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Original Research Article

SERUM ZINC LEVELS AND THEIR ASSOCIATION WITH SIMPLE FEBRILE SEIZURES IN CHILDREN: A PROSPECTIVE OBSERVATIONAL STUDY

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Abstract

Background: Febrile seizures affect 2-5% of children aged 6 months to 5 years, with zinc playing a vital role in neuronal excitability and seizure control. Studies suggest that zinc deficiency may contribute to seizure susceptibility. This study aimed to investigate the association between serum zinc levels and simple febrile seizures in children. **Materials and Methods:** This prospective observational study included 60 children aged 6 months to 5 years with simple febrile seizures. Serum zinc levels were measured at admission and categorised for comparative analysis. The seizure characteristics, including duration, were documented. Additionally, a history of febrile seizures and nutritional status were noted. Data were presented as mean, standard deviation, frequency, and percentage. **Result:** Among the children, 48% were aged 6-12 months, and 52% were 13-60 months. Males comprised 54% of the study population. The mean serum zinc level was 91.4 ± 18.62 mcg/dl. Zinc levels varied with age: 86.11 ± 12.58 mcg/dl (6-12 months) and 84.32 ± 13.37 mcg/dl (13-60 months). Zinc levels also differed by seizure duration: 81.28 ± 11.05 mcg/dl (<5 min), 83.56 ± 16.13 mcg/dl (5-10 min), and 76.41 ± 7.8 mcg/dl (10-15 min). Children with febrile seizures had lower zinc levels (77.15 ± 14.08 mcg/dl) than those without (81.82 ± 12.18 mcg/dl). Malnourished children had higher zinc levels (87.9 ± 16.23 mcg/dl) than well-nourished children (78.85 ± 12.9 mcg/dl). **Conclusion:** Our study concluded that the mean serum zinc concentrations were normal but varied according to age, seizure duration, and febrile seizure history. Children with prolonged seizures exhibit lower serum zinc levels, indicating a potential role for zinc in regulating seizure susceptibility.

INTRODUCTION

Febrile seizures are common childhood events occurring in 2-5% of children aged 6 months to 5 years, associated with fever but without central nervous system infection.1 The International League Against Epilepsy defines them as seizures in children over the age of 1 month with a febrile illness, excluding those with prior unprovoked seizures or meeting criteria for other acute symptomatic seizures.[2] The global occurrence rate varies, with figures ranging from 2-5% in the United States and Western Europe to 14% in India and Guam.[2] These are categorised as either simple or complex, with complex seizures characterised by a duration exceeding 15 minutes, the presence of focal characteristics, or recurrence within 24 hours.[1] Risk factors include viral illnesses, certain vaccinations, and genetic predisposition.[1] For simple febrile seizures in well-appearing children, routine diagnostic tests are unnecessary.[1] Management involves ruling out other underlying causes and addressing parental concerns.[2]

Zinc plays a key role in neurological function across the lifespan, from early brain development to adult brain maintenance.[3] Zinc plays a crucial role at both molecular and cellular levels. At the molecular level, it affects gene expression and enzyme activity. At the cellular level, zinc influences synaptic processes and neuronal plasticity.[4] Zinc plays a role in neurogenesis, cell survival, redox signalling, and immune modulation.4 Zinc acts as a neuromodulator in the olfactory bulb and other regions of the brain, modulating both excitatory and inhibitory neurotransmission by its action on varied receptors and ion channels.[5] Although zinc deficiency may compromise neurogenesis and immune function, excessive zinc deposition may cause oxidative stress, mitochondrial dysfunction, and neurodegeneration.[4] Alterations in zinc levels in the brain have been linked to a variety of neurological disorders,

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including neurodegenerative diseases, affective disorders, and epileptic seizures.[3]

Zinc deficiency is also linked to an elevated risk of seizures, especially febrile seizures in children. Lower blood and cerebrospinal fluid zinc concentrations have been found in children with febrile seizures.[6,7] Zinc signalling in epilepsy is intricate since both

intracellular and extracellular zinc may play protective or deleterious roles.8 The modulation of zinc homeostasis and supplementation might provide potential treatments for epilepsy and febrile seizures in high-risk patients.[7,8] As zinc has the potential to be involved in seizure regulation and neuronal excitability, its function in simple febrile seizures should be investigated. While previous research has provided inconsistent findings, more work is needed to determine a cause-and-effect relationship. This prospective observational study assessed the serum zinc levels in children with simple febrile seizures.

Aim

This study aimed to investigate the association between zinc levels and simple febrile seizures in children.

MATERIALS AND METHODS

This observational study included 60 children and was conducted at the Department of Neurology, Government Medical College, Ramanathapuram, from January 2024 to June 2024. Before initiation, the study was approved by the Institutional Ethics Committee (IEC). Informed consent was obtained from the parents before they participated in the study.

Inclusion criteria

Children aged 6 months to 5 years who presented with and were diagnosed with simple febrile seizures were included.

Exclusion criteria

Children aged <6 months and > 5 years, with congenital anomalies, and with a known history of seizures were excluded.

Methods

Data collection included demographic details such as age, sex, and body weight. Serum zinc levels were measured upon admission. The children were categorised into two groups: 6–12 months and 13–60 months. Zinc levels were classified into predefined ranges for comparative analysis. The seizure characteristics, including duration, were documented. Additionally, a history of febrile seizures and nutritional status were recorded to assess their association with serum Zn levels. Data were presented as mean, standard deviation, frequency, and percentage.

RESULTS

Regarding age distribution, 48% were aged 6-12 months, while 52% were 13-60 months. Male children comprised 54% of the study population, while female children comprised 46% [Table 1].

Table 1: Demographic characteristics.

