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SERUM ZINC AND IRON STATUS IN CHILDREN WITH FEBRILE SEIZURES: A PROSPECTIVE CASE CONTROL STUDY

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ABSTRACT

Background: Febrile seizures are the most common neurological disorder in early childhood. Micronutrients such as iron and zinc play a crucial role in neurodevelopment and neuronal excitability. Deficiency of these micronutrients may predispose children to febrile seizures. **Objectives:** To evaluate serum iron and zinc levels in children with febrile seizures and compare them with febrile children without seizures. **Methods:** This prospective case control study was conducted at a tertiary care centre over one year. Children aged 6–60 months presenting with febrile seizures were enrolled as cases, while age- and sex-matched febrile children without seizures served as controls. Serum iron, ferritin, and zinc levels were estimated. **Results:** A total of 120 children were included (60 cases and 60 controls). Mean serum iron (57.12 ± 23.64 µg/dL), ferritin (59.63 ± 30.55 µg/dL), and zinc levels (56.1 ± 9.1 µg/dL) were significantly lower in children with febrile seizures compared to controls ($p < 0.001$). Iron deficiency was observed in 66.6% of cases and zinc deficiency in 60%. Haemoglobin and red cell indices were also significantly reduced among cases. **Conclusion:** Children with febrile seizures have significantly lower iron and zinc levels compared to febrile children without seizures. Routine screening for iron and zinc deficiency should be considered in children presenting with febrile seizures.

KEYWORDS :

INTRODUCTION

Febrile seizures are seen approximately 2–5% of children between the ages of 6 months and 5 years[1] and cause parental anxiety and result in emergency department visits [2].

The pathophysiology of febrile seizures is complex and multifactorial. Several mechanisms have been proposed, including genetic susceptibility, immature neuronal networks, altered neurotransmitter balance, inflammatory cytokine and environmental influences[3]., Exact mechanism remains incompletely understood. Increasing attention has been directed toward the role of nutritional deficiencies, particularly micronutrients, in modulating neuronal excitability and seizure threshold.

Iron is a critical micronutrient involved in numerous neurophysiological processes, including neurotransmitter synthesis, myelination, energy metabolism, and regulation of neuronal growth and differentiation. Iron deficiency during early childhood can impair cognitive development, alter neurotransmitter metabolism, and disrupt normal brain maturation[4]. Iron deficiency may reduce seizure threshold by altering dopamine and gamma-aminobutyric acid (GABA) metabolism, thereby increasing neuronal excitability.

Zinc acts as a neuromodulator in both excitatory and inhibitory synapses, particularly within the hippocampus, a region critically involved in seizure generation[5]. Zinc influences the function of N-methyl-D-aspartate (NMDA) receptors and GABAergic pathways, thereby regulating neuronal excitability.

Several clinical studies have explored the association between iron deficiency and febrile seizures. While some authors reported lower serum iron, ferritin and zinc levels in children with febrile seizures, others have failed to demonstrate a consistent association[6-8]. These discrepancies may be due to differences in study design, population characteristics, nutritional status, and laboratory methods[9,10].

In India, nutritional deficiencies remain highly prevalent due to multiple factors. In this context, the present study was undertaken to evaluate serum iron and zinc levels in children presenting with febrile seizures and to compare them with age- and sex-matched febrile children without seizures.

MATERIALS AND METHODS

This prospective comparative study was conducted at Pragna Children's Hospital.

Children aged 6–60 months presenting with fever were screened for inclusion. Cases included children with simple febrile seizures, defined as generalized seizures lasting less than 15 minutes and not recurring within 24 hours. Controls were age- and sex-matched febrile children without seizures. Children with central nervous system infections, metabolic disorders, developmental delay, epilepsy, or those receiving iron or zinc supplementation were excluded. Written informed consent was obtained from parents or guardians.

Detailed clinical evaluation was performed, including history, anthropometry, and neurological examination. Blood samples were collected for estimation of haemoglobin, mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), serum iron, ferritin, and zinc.

