

## Original Research Article

# Low serum zinc and magnesium—a possible risk factor for first episode Simple febrile seizures in children between 6 months to 5 years of age

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### ABSTRACT

**Background:** Febrile seizure is the most common type of seizure in children. The incidence of febrile seizure is 5-10% in India. There are multiple aetiologies like high grade fever; genetic predisposition, viral infections and trace elements deficiency like iron, zinc, magnesium and calcium are postulated to be risk factors for developing febrile seizures. Recent studies had shown there is a significant association between low serum zinc, low serum magnesium levels and febrile seizures in children.

**Methods:** This was a case control study with 40 children in each group. Children aged 6 months to 5 years with first episode of simple febrile seizures who attends the out-patient department/emergency room (OPD/ER) were included in case group consecutively and 40 children with acute febrile illness without febrile seizures were included in control group. Serum zinc and magnesium levels were estimated for all the children along with other investigations after proper consent from parents. Using statistical package for the social sciences (SPSS) software, independent sample t test was used to analysis the observations between the two groups. Normal lab reference value of serum zinc was 60-120 µg/dl and serum magnesium was 1.7-2.5 mg/dl.

**Results:** The incidence of febrile seizure was high (37.5%) in children between 1-2 years and male (55%) children had increased incidence when compared to female children in case group. The children with febrile seizure had significantly low levels of serum zinc with mean value of 35.08 µg/dl (±8.56) when compared to control group with mean value of 70.23 µg/dl (±13.41) and serum magnesium level in case group was 1.35 mg/dl (±0.29) versus 1.68 mg/dl (±0.42) in control group, which was also statistically significant.

**Conclusions:** The incidence of febrile seizure was high in children between 1-2 years of age with male preponderance. The serum levels of both zinc and magnesium is significantly low in children with febrile seizure pointing a need of further studies in role of supplemental zinc and magnesium in this age group to reduce the incidence of febrile seizures.

**Keywords:** Febrile seizure, Serum zinc, Serum magnesium

### INTRODUCTION

Fever in a child below 5 years is a common problem and febrile seizures in this age group are still an unpredictable illness. There is no specific single risk factor or aetiology for developing febrile seizures in children. The recurrence of febrile seizure is also unpredictable. Reduced zinc level had been found in children with febrile seizures. Zinc is an

essential trace element associated with all the enzymatic function of our cells. In the central nervous system zinc plays a critical role as neuromodulator, it helps in communication between neurons. Dietary zinc deprivation affects zinc homeostasis in brain and enhances susceptibility to epileptiform discharges. Zinc has an important role in gamma aminobutyric acid (GABA) synthesis. Zinc has a regulatory effect on GABA synthesis.

Low serum zinc level can reduce GABA concentration and lead to lower seizure threshold.<sup>1</sup> Magnesium is essential for maintaining cell membrane stability and conduction of signals in neurons. Reduced magnesium level can cause cell membrane excitability leading to seizures.<sup>2</sup> Magnesium may be an endogenously occurring neuromodulator in epilepsy and seizures would be caused by magnesium depletion. In our study we try to find the correlation between serum zinc and magnesium levels in children with first episode simple febrile seizures.

## METHODS

This was a case-control study done at Shri Sathya Sai Medical College and Research institute, Tamil Nadu, India from June 2019 to February 2020.

### Inclusion criteria

First 40 consecutive samples of children age between 6 months to 5 years attending outpatient department/emergency room (OPD/ER) in our hospital with first episode of febrile seizures were included in the case group after parental consent

Age and sex matched first 40 children presented with acute febrile illness who needed blood investigation as part of treatment during the study period were included in the control group after parental consent.

### Exclusion criteria

Age less than 6 months and more than 5 years, recurrent febrile seizures, children with neurological disability, suspected meningitis, children on mineral supplements and parental non consent.

### Procedure

Detailed history and clinical examination was done and entered in proforma.

Blood samples were collected in both controls and cases on first sampling indication as part of fever evaluation. Serum zinc and serum magnesium level were measured in both the groups as one time testing at our hospital lab. Calorimetric method using 5-nitro 2 pyridoxylazo-5-n-propyl-3 sulfopropyl amino phenol disodium salt (NITRO PAPS) was used for the estimation of serum zinc and calorimetric assay with chlorophosphonazo III method was used for the estimation of magnesium. The normal lab reference value given by our lab for serum zinc was 60-120 µg/dl and serum magnesium was 1.7-2.5 mg/dl.

