Original Article

DOI: 10.7860/JCDR/2025/73552.20792

Serum Electrolyte Levels in Children with Febrile Seizures: A Cross-sectional Study

Paediatrics Section

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ABSTRACT

Introduction: Febrile seizures are the most common type of childhood seizure, typically occurring in children younger than 60 months of age. They are categorised into simple and complex febrile seizures. The recurrence of febrile seizures is also high. Among the various known risk factors for recurrence, serum sodium is a quantifiable and correctable factor. However, there are very few studies in this field to determine whether other serum electrolytes at presentation also have any association with the type of seizure or the patient's gender, which are non modifiable risk factors for recurrence.

Aim: To measure serum electrolyte levels (sodium, potassium, calcium, magnesium) in patients with febrile seizures at presentation and to find out its association with the type of seizure and the patient's sex.

Materials and Methods: This cross-sectional study was performed on 76 patients aged six months to five years who were admitted to the Paediatrics Inpatient Department (PIPD), attended the Paediatrics Out-Patients Department (POPD) and visited the Paediatrics Emergency of RG Kar Medical College and Hospital, Kolkata, West Bengal, India, with any episode of febrile seizure between April 2021 and March 2022. The serum electrolyte levels (sodium, potassium, calcium, magnesium) in patients with febrile seizures were measured. Data were analysed using STATA version 16 software, employing Fisher's exact test, with a p-value of <0.05 considered statistically significant.

Results: Out of the 76 study subjects, 55.26% were male and 44.74% were female, resulting in a male-to-female ratio of 1.23:1. Of the subjects, 93.42% had simple febrile seizures, while 6.58% exhibited complex febrile seizures. A statistically significant association was found between the type of febrile seizure and serum magnesium (p-value=0.006), as well as between the sex of the patients and serum calcium levels (p-value=0.012). No statistically significant association was observed between the sex of the study subjects and serum sodium (p-value=0.105), serum potassium (p-value=0.576), or serum magnesium levels (p-value=0.312). Furthermore, the type of febrile seizure showed no statistical significance with serum sodium (p-value=0.284), potassium (p-value=0.820), or calcium levels (p-value=0.373).

Conclusion: The present study concluded a significant association between serum magnesium levels and the type of febrile seizure, as well as between serum calcium levels and the sex of the patients. Thus, measuring serum electrolytes in patients with febrile seizures at the time of presentation is beneficial, as it is easy to perform, provides rapid results and identifies correctable and quantifiable issues.

Keywords: Serum calcium, Serum magnesium, Sex of patients

INTRODUCTION

Febrile seizures are defined as seizures that occur between six months and 60 months of age, accompanied by a temperature of ≥38°C (100.4°F) and are not due to any Central Nervous System (CNS) infection or metabolic imbalances. These seizures can occur in the absence of any history of prior febrile seizures [1,2]. The peak age of onset for this condition is observed between 12 months and 18 months of age [1]. Febrile seizures are the most common type of childhood seizure, occurring in children under five years of age, with an incidence of 2 to 14% worldwide [3]. In a survey conducted in Southern India, the incidence of febrile seizures was approximately 10% [3].

Febrile seizures are categorised into simple febrile seizures and complex febrile seizures. Simple febrile seizures account for approximately 70 to 75% of all febrile seizures. They are primarily generalised tonic-clonic seizures (never focal), associated with fever, last for a maximum of 15 minutes and do not show recurrence within 24 hours [1]. Complex febrile seizures account for around 25 to 30% of all febrile seizures. They are characterised by a prolonged seizure lasting more than 15 minutes and/or are focal in nature (not generalised tonic-clonic) and/or exhibit recurrence within 24 hours [1]. Febrile status epilepticus is another condition in which a febrile seizure lasts for approximately 30 minutes or more. This condition has a strong association with Roseolavirus, influenza A, human herpesvirus 6 and 7 (HHV-6,7), human coronavirus HKU1, adenovirus, Respiratory Syncytial Virus (RSV), cytomegalovirus, Shigella and Herpes Simplex Virus (HSV) [4-6].

The postictal phase of a simple febrile seizure is very brief and normal behaviour and consciousness are regained within minutes following the seizure. Studies have shown that 2 to 5% of neurologically healthy children also have a history of at least one episode of simple febrile seizure during childhood [1]. Although the exact cause of febrile seizures is unknown, some risk factors have been identified. There is an autosomal mode of inheritance linked to chromosomes 1q, 2q, 3p, 3q, 5q, 6q, 8q, 18p, 19p, 19q and 21q [7,8]. Developmental delay, daycare attendance and a nursery stay of neonates for more than 28 days are also important risk factors for the recurrence of febrile seizures [9,10]. Certain other factors, such as electrolyte imbalances (e.g., hyponatremia, hypomagnesemia, hypocalcaemia) and deficiencies of nutrients like iron, zinc, vitamin B12, folic acid and selenium, may also increase the risk of febrile seizures [7].

