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Original Research Article

THE ROLE OF ZINC DEFICIENCY IN FEBRILE SEIZURES AMONG CHILDREN: A CROSS-SECTIONAL ANALYSIS

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ABSTRACT

Background: Febrile seizures are the most common neurological condition in children aged 6 months to 6 years. Zinc deficiency has been proposed as a potential risk factor, but its role remains unclear. This study aimed to evaluate serum zinc levels in children with febrile seizures compared to febrile children without seizures.

Material and Methods: A comparative cross-sectional study was conducted on 100 children aged 6 months to 6 years, with 50 children in each group. Serum zinc levels were measured using atomic absorption spectrophotometry. Zinc levels below 0.3 mg/L were classified as deficient. Data on age, gender, socioeconomic status, nutritional status, and seizure type were analyzed, and statistical tests were applied to identify significant associations.

Results: The median zinc levels in children with febrile seizures were 146.5 µg/dL (IQR: 101.7–169), compared to 141 µg/dL (IQR: 95.75–180.5) in children without febrile seizures, with no statistically significant difference ($p = 0.733$). Low zinc levels were more prevalent in older children, females, and those from lower socioeconomic backgrounds in both groups, but these differences were not statistically significant. Children with simple febrile seizures had a higher prevalence of low zinc levels compared to those with complex febrile seizures (85.7% vs. 14.3%, $p = 0.657$).

Conclusion: This study found no significant difference in serum zinc levels between children with febrile seizures and those without. Zinc deficiency may not be a universal risk factor for febrile seizures, but further large-scale studies are needed to clarify its role.

Keywords: Febrile seizures, zinc deficiency, serum zinc levels, children, risk factors, nutritional status.

INTRODUCTION

Febrile seizures (FS) are one of the most common neurological disorders observed in children, with a prevalence of 2–5% among those aged 6 months to 6 years.[1] These seizures occur during episodes of fever (temperature >38.4°C or 101°F) without evidence of acute central nervous system (CNS) infections, metabolic disturbances, or previous afebrile seizures.[2] The exact mechanisms underlying febrile seizures remain unclear, but genetic predispositions, electrolyte imbalances, and micronutrient deficiencies are suspected contributors.[3]

Zinc is an essential trace element involved in numerous biochemical and physiological processes, including neurotransmission, enzymatic activities, and immune modulation.[4] Its role in the central nervous system is particularly critical, as it participates in synaptic signaling and the regulation of excitatory and inhibitory neurotransmitters.[5] Zinc deficiency has been hypothesized to affect the function of gamma-aminobutyric acid (GABA) receptors, potentially increasing neuronal excitability and lowering the seizure threshold.[6] Several studies have indicated that children with febrile seizures may have lower serum zinc levels compared to febrile children without seizures.[7]

However, the evidence remains inconsistent, and further investigation is needed to clarify this association.[8] Understanding the relationship between zinc deficiency and febrile seizures could provide valuable insights into preventive strategies and therapeutic interventions for at-risk children.

This study aims to evaluate serum zinc levels in children with febrile seizures compared to children without febrile seizures, exploring the potential role of zinc deficiency as a risk factor for febrile seizures.

MATERIALS AND METHODS

This study was designed as a comparative cross-sectional analysis conducted in the Department of Pediatrics, D.Y. Patil Hospital and Research Centre, Nerul, Navi Mumbai, over a period of one and a half years, from August 2022 to February 2024. The primary objective was to evaluate serum zinc levels in children with febrile seizures compared to children without febrile seizures. A purposive sampling technique was employed to recruit participants aged between 6 months and 6 years who met the inclusion and exclusion criteria.

Children with febrile seizures were identified based on the American Academy of Pediatrics definition, while the group without febrile seizures included febrile children who did not experience seizures. Children who had received zinc supplements within the last two weeks, those with a history of epilepsy, and febrile children with central nervous system manifestations were excluded from the study. Informed consent was obtained from the parents or guardians of all participants prior to enrollment.