Serum iron and ferritin were measured using automated biochemical analysers using colorimetric method, and serum zinc levels were estimated using atomic absorption spectrophotometry. Iron deficiency was defined as serum iron <50 µg/dL, and zinc deficiency as serum zinc <60 µg/dL.[11,12] Serum ferritin level is assessed by immunoassay, cutoff of <12 ng/mL was taken as ferritin deficiency.[1] Analyser equipment is calibrated and validated with internal and external quality controls.

Statistical analysis was performed using SPSS version 24. Continuous variables were expressed as mean ± standard deviation. Independent sample t-test was used for comparison of means, and chi-square test was applied for categorical variables. A p-value <0.05 was considered statistically significant.

Ethical approval was obtained from the Institutional Ethics Committee.

RESULTS

Demographic Profile of the Study Population

A total of 120 children were enrolled in the present study, comprising 60 cases (children with febrile seizures) and 60 controls (febrile children without seizures). The mean age of children in the case group was 20.4 ± 13.2 months, while that of the control group was 19.5 ± 12.08 months.

63.3% of cases and 60% of control children were male. Based on the modified Kuppuswamy socioeconomic classification, among the cases, 48 children belonged to the middle socioeconomic class and 12 to the lower class. Among the controls, 50 belonged to the middle class and 10 to the lower class.

Clinical Characteristics

The mean recorded temperature among cases was 100.67 ± 0.63°F, whereas among controls it was 100.24 ± 0.84°F.

Regarding nutritional status, among the 60 cases, 36 (60%) had normal nutrition, 12 (20%) had Grade I malnutrition, 6 (10%) had Grade II malnutrition, 3 (5%) had Grade III malnutrition, and 3 (5%) had Grade IV malnutrition. Among the controls, 45 (75%) were normally nourished, 9 (15%) had Grade I malnutrition, and 6 (10%) had Grade II malnutrition.

Among the cases, 42% had viral fever, 28% had lower respiratory tract infections (LRTI), 20% had acute gastroenteritis, 5% had upper respiratory tract infections (URTI), and 5% had malaria. In the control group, 40% had viral fever, 30% had LRTI, 20% had acute gastroenteritis, 5% had URTI, and 5% had malaria.

There was no statistically significant difference between the two groups with respect to age or sex, indicating adequate matching

Peripheral Smear Findings

Among the cases, 40% had a normal peripheral smear, while 60% showed abnormal findings. In contrast, 80% of controls had normal peripheral smears and 20% had abnormal findings. The difference was statistically significant ($\chi^2 = 10.72$; $p = 0.001$).

Haematological Parameters

Lower haemoglobin levels in children with febrile seizures (9.67 ± 1.2 g/dL) compared to controls (10.91 ± 0.9 g/dL). Red cell indices, including mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), and mean corpuscular haemoglobin concentration (MCHC), were also lower among cases, suggesting a predominance of microcytic hypochromic anaemia.

The mean packed cell volume (PCV) among cases was 29.6 ± 2.7%, compared to 34.05 ± 1.7% in controls; however, this difference was not statistically significant ($p = 0.5$).

Iron Profile

Mean serum iron levels were significantly lower in the febrile seizure group (57.12 ± 23.64 µg/dL) compared to controls (143.54 ± 21.85 µg/dL) with a p value < 0.001. Iron deficiency (serum iron < 50 µg/dL) was observed in 66.6% of cases, compared to 15% among controls.

Mean serum ferritin levels were also significantly reduced in cases (59.63 ± 30.55 ng/mL) compared to controls (158.34 ± 95.76 ng/mL, p = 0.001). Ferritin levels <50 ng/mL were observed in 83.3% of children with febrile seizures, whereas only 2 children in the control group had values below this threshold.

Serum Zinc Levels

Children with febrile seizures demonstrated significantly lower serum zinc levels (56.1 ± 9.1 µg/dL) compared to controls (89.2 ± 11.7 µg/dL), with a p value < 0.001. Zinc deficiency (serum zinc <60 µg/dL) was observed in 60% of cases, compared to 10% among controls.