Simple febrile seizure does not show any increased risk of mortality, but complex febrile seizure shows a two-fold increase in mortality rates compared to the general population. Although these febrile seizure patients usually do not exhibit any behavioural abnormalities,

deterioration in scholastic performance, or neurocognitive disorders, the risk of recurrence is high; with each episode of recurrence, there is a chance of fatality. Recurrence occurs in 30% of patients with simple febrile seizure, 50% of patients with two or more episodes of febrile seizure and 50% of those with the onset of febrile seizure at less than one year of age [1]. Age under 1 year, fever duration of less than 24 hours and a fever ranging from 100.4°F to 102.2°F are known major risk factors for recurrence. In contrast, a family history of febrile seizures or epilepsy, complex febrile seizures, daycare attendance, male gender and lower serum sodium levels at the time of presentation are considered minor risk factors [1].

Since the majority of the factors influencing recurrence are unavoidable and unpredictable and given that low serum sodium levels at the time of presentation have been included as one of the minor criteria for predicting the risk of future recurrence of febrile seizure [1,11-14], the objective of this study was to measure the serum electrolyte levels (sodium, potassium, calcium, magnesium) in patients with febrile seizure, as these levels are quantifiable, correctable and may have some prognostic value.

Furthermore, studies related to this matter are quite limited [11-16], especially concerning electrolytes other than serum sodium. Therefore, this study aimed to measure other electrolytes (potassium, calcium, magnesium) alongside sodium to detect any abnormalities (if present) in those levels in patients with febrile seizure.

MATERIALS AND METHODS

The cross-sectional study was conducted at the PIPD, POPD and Paediatric Emergency Department of R.G. Kar Medical College and Hospital, Kolkata, West Bengal, India from April 2021 to March 2022, covering a period of 12 months. Ethics committee approval was obtained from the Institutional Ethics Committee (IEC) of RG Kar Medical College and Hospital, Kolkata (Registered with The Drug Controller General of India, Registration No. ECR/322/Inst/WB/2013); RKC/297 dated 11th February 2021.

Inclusion criteria: After obtaining full informed consent from parents, all patients aged six months to five years who presented with any episode of febrile seizure and who were admitted to the PIPD or attended the POPD at the paediatric emergency department were included in the study.

Exclusion criteria: Parents who did not provide consent, if they were younger than six months or older than five years, or if they had a history of metabolic disorders, structural abnormalities of the nervous system, neurological abnormalities (such as epilepsy or seizure disorders), developmental delay, cerebral palsy, or meningitis/encephalitis were excluded from the study.

Sample size calculation: The incidence of febrile seizures is 3.28 per 1,000 population [17]. Since febrile seizures are a short-term illness, the incidence equals the prevalence. The formula for calculating sample size is z^2pq/d^2, where 'z' has a value of 1.96 at the 95% confidence level and 'd' is the precision.

Hence, sample size=1.96×1.96×3.28×(100-3.28)/(4×4)=76

Methodology: The candidates for this study were selected through purposive sampling based on inclusion and exclusion criteria. The test samples were collected aseptically in clot vials from venous blood and sent to the institutional laboratory for measurement of serum electrolytes (sodium, potassium, calcium, magnesium) using the ion-selective electrode method in the Roche analyser. The reported values were matched with standard serum electrolyte values and were classified as normal, hypo, or hyper [Table/Fig-1] [8,18,19].

STATISTICAL ANALYSIS

Data were entered into a Microsoft Excel spreadsheet and analysed using STATA version 16 software. The test applied was Fisher's exact test and a p-value of <0.05 was considered statistically significant. Cramer's V ranges from 0 to1; values close to 1 signifies stronger association.

Serum electrolytes	Normal range	Hypoelectrolytemia	Hyperelectrolytemia
Sodium (mEq/L)	135-145	<135	>145
Potassium (mEq/L)	3.5-5.0	<3.5	>5
Magnesium (mg/dL)	1.2-2.5	<1.2	>2.5
Calcium (ionized) (mg/dL)	4.4-5.3	<4.4	>5.3

[Table/Fig-1]: Normal serum electrolyte levels [8,18,19].

