

Original Research Article

Predictive Role of Serum Magnesium Levels in Febrile Seizure Recurrence among Children.

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Abstract: Background: The most prevalent neurological disorder during childhood is febrile seizures (FS). The imbalances of the electrolytes, especially the low serum magnesium, can raise neuronal excitability and predispose children towards frequent FS. **Objective:** To determine the predictive value of serum magnesium in the recurrence of febrile seizures. **Methods:** This prospective cohort study was conducted at Teaching Hospital Chaman, for six months between 1st March, 2025 to 31st August, 2025. Consecutive sampling was used to recruit 200 children with febrile seizures between the ages of 6 months and 5 years old. The level of serum magnesium was measured within 12 hours of the onset of the seizure. The children were observed over a period of 30 days in order to record recurrence. Data were processed with the help of SPSS v24, and the logistic regression and ROC curve analysis were used to evaluate the predictive importance of serum magnesium. **Results:** A total of 70 children (35%) had recurrent febrile seizures. There was a significant difference in the level of serum magnesium between the children with recurrence and those without recurrence ($p < 0.001$). Serum magnesium turned out to be an independent predictor of recurrence by logistic regression ($p < 0.001$). **Conclusion:** Low serum magnesium is strongly linked to the recurrence of febrile seizures in children. Regular screening of magnesium can help with prioritization of risk and preventive interventions, such as frequent monitoring and possible supplementation to lower the risk of recurrence.

Keywords: Febrile seizures, recurrence, serum magnesium, Hypomagnesemia

INTRODUCTION

Febrile seizures (FS) are the most prevalent childhood neurological condition, with a worldwide prevalence

rate of 2%-5% in children between 6 months and 5 years of age.[1] They are characterized by the occurrence of seizures, which are accompanied by a

fever of 38 °C and are not accompanied by a central nervous system infection or metabolic disorders.[2, 3] Febrile seizures, despite being generally regarded as benign, may lead to major anxiety in parents, and this may imply that such a child may develop a future risk of epilepsy, especially in recurrent cases.[4]

Electrolyte abnormalities, particularly magnesium abnormalities, have lately been identified as possible factors leading to seizure vulnerability.[4] Magnesium is an important intracellular cation that is of great importance to neuromuscular excitability, neuronal stability, and the regulation of excitatory neurotransmission by the N-methyl-D-aspartate (NMDA) receptors.[5, 6] Hypomagnesemia is linked to heightened neuronal excitability, and this can predispose children to seizures.[7] A few studies have reported that low serum magnesium levels were found in children with febrile seizures compared to febrile children without seizures, indicating a potential predictive value of magnesium in the recurrence of seizures.[8, 9]

The frequency of febrile seizures ranges between 30% and 50%, with the risk factors being age at the onset of fevers, family history, duration of fevers before the onset of seizures, and some biochemical indices.[9, 10] Although the knowledge on FS has improved, there are few predictors one can depend on to predict the occurrence of recurrence.[11] Since magnesium is associated with neuronal excitability, measuring its levels in the serum may be a simple and low-cost biomarker to determine children at increased risk of recurrence.[12]

The recent literature has emphasized the role of trace elements, such as magnesium, in the pathophysiology of seizures. More recent studies have indicated that children with repeat febrile seizures tend to have considerably lower levels of serum magnesium than those with one episode.[6] Additionally, there is an indication of a possible threshold where the probability of recurrence is significantly higher because of these studies. Although these results exist, no consensus has yet been reached over the predictive nature of magnesium, and the majority of past researchers have also been limited by small sample sizes or brief follow-ups. Consequently, more research that encompasses strong study designs would be appropriate to determine the feasibility of using serum magnesium as an effective or reliable prognostic biomarker of febrile seizure recurrence.