A total of 100 children were enrolled, with 50 participants in the group with febrile seizures and 50 in the group without febrile seizures. A detailed history and clinical examination were conducted, and data on socio-demographic details, past medical history, and clinical findings were collected using a pre-validated questionnaire. Blood samples of 1 mL were obtained from each participant within the first six hours of admission. The samples were centrifuged to separate serum, which was then stored at -8°C for subsequent analysis. Serum zinc levels were measured using the atomic absorption spectrophotometry technique, ensuring precision and reliability. Zinc levels below 0.3 mg/L (30 µg/dL) were classified as deficient, based on established reference ranges.

Data were analyzed to compare serum zinc levels between the two groups, with age, gender, nutritional status, and socio-economic status considered as potential confounding factors. Statistical tests, including the chi-square test and Mann-Whitney U test, were used to evaluate differences between groups. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The results of the study reveal detailed observations regarding serum zinc levels in children with febrile seizures compared to those without febrile seizures. Among children with febrile seizures, low zinc levels were noted in 15.4% of children aged 2–3 years, 14.3% of those aged 3–4 years, and 44.4% of those aged 5–6 years. In contrast, no children under the age of 2 years in this group exhibited low zinc levels. For children without febrile seizures, low zinc levels were observed in 11.1% of those aged 5–6 years, 20% of those aged 4–5 years, and 8.3% of those aged 3–4 years. Despite these differences, the statistical analysis did not show any significant association between age and zinc levels, with p-values of 0.06 for the febrile seizure group and 0.299 for the group without febrile seizures.

When examining gender differences, children with febrile seizures showed a higher prevalence of low zinc levels among females (71.4%) compared to males (28.6%). Conversely, in the group without febrile seizures, all observed low zinc levels were seen in males, while 66.7% of high zinc levels were also noted in males. However, these gender-based differences in zinc levels were not statistically significant, with p-values of 0.115 for the febrile seizure group and 0.431 for the group without febrile seizures. [Table 1]

The study also analyzed serum zinc levels based on socioeconomic status. Among children with febrile seizures, the highest prevalence of low zinc levels was seen in the upper class (42.9%) and the lower middle class (42.9%). In the group without febrile seizures, low zinc levels were predominantly observed in children belonging to the upper lower class (66.7%) and the lower middle class (33.3%). Despite these variations, there was no statistically significant association between socioeconomic status and zinc levels in either group, with p-values of 0.106 for the febrile seizure group and 0.266 for the group without febrile seizures. [Table 2]

Nutritional status was also evaluated in relation to serum zinc levels. In the group with febrile seizures, children with normal nutritional status accounted for 85.7% of all low zinc cases. Similarly, in the group without febrile seizures, 66.7% of the low zinc levels were observed in children with normal nutritional status. Other nutritional categories, such as moderate acute malnutrition, severe acute malnutrition, and stunting, did not show significant differences in zinc levels. The relationship between nutritional status and zinc levels was not statistically significant, with p-values of 1 for the febrile seizure group and 0.593 for the group without febrile seizures. [Table 3]

Further analysis was performed to assess the relationship between zinc levels and the type of febrile seizures. Among children with simple febrile seizures, 85.7% had low serum zinc levels, compared to 14.3% in those with complex febrile

seizures. However, this difference did not reach statistical significance, with a p-value of 0.657. [Table 4]

When comparing overall serum zinc levels between the two groups, the median zinc level in children with febrile seizures was 146.5 µg/dL (IQR: 101.7–169), while the median level in children without febrile seizures was 141 µg/dL (IQR: 95.75–180.5). This difference was not statistically significant, with a Mann-Whitney U test p-value of 0.733. [Table 5]

Finally, haemoglobin levels were also evaluated. The mean haemoglobin levels in children with febrile seizures were 10.77 ± 1.58 g/dL, while the mean haemoglobin levels in children without febrile seizures were 10.32 ± 1.62 g/dL. Although the haemoglobin levels were slightly higher in the febrile seizure group, the difference was not statistically significant, with a p-value of 0.191. [Table 7]

Table 1: Distribution of Serum Zinc Levels Across Age Groups in Children with and without Febrile Seizures

