

A STUDY OF SERUM ZINC LEVELS IN CHILDREN WITH FEBRILE SEIZURE IN COMPARISON WITH FEBRILE CHILDREN WITHOUT SEIZURE

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Received : 10/06/2024
Received in revised form : 04/08/2024
Accepted : 19/08/2024

Keywords:

Febrile seizures, serum zinc, pediatric neurology, febrile children, zinc deficiency, seizure prevention, complex febrile seizures.

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DOI: 10.47009/jamp.2024.6.4.154

Source of Support: Nil,

Conflict of Interest: None declared

Int J Acad Med Pharm

2024; 6 (4); 778-781



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Abstract

Background: Febrile seizures are the most common seizure disorder in pediatric patients, particularly affecting children aged 6 to 60 months. These seizures, triggered by fever, can be a source of significant anxiety for parents and caregivers. Zinc, a critical trace element, plays a vital role in numerous physiological processes, including immune function, protein synthesis, and neuronal activity. This study evaluates and compares serum zinc levels in children with febrile seizures to those in febrile children without seizures to determine whether zinc deficiency could be a contributing factor in the pathogenesis of febrile seizures. **Materials and Methods:** This prospective, observational study was conducted over 18 months at a tertiary care hospital in Jharkhand, India. The study involved 60 children aged 6 to 60 months, divided into two groups: 30 children with febrile seizures (Group A) and 30 children without seizures (Group B). Serum zinc levels were measured using a colorimetric method. Statistical analyses were performed to identify significant differences in zinc levels between the two groups and to explore potential correlations between zinc levels and seizure characteristics. **Result:** The mean serum zinc levels in Group A were significantly lower than in Group B. Children with febrile seizures had a mean zinc level of $60.5 \pm 14.2 \mu\text{g/dL}$, while those without seizures had a mean zinc level of $92.7 \pm 17.6 \mu\text{g/dL}$ ($p < 0.001$). Additionally, the study found that 73.3% of children with febrile seizures had zinc levels below $70 \mu\text{g/dL}$, compared to 26.7% in the febrile children without seizures group. The study also observed that children with complex febrile seizures had lower zinc levels compared to those with simple febrile seizures. **Conclusion:** The study concludes that children with febrile seizures have significantly lower serum zinc levels compared to febrile children without seizures. These findings suggest that zinc deficiency could play a role in the pathogenesis of febrile seizures. Zinc supplementation might be a potential preventive strategy in children at risk of developing febrile seizures, particularly in regions with a high prevalence of zinc deficiency.

INTRODUCTION

Febrile seizures are a significant concern in pediatric healthcare, representing the most common neurological disorder encountered in young children. Defined as seizures that occur in association with a fever, febrile seizures typically affect children between the ages of 6 months and 5 years. The global incidence of febrile seizures varies widely, with estimates ranging from 2% to 5% in Western populations, and higher rates reported in some Asian and African countries. In India, the incidence of febrile seizures is reported to be approximately 3% to

5%, making it a prevalent condition that warrants careful consideration in pediatric practice.^[1-3]

The pathophysiology of febrile seizures is complex and not fully understood. However, it is believed to involve a combination of genetic predisposition, environmental factors, and neurochemical imbalances. Among the various factors implicated in the development of febrile seizures, zinc deficiency has emerged as a potential contributor.^[4] Zinc is an essential micronutrient involved in numerous biological processes, including DNA synthesis, cell division, and protein synthesis. It also plays a critical role in maintaining the integrity of neuronal

membranes and modulating neurotransmitter release, both of which are crucial for proper neural function.^[5] Previous studies have suggested a possible link between zinc deficiency and the occurrence of febrile seizures. Zinc's role in modulating neurotransmitter activity and maintaining neuronal stability suggests that insufficient levels of this trace element may lower the seizure threshold, making children more susceptible to febrile seizures. However, the relationship between serum zinc levels and febrile seizures remains a topic of ongoing research, with some studies reporting conflicting results.^[6] This study aims to investigate serum zinc levels in children with febrile seizures and compare them to those in febrile children without seizures. By exploring the potential association between zinc deficiency and febrile seizures, this research seeks to provide insights that could inform clinical practice and guide the development of preventive strategies. Specifically, the study will address the following questions:

1. Are serum zinc levels significantly lower in children with febrile seizures compared to febrile children without seizures?
2. Is there a correlation between the severity or type of febrile seizure (simple vs. complex) and serum zinc levels?
3. Can zinc supplementation serve as a preventive measure in children at risk of febrile seizures?

By answering these questions, the study hopes to contribute to the understanding of febrile seizures and identify potential interventions that could reduce the burden of this condition in pediatric populations.

MATERIALS AND METHODS

Study Design and Setting

This study was designed as a prospective, observational study and was conducted at a tertiary care hospital in Jharkhand, India, over 18 months, from January 2020 to June 2021. The hospital serves a large catchment area, providing healthcare services to a diverse population, including a significant number of pediatric patients. Ethical approval for the study was obtained from the hospital's ethics committee, and informed consent was obtained from the parents or guardians of all participating children.

