e-ISSN: 0975-1556, p-ISSN:2820-2643
Available online on www.ijpcr.com
International Journal of Pharmaceutical and Clinical Research 2024; 16(3); 1094-1099
Original Research Article

A Clinical Study of Serum Zinc Levels in Children with Simple Febrile Convulsions

A Narendra[1], P Pramod Kumar[2], B Subash[3], Sri Divya. R[4]

[1]Assistant Professor, Department of Pediatrics Government Medical College and Hospital, Wanaparthy, Telangana State.
[2]Assistant Professor, Department of Pediatrics Government Medical College and Hospital, Wanaparthy, Telangana State.
[3]Assistant Professor, Department of Pediatrics Government Medical College and Hospital, Wanaparthy, Telangana State.
[4]Assistant Professor, Department of Pediatrics Government Medical College and Hospital, Wanaparthy, Telangana State

Received: 15-01-2024 / Revised: 20-02-2024 / Accepted: 26-03-2024
Corresponding Author: Dr. Sri Divya R.
Conflict of interest: Nil

Abstract:

Background: Seizures are common among pediatric populations, occurring in approximately 10% of children. In most cases, seizures in children are triggered by somatic disorders originating externally to the brain, such as high fever, infections, syncope, head trauma, hypoxia, or exposure to toxins. This study aimed to assess whether children experiencing febrile convulsions exhibit lower serum zinc levels compared to both normal children and children with fever but without convulsions.

Methods: The study recruited children admitted with fever to Pediatrics wards of Government Medical College and Hospital, Wanaparthy, Telangana state. We recruited three groups for the study 1) Children with febrile convulsions, 2) Children with fever but without convulsions, and 3) Normal children. Each group consisted of 25 participants.

Results: Among children with febrile convulsions, the mean serum zinc level was 41.53 µg/dl, while it was 69.65 µg/dl in children with fever and 71.29 µg/dl in normal children. Statistical analysis revealed significant differences in serum zinc levels among the three groups, particularly between children with febrile convulsions and the other two groups. Statistical analysis found that the mean serum zinc levels were significantly reduced in children with fever and febrile convulsions as compared to normal controls while there were no significant differences in cases of fever without seizures and normal controls.

Conclusions: The findings of this study suggest that serum zinc levels are diminished in children experiencing febrile convulsions, indicating a potential role of zinc deficiency in the pathogenesis of these convulsions.

Keywords: Febrile seizures, Posthoc multiple comparisons, Zinc level.

Introduction

A seizure is defined as a transient, time-limited alteration in motor activity and/or behavior due to abnormal electrical activity in the brain. Seizures are prevalent among the pediatric population, affecting approximately 10% of children. [1] Most seizures in children are triggered by somatic disorders originating externally to the brain, such as high fever, infections, syncope, head trauma, hypoxia, or exposure to toxins. Epilepsy, characterized by two or more unprovoked seizures occurring at intervals greater than 24 hours apart, accounts for less than one-third of seizures in children. [2] Infants and children exhibit a higher susceptibility to seizures compared to adults, reflecting greater neuronal excitability at certain developmental stages when the excitatory glutamate system and inhibitory GABA system are not always in equilibrium [3]. Consequently, there is a propensity to manifest symptomatic seizures in response to factors like high fever, infections, minor asphyxia, medication, bacterial toxins, and biochemical imbalances such as hyponatremia, hypernatremia, and hypocalcemia, among others [4]. Febrile seizures manifest in young children during a developmental stage characterized by a low seizure threshold. Typically, they occur early in the course of an infectious illness, often during

the febrile ascent phase when the rectal temperature may rise above 39.2°C, with around one-fourth of seizures occurring at temperatures exceeding 40.2°C [5]. These seizures are commonly associated with childhood infections such as upper respiratory tract infections, lower respiratory tract infections, otitis media, and acute gastroenteritis, which elicit comparably higher temperatures in affected children [6]. The onset of febrile seizures typically follows a bell-shaped pattern, with 94% occurring within the first 3 years of life, and only 6% occurring thereafter. Approximately half of these seizures present during the second year of life, with a peak incidence observed between 18 to 24 months. Notably, febrile seizures before 6 months of age should prompt consideration of serious infections like bacterial meningitis [7]. Conversely, febrile seizures occurring after 5 years of age require cautious management, as benign causes are less common in older children [8].