	Zinc levels - (FS)				Zinc levels-(NS)			
Age category	**Low (%)**	**Normal (%)**	**High (%)**	**p- value**	**Low (%)**	**Normal (%)**	**High (%)**	**p- value**
<1years	0	7	0	0.06	0	4	1	0.299
		(100)	0		0	(80)	20	
1-2years	0	13	0		0	7	0	
	0	(100)	0		0	(100)	0	
2-3years	2	11	0		0	3	0	
	15.4	(84.6)	0		0	(100)	0	
3-4years	1	6	0		0	11	1	
	14.3	(85.7)	0		0	(91.7)	8.3	
4-5years	0	1	0		1	3	1	
	0	(100)	0		20	(40)	20	
5-6years	4	5	0		2	16	0	
	44.4	(55.6)	0		11.1	(88.9)	0	

Table 2: Gender-Wise Distribution of Serum Zinc Levels in Children with and without Febrile Seizures

	Zinc levels- (FS)				Zinc levels- (NS)			
Gender	**Low (%)**	**Normal (%)**	**High (%)**	**p-value**	**Low (%)**	**Normal (%)**	**High (%)**	**p-value**
Males	2	27	0	0.115	3	23	2	0.431
	(28.6)	(62.8)	0		(100)	(52.3)	(66.7)	
Females	5	16	0		0	21	1	
	(71.4)	(37.2)	0		0	(47.7)	(33.3)	

Table 3: Distribution of Serum Zinc Levels Based on Socioeconomic Status in Children with and without Febrile Seizures

Socioeconomic status (Modified Kuppuswamy classification)	Zinc levels- (FS)				Zinc levels- (NS)			
	Low (%)	**Normal (%)**	**High (%)**	**p- value**	**Low (%)**	**Normal (%)**	**High (%)**	**p- value**
Upper class	3	8	0		0	0	0	0.266
	(42.9)	(18.6)	0	0.106	0	0	0	
Upper middle	0	11	0		0	2	0	
	0	(25.6)	0		0	(4.5)	0	
Lower middle	3	23	0		1	5	0	
	(42.9)	(53.5)	0		(33.3)	(11.4)	0	
Upper lower	1	1	0		2	13	0	
	(14.2)	(2.3)	0		(66.7)	(29.5)	0	
Lower class	0	0	0		0	24	3	
	0	0	0		0	(54.5)	(100)	

Table 4: Nutritional Status and Serum Zinc Levels in Children with and without Febrile Seizures

Nutritional Status	Zinc levels- (FS)				Zinc levels- (NS)			
	Low (%)	**Normal (%)**	**High (%)**	**p-value**	**Low (%)**	**Normal (%)**	**High (%)**	**p-value**
Normal	6	32	0	1	2	28	2	0.593
	(85.7)	(74.3)	0		(66.7)	(63.6)	(66.7)	
Moderate acute malnutrition	0	5	0		0	6	0	
	0	(11.6)	0		0	(13.6)	0	
Severe acute malnutrition	1	4	0		1	5	0	
	(14.3)	(9.3)	0		(33.3)	(11.4)	0	
Moderate underweight	0	0	0		0	3	0	
	0	0	0		0	(6.8)	0	
Moderate stunting	0	1	0		0	2	1	
	0	(2.3)	0		0	(45)	(33.3)	
Underweight+ Stunting	0	1	0		0	0	0	
	0	(2.3)	0		0	0	0	

Table 5: Distribution of Serum Zinc Levels Based on the Type of Febrile Seizures

Type of convulsion	Zinc levels- (FS)			
	Low (%)	Normal (%)	High (%)	p- value
Simple febrile convulsion	6	30	0	0.657
	(85.7)	(69.8)	0	
Complex febrile convulsion	1	13	0	
	(14.3)	(30.2)	0	

Table 6: Comparative Analysis of Haemoglobin Levels Between Children with Febrile Seizures and Those Without Febrile Seizures

Variables	Group	Mean	Std. Deviation	Mean difference	t-value	p-value
Haemoglobin levels	Febrile Seizures	10.77	1.58	0.445	1.318	0.191
	Febrile illness	10.32	1.62			
Independent t-test						