Study Population

The study included 60 children aged 6 to 60 months who presented to the hospital with febrile illnesses. The children were divided into two groups based on the presence or absence of seizures:

- **Group A:** 30 children with febrile seizures. This group included children who experienced either simple or complex febrile seizures.
- **Group B:** 30 febrile children without seizures. These children had febrile illnesses but did not experience any seizure activity.

The inclusion criteria were as follows:

- Children aged 6 to 60 months.

- Children presenting with a febrile illness, defined as a rectal temperature of 38°C (100.4°F) or higher.
- For Group A, children must have experienced a seizure associated with the febrile illness.

Exclusion criteria included:

- Children with known chronic illnesses, such as epilepsy, metabolic disorders, or neurological conditions.
- Children who had received zinc supplementation in the past six months.
- Children with a history of developmental delay or neurodevelopmental disorders.

Data Collection

Data collection involved detailed history-taking, clinical examination, and laboratory investigations. The following data were recorded for each participant:

- **Demographic Information:** Age, gender, and socioeconomic status.
- **Clinical History:** Details of the febrile illness, including the duration of fever, peak temperature, and any associated symptoms (e.g., cough, diarrhea, vomiting).
- **Seizure Characteristics (Group A):** Type of seizure (simple or complex), duration of the seizure, frequency of seizures, and any postictal symptoms.

Blood samples were collected from all participants to measure serum zinc levels. The blood samples were obtained using standard venipuncture techniques and were processed immediately. Serum zinc levels were measured using a colorimetric method, with results expressed in micrograms per deciliter (µg/dL). The normal reference range for serum zinc levels in children is typically 70-120 µg/dL.

Statistical Analysis

Data analysis was conducted using SPSS software (version 27.0). Continuous variables were presented as means and standard deviations, while categorical variables were expressed as frequencies and percentages. The independent t-test was used to compare mean serum zinc levels between the two groups. The chi-square test was used to assess the association between zinc deficiency and the occurrence of febrile seizures. A p-value of <0.05 was considered statistically significant.

Additional analyses were performed to examine the correlation between serum zinc levels and the type of febrile seizure (simple vs. complex). The results were presented in the form of tables and graphs to provide a clear and comprehensive understanding of the findings.

RESULTS

Demographic and Clinical Characteristics

The demographic and clinical characteristics of the study participants are summarized in Table 1. The mean age of children in Group A (febrile seizures) was 24.5 ± 10.2 months, while the mean age in Group

B (febrile without seizures) was 26.3 ± 11.5 months. The gender distribution was similar in both groups, with a slight male predominance. The mean peak temperature recorded during the febrile illness was $39.1 \pm 0.7^\circ\text{C}$ in Group A and $38.9 \pm 0.6^\circ\text{C}$ in Group

B. Serum Zinc Levels

The mean serum zinc levels in Group A (febrile seizures) were significantly lower than in Group B (febrile without seizures). Children in Group A had a mean serum zinc level of $60.5 \pm 14.2 \mu\text{g/dL}$, while those in Group B had a mean serum zinc level of $92.7 \pm 17.6 \mu\text{g/dL}$ ($p < 0.001$). Furthermore, 73.3% of children in Group A had serum zinc levels below $70 \mu\text{g/dL}$, compared to 26.7% in Group B ($p < 0.001$).

Seizure Characteristics in Group A

The study also analyzed the seizure characteristics in children with febrile seizures (Group A). Of the 30 children in this group, 20 (66.7%) had simple febrile

seizures, and 10 (33.3%) had complex febrile seizures. The mean serum zinc level in children with complex febrile seizures was lower ($57.2 \pm 12.8 \mu\text{g/dL}$) compared to those with simple febrile seizures ($62.3 \pm 15.1 \mu\text{g/dL}$), although this difference was not statistically significant ($p = 0.08$).

Correlation Between Serum Zinc Levels and Seizure Frequency

The study further explored the correlation between serum zinc levels and the frequency of seizures in Group A. Children with recurrent febrile seizures (defined as two or more seizure episodes within the same febrile illness) had lower mean serum zinc levels ($58.1 \pm 13.5 \mu\text{g/dL}$) compared to children with a single seizure episode ($61.8 \pm 14.0 \mu\text{g/dL}$), although the difference was not statistically significant ($p = 0.15$).

Table 1: Demographic and Clinical Characteristics of Study Participants.

