¹⁷

Age

In this study, 16 cases (53.33%) were in the age group of 6 months to 2 years and 14 cases (46.66%) were between 2 to 5 years. The mean age of cases and controls in this study was 27.3 ± 12.14 months and 30.03 ± 12.99 months. The mean serum zinc levels were 80.1 ± 13.64 and 97.9 ± 10.5 in cases and controls between 6 months to 2 years respectively. The mean serum zinc levels were 77.2 ± 12.9 and 96.1 ± 11.8 in cases and controls between 2 to 5 yrs respectively.

These findings were similar to Mahyar et al and Ganesh et al, who reported a mean age of 27.13 ± 15.12 and 23.8 months in cases respectively. Hartfield et al and Gayathri D et al reported that maximum children with febrile seizures were in the age group less than 24 months and mean age was 17.9 months.¹⁸ Guzman A R et al, found that 55% of children with febrile seizures were aged between 6 months and 24 months.

Bhat J A et al found that more than three fourth of the patients with febrile seizures were below 24 months with a mean age of 22.14 ± 15 months.¹⁹

Gender

In this study, most of the children with SFS, both males (85%) and females (70%) had serum zinc levels <90 mcg/dl. The mean serum zinc levels were 75.6 ± 12.6 in males and 85.5 ± 13.9 in females. In the control group, the mean serum zinc levels were 92.8 ± 12.8 in males and 101.6 ± 8.1 in females. Males predominated in the study by Bhat J A et al with a male: female ratio of 2.9:1 in total 150 study population. Talebian A et al, in their case control study found no relationship between serum zinc levels with gender, duration or type of seizures.²⁰

Duration of Seizures/Past history of Seizures/ Nutrition status

There was no correlation between the duration of seizures and mean serum zinc levels in this study. The mean

serum zinc level was 79.3 ± 13.3 , 82 ± 18.3 and 74.1 ± 5.8 in children with seizure duration lasting <5 min, 5-10 min and 10-15 min respectively. Only 7 children in this study had a past history of febrile convulsions. The mean serum zinc levels were 80.2 ± 13.8 in children with past history of febrile seizures and 78.5 ± 13.8 in children with no febrile seizures in the past. In this study, only 5 children had grade- I malnutrition and the mean serum zinc level was 85.8 ± 15.3 in children with febrile seizures and malnutrition and 77.5 ± 13.1 in children with febrile seizures and no malnutrition.

The serum zinc levels did not show any significant correlation with age of onset, gender, family history and nutritional status in studies by Talebian A et al, and Sampathkumar P et al.^{20,12}

Margaretha L et al, and Gayathri D et al, found that children with longer duration of seizures had lower serum zinc levels.^{21,3}

CONCLUSION

The mean serum zinc levels were lower in children with simple febrile seizures when compared to febrile children without seizures. Low serum zinc level may have a role in SFS. Further studies with larger numbers would be needed for more definitive correlation of serum zinc levels in SFS.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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