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THE PREDICTIVE VALUE OF LOW SERUM SODIUM LEVELS IN THE RECURRENCE OF SIMPLE FEBRILE CONVULSIONS

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ABSTRACT

Introduction: Febrile seizures are common in children aged 3 to 60 months, defined by the occurrence of seizures in the presence of fever (≥38°C) without central nervous system infections, lesions, trauma, or poisoning. Factors contributing to recurrence include a positive family history, age under 18 months, and low serum sodium levels. Previous studies indicate that low sodium levels significantly correlate with the recurrence of febrile convulsions. **Objective:** To investigate the relationship between low serum sodium levels and the recurrence of simple febrile seizures during the same febrile illness. **Methods:** Children presenting to the pediatric emergency department with febrile seizures underwent clinical evaluations and serum sodium assessments. Descriptive statistics summarized sample characteristics, while Chi-square and independent t-tests analyzed variable relationships. The area under the curve (AUC) method determined optimal serum sodium cutoffs for predicting seizure recurrence. **Results:** The study comprised 95 children (31 females, 64 males) aged 6 to 60 months (mean = 31 months). The primary causes of hyperthermia included respiratory and urinary tract infections. Recurrent febrile seizures occurred in 27.4% of cases. Median serum sodium was 138 ± 6.2 mEq/L in non-recurrent cases and 131.6 ± 3.9 mEq/L in recurrent cases. A significant difference was noted between low sodium levels and seizure recurrence, as well as between family history and recurrence. **Conclusion:** Hyponatremia and positive family history were significantly associated with the recurrence of febrile seizures, while age and gender do not appear to influence this outcome. A serum sodium threshold of 135 mEq/L is recommended as a predictive cutoff for seizure recurrence.

KEYWORD:- Simple febrile seizures, Low serum sodium levels, Family history of febrile seizures.

INTRODUCTION

Febrile seizures are the most common convulsive disorder in children aged 3 to 60 months, occurring in association with fever and in the absence of intracranial infection, metabolic disturbances, or a history of recurrent afebrile seizures. Approximately two to five percent of children experience febrile seizure during the childhood.[1] About 65-90% of febrile seizures are simple characterized by generalized seizures without repetition within the first 24 hours.[2] Several underling factors have been linked with febrile seizures including a history of antenatal complication, zinc deficiency, iron deficiency, anemia, and hypomagnesemia.[3,4]

Numerous studies have explored risk factors for recurrent febrile seizures occurring during the same febrile illness. Key factors identified include age (Under one year), the duration of fever (less than 24 hours), low-grade fever, a family history of febrile convulsions, and low serum sodium levels.[1] Recent research has highlighted serum sodium deficiency as a significant predictor of recurrent febrile convulsions during the same illness, although findings across studies have been inconsistent.[5,8,13]

One of the most pressing concerns for parents is the likelihood of recurrence of the convulsion, which can generate considerable anxiety and fear. In this paper, we aim to evaluate the potential role of low serum sodium levels as a predictive biomarker for the recurrence of febrile seizures during the same episode of illness.

MATERIALS AND METHODS

Study design and Population

We conducted a prospective cohort study. The primary aim is to evaluate the predicting value of low serum sodium level in the recurrence of febrile seizures during the same febrile disease. Also, we assessed the relationship between the recurrent febrile convulsions and demographic variables.

Participants were recruited from Latakia University Hospital over a period of one year. The inclusion criteria comprised: children with simple febrile seizures aged (3-60) months while, Children with history of afebrile seizures, evidence of central nervous system infection, gastroenteritis, developmental delay and neurological disorder were excluded.

Data collection

The following variables were obtained: Demographic variables: Age (In months), sex (Male/Female), the type of convulsions, the nutrition status, the temperature degree, the infection disease, that causing the fever, and the family history of febrile convulsions. A complete blood count (CBC), measurement of C-reactive protein (CRP), serum sodium level, and a lumbar puncture if there are clinical indications for meningitis or encephalitis were performed.