Material and Methods

This cross-sectional study was conducted in the Department of Pediatrics, Government Medical College and Hospital, Wanaparthy, Telangana. Institutional Ethical approval was obtained for the study. Written consent was obtained from all the parents and guardians of the children involved in the study after explaining the nature of the study in vernacular language.

Inclusion Criteria

1. Children aged 6 months to 5 years with first episodes of simple febrile convulsions.
2. Males and females
3. Children aged 6 months to 5 years with fever without convulsions.
4. Age and sex-matched healthy children as controls.

Exclusion Criteria

1. Cerebral palsy, epilepsy,
2. chronic illnesses, weight below 70% of expected,
3. severe febrile seizures,
4. children taking zinc supplements,
5. recurrent febrile seizures,
6. children prescribed anticonvulsant medication.

A total of 75 cases which included n=25 cases of simple febrile convulsions n=25 cases with fever without convulsions and n=25 normal cases as controls. Before enrolling the children in the study, a comprehensive history of their presenting symptoms was documented, including details such as the duration of fever, onset time of seizures, seizure type, seizure duration, past seizure history, and family seizure history. Additionally, any suggestive history of potential triggers for the febrile episode, such as cough, cold, nasal discharge, ear discharge, burning sensation during urination, or crying during urination, was noted. Vital signs, including heart rate, respiratory rate, and blood pressure, were measured and recorded. Axillary temperature was measured using a mercury thermometer placed in the axilla for three minutes. Anthropometric measurements, such as weight, height, mid-arm circumference, and head circumference, were taken. Children with weight less than 70% of expected, height less than 12.5 cm, mid-arm circumference less than 12.5 cm (applicable to children aged 1-4 years), and head circumference less than the third centile were excluded from the study.

Subsequently, a general examination and detailed systemic examination were conducted. Children displaying features of any chronic congenital or acquired illnesses were excluded, as were those exhibiting signs suggestive of intracranial infection, such as altered mental status, meningeal signs, or bulging anterior fontanelle. 3ml of whole blood was collected via venipuncture under strict aseptic conditions using sterile metal-free acid propylene-washed plastic test tubes. They were sent to the laboratory for estimation of complete blood count and serum zinc levels. Other investigations included CSF analysis was only done in children with febrile seizures less than one year of age. Given that the cases in our study involved only simple febrile seizures, and considering ethical considerations, CSF analysis was not conducted in children with fever alone or otherwise healthy children.

Statistical Analysis: All the available data was refined and uploaded to MS Excel and analyzed by SPSS version 21 (Amarok USA). Continuous variables were represented as mean, standard deviation, and percentages. Categorical variables were calculated using ANOVA analysis to find differences between the groups. The p-value of (<0.05) was considered significant.

Results

Table 1 shows the distribution of children included in a study categorized by age group and presence or absence of febrile convulsions (fevers with seizures) compared to a normal control group defined as children who came for regular check-ups without fever or convulsions. *Age Distribution:* All groups have a similar distribution of ages across the four categories (less than 2 years, 2-3 years, 3-4 years, 4-5 years). The majority (60%) of children with febrile convulsions were under 2 years old. The prevalence of febrile convulsions decreased with increasing age groups. The table suggests that there is a potential link between younger age (less than 2 years) and a higher prevalence of febrile convulsions.

Table 1: Showing the distribution of cases of febrile children included in this study

	< 2 years		2 – 3 years		3 – 4 years		4 – 5 years		Total
	N	%	N	%	N	%	N	%	
Febrile with convulsions	15	60.0	6	24.0	2	8.0	2	8.0	25(100%)
Febrile without convulsions	10	40.0	6	24.0	5	20.0	4	16.0	25(100%)
Normal controls	10	40.0	5	20.0	5	20.0	5	20.0	25(100%)

*Gender Distribution***:** Children experiencing febrile convulsions (fevers with seizures) were slightly more likely to be male (52%) than female (48%). Conversely, children with fever but without convulsions had a slightly higher proportion of females (52%) compared to males (48%). The normal control group, consisting of children without fever or seizures, showed a more prominent male predominance, with 60% being male and 40% female.