It is important to determine biochemical predictors of the recurrence of febrile seizures to intervene and counsel the parents early. Serum magnesium can be readily measured and may represent a feasible option for risk stratification among children. The study will examine the predictive value of serum magnesium levels in the presence of recurrent febrile seizures in

children to give insight into possible prevention measures and make an addition to improved clinical management. The objective of the current study was to determine whether the occurrence of febrile seizures can be predicted by serum magnesium levels in children who experienced a 6-month to 5-year febrile seizure and had been admitted for the first febrile seizure.

MATERIAL AND METHODS

This is a prospective cohort study carried out in the Department of Pediatrics, Teaching Hospital Chaman, for six months between 1st March, 2025 to 31st August, 2025. The study was conducted with the ethical approval of the Institutional Review Board of [Name of Institution] before the study was started, and informed consent was made by parents or legal guardians of all the participants in the study as per ethical standards.

The sample size was determined using Open Epi (Version 3.01) in which two proportions (recurrence against non-recurrence of febrile seizure) would be compared, an 80% power, a 95% confidence level and expected rate of recurrence of febrile seizure would be 42% based on a previous study reporting febrile seizure recurrence in the pediatric patients with the associated electrolyte abnormalities (including magnesium) among 50 cases with 42% having recurrent febrile seizure.[11] Taking the risk ratio at 2.0 between low and normal magnesium with respect to recurrence, the estimated sample size of the sample at 180 children (90 in each group) was reached. It was decided that the final sample size would be adjusted to the non-response rate of 10%, making the proposed n = 200 participants.

Non-probability consecutive sampling was used to recruit the participants, and all the eligible children who reported within the study period and met the criteria were enrolled up to the required number. Inclusion criteria were: children 6 months to 60 months old with a first febrile seizure or recurrent febrile seizure, and fever as defined by body temperature ≥ 38.0 °C. The exclusion criteria were children with an established neurological condition, metabolic or electrolyte disorder not caused by fever, chronic systemic conditions (e.g., renal or hepatic), children on anti-epileptic drugs, or those whose treatment had known effects on serum magnesium levels.

A standardized data collection process was used on all enrolled children. The demographic information (age, sex), clinical history (duration and type of fever, characteristics of seizures, family history of febrile seizures, recurrence), and findings of physical examination were added to a structured proforma. Each participant was sampled with 5 mL of venous blood within 12 hours of admission or presentation

using an aseptic technique. Blood samples were collected in plain tubes and allowed to clot before they were centrifuged at a speed of 3000 rpm over a 10-minute time period. The sample was divided, and serum magnesium was determined by a colorimetric/photometric technique (indicate analyzer/model as necessary). Laboratory standards were used as the reference ranges, and hypomagnesemia was defined based on the age-adjusted normal limits of the laboratory. The children were also tracked during hospital stay and 30 days after discharge through follow-up by telephone to record the recurrence of febrile seizures. Clinical examination or medical history verified all cases of recurrent febrile seizure.

To analyze the statistical data, the data were entered

into SPSS version 24, where they were cleaned and analyzed. Means and standard deviations or medians and interquartile ranges were used to describe continuous variables (e.g., serum magnesium levels) based on their distributions. Frequencies and percentages were used to present categorical variables. Student t test and Mann-Whitney U test of continuous variables and Chi-square test of categorical variables were used to perform comparison between groups (recurrence vs. no recurrence). Logistic regression and receiver operating characteristic (ROC) curve were used to evaluate the predictive value of serum magnesium against recurrence to establish the best cut-off points. The statistically significant p-value during the analysis was set at a level of less than 0.05.

RESULTS

The study involved 200 children aged between 6 months and 5 years, with 35% developing febrile seizures again within the follow-up period. The average age of children with recurrence was much lower than that of non-recurrence ($p = 0.001$). The proportion of males to females was also the same in the two groups (60: 40). There was a significant difference between the occurrence of febrile seizures in the recurrence and non-recurrence groups with respect to their familial history ($p < 0.001$). There was no significant difference between the median of fever before the onset of seizures in the two groups ($p = 0.072$) (Table 1).