Statistical analysis

Descriptive statistics were computed for all variables, presenting means ± standard deviation for continuous variables and counts/percentages for categorical variables. We utilized chi-square test to assess the relation between serum sodium levels and the recurrence of febrile convulsions. we utilized the area under the curve (AUC) method to determine the optimal cutoff of hyponatremia that predicts recurrence of febrile convulsions with balanced sensitivity and specificity. All analysis was performed using SPSS statistical software (edition 25), with a significance level set at $p < 0.05$. The t-test student was employed to compare between the means of two different groups.

Ethical considerations

The study protocol was reviewed and approved by the ethics committee at the Faculty of Medicine – Latakia University, ensuring compliance with ethical standards for research involving human subjects. Informed consent was obtained from all participants prior to data collection, with assurances provided regarding confidentiality and the voluntary nature of participation.

RESULTS

The study sample comprised 95 children with simple febrile seizures who were referred to Latakia University Hospital. Among them, 31 were female (32.6%), and 64 were male (67.4%). The ages of the children ranged from 6 months to 60 months, with a mean age of 31 months (±11.3). The distribution of the underlying causes of fever was as follows: upper respiratory infection in 53 children (55.8%), acute tonsillitis in 22 (23.2%), lower respiratory infection in 12 (12.6%), and urinary tract infection in 8 (8.4%). Out of the total sample, 26 children (27.4%) experienced recurrent febrile seizures during the same febrile illness.

The median serum sodium level in children who developed febrile seizures without recurrence was 138 ± 6.2 mEq/L. In contrast, the median serum sodium level among those who experienced recurrent febrile seizures was 131.6 ± 3.9 mEq/L. Among the 26 children (27.4%) with recurrent febrile seizures, 20 (21%) had serum sodium levels below 135 mEq/L, while 6 (6%) had levels above this threshold. The risk of recurrent febrile seizures increased as serum sodium levels decreased.

Table 1: The relation between the recurrence of simple febrile convulsions and the studied variables.

Variable	Single convulsion	Recurrent convulsion	P-value
Age	32 ± 12.1	27.4 ± 7.4	P = 0.075 *
Sodium level	137 ± 3.7	131.6 ± 3.9	P < 0.001 *
Gender			
Boys	46 (48.4%)	18 (19%)	P = 0.81 **
Girls	23 (24.2%)	8 (8.4%)	
Family history			
Positive	36 (37.9%)	20 (21.1%)	P = 0.031 **
Negative	33 (34.7%)	6 (6.3%)	

* Student t-test || ** Chi-Square test || P-values are considered significant at 0.05

Table 2: Association between the serum sodium levels and the recurrence of simple febrile convulsions.

Serum Sodium	Single	Recurrent	Total	P-value
Normal (≥ 135 mEq/L)	51 (53.7%)	6 (6.3%)	57 (60%)	P < 0.001*
Low (< 135 mEq/L)	18 (18.9%)	20 (21.1%)	38 (40%)	
Total	69 (72.6%)	26 (27.4%)	95 (100%)	

* Chi-Square test || P-values are considered significant at 0.05

Figure 1: The distribution of the sample according to the infection disease that causing the fever.