		N (%)
Age	6-12 months	29(48%)
	13-60 months	31(52%)
Sex	Male	32(54%)
	Female	28(46%)

The children's mean age was 29.5 ± 20.43 months, mean weight was 15.28 ± 5.01 kg, and mean zinc level was 91.4 ± 18.62 mcg/dl [Table 2].

Table 2: Mean Demographic and biochemical characteristics

	Mean±SD
Mean Age (months)	29.5±20.43
Mean Weight (kg)	15.28±5.01
Mean Zinc Level (mcg/dl)	91.4±18.62

Zinc levels were predominantly within the 60–90 mcg/dL range in both age groups, with a higher proportion in the 13–60 months' group (74.2% vs. 65.6%). Mean zinc levels were comparable between the groups (86.11 ± 12.58 mcg/dL vs. 84.32 ± 13.37 mcg/dL), indicating minimal variation with age [Table 3].

Table 3: Zinc levels across age groups

		6-12 months	13-60 months
Zinc Level (mcg/dl)	60-90	19(65.6%)	23(74.2%)
	90-120	10(34.4%)	8(25.8%)
	Mean	86.11±12.58	84.32±13.37

The mean serum zinc level was highest among children with a seizure duration of 5–10 min (83.56 ± 16.13 mcg/dL), followed by those with a duration of <5 min (81.28 ± 11.05 mcg/dL), and lowest in those with a duration of 10–15 min (76.41 ± 7.8 mcg/dL). Children with a history of febrile seizures had a higher mean serum zinc level (81.82 ± 12.18 mcg/dL) than those without (77.15 ± 14.08 mcg/dL). Children with malnutrition had a higher serum zinc level (87.9

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± 16.23 mcg/dl) than those without (78.85 ± 12.9 mcg/dl) [Table 4].

Table 4: Serum zinc levels to seizure duration, febrile seizures, and malnutrition

		Mean±SD
		Serum Zinc level
Seizure duration (minutes)	< 5	81.28±11.05
	5-10	83.56±16.13
	10-15	76.41±7.8
H/O febrile seizure	Yes	81.82±12.18
	No	77.15±14.08
Febrile seizures with malnutrition	Yes	87.9±16.23
	No	78.85±12.9

DISCUSSION

In our study, febrile seizures were observed across different age groups, with a nearly equal distribution between younger and older children. Male children were slightly more affected than females were. A study by Hussain et al. found that febrile seizures were more common in younger male children with 68(68%) males and 32(32%) females with a mean age of 22.58±12.50 months.[9] The prospective observational study by Shajahan and Manuel reported febrile seizures are common in young children, with a slightly higher prevalence in males.[10] Also a study by Priyanishaben et al. reported the male-to-female ratio as 1.75:1.[11]

In our study, the mean serum zinc levels were within the normal range; however, they varied based on age, seizure duration, and history of febrile seizures. A higher proportion of younger children had lower serum zinc levels than older children. A study by Sowjan reported the mean serum zinc levels in children with simple febrile seizures was 58.4 micrograms/dl.[12] Tamilarasu et al. reported the mean serum zinc levels in the simple febrile seizures group was 57.69 mcg/dL about 66% of children with simple febrile seizures had low serum zinc levels.[13] A study by Lee and Kim reported the mean serum zinc level was 60.5±12.7 µg/dL in the febrile seizure group.[14]

In our study, serum zinc levels decreased with increasing seizure duration, with the lowest levels observed in children experiencing prolonged seizures. A survey by Sowjan reported that serum zinc levels were significantly low in children who had febrile seizures of prolonged duration.[12] Study by Margaretha and Masloman reported mean serum zinc levels in simple febrile seizure children with seizure periods <5, 5-10, and 10-15 minutes were 10.27 (±0.25) µmol/L, 9.02 (±0.81) µmol/L and 6.90 (±0.98) µmol/L, respectively.[15] A study by Santappanawar et al. reported that most cases (80%) had serum zinc levels <90 mcg/dl and the mean serum zinc level was 78.9±14.26 mcg/dl in cases with simple febrile seizures.[16]

In our study, children with a history of febrile seizures had lower serum zinc levels than those without. Nutritional status also influenced serum zinc levels, with malnourished children showing higher zinc concentrations than well-nourished ones. A study by Ganesh et al. reported children with a history of febrile seizures had lower serum zinc levels compared to those without.[17] A study by Santappanawar et al. reported children with simple febrile seizures have significantly lower serum zinc levels compared to well-nourished controls.[16] In A study by Arul et al. children with febrile seizures had lower serum zinc levels compared to febrile children without seizures.[18]

Limitations

The small sample size of 60 children limits generalisability, and as a single-centre study, findings may not represent broader populations. The study lacked a control group, making it difficult to determine whether zinc deficiency is specific to febrile seizures. The cross-sectional nature of the study, involving serum zinc measurements at a single point, limited our ability to evaluate changes over time or the effects of zinc supplementation. Serum zinc measurements may not accurately reflect zinc homeostasis in the brain, where its role in seizure susceptibility is crucial. While seizure duration was analysed, other aspects such as recurrence, severity, and treatment response were not evaluated. The findings suggest an association between zinc levels and febrile seizures but do not establish causality, highlighting the need for larger studies to confirm these findings.

CONCLUSION

Our study concluded that the mean serum zinc concentrations were normal but varied by age, seizure duration, and febrile seizure history. Children with prolonged seizures exhibit lower serum zinc levels, indicating a potential role for zinc in regulating seizure susceptibility. Children with a history of febrile seizures had lower zinc levels than those without, supporting zinc deficiency as an etiological factor. While these results support prior evidence, larger trials are needed to determine causality and whether zinc supplementation can prevent febrile seizures.

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