*Kuppusamy Classification***:** Within the febrile convulsions group, the majority (60%) belonged to Kuppusamy class II, while 40% fell into class III. The fever group (children with fever but no seizures) mirrored this distribution almost exactly, with 58% in class II and 42% in class III. The normal control group again differed slightly, with 56% classified as Kuppusamy class II and 44% in class III.

Table 2: Showing the distribution of cases of simple febrile convulsions cases with family history

Family History	Groups		
	Febrile with convulsions	Febrile without convulsions	Normal controls
NIL	21(84%)	25(100%)	25(100%)
Father	1(4%)	0(0.00%)	0(0.00%)
Mother	1(4%)	0(0.00%)	0(0.00%)
Siblings	2(8%)	0(0.00%)	0(0.00%)
Total	25(100%)	25(100%)	25(100%)

Table 2 shows the distribution of cases of simple febrile convulsions cases with a family history of febrile convulsions recorded in the cases of the study. *No Family History (NIL):* The majority of children in all three groups (84% in the febrile convulsion group, 100% in both the febrile without convulsions and normal control groups) did not have a reported family history of febrile convulsions. *Family History:* A small percentage of children in the febrile convulsions group had a family history reported from either the father (4%), mother (4%), or siblings (8%). However, none of the children in the febrile without convulsions or normal control groups had a reported family history.

Table 3: Shows the distribution of cases of simple febrile convulsions cases with Nutritional status recorded in the cases of the study.

	Grade I PEM		Normal		Total
	N	%	N	%	
Febrile with convulsions	12	48	13	52	25(100%)
Febrile without convulsions	11	44	14	56	25(100%)
Normal controls	10	40	15	60	25(100%)

Table 3 describes the distribution of nutritional status among three groups in a study. *Grade I PEM:* A significant proportion of children in the febrile convulsions group (48%) were classified as having Grade I PEM. A smaller percentage of children with fever but no seizures (44%) and normal controls (40%) fell under this category. *Normal:* The remaining children in each group were categorized as having normal nutritional status. This suggests a potential association between poorer nutritional status (Grade I PEM) and febrile convulsions. The highest percentage of children with PEM were in the febrile convulsions group. However, a significant portion of children with febrile convulsions (52%) also had normal nutritional status. This indicates that malnutrition might not be the sole factor influencing febrile convulsions.

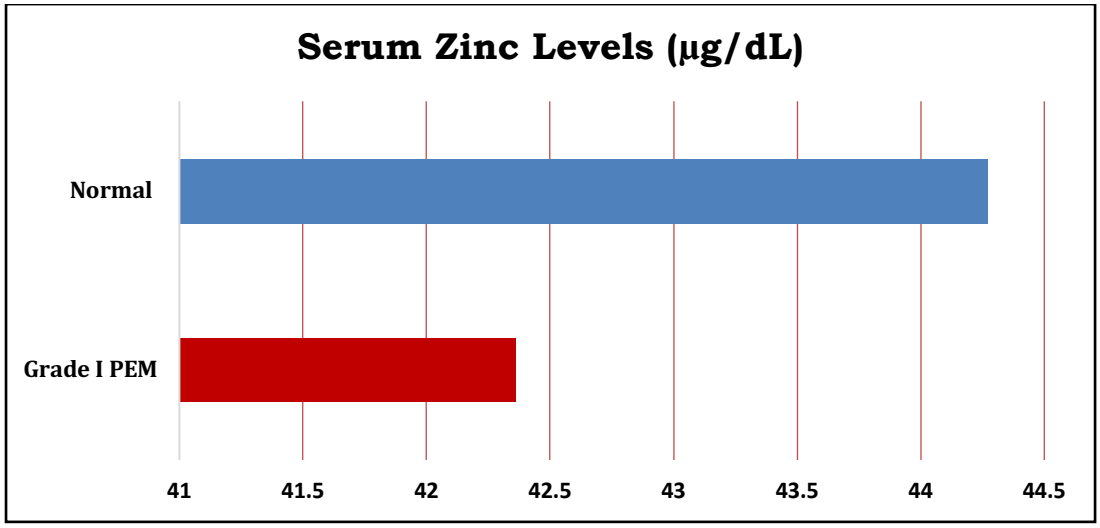

Figure 1: showing the mean serum zinc levels in children based on the nutritional status.

