

## INCIDENCE AND ASSOCIATION OF SERUM HYPOMAGNESEMIA WITH FEBRILE SEIZURES IN YOUNG CHILDREN

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**Abstract:** Febrile seizures (FS) are a common occurrence in pediatric patients, affecting 2-5% of children between 6 months and 5 years of age. Various factors have been implicated in the pathogenesis of febrile seizures, including electrolyte imbalances such as hypomagnesemia, which can influence neuronal excitability and seizure susceptibility. **Objective:** The study aimed to assess the incidence of serum hypomagnesemia in children with febrile seizures and to examine the association between hypomagnesemia and the occurrence of febrile seizures. **Methods:** This retrospective case-control study was conducted at the Emergency Department of Shifa International Hospital from September 2023 to August 2024. A total of 300 children aged 6 months to 5 years were included in the study. Of these, 150 children presented with febrile seizures (case group), while 150 febrile children without seizures (control group) were selected as the comparison group. Patient data, including gender, body temperature, birth weight, age of onset, history of febrile seizures, gestational age, family history of seizures, and serum magnesium levels, were recorded. Serum magnesium levels were measured within 12 hours of a seizure episode, and results outside the reference range of 0.85-1.15 mmol/L were considered abnormal. Statistical analysis was performed using SPSS, and a Pearson correlation test was conducted to assess the association between serum magnesium levels and febrile seizures. **Results:** The mean serum magnesium level was significantly higher in the control group ( $0.99 \pm 0.0957$  mmol/L) than in the case group ( $0.95 \pm 0.133$  mmol/L) ( $p < 0.01$ ). Hypomagnesemia was observed in 42 (28%) of the children with febrile seizures compared to 15 (10%) of the control group. A negative correlation was found between serum magnesium levels and the occurrence of febrile seizures (Pearson's coefficient = -0.1709), indicating that lower magnesium levels were associated with a higher likelihood of febrile seizures. **Conclusion:** Children with febrile seizures exhibit significantly lower serum magnesium levels compared to febrile children without seizures. Hypomagnesemia appears to be associated with an increased risk of febrile seizures, particularly in those with a personal or family history of febrile seizures. Early identification and correction of hypomagnesemia in children presenting with fever may help in preventing febrile seizures.

**Keywords:** Febrile seizures, Magnesium, Pediatrics, Seizures

### Introduction

Febrile seizures, characterized by high body temperature and convulsions, are common in pediatric populations younger than 5 years (1). Seizures can occur as early as 6 months with body temperature above 38 °C without any neurological or metabolic disorders. The annual incidence of febrile seizures in the United States and Western Europe is 2-5%, whereas this incidence is 8-10% in Asia (2, 3, 4). A definite etiology of febrile seizure has not been established yet but some risk factors include an imbalance in neurotransmitter levels, electrolyte imbalance, and genetic predisposition (5).

An average human being requires 200-400 mg of magnesium among which 50-60% is stored in bones and soft tissues. It is responsible for the establishment and maintenance of electrical pathways for the transport of sodium and calcium across the cell membrane. A magnesium deficiency can lead to the release of voltage-gated calcium channels, inducing muscle and nerve excitability. NDMA receptor of glutamate, a neurotransmitter is inhibited by the production of extracellular magnesium. Hypomagnesemia causes

activation of NDMA, increasing the epileptiform electrical activity.

Literature has indicated a link between hypomagnesemia and febrile seizures (6). A study reported elevated magnesium levels in CSF of epileptic children possibly due to dysfunction in the cell membrane during epilepsy (7). Although most children with febrile seizures recover, their occurrence is risky as 2-8% of these children develop epilepsy later (8). This study was conducted to assess the incidence and association of serum hypomagnesemia in children with febrile seizures.

### Methodology

A retrospective case-control study was conducted in the Emergency Department of Shifa International Hospital from Sep 2023 to Aug 2024. A total of 150 children with febrile seizures and 150 febrile children without seizures were included in the study. The ages of the study population were ages 6 months to 5 years and children were healthy and had normal development. Children with CNS infection, congenital anomalies, history of magnesium supplement intake, and metabolic disorders were excluded. Parental

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consent was taken from all guardians. The study was approved by the ethical committee of the hospital.

Patients' data including gender, body temperature, birth weight, age of onset, history of febrile seizures, gestation age, family history of seizures, and levels of serum magnesium at admission were recorded. Mg was tested within 12 hours after a seizure episode and results outside the reference range of 0.85-1.1.5 mmol/l were considered abnormal.

SPSS version 24 was used for data collection and analysis. Mean and standard deviation was used to present continuous data and percentage was used for categorical data. Continuous variables were compared by independent t-tests and categorical variables were compared by chi-squared test. Pearson's correlation coefficient was used to assess the association between hypomagnesemia and febrile seizures. Statistical significance was determined by a two-tailed p-value less than 0.05.

## Results

The mean age in the cases group was  $31.20 \pm 14.3$  months and  $34.68 \pm 12.26$  in the control group. 12 children (8%) in the cases group and 3 children (2%) in the control group were born preterm. Febrile seizures were caused by respiratory tract infection in 98% of children while all control group patients had respiratory infections. An individual history of febrile seizures was more common in the cases group (37.4%) than the control group (4%). 95% of the population had simple febrile seizures and 5% had complex febrile seizures (Table 1).