The study proposal was approved by our institutional ethical committee.

The results were analysed using independent t test using statistical package for the social sciences (SPSS) software.

P value of less than 0.05 was taken as statistical significance.

## RESULTS

Children between ages 12 months to 24 months had higher incidence of febrile seizure in case group. This is shown in the Table 1, with 15 out of 40 children; about 37.5% were in the age group of 1-2 years.

**Table 1: Incidence of febrile seizures in cases with respect to age.**

Age	Frequency (n=40)	Percent
6 months–1 year	9	22.5
1 year–2 years	15	37.5
2 years–3 years	10	25
3 years–4 years	2	5
4 years–5 years	4	10

Male children had an increased incidence of developing febrile seizures in our study. 12/40 (55%) male children and 18/40(45%) female children had febrile seizures (Table 2).

**Table 2: Incidence of febrile seizures in cases with respect to gender.**

Sex (children)	Frequency (n=40)	Percent
Male	22	55
Female	18	45

11 children (22.5%) in case group had family history of febrile seizures while no children in control group had such family history (Table 3).

**Table 3: Family history of febrile seizures among both groups.**

Group	Cases, n=40 (percent)	Controls
With positive family history	11 (22.5)	0
With negative family history	29 (77.5)	0

Mean serum zinc level was 35.08 µg/dl in children with febrile seizure which was significantly lower than the control group children whose mean was 70.23 µg/dl. The statistical p value was less than 0.001 (Table 4).

**Table 4: Mean value of serum zinc among cases and controls.**

Parameter	Case (SD)	Control (SD)	T statistics	P value
Mean serum zinc in µg/dl	35.08 (8.56)	70.23 (13.41)	-13.96	<0.001

Mean serum magnesium level was 1.19 mg/dl in children with febrile seizure which was significantly lower when compared to control group children who had mean serum magnesium of 1.92 mg/dl. The statistical p value was less than 0.001 (Table 5).

**Table 5: Mean value of serum magnesium among cases and controls.**

Parameter	Case (SD)	Control (SD)	T statistics	P value
Mean serum magnesium in mg/dl	1.35 (0.29)	1.68 (0.42)	-3.946	<0.001

## DISCUSSION

In the present study we found that the peak incidence of febrile seizures was occurring between 1 to 2 years. This is comparable to the previous studies. In a study done by Berg et al the incidence of febrile seizures was more between 18-24 months of age.<sup>3</sup>

In our study the incidence of febrile seizures was slightly higher among the boys than the girl children, with a male to female ratio of 1.2: 1. Berg et al study also had more incidence among male children.<sup>3</sup> Rehman et al have done a similar study, in which no gender difference was observed.<sup>4</sup>

In our study children with positive family history developing febrile seizures were 22.5%. Prediction of febrile seizures in children- a study done by Esch et al showed a risk of 10-45% exists if a first degree relative or a sibling had febrile seizures.<sup>5</sup>

Mean serum zinc and magnesium levels are significantly below the lower limit in our children with febrile seizures. Izumi et al in his study proposes that low level of zinc during fever triggers N-methyl-D-aspartate (NMDA) receptors which leads to epileptiform discharges.<sup>6</sup>

Zinc acts as a neurotransmitter and helps in communication between neurons, deficiency of zinc diminishes hippocampal zinc and leads to seizures. Ganesh et al in a prospective case control study on serum zinc level in children with simple febrile seizures done at KKCTH, Chennai with 76 children, found the mean serum zinc level in cases as 32.17 µg/dl and among controls as 87.6 µg/dl which was statistically significant.<sup>7</sup>

Study done by Talebian et al showed a significant level of low serum magnesium in children with febrile seizures which is more similar to our study.<sup>8</sup> Goutham et al done a study on serum magnesium level in febrile convulsion at KIMS hospital Bangalore in 2017 showed a significant low level of magnesium among children with febrile seizures when compared to controls.<sup>9</sup>

## Limitations

Zinc homeostasis during illness is not an established concept hence large studies are needed to give recommendations on zinc supplements.

Follow up with zinc supplement would also have given a better idea on role zinc in children with febrile seizures.

## CONCLUSION

In our study the serum zinc and magnesium levels are significantly low in children presenting with first episode simple febrile seizures. The occurrence of febrile seizures is more between 12-24 months of age. Male children are more affected than female children.

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