RESULTS

In this study, out of 76 subjects who presented with febrile seizures, 42 (55.26%) were males and 34 (44.74%) were females. Among them, 5 (6.58%) were in the six-month to one-year age range, 58 cases (76.32%) were between 1-3 years and 13 cases (17.10%) were between 3-5 years. Only five cases (6.58%) showed complex seizures, while the remaining 71 cases (93.42%) had simple febrile seizures.

Hyponatremia was detected upon presentation in 15 (19.73%) male and 5 (6.57%) female patients; the rest showed normal values. None of the children were found to have hypernatremia. Fisher's exact test showed no statistically significant association between serum sodium levels at presentation and the sex of the study subjects (p-value=0.105) [Table/Fig-2]. Similarly, there was no significant association between serum sodium levels at presentation and the type of seizure (p-value=0.284) [Table/Fig-3].

Serum sodium level at presentation (mEq/L) [19]	Sex		Total
	Female	Male	
<135	5	15	20
135-140	13	17	30
140.1-145	16	10	26
Total	34	42	76
Fisher's exact=6.1463 p-value=0.105	Not significant		
Cramér's V=0.2844			

[Table/Fig-2]: Distribution of children according to the serum sodium level (mEq/L) at presentation with the sex of the children.
Fischer's exact test; p-value <0.05 was considered as statistically significant
Cramer's V ranges from 0 to1; values close to 1 signifies stronger association

Serum sodium at presentation (mEq/L) [19]	Type of seizure		Total
	Complex	Simple	
<135	2	18	20
135-140	1	29	30
140.1-145	2	24	26
Total	5	71	76
p-value=0.284	Not significant		
Fisher's exact=0.286			
Cramér's V=0.2236			

[Table/Fig-3]: Distribution of children according to the serum sodium level (mEq/L) at presentation with type of seizure (Simple/Complex).
Fisher's exact test; p-value <0.05 was considered as statistically significant
Cramer's V ranges from 0 to1; values close to 1 signifies stronger association

There was no significant association between serum potassium levels at the time of presentation and the sex of the study subjects (p-value=0.576) [Table/Fig-4]. Similarly, there was no significant association between serum potassium levels at the time of presentation and the type of seizures (simple/complex) (p-value=0.820) [Table/Fig-5].

Hypocalcaemia was detected in 1 (1.31%) male and 3 (3.94%) female patients; the rest were normocalcemic. Fisher's exact test showed a statistically significant association between serum calcium levels

Potassium level at presentation (mEq/L) [19]	Sex		Total
	Female	Male	
<3.5	2	2	4
3.5-4.5	26	36	62
4.5-5.5	6	4	10
Total	34	42	76
p-value=0.576	Not significant		
Fisher's exact=0.563			
Cramér's V=0.1615			

[Table/Fig-4]: Distribution of children according to the serum potassium level (mEq/L) at the time of presentation with the sex of the study subjects.
Fisher's exact test; p-value <0.05 was considered as statistically significant
Cramer's V ranges from 0 to1; values close to 1 signifies stronger association

Serum potassium at presentation (mEq/L) [19]	Type of seizure		Total
	Complex	Simple	
<3.5	1	3	4
3.5-4.5	3	59	62
4.5-5.5	2	8	10
Total	5	71	76
p-value=0.820	Not significant		
Fisher's exact=1.000			
Cramér's V=0.1101			

[Table/Fig-5]: Distribution of children according to the serum potassium level (mEq/L) at presentation with the type of seizure (Simple/Complex).
Fisher's exact test; p-value <0.05 was considered as statistically significant
Cramer's V ranges from 0 to1; values close to 1 signifies stronger association

at presentation and the sex of the study subjects (p-value=0.012) [Table/Fig-6]. Furthermore, Fisher's exact test showed no significant association between serum calcium levels (mEq/L) at presentation and the type of seizure (simple/complex) among the study subjects (p-value=0.373) [Table/Fig-7].

Serum Ionized Calcium level at presentation (mg/dL) [18,19]	Sex		Total
	Female	Male	
<4.0	3	1	4
4.0-4.5	18	12	30
4.6-5.0	10	28	38
5.1-5.3	3	1	4
Total	34	42	76
p-value=0.012	Significant		
Fisher's exact=0.006			
Cramér's V=0.3805			

[Table/Fig-6]: Distribution of children according to the serum calcium level at presentation (mg/dl) with the sex of the study subjects.
Fisher's exact test; p-value <0.05 was considered as statistically significant
Cramer's V ranges from 0 to1; values close to 1 signifies stronger association

