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**Original Research Article**

# Comparison of serum electrolytes in children with febrile seizures to febrile children without seizures: a case control study

**K. Jayasurya*, Pankaj Kumar Singhal, Manav Gaba, Gaurav Mathur**

Department of Pediatrics, Jaykaylon Mother and Child Hospital, Government Medical College, Kota, India

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***Correspondence:**
Dr. K. Jayasurya,
E-mail: jayasuryakumaran06@gmail.com



## ABSTRACT

**Background:** Febrile seizures (FS) are the most common type of seizures in children aged 6 to 60 months, occurring during fever episodes without underlying CNS infections or prior afebrile seizures. Electrolyte imbalances are thought to contribute to FS, but their exact role remains unclear. This study aimed to investigate the association between serum electrolyte levels (sodium, potassium, calcium and magnesium) in children with febrile seizures and compare them to febrile children without seizures.
**Methods:** A case-control study was conducted at the JK Lon Children and Mothers Hospital, Government Medical College, Kota, Rajasthan, over four months. Sixty-one children with febrile seizures were identified as cases and 60 febrile children without seizures served as controls. Data on sociodemographic and clinical parameters, including serum electrolyte levels, were collected. Chi-square tests and t-tests were used to analyse categorical and continuous variables, respectively.
**Results:** Significant differences were found in serum calcium and potassium levels between the two groups. Hypocalcemia was more prevalent in controls (75%) compared to cases (29.51%) (p=0.000), while hypokalemia was also higher in controls (35%) than in cases (6.56%) (p=0.000). No significant differences were observed in sodium and magnesium levels between the groups.
**Conclusions:** Calcium and potassium levels appear to be associated with the occurrence of febrile seizures in children, while sodium and magnesium levels showed no significant differences. Further studies are needed to clarify the role of electrolytes in FS pathogenesis.

**Keywords:** Epilepsy, Febrile children, Febrile seizures, Paediatric neurology, Serum electrolytes

## INTRODUCTION

Febrile seizures (FS) are the most common cause of seizures in children. FS occur between the ages of 6 and 60 months with a peak incidence at 12-18 months, associated with a temperature of 38°C (100.4°F) or higher. These seizures are not the result of CNS infection or metabolic imbalance and occur in the absence of a history of prior afebrile seizures.[1] Although FS do not constitute epilepsy, they are a common concern in paediatric neurology and epilepsy clinics. Between 2% and 5% of neurologically healthy infants and children experience at least one, usually simple, febrile seizure.[2-4] Two-thirds of children with FS have no evident risk factors, while one-third have a positive family history of FS or epilepsy.[5] Understanding FS is crucial as 30-40% of children experience recurrences after the first episode.[6] FS is a multifactorial disorder, with known risk factors including serum electrolyte imbalances, genetic predisposition, changes in neurotransmitter levels, degree and duration of fever, age, and sex.[7-9] The roles of trace elements such as sodium, calcium, potassium and

magnesium in causing FS have been identified.[10,11] Magnesium, the most abundant intracellular divalent cation, is crucial for numerous cellular functions and significantly impacts neural excitability. It is the fourth most common cation in the body, with normal plasma levels between 1.5 to 2.3 mg/dl.[10] It serves as an essential cofactor for enzymes such as ATPases, Cyclase and Kinases, important for nerve conduction and maintaining cell membrane stability.[13] Magnesium is predominantly found in muscles, soft tissues, bones and red blood cells, and its key functions include establishing and maintaining electrical potentials across cell membranes and inhibiting voltage-gated calcium channels.[14]

The small ionized pool of calcium in the circulatory system, extracellular fluid, and various tissues mediates blood vessel contraction and dilation, muscle function, blood clotting, nerve transmission and hormonal secretion.15 Maintaining normal levels of these trace electrolytes is crucial for the central nervous system to function normally.

Potassium has a strong relationship with sodium, the main regulator of extracellular fluid volume, including plasma volume.16 Normal serum concentrations of potassium range from about 3.6 to 5.0 mmol/L.16,17 The sodium-potassium (Na+/K+) ATPase transporter maintains a transmembrane electrochemical gradient as intracellular potassium concentration is approximately 30 times higher than the extracellular concentration.18 This gradient is essential not only for cellular tonicity but also for proper nerve signaling, muscle contraction and kidney function.

Sodium is the major cation of extracellular fluid. The concentration gradient between the ECF and intracellular fluid is maintained by the sodium–potassium pump activity. It's role is crucial for maintaining ECF volume because of its important osmotic action and is equally important for the excitability of muscle and nerve cells and for the transport of nutrients and substrates through plasma membranes.19

Alterations in these electrolytes can disrupt the ion gradient across cell membranes, leading to abnormal nerve discharges and potentially resulting in convulsions, especially in children.9 This study aims to study about the association between serum electrolytes (sodium, potassium, calcium, magnesium) in children with febrile seizures and compare with febrile children without seizures.