The mean serum magnesium was significantly higher in the control group ( $0.99 \pm 0.0957$ ) than in cases ( $0.95 \pm 0.133$ ) ( $p < 0.01$ ). 42 (28%) cases and 15 (10%) controls had hypomagnesemia. Serum magnesium levels were inversely associated with the incidence of FS (Pearson's coefficient =  $-0.1709$ ,  $p < 0.05$ ) indicating that hypomagnesemia can lead to the occurrence of FS (Table 2).

**Table 1: Comparison of Baseline Features Between Study Groups**

Variables	Cases group	Control group	P
Age in months	31.20 ± 14.3	34.68 ± 12.26	1.722
<b>Sex</b>			
Male	99 (66%)	99 (66%)	0.563
Female	101 (44%)	101 (44%)	
Birth weight in kilograms	3.31 ± 0.5140	3.32 ± 0.509	0.836
<b>Gestation age</b>			
Preterm	12 (8%)	3 (2%)	
Full term	138 (92%)	147 (98%)	0.02
Body temperature	39.33 ± 0.73	39.11 ± 0.64	0.999
<b>Aetiology of febricity</b>			
Respiratory infection	147 (98%)	150 (100%)	
Urinary tract infection	3 (2%)	-	0.497
History of febrile seizures	56 (37.4%)	6 (4%)	
Family history of seizures	51 (34%)	-	

**Table 2: Serum Magnesium Levels and Incidence of Hypomagnesemia**

Variables	Cases group	Control group	P
Mean serum magnesium levels	0.95 ± 0.133	0.99 ± 0.0957	0.005
Hypomagnesemia	42 (28%)	15 (10%)	0.0
Normal range	108 (72%)	135 (90%)	

## Discussion

This study was conducted to assess the incidence and association of serum hypomagnesemia with febrile seizures in children. The results revealed a negative relationship between hypomagnesemia and FS, indicating hypomagnesemia as the cause of febrile seizures in children. The study groups did not differ significantly concerning demographics. The mean age in the cases group was  $31.20 \pm 14.3$  months and  $34.68 \pm 12.26$  in the control group. These results were higher than Tarhani et al and Namakin et al where the mean age of children with FS was  $29.4 \pm 17.6$  and  $24.1 \pm 13.4$ , respectively (9) Children in Kumar et al were older than children in our study i.e.  $35.3 \pm 2.5$  months (10) Febrile seizures were more common in boys (66%) than girls (44%). This finding is similar to Jisha et al and Rice et al where 56% and 60% study population with FS were males, respectively, implying male disposition to febrile

seizures (11, 12). Kobuta et al reported a sensitivity of 88.9% and specificity of 76.2% of the male gender as a risk factor of FS (13).

The birth weights in both groups did not differ significantly i.e.  $3.31 \pm 0.5140$  vs  $3.32 \pm 0.509$ . Children with febrile seizures were more likely to be born preterm (8%) as compared to ones without seizures (2%). Christensen et al

Comply with these study results (14). The mean body temperature of FS children was  $39.3$  °C similar to  $39.4$  °C as reported by Baaker et al (15) Studies have also shown that fever with temperature  $< 39$  °C in viral infections induces convulsions in patients (16). 98% of children with febrile seizures had respiratory tract infections and 34% had a family history of FS. Debroy et al and Peng et al reported similar results. (17, 18). 95% of the population had simple seizure episodes, this incidence is higher than in Thakur et al where 78% of children had simple seizures. However, the

incidence of complex seizures was 21% which is higher than 5% as reported in our study (19).

FS children had significantly lower magnesium levels ( $0.95 \pm 0.133$ ) than children without FS ( $0.99 \pm 0.0957$ ) and were negatively associated with the incidence of febrile seizures. Pabani et al and Debroy et al agreed with these results (17, 20). and Baek et al concluded that deficiency of magnesium was an independent predictor of FS.21 Magnesium and zinc levels in FS children aged from 6 months to 6 months in Kashlan et al were significantly low and supplements were prescribed (22). An assessment of magnesium and copper in FS showed that Mg was significantly low but Cu was higher as compared to children without FS and both elements were associated with FS (23).

Our study has some limitations. The sample size of febrile Seizure patients limited the generalizability of the findings hence larger studies are needed to back these results.

### Conclusion

Febrile seizure children have low serum magnesium as compared to children without FS. Hypomagnesemia is negatively associated with the occurrence of FS which is common in children with personal and family history of febrile seizures.

### Declarations

#### Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

#### Ethics approval and consent to participate

Approved by the department concerned. (IRBEC-SIISB-93/23)

#### Consent for publication

Approved

#### Funding

Not applicable

### Conflict of interest

The authors declared the absence of a conflict of interest.

### Author Contribution

#### MUHAMMAD HAMZA AKRAM (PGY4)

Coordination of collaborative efforts.

Study Design, Review of Literature.

#### ANWAAR KHURSHID (PGY4)

Conception of Study, Development of Research Methodology Design, Study Design, Review of manuscript, final approval of manuscript.

Conception of Study, Final approval of manuscript.

#### HUSNAIN MAZHAR (SMO)

Manuscript revisions, critical input.

Coordination of collaborative efforts.

Data entry and Data analysis, drafting article.

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