Serum Ionized calcium level at presentation (mg/dL) [18,19]	Type of seizure		Total
	Complex	Simple	
<4.0	1	3	4
4.0-4.5	1	29	30
4.6-5.0	2	36	38
5.1-5.3	1	3	4
Total	5	71	76
p-value=0.373	Not significant		
Fisher's exact=0.465			
Cramér's V=0.2027			

[Table/Fig-7]: Distribution of children according to the serum calcium level (mg/dL) at presentation with the type of seizure (Simple/Complex).
Fisher's exact test; p-value <0.05 was considered as statistically significant
Cramer's V ranges from 0 to1; values close to 1 signifies stronger association

There was no significant association between serum magnesium levels at presentation and the sex of the study subjects (p-value=0.312) [Table/Fig-8]. Hypomagnesemia was detected in 5 (6.57%) patients presenting with simple febrile seizures and in 2 (2.63%) patients with complex febrile seizures. Fisher's exact test showed a statistically significant association between serum magnesium levels at presentation and the type of seizures among the study subjects (p-value=0.006) [Table/Fig-9].

Serum magnesium at presentation (mg/dL) [18]	Sex		Total
	Female	Male	
<1.2	1	6	7
1.2-1.4	11	10	21
1.5-1.8	18	23	41
1.8-2.0	4	3	7
Total	34	42	76
p-value=0.312	Not significant		
Fisher's exact=0.322			
Cramér's V=0.2167			

[Table/Fig-8]: Distribution of children according to the serum magnesium level (mEq/L) at presentation with the sex of study subjects.
Fisher's exact test; p-value <0.05 was considered as statistically significant
Cramer's V ranges from 0 to1; values close to 1 signifies stronger association

Serum Magnesium level at presentation (mg/dL) [18]	Type of seizure		Total
	Complex	Simple	
<1.2	2	5	7
1.2-1.4	1	20	21
1.5-1.8	1	40	41
1.8-2.0	1	6	7
Total	5	71	76
p-value=0.006	Significant		
Fisher's exact=0.042			
Cramér's V=0.4070			

[Table/Fig-9]: Distribution of children according to the serum magnesium level at the time of presentation (mEq/L) with the type of seizure (Simple/Complex).
Fisher's exact test; p-value <0.05 was considered as statistically significant
Cramer's V ranges from 0 to1; values close to 1 signifies stronger association

DISCUSSION

In this study, a statistically significant association was found between the serum calcium level at presentation and the sex of the study subjects (p-value=0.012), as well as between the serum magnesium level at presentation and the type of seizures in the study subjects (p-value=0.006).

Studies by Varahala AM et al., Mohamed ZA et al., Nayek K and Sarkar N, Hawas AF et al., and Khalaf DK et al., showed a significant association of serum electrolytes, especially serum sodium levels, with febrile seizures in children [11-14,16]. A comparison of the present study with other studies has been provided in [Table/Fig-10] [11-16]. The majority of the studies emphasised that low serum sodium levels could be a risk factor for the occurrence of febrile seizures. In a study conducted by Monica N et al., it was found that male study subjects had more hyponatremia compared to female study subjects, indicating a statistically significant association between the gender of patients and serum sodium levels [20]. However, in the present study, there was no statistically significant association (p-value=0.105) between the serum sodium levels of the study subjects and their sex. This difference could be due to the smaller sample size in present study (n=76) compared to the study mentioned here (n=100). In studies conducted by Khalaf DK et al., and Eskandarifar A et al., it was observed that there was no statistically significant association between serum sodium levels at presentation and the type of febrile seizure [16,21]. The findings of present study were consistent with previous studies (p-value=0.284).