Combined deficiency

Iron deficiency was observed in 66.6% of cases compared with 15% of controls, while zinc deficiency affected 60% of cases and 10% of controls. Combined iron and zinc deficiency was present in more than 40% of cases but only 5% of controls.

DISCUSSION

Febrile seizures often cause considerable parental anxiety and healthcare utilization. Micronutrient deficiencies—particularly iron and zinc—may play a significant role in lowering seizure threshold.

Comparison of Haemoglobin Levels with Other Studies

In the present study, children with febrile seizures had significantly lower haemoglobin levels (9.67 ± 1.2 g/dL) compared to controls (10.91 ± 0.9 g/dL; p < 0.001). Similar findings have been reported by Daoud et al., who documented mean haemoglobin levels of 9.8 ± 1.1 g/dL in cases compared to 11.2 ± 1.0 g/dL in controls[6]. Kumar et al. also observed significantly lower haemoglobin levels in children with febrile seizures (9.6 ± 1.3 g/dL) compared to febrile controls (11.0 ± 0.8 g/dL) [7].

Comparison of Serum Iron Levels with Other Studies

In the present study, mean serum iron levels were significantly lower in cases (57.12 ± 23.64 µg/dL) compared to controls (143.54 ± 21.85 µg/dL), with iron deficiency observed in 66.6% of cases. Daoud et al. reported mean serum iron levels of 46.2 ± 19.4 µg/dL in children with febrile seizures compared to 82.4 ± 29.1 µg/dL in controls[6]. Similarly, Kuntari et al. observed mean serum iron levels of 52.8 ± 18.6 µg/dL among cases versus 89.6 ± 24.3 µg/dL among controls[7].

Comparison of Serum Ferritin Levels with Other Studies

Serum ferritin levels in the present study were significantly lower in cases (59.63 ± 30.55 µg/dL) compared to controls (158.34 ± 95.76 µg/dL). Low ferritin levels (<50 µg/dL) were observed in 83.3% of children with febrile seizures. Daoud et al. reported mean ferritin levels of 29.5 ± 21.3 µg/dL in cases versus 53.7 ± 35.6 µg/dL in controls[14]. Similarly, Mahmoud et al. observed significantly reduced ferritin levels (34.2 ± 18.9 µg/dL) in children with febrile seizures compared to controls (76.5 ± 42.3 µg/dL) [9]. Although ferritin is an acute-phase reactant, the consistently low levels observed across studies suggest true iron depletion rather than inflammation alone.

Comparison of Serum Zinc Levels with Other Studies

In the present study, mean serum zinc levels were significantly lower in children with febrile seizures (56.1 ± 9.1 µg/dL) compared to controls (89.2±11.7 µg/dL). Zinc deficiency was present in 60% of cases. Mahmoud et al. reported mean zinc levels of 55.4 ± 8.2 µg/dL in cases compared to 87.6±10.4 µg/dL in controls[9]. Abdel Hameed et al. similarly reported reduced serum zinc levels (58.3 ± 7.6 µg/dL) among children with febrile seizures compared to controls (91.2±9.8 µg/dL) [10].

Combined Effect of Iron and Zinc Deficiency

Combined iron and zinc deficiency was present in more than 40% of cases but only 5% of controls. Similar observations have been reported in previous studies[9,15].

Strengths and Limitations

Strengths are prospective design, age- and sex-matched controls, and standardised biochemical assessment of iron and zinc status.

Limitations are single-centre design and relatively small sample size. The cross-sectional nature of the study precludes causal inference between micronutrient deficiency and febrile seizures. Dietary intake and inflammatory markers were not assessed. Long -term outcomes and seizure recurrence were not evaluated.

Clinical implications.

Screening for iron and zinc deficiency in children presenting with febrile seizures may help identify at-risk individuals. While routine supplementation for all children with febrile seizures cannot yet be universally recommended, targeted screening in high-risk populations may be beneficial. Future large-scale, multicentric, and longitudinal studies are required.

CONCLUSION

Children with febrile seizures have significantly lower serum iron and zinc levels compared to febrile children without seizures.

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