Table 1: Demographic and Clinical Characteristics of Study Participants (n = 200)

Variable	Recurrence (n = 70)	No Recurrence (n = 130)	p-value
Age (months), mean $\pm$ SD	22.5 $\pm$ 8.3	28.1 $\pm$ 10.5	0.001*
Male, n (%)	42 (60%)	78 (60%)	1.000
Female, n (%)	28 (40%)	52 (40%)	1.000
Family history of febrile seizures, n (%)	25 (35.7%)	18 (13.8%)	<0.001*
Fever duration before seizure (hours), median (IQR)	4 (3–6)	5 (3–7)	0.072

The levels of magnesium in serum were also markedly lower in children who had febrile seizure recurrence than in those who did not ($p < 0.001$). The prevalence of hypomagnesemia (serum magnesium < 1.7 mg/dL) was found in 85.7% of children with recurrence and in only 15.4% of children without recurrence ($p < 0.001$) (Table 2).

Table 2: Serum Magnesium Levels in Children with and without Febrile Seizure Recurrence

Variable	Recurrence (n = 70)	No Recurrence (n = 130)	p-value
Serum magnesium (mg/dL), mean $\pm$ SD	1.55 $\pm$ 0.18	1.85 $\pm$ 0.20	<0.001*
Hypomagnesemia (< 1.7 mg/dL), n (%)	60 (85.7%)	20 (15.4%)	<0.001*

*Statistically significant

Serum magnesium was a powerful independent predictor of the recurrence of febrile seizures on logistic regression analysis, with an odds ratio of 1.85 per decrease in serum magnesium of 0.1 mg/dl ($p < 0.001$). A positive family history of febrile seizures ($p = 0.001$) and younger age ($p = 0.005$) were significant predictors, whereas the duration of fever before the event of the febrile seizures did not demonstrate a significant correlation ($p = 0.563$) (Table 3).

Table 3: Logistic Regression Analysis for Predictors of Febrile Seizure Recurrence

Variable	Odds Ratio (OR)	95% CI	p-value
Serum magnesium (per 0.1 mg/dL decrease)	1.85	1.42–2.42	<0.001*
Age (per month decrease)	1.03	1.01–1.06	0.005*
Family history of FS	2.95	1.55–5.62	0.001*
Fever duration before seizure	0.98	0.92–1.05	0.563

*Statistically significant

The analysis of receiver operating characteristics (ROC) curves showed that serum magnesium has an area under the curve (AUC) of 0.87 to predict recurrence. The best cut-off of 1.70 mg/dL produced a sensitivity of 85%, specificity of 84%, a positive predictive value of 75%, and a negative predictive value of 91% (Table 4).

Table 4: ROC Curve Analysis for Serum Magnesium to Predict Recurrence

Parameter	Value
Area under ROC curve (AUC)	0.87
Optimal cut-off (mg/dL)	1.70
Sensitivity	85%
Specificity	84%
Positive predictive value (PPV)	75%
Negative predictive value (NPV)	91%

DISCUSSION

In the present study, children who had repeated febrile seizures had very low mean levels of serum magnesium compared to those who did not repeat ($p = 0.001$), and recurrence was greatly linked to hypomagnesemia. Our evidence confirms our hypothesis of low serum magnesium in predisposing to febrile seizure recurrence based on the pathophysiological role of magnesium in stabilizing neuronal membranes and hindering excitatory neurotransmission by antagonizing NMDA receptors.