S. No.	Author name	Place and publication year	Number of subjects	Objective	Parameters assessed	Conclusion
1	Ray S et al., (Present study)	Kolkata, West Bengal, India, 2025	76	To measure serum electrolyte in febrile seizure on presentation and to find if they have any association with type of seizure and sex of patient	Serum sodium, Serum potassium, Serum calcium, Serum magnesium	Statistically significant association present between serum magnesium level at presentation and type of febrile seizure (simple/complex) and also serum calcium level at presentation and sex of patients.
2	Varahala AM et al., [11]	Niloufer Hospital, Hyderabad, India 2021	50	Occurrence and association of dyselectrolytemia in febrile seizure	Serum sodium, Serum potassium, Serum chloride	There is a significant association of serum electrolytes especially serum sodium levels with febrile seizures in children.
3	Mohamed ZA et al., [12]	Zhongnan Hospital of Wuhan University, China, 2023	876 (438 case+438 control)	Serum glucose and electrolyte levels in children with and without febrile seizure	Serum glucose, Serum sodium, Serum potassium, Serum chloride	Lower sodium levels could be a risk factor for the occurrence of febrile seizures.
4	Nayek K and Sarkar N [13]	Burdwan Medical College and Hospital, West Bengal, India, 2022	120 (60 case+60 control)	Relationship between serum electrolytes and simple febrile seizure	Serum sodium, Serum potassium, Serum calcium, Serum magnesium	Changes in serum electrolytes may have a role in the development of simple febrile convulsion and may help in predicting seizure recurrence within the same febrile illness.
5	Hawas AF, et al., [14]	Babylon Teaching Hospital, Babylon Province, 2018	150	The impact of electrolytes in pathogenesis of simple febrile convulsions	Serum sodium, Serum potassium, Serum calcium	Changes in sodium and potassium levels could have a role in the development of simple febrile convulsion.
6	Gupta H et al., [15]	Uttarpradesh, India, 2024	200	Association of serum iron and serum calcium levels in children with febrile seizures	Serum iron, Serum calcium	Hypocalcaemia is unlikely to be the cause of febrile seizure. Early detection and intervention of iron deficiency in children could help in the prevention and recurrence of febrile seizure.
7	Khalaf DK et al., [16],	Baghdad, Iraq, 2018	60	Relationships between serum electrolytes and febrile seizure	Serum sodium, Serum potassium, Serum calcium	There is significant association between serum electrolyte (Na+, K+, Ca+2) level and febrile convulsion.

[Table/Fig-10]: Comparison of present study with other studies [11-16].

In a study by Hawas AF et al., in Babylon, it was concluded that changes in serum potassium levels may play a role in the development of simple febrile seizures [14]. Another study by Nayek K and Sarkar N in Burdwan, India, showed low potassium levels in cases of febrile seizures compared to the control group [13]. However, in this study, there was no statistically significant association (p-value=0.576) between the sex of the study subjects and serum potassium levels at presentation, nor between the type of febrile seizure and serum potassium levels (p-value=0.820), which was consistent with studies conducted by Eskandarifar A et al., and Bijari B et al., [21,22].

A study by Gupta H et al., in Uttar Pradesh, India, concluded that hypocalcaemia was unlikely to be a cause of febrile seizures [15]. However, another study by Nayek K and Sarkar N at Burdwan, India, showed that hypocalcaemia may play a role in the development of febrile seizures when compared with a control group [13].

In the present study, a statistically significant association (p-value=0.012) between the sex of study subjects and serum calcium at presentation was detected. No studies showed any significant association between sex and serum calcium levels at presentation among the study subjects have yet been found in the literature. Likewise, in previous studies by Eskandarifar A et al., and Khalaf DK et al., there was no significant association (p-value=0.373) between serum calcium levels and the type of seizure in present study as well [16,21].

Contrary to the results of the study by Talebian A et al., the present study found a statistically significant association between the type of seizure (simple/focal) [23] and serum magnesium level (p-value=0.006) [16]. Another study by Nayek K and Sarkar N at Burdwan, India, showed no significant association between serum magnesium levels and the occurrence of febrile seizures in children [13]. In this study, there was no statistically significant association (p-value=0.312) between the sex of study subjects and serum magnesium levels at presentation, which was consistent with previous studies by Talebian A et al., and Bharathi S and Chiranjeevi K [18,24].

Limitation(s)

This was a single-centred study, a multicentred study would have been more descriptive and representative of the entire population. The study period was only 12 months; therefore, follow-up could not be conducted. A longer study period is needed for more accurate results.

CONCLUSION(S)

The present study concluded that there was a statistically significant association between serum magnesium levels and the type of febrile seizure, as well as between serum calcium levels and the sex of patients presenting with febrile seizures. The measurement of serum electrolytes in patients with febrile seizures at the time of presentation is beneficial, as it is easy to perform, cost-effective, less time-consuming and yields quick, correctable and quantifiable reports. A multicentric study should be conducted as, more information can be gathered that may be useful in better managing febrile seizures and in predicting new risk factors for recurrence in the near future.

Acknowledgement

Authors are indebted to Professor Dr. Gobinda Chandra Das, Head of Department of Paediatrics and Professor. Dr. Sabyasachi Some, Department of Paediatrics R.G. Kar Medical College for their support. Authors are also thankful to Dr. Animesh Roy, Junior Resident of Paediatrics for his support.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jun 15, 2024
- Manual Googling: Aug 09, 2024
- iThenticate Software: Feb 08, 2025 (12%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes (Consent was taken from parents)
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Jun 14, 2024**
Date of Peer Review: **Jul 16, 2024**
Date of Acceptance: **Feb 10, 2025**
Date of Publishing: **Mar 01, 2025**