## METHODS

### *Study place*

We conducted a case-control study in the department of paediatrics at JK Lon children and mothers' hospital, Government Medical College, Kota Rajasthan.

### *Study duration*

Study was done for a period of 4 months.

### *Sample size*

A total of 121 children were recruited, with 61 identified as cases and 60 as controls. The cases were defined as children experiencing febrile seizures, whereas the controls were children who had a fever but no seizures within age group of 6-60 months.

### *Inclusion criteria*

All consequent cases of febrile seizures were included and febrile children reporting to the hospital during the same period were recruited as controls.

### *Exclusion criteria*

Children with known neurological disorder were excluded.

### *Data collection*

A structured questionnaire was used to collect data on various sociodemographic and clinical parameters. Sociodemographic variables included age and sex. Clinical parameters included duration of fever, type of seizure, duration of seizure, serum levels of sodium, potassium, calcium and magnesium.

### *Data analysis*

All Continuous variables such as age, duration of fever, duration of seizure and serum levels of sodium, potassium, calcium and magnesium were summarized as median with Interquartile range. Serum levels of sodium, potassium, calcium and magnesium were then categorized into hypo, normal, and hyper states to facilitate a comparative analysis between the cases and controls.

Other categorical variables such as sex and type of seizure were summarized as frequency with proportion. To compare categorical variables between the groups, the chi-square test was applied, whereas the t-test was employed for comparing the means of continuous variables. A p-value of less than 0.05 was considered statistically significant, ensuring the reliability of the results.

## RESULTS

### *Baseline characteristics*

Table 1 presents the baseline characteristics of the study participants. The median age for cases was 2.5 years (IQR: 1.0-3.5) compared to 3.0 years (IQR: 3.0-4.0) for controls, with a statistically significant difference

(p=0.0002). The sex distribution was not significantly different between the groups, with 29.51% males in the cases and 43.33% males in the controls (p=0.114). The median duration of fever was significantly shorter in cases (12 hours IQR: 10 hours-1 day) compared to controls (3.0 days, IQR: 3.0-4.0), with a p-value of 0.0000. Table 2 compares the duration of seizures between focal seizures and generalized tonic-clonic seizures (GTCS). The median duration of focal seizures was 10 minutes (IQR: 8-15) compared to 10 minutes (IQR: 8-10) for GTCS, with a statistically significant difference (p=0.0044).

Table 3 presents the comparison of electrolyte levels between cases and controls. The study found significant differences in the levels of calcium and potassium between the two groups. Hypocalcemia was significantly more prevalent in controls (75.00%) compared to cases (29.51%), with a p-value of 0.000. Hypokalemia was also more common in controls (35.00%) than in cases (6.56%), with a p-value of 0.000. However, there were no significant differences in the levels of magnesium and sodium between the groups. Figure 1 is a box and whisker plot displaying the median and IQR values of serum electrolytes among cases and controls. The median (IQR) of serum potassium among febrile children was 3.75 (3.3-4.2) and those with febrile seizure was 4.2 (3.7-4.4) (1a). The median (IQR) of serum magnesium among febrile children was 2 (1.8-2) and those with febrile seizure was 2 (1.8-2) (1b).

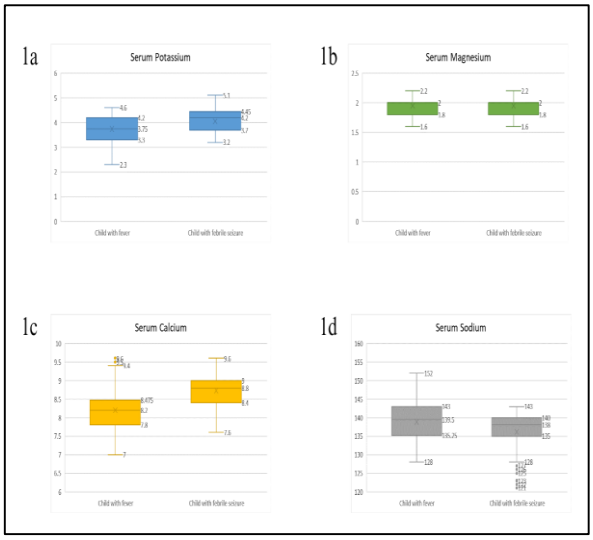


**Figure 1 (a-d): Comparison of serum electrolyte levels among cases and controls.**

The median (IQR) of serum calcium among febrile children was 8.2 (7.8-8.45) and those with febrile seizure was 8.8 (8.4-9.0) (1c). The median (IQR) of serum sodium among febrile children was 139.5 (135.5-143) and those with febrile seizure was 138 (135-140) (1d). We could not find any statistically significant difference in electrolytes between the focal seizures and GTCS.