The average serum zinc level was 42.36 ± 3.54 µg/dL in normal children and 44.27 ± 6.47 µg/dL in children with grade I protein-energy malnutrition (PEM). There was no significant variation observed in relation to the nutritional status of the children (p=0.436, not significant) depicted in Figure 1. The average age of onset for febrile convulsions was determined to be 1.5 years, equivalent to 18 months. The mean axillary temperature recorded at the time of convulsion was 103.5 degrees Fahrenheit. Additionally, the average interval between fever onset and seizure occurrence was found to be 7.0 hours.

Table 4: The serum zinc levels in three groups of children

	Frequency	Minimum	Maximum	Mean	SD	P value
Febrile with convulsions	25	40.332	44.621	41.53	3.74	0.021*
Febrile without convulsions	25	66.54	70.64	69.95	8.25	0.125
Normal controls	25	69.88	7.94	71.29	9.41	---

*Significant

This table compares the serum zinc levels among three groups of children in a study. *Febrile with Convulsions:* The mean serum zinc level in this group (41.53) is lower than the other two groups. The P value (0.021) is statistically significant, indicating a possible difference in zinc levels compared to the normal controls. *Febrile without Convulsions:* The mean serum zinc level (69.95) is higher than the febrile convulsions group but similar to the normal controls (71.29). The P value (0.125) suggests no statistically significant difference compared to the normal controls. *Normal Controls:* This group has the highest mean serum zinc level (71.29). The zinc levels of < 65µg/dL were considered as zinc deficiency. Children with febrile convulsions may have lower serum zinc levels compared to those without convulsions or those in the normal control group.

Discussion

The objective of this study was to investigate whether children experiencing febrile convulsions exhibited lower serum zinc levels compared to children with fever alone and those considered normal. The mean age of onset for febrile convulsions in this study was determined to be 18 months and the majority (60%) of children with febrile convulsions were under 2 years old. In comparison, Hartfield et al. [9] also reported a similar mean age of onset at 18 months, while other similar studies cited a mean age of onset ranging between 20 and 25 months [10-12] Additionally, a positive family history was found in only 16% of children experiencing febrile convulsions in this study, the similar prevalence to findings reported in other studies. [13-15] Frantzen, et al. [16] documented a positive family history in 20% of children in their study aggregating with the observations of the current study. Farwell et al. [17] reported a higher prevalence, with positive family history observed in 29% of cases. However, the observation that children with a positive family history exhibited an earlier onset of febrile convulsions, as demonstrated in these studies, was also evident in our study. Specifically, the mean age of onset was found to be 18 months in children with a positive family history, which is lower compared to the overall mean age of 20 months. This finding aligns with results reported by Gatti S, et al. [12] Additionally, mean serum zinc levels were 42.9 µg/dl, 70 µg/dl, and 71.3 µg/dl in children with febrile convulsions, children with

fever alone, and normal healthy children, respectively. Statistically significant reductions in serum zinc levels were observed in children with febrile convulsions compared to both children experiencing fever alone and those considered normal. Conversely, children with fever alone did not exhibit a significant decline in serum zinc levels compared to normal children, consistent with previous findings indicating that while serum zinc levels decrease in children with fever, the extent of reduction is not as pronounced as in cases of febrile convulsions. Moreover, in this study, serum zinc levels did not demonstrate any significant correlation with factors such as age of onset, sex, axillary temperature, or the interval between fever onset and seizure occurrence [18]. All preceding studies have yielded similar findings in this regard [19]. In our study, the mean serum zinc level among normal children was determined to be 41.53 µg/dl, which is lower than the reference range of 70 to 110 µg/dl. Comparatively, the mean serum zinc levels in children with fever were 85.7 96.65 µg/dl, and in those with febrile convulsions, it was 71.29 µg/dl. Among children with fever in this study, the mean serum zinc level was 41.53 µg/dl, again lower than the corresponding values reported by Hauser WA et al. As serum zinc levels within any population are influenced by factors such as dietary patterns, deficiencies in vitamins A and D, and zinc levels in soil and water, further investigations are warranted to elucidate the potential underlying cause of this observation [20].

Conclusion

Zinc has been advocated to be used in children with acute watery diarrhea. The present showed that the zinc levels in children were significantly reduced in cases of children with fever as compared to normal controls. Given the multifaceted benefits of zinc in various bodily functions, supplementation with zinc may still offer a cost-effective preventive measure against febrile convulsions, particularly among vulnerable age groups, especially in cases where there is a positive family history.