Characteristic	Febrile Seizure Group (n=30)	Febrile Without Seizure Group (n=30)	p-value
Mean Age (months)	24.5 ± 10.2	26.3 ± 11.5	0.34
Male	19 (63.3%)	17 (56.7%)	0.59
Female	11 (36.7%)	13 (43.3%)	0.59
Mean Temperature ($^\circ\text{C}$)	39.1 ± 0.7	38.9 ± 0.6	0.45
Rural Residence	20 (66.7%)	22 (73.3%)	0.54
Urban Residence	10 (33.3%)	8 (26.7%)	0.54

Table 2: Serum Zinc Levels in Study Participants

Serum Zinc Level ($\mu\text{g/dL}$)	Febrile Seizure Group (n=30)	Febrile Without Seizure Group (n=30)	p-value
Mean	60.5 ± 14.2	92.7 ± 17.6	$< 0.001^*$
$< 70 \mu\text{g/dL}$	22 (73.3%)	8 (26.7%)	$< 0.001^*$
$> 70 \mu\text{g/dL}$	8 (26.7%)	22 (73.3%)	$< 0.001^*$

Table 3: Seizure Characteristics and Serum Zinc Levels in Group A

Seizure Type	Number of Patients (n=30)	Percentage (%)	Mean Serum Zinc Level ($\mu\text{g/dL}$)	p-value
Simple Febrile Seizure	20	66.7%	62.3 ± 15.1	0.08
Complex Febrile Seizure	10	33.3%	57.2 ± 12.8	0.08

Table 4: Correlation Between Serum Zinc Levels and Seizure Frequency in Group A

Seizure Frequency	Number of Patients (n=30)	Percentage (%)	Mean Serum Zinc Level ($\mu\text{g/dL}$)	p-value
Single Seizure Episode	18	60.0%	61.8 ± 14.0	0.15
Recurrent Seizures	12	40.0%	58.1 ± 13.5	0.15

DISCUSSION

The findings of this study provide compelling evidence for the association between low serum zinc levels and the occurrence of febrile seizures in children. The significantly lower mean serum zinc levels observed in children with febrile seizures compared to febrile children without seizures suggest that zinc deficiency may be a contributing factor in the pathogenesis of febrile seizures.^[7]

Zinc and Its Role in Seizure Pathophysiology

Zinc is a vital trace element that plays an essential role in maintaining cellular and molecular functions within the central nervous system (CNS). It acts as a cofactor for numerous enzymes involved in neurotransmitter synthesis, such as glutamate and gamma-aminobutyric acid (GABA), which are critical for maintaining the excitatory-inhibitory

balance in the brain. Zinc also stabilizes neuronal membranes by modulating ion channels and influencing synaptic plasticity.^[8]

In the context of febrile seizures, zinc deficiency may disrupt these neurochemical processes, leading to an imbalance between excitatory and inhibitory neurotransmission. This imbalance could lower the seizure threshold, making the brain more susceptible to abnormal electrical activity during a febrile illness. The lower serum zinc levels observed in children with complex febrile seizures, although not statistically significant, further support this hypothesis. Complex febrile seizures, which are characterized by prolonged duration, focal onset, or multiple episodes within 24 hours, may represent a more severe manifestation of zinc deficiency's impact on neural function.^[9-11]

The findings of this study are consistent with previous research that has reported an association between zinc deficiency and febrile seizures. For example, a study conducted found that children with febrile seizures had significantly lower serum zinc levels compared to febrile children without seizures. Similarly, a study concluded that low serum zinc levels are associated with an increased risk of febrile seizures in children.^[12,13]

However, not all studies have reported a consistent relationship between zinc levels and febrile seizures. Some researchers have suggested that the observed differences in zinc levels may be influenced by factors such as dietary intake, regional variations in zinc deficiency, and the timing of blood sample collection. Despite these inconsistencies, the overall body of evidence supports the notion that zinc plays a critical role in seizure susceptibility, particularly in the context of febrile illnesses.

Clinical Implications and Future Directions

The results of this study have important clinical implications for the management of febrile seizures in pediatric patients. Given the association between low serum zinc levels and febrile seizures, zinc supplementation could be considered a preventive measure in children at risk of developing febrile seizures, especially in regions with a high prevalence of zinc deficiency. Zinc supplementation is a safe and cost-effective intervention that could potentially reduce the incidence of febrile seizures and improve neurological outcomes in children.

Further research is needed to explore the long-term effects of zinc supplementation on seizure prevention and to determine the optimal dosage and duration of supplementation. Additionally, studies investigating the underlying mechanisms by which zinc influences seizure activity could provide valuable insights into the pathophysiology of febrile seizures and inform the development of targeted therapeutic strategies.

Study Limitations

This study has several limitations that should be considered when interpreting the results. First, the sample size was relatively small, which may limit the generalizability of the findings. Larger studies with more diverse populations are needed to confirm the observed associations and to identify potential confounding factors. Second, the study was conducted at a single tertiary care hospital, which may introduce selection bias. Finally, the cross-sectional design of the study precludes the establishment of a causal relationship between zinc deficiency and febrile seizures.

Despite these limitations, the study provides valuable insights into the potential role of zinc in the

pathogenesis of febrile seizures and highlights the need for further research in this area.

CONCLUSION

This study confirms that children with febrile seizures have significantly lower serum zinc levels compared to febrile children without seizures. The findings suggest that zinc deficiency may contribute to the development of febrile seizures and that zinc supplementation could be a potential preventive strategy in at-risk populations. Further research is warranted to explore the benefits of zinc supplementation and to elucidate the mechanisms underlying the relationship between zinc and seizure susceptibility.

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