**Table 1: Characteristics of study participants.**

| S. no. | Characteristic | Cases (n=61) | Controls (n=60) | P value |
|---|---|---|---|---|
| **1** | **Age (years)** | | | |
| | Median (IQR) | 2.5(1.0-3.5) | 3.0 (3.0 - 4.0) | 0.0002 |
| **2** | **Sex** | | | |
| | Male (%) | 18 (29.51) | 26 (43.33) | |
| | Female (%) | 43 (70.49) | 34 (56.67) | 0.114 |
| **3** | **Duration of fever (days)** | | | |
| | Median (IQR) | 0.5 (0.42 - 1.0) | 3.0 (3.0-4.0) | 0 |

**Table 2: Duration of seizure according to type of seizure among the study participants.**

| S. no. | Seizure type | Median duration (IQR) | P value |
|---|---|---|---|
| **1** | **Focal seizures** | 10 days (8 - 15) | |
| **2** | **Generalized tonic-clonic seizures (GTCS)** | 10 days (8 - 10) | 0.0044 |

**Table 3: Comparison of serum electrolyte levels among study participants.**

| S. no. | Electrolyte | Cases (n=61) | Controls (n=60) | P value |
|---|---|---|---|---|
| **1** | **Calcium (Ca)** | | | |
| | Hypocalcaemia (%) | 18 (29.51) | 45 (75.00) | |
| | Normal (%) | 43 (70.49) | 15 (25.00) | 0.000 |
| **2** | **Magnesium (Mg)** | | | |
| | Hypomagnesemia (%) | 2 (3.28) | 4 (6.67) | |
| | Normal (%) | 59 (96.72) | 56 (93.33) | 0.391 |
| **3** | **Sodium (Na)** | | | |

Continued.

| S. no. | Electrolyte | Cases (n=61) | Controls (n=60) | P value |
|---|---|---|---|---|
| | Hyponatremia (%) | 13 (21.31) | 12 (20.00) | |
| | Normal (%) | 48 (78.69) | 44 (73.33) | |
| | Hypernatremia (%) | 0 (0.00) | 4 (6.67) | 0.122 |
| **4** | **Potassium (K)** | | | |
| | Hypokalemia (%) | 4 (6.56) | 21 (35.00) | |
| | Normal (%) | 57 (93.44) | 39 (65.00) | 0.000 |

## DISCUSSION

Our study aimed to investigate the association between serum electrolyte levels and the onset of febrile seizures (FS) in children. We found significant differences in calcium and potassium levels between the case and control groups, while magnesium and sodium levels did not show significant differences.

Our results revealed that children with febrile seizures had significantly higher serum calcium levels compared to the control group. This finding is in contrast with previous studies, such as Sharma et al, who reported a significant difference in ionized calcium levels between children with and without febrile seizures (mean ionized calcium levels of 4.62±0.26 mg/dl in the study group and 4.88±0.27 mg/dl in the control group).[20] Similarly, Akbayram et al and Chiarelli et al found significantly lower serum calcium levels in children with febrile seizures compared to controls.

Our study also found a significant difference in potassium levels, with hypokalemia being more common in controls compared to cases. This is in contrast to the findings of Namakin et al. (2016) and Akbayram et al. (2012), who reported significantly lower potassium levels in children with febrile seizures compared to febrile children without seizures.[7] The discrepancy in calcium and potassium levels across studies indicates a complex relationship between potassium and febrile seizures, warranting further investigation.

Many studies have reported lower serum levels of sodium (Namakin et al, and Chiarelli et al, and magnesium (Iyshwarya et al, and Papierkowski et al, among children with febrile seizures.[21-23] However, we could not demonstrate any significant difference in serum levels of sodium and magnesium among children with febrile seizures and febrile children without seizures. Magnesium's role in modulating neural excitability and its anticonvulsant properties make it a crucial element in the study of febrile seizures. Our findings reveal a more complex relationship between electrolyte levels and febrile seizures than previously understood. While we did not observe significant abnormalities in certain electrolytes typically associated with seizures (such as potassium, calcium, sodium, and magnesium), the reduction in values seen in the control group suggests that the pathogenesis of febrile seizures might involve mechanisms beyond straightforward electrolyte imbalances. The lower electrolyte levels in the control group could indicate possible protective or adaptive mechanisms that prevent the development of seizures in febrile conditions. One of the strengths of this study is the detailed comparison of electrolyte levels and seizure characteristics, providing valuable insights into the potential factors contributing to febrile seizures. Additionally, the use of a well-defined case-control design allows for a clear comparison between children with and without febrile seizures.

However, the study has some limitations. The sample size is relatively small, which may limit the generalizability of the findings. Moreover, the study did not account for other potential confounding factors such as genetic predisposition, previous medical history and environmental influences, which could affect the results. Future research should aim to include larger sample sizes and consider these additional factors to provide a more comprehensive understanding of febrile seizures.

## CONCLUSION

Our study contributes to the growing body of evidence that the relationship between electrolyte levels and febrile seizures is complex, it also opens the door for future research to explore the multifaceted nature of febrile seizures, ultimately aiming to improve outcomes for affected children.

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