References

1. Practice parameter: long-term treatment of the child with simple febrile seizures. American Academy of Pediatrics. Committee on Quality Improvement, Subcommittee on Febrile Seizures. Pediatrics. 1999 Jun;103(6 Pt1):1307-09
2. Annegers JF, Hauser WA, Shirts SB, Kurland LT. Factors prognostic of unprovoked seizures after febrile convulsions. New Eng J Med. 1987 Feb 26; 316(9):493-98.
3. Audenaert D, Van Broeckhoven C, De Jonghe P. Genes and loci involved in febrile seizures and related epilepsy syndromes. Human Muta. 2006 May; 27(5):391-401.
4. Nardone R, Brigo F, Trinka E. Acute Symptomatic Seizures Caused by Electrolyte Disturbances. J Clin Neurol. 2016; 12(1):21-33.
5. Berg AT, Shinnar S, Darefsky AS, Holford TR, Shapiro ED, Salomon ME, et al. Predictors of recurrent febrile seizures: a prospective cohort study. Archiv Pediatr Adolesce Med. 1997 Apr 1; 151(4):371-78.
6. Chang YC, Guo NW, Wang ST, Huang CC, Tsai JJ. Working memory of school-aged children with a history of febrile convulsions: a population study. Neurology. 2001 Jul 10; 57 (1):37-42.
7. Consensus statement Febrile seizures: long term management of children with fever associated seizures, Pediatrics. Dec 1980;(6):1009-12.
8. Mishra, Deepak Singhal, Ram S Upadhyay, Rajniti Prasad, Divya Atri. CSF zinc, magnesium, copper and GABA levels in febrile seizures-Op J Pediatr Neurol. 2007; 5:39-44.
9. Hartifeld DS, Tan J, Yager JY, et al. The association between iron deficiency and febrile seizures in childhood. Clinical Pediatr 2009; 48 (4):420-426.
10. Doose H, Ritter K, Völzke E. EEG Longitudinal Studies in Febrile Convulsions1. Neuropediatric. 1983 May; 14(02):81-87.
11. Frantzen E, Lennox-Buchthal M, Nygaard A, Stene J. A genetic study of febrile convulsions. Neurology. 1970 Sep 1; 20(9):909.
12. Gatti S, Vezzani A, Bartfai T. Mechanisms of fever and febrile seizures: putative role of the interleukin-system. Feb Seiz. 2002:169-88.
13. Graves RC, Oehler K, Tingle LE. Febrile seizures: Risks, evaluation, and prognosis. Am Fam Physician. 2012; 85:149–53.
14. Annegers JF, Blakley SA, Hauser WA, Kurland LT. Recurrence of febrile convulsions in a population-based cohort. Epilepsy Res. 1990; 5:209–16.
15. Berg AT, Shinnar S, Hauser WA, Alemany M, Shapiro ED, Salomon ME, et al. A prospective study of recurrent febrile seizures. N Engl J Med. 1992; 327:1122–27.
16. Frantzen E, Lennox-Buchthal M, Nygaard A. The electroencephalogram in children with febrile convulsions. Electroencephalogr Clin Neurophysiol. 1967;23(4):396.
17. Farwell JR, Lee YJ, Hirtz DG, Sulzbacher SI, Ellenberg JH, Nelson KB. Phenobarbital for febrile seizures--effects on intelligence and on seizure recurrence [published erratum appears in New England Journal of Medicine 1992 Jan 9;326(2):144. New England Journal of Medicine 1990;322(6):364-69.
18. Hamati-Haddad A, Abou-Khalil B. Epilepsy diagnosis and localization in patients with antecedent childhood febrile convulsions. Neurology. 1998 Apr 1;50(4):917-22.

19. Haspolat S, Mihçi E, Coşkun M, Gümüslü S, Özbenm T, Yegin O. Interleukin-1β, tumor necrosis factor-α, and nitrite levels in febrile seizures. J Child Neurol. 2002 Oct;17(10):749-51.
20. Hauser WA. The prevalence and incidence of convulsive disorders in children. Epilepsia. 1994 Apr;35: S1-S6.