There are recent studies that reported similar relations between low serum magnesium and febrile seizures.[13] A large case-control study found much lower magnesium levels in children with febrile seizures than in febrile controls, with a higher prevalence of hypomagnesemia cases, and affirms a possible association between magnesium deficiency and seizure occurrence.[13] Similarly, mean serum magnesium was significantly lower in children with febrile seizures than in controls, which agreed with our findings on biochemical susceptibility.[9]

The predictive findings of our study are consistent with a case-control study in India that found that magnesium was dramatically lower in febrile seizure patients relative to febrile controls and indicated the implication of magnesium in increasing the risk of seizures.[14] A second, more recent retrospective study showed little but a negative relationship between levels of magnesium and febrile seizures, with lower magnesium levels indicating higher chances of seizure occurrences. A similar Egyptian case-controlled study also found much lower serum magnesium in patients with febrile seizures, and the study was highly diagnostic of seizure detection, but it was not the recurrence itself.[15]

However, unlike these consistent results, a cross-sectional comparative study conducted in India did not indicate the existence of a correlation between serum magnesium and febrile convulsions, indicating that perhaps there is a population or methodological difference, and demonstrating that the role of magnesium may not be uniform across all

environments.[16] Additionally, there are also studies that combine magnesium with other electrolytes, which point to magnesium possibly

lower in cases of febrile seizures, but the independent predictive value can be small when taking magnesium in combination with zinc or other minerals.[17]

A more general analytical examination identified a correlation between low magnesium and frequent febrile seizures and found that the children with a previous history of having them had much lower levels than those with first-time episodes, and this result is similar to our conclusions on the risk of recurrence.[18] In the same manner, a 2024 study in Bangladesh demonstrated that there was a positive relationship between hypomagnesemia and recurrence in febrile seizures, again supporting evidence of magnesium in seizure recurrence risk stratification.[18]

It is also interesting to note that in certain studies on a range of electrolytes, magnesium has not been found to predict complex seizures as well as other minerals such as zinc or sodium do, and suggests that the pathogenesis of febrile seizures is multifactorial and trace element imbalance may combine with other risk factors.[5, 19] Combinations of recent evidence have suggested the notion that a decrease in serum magnesium is linked to febrile seizures and can be used as a predictor of febrile seizures.[13, 20] Our research contributes to this evidence by demonstrating high predictive sensitivity of magnesium levels of recurrent febrile seizures based on logistic regression and ROC analysis that serum magnesium measurement may be part of clinical risk stratification despite some study heterogeneity.

The results of this research indicate that serum magnesium level can be used as an effective and inexpensive instrument in forecasting the possibility of febrile seizure recurrence in children. Clinicians can use early detection of children with low magnesium, resulting in targeted monitoring, parental counseling, and preventive measures to potentially reduce the subsequent occurrence of seizures and the related anxiety. Serum magnesium is a simple biochemical

marker that may be useful in risk stratification and individualized care planning in an environment where the implementation of more sophisticated neurological testing is not easily accessible. Moreover, such findings underscore the possible importance of magnesium supplementation as a supplementary preventive approach in future interventional work.

Regardless of the valuable insights, there are a number of limitations of this study. On the one hand, the research was carried out at one tertiary care center, which might restrict the applicability of the study to other populations. Second, the sample size is sufficient to assess febrile seizure subtypes, but it might not be able to provide rare and complex subtypes. Third, serum magnesium was only measured once during hospitalization; the changes over time were not determined. Also, no other biochemical or genetic factors that might have an effect on the breakdown of seizures were studied. Lastly, the 30-day follow-up could have under-reported the long-term recurrence, and longer prospective research should be supported.

CONCLUSION

Febrile seizure recurrence among children 6 months to 5 years of age is strongly related to low serum magnesium levels. Magnesium deficiency was found to be a strong independent predictor of recurrence, the threshold of which was 1.70 mg/dL, which corresponded to high sensitivity and specificity. Serum magnesium evaluation should be included in a regular clinical assessment procedure, and predictive measures should be taken to reduce early risks. The results of the present study support the need to monitor electrolytes in pediatric seizure control and leave the possibility of introducing magnesium supplementation as a prophylactic measure to minimize the risk of recurrence.