Table 7: Comparative Analysis of Median Serum Zinc Levels in Children with and Without Febrile Seizures

Variables	Group	Median	Interquartile range	Z-value	p-value
Zinc levels	Febrile Seizures	146.5	101.73-169	0.341	0.733
	Febrile illness	141	95.75-180.5		

DISCUSSION

This study aimed to evaluate the association of serum zinc levels with febrile seizures in children, comparing those with febrile seizures to those without. Variables such as age, gender, socioeconomic status, nutritional status, and type of febrile seizures were analyzed to understand their potential influence on zinc levels.

In our study, low serum zinc levels were more prevalent in older children with febrile seizures, particularly those aged 5–6 years, while younger children (<2 years) had normal zinc levels. This contrasts with findings from Sakr et al., who reported significant zinc deficiencies in younger children with febrile seizures, particularly those aged 6–24 months, suggesting that age-specific metabolic demands may play a role in zinc deficiency.[9] Similarly, Baaker Hommadi et al. found younger children to be more susceptible to hypozincemia associated with febrile seizures.[10] The variation in findings may reflect differences in dietary patterns, age-specific nutritional requirements, or population demographics.

Low serum zinc levels were more common in females with febrile seizures (71.4%) compared to males (28.6%) in our study. However, in the group without febrile seizures, low zinc levels were predominantly observed in males. Madhubalan et al. reported no significant gender differences in serum zinc levels among children with febrile seizures, suggesting that gender may not be a critical factor in zinc metabolism.[11] This discrepancy highlights the need for further research to explore potential gender-related differences in zinc levels.

Children from lower socioeconomic backgrounds exhibited higher rates of zinc deficiency in both groups in our study. Among those with febrile seizures, the lower middle and upper lower socioeconomic classes had the highest prevalence of low zinc levels. These findings are consistent with Maheshwari et al., who observed that lower socioeconomic status contributes to nutritional deficiencies, including hypozincemia, increasing susceptibility to febrile seizures.[12] Addressing disparities in nutritional intake and access to zinc-rich foods remains crucial, particularly in resource-constrained populations.

In terms of nutritional status, our findings indicated that most children with low zinc levels had normal nutritional status in both groups. This contrasts with Achanta et al., who reported significant zinc deficiencies in malnourished children with febrile seizures.[13] This discrepancy may be attributed to differences in the assessment of nutritional status or sample size. Malnutrition could exacerbate deficiencies in zinc, but it may not fully explain the prevalence of low zinc levels in children with febrile seizures.

Among children with simple febrile seizures, 85.7% had low zinc levels compared to 14.3% in those with complex febrile seizures. These findings are consistent with Shaikh et al., who found a higher prevalence of hypozincemia in simple febrile seizures, suggesting that zinc may play a role in reducing neuronal excitability, potentially lowering the seizure threshold.[14] However, this association requires further exploration, particularly regarding its clinical implications.

Comparative analysis showed no statistically significant difference in median serum zinc levels between the two groups, with similar findings reported by Singh and Yadav.[15] Conversely, studies such as those by Santappanawar et al. and Rehman et al. demonstrated significantly lower zinc levels in children with febrile seizures, highlighting regional and methodological differences in results.[16,17] These discrepancies underscore the complexity of zinc's role in febrile seizures, influenced by genetic, dietary, and environmental factors.

Our findings suggest that while zinc deficiency may be observed in some children with febrile seizures, it is not a universal predictor. Variability in study outcomes may result from differences in population

characteristics, dietary zinc intake, or laboratory methodologies. Zinc deficiency should be considered one of many potential contributing factors to febrile seizures rather than a definitive risk factor.

CONCLUSION

This study found no significant difference in serum zinc levels between children with febrile seizures and those without, nor any significant associations with age, gender, socioeconomic status, nutritional status, or seizure type. While zinc deficiency has been proposed as a potential risk factor, our findings do not support routine zinc assessment in febrile seizures. Further large-scale research is needed to clarify zinc's role and guide interventions such as supplementation in at-risk populations.

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