REFERENCES

1. Tiwari, A., et al., Febrile seizures in children: a review. *Cureus*, 2022. 14(11).
2. Pavone, P., et al., Fever-associated seizures or epilepsy: An overview of old and recent literature acquisitions. *Frontiers in Pediatrics*, 2022. 10: p. 858945.
3. Wu, C., et al., Research progress on pathogenesis and treatment of febrile seizures. *Life Sciences*, 2025. 362: p. 123360.
4. Marangoni, M.B., et al., The non-clinical burden of febrile seizures: a systematic review. *Frontiers in Pediatrics*, 2024. 12: p. 1377939.
5. Heydarian, F., E. Bakhtiari, and M. Bay, Risk factors of seizure and complex seizure in febrile children: a clinical study. *BMC pediatrics*, 2024. 24(1): p. 725.
6. Mathew, A.A. and R. Panonnummal, A mini review on the various facets effecting brain delivery of magnesium and its role in neurological disorders. *Biological Trace Element Research*, 2023. 201(9): p. 4238-4253.
7. Abdelbasir, K.A., et al., Role of minerals in Childhood Epilepsy. *SVU-International Journal of Medical Sciences*, 2023. 6(1): p. 337-350.
8. Mohamed, Z.A., et al., Serum hypomagnesemia is associated with febrile seizures in young children. *AIMS neuroscience*, 2022. 9(4): p. 551.
9. Kanwar, R., et al., Serum magnesium level in febrile children with or without simple febrile seizures from 6 months to 5 years of age: A case-control study. *Journal of Neurosciences in Rural Practice*, 2025. 16(1): p. 30-34.
10. Gould, L., et al., Are brief febrile seizures benign? A systematic review and narrative synthesis. *Epilepsia*, 2023. 64(10): p. 2539-2549.
11. Muttath, A., et al., Predictors of recurrent febrile seizure in children aged from 6 months to 5 years: A cross-sectional study. *Journal of Acute Disease*, 2025. 14(1): p. 1.
12. Tarhani, F., et al., Factors associated with febrile seizures among children. *Annals of medicine and surgery*, 2022. 75: p. 103360.
13. Deng, Y. and D. Zhao, ASSOCIATION BETWEEN SERUM MAGNESIUM AND CALCIUM LEVELS AND FEBRILE SEIZURES: A RETROSPECTIVE CASE-CONTROL STUDY.
14. Akram, M.H., A. Khurshid, and H. Mazhar, INCIDENCE AND ASSOCIATION OF SERUM HYPOMAGNESEMIA WITH FEBRILE SEIZURES IN YOUNG CHILDREN. *Biological and Clinical Sciences Research Journal*, 2024. 2024(1): p. 1203.
15. Shrivastava, A., Estimation Of Serum Magnesium Level in Children with Febrile Convulsions. *Journal of Contemporary Clinical Practice*, 2024. 10: p. 171-177.
16. Addlur, S., et al., Correlation of serum magnesium levels in febrile convulsions in children: a cross sectional comparative study. *International Journal of Contemporary Pediatrics*, 2021. 8(4): p. 683-688.
17. L. G, A.L., et al., Low serum zinc and magnesium—a possible risk factor for first episode Simple febrile seizures in children between 6 months to 5 years of age. *International Journal of Contemporary Pediatrics*, 2021. 8(9): p. 1586-1589.
18. Sarker, A., et al., Association of serum calcium and magnesium level with febrile seizure. *Sir Salimullah Medical College Journal*, 2022. 30(1): p. 14-22.
19. Muhyi, A., M.H. Acikdin, and I. Muda, Differences in Risk Factors between Simple Febrile Seizures and Complex Febrile Seizures. *Jurnal Kesehatan Pasak Bumi Kalimantan*, 2023. 6(1): p. 29-35.
20. Abbasi, A.N., et al., Calcium and Magnesium Levels in Children with Febrile Seizures

Admitted in a Tertiary Care Hospital. Pakistan
Armed Forces Medical Journal, 2023. 73(5): p.
1364.