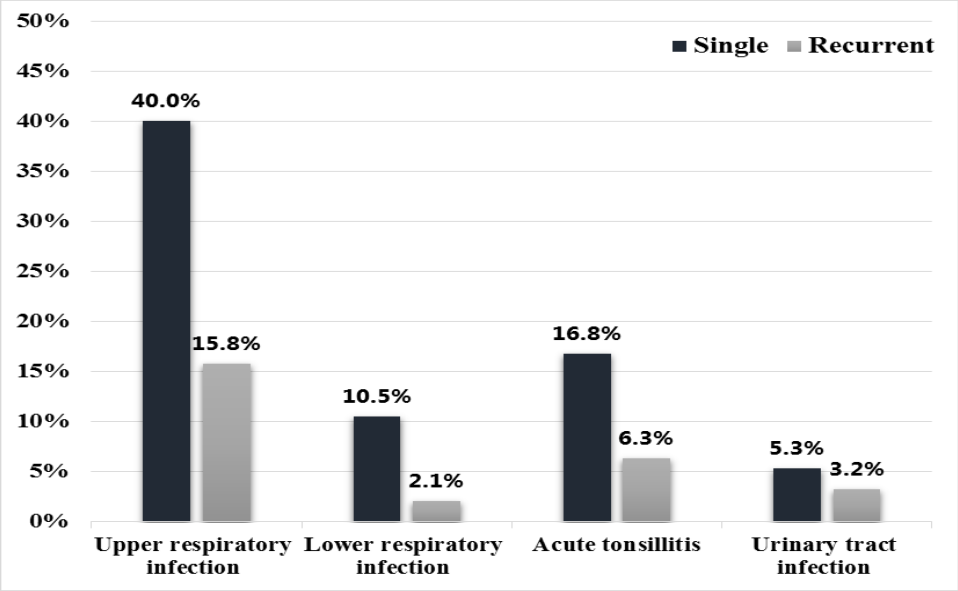

Figure 2: ROC Curve Analysis of hyponatremia as a Predictor of Recurrent Febrile Seizures.

The area under the curve (AUC) is 0.84, indicating a strong predictive capacity with an accuracy of 84%. The optimal cutoff value identified is approximately 134.2 mEq/L, suggesting this threshold effectively identifies children at higher risk for recurrent seizures during febrile episodes.

DISCUSSION

This study found that the majority of children with low serum sodium levels at the time of presentation were more likely to develop a recurrent febrile convulsion during the same febrile illnesses where the probability of a repeat convulsion within the same febrile period appeared to be significantly related to the serum sodium levels, this can be explained by the fact that that hyponatremia lowers the threshold for febrile convulsions.[7] The bursting activity is caused by a relatively long-lasting depolarization of the neural membrane due to the influx of extracellular calcium, which leads to the opening of voltage-dependent sodium channels and an influx of sodium. In cases of hyponatremia, there is more calcium influx, which can generate potential repetitive convulsions.[9] Fever often causes poor appetite in children, resulting in inadequate sodium intake; this may vary from child to child due to contributing genetic factors.[10] Additionally, fever plays a role in the inappropriate secretion of antidiuretic hormone (ADH), which may lead to a deficiency in serum sodium levels. This deficiency carries a high risk, particularly for neurological cells, as it can cause cellular swelling and cerebral edema, potentially leading to repeated convulsions during the same febrile illness.[11]

Several studies have suggested a statistically significant association between low serum sodium levels and the occurrence of febrile seizures, including both initial and recurrent events. For example, a systematic review and meta-analysis by Navaeifar et al. (2020) showed that children with febrile seizures were more likely to have hyponatremia compared to febrile children without seizures.[6] Hugen et al found that the measurement of serum sodium level has an investigation role in case of febrile convulsions where the lower the serum sodium level, the higher opportunity for the recurrence of febrile seizures.[12] Kiviranta et al reported that levels of serum sodium were lower in repeated febrile convulsions.[6] Maksikharin et al showed that sodium does not play a predictive role in the recurrence of febrile convulsions.[13]

In this study, we had six patients with recurrent febrile convulsions who presented with normal serum sodium levels. This may be explained by genetic factors, iron deficiency, or hypomagnesemia. We found that a family history of recurrent febrile seizures is a risk factor for developing recurrent convulsions. The genetic mechanisms involved are complex and involve multiple genes that contribute to neuronal excitability and synaptic function. Variants in ion channel genes, such as sodium (SCN1A, SCN2A) and calcium (CACNA1A), have been implicated in susceptibility to febrile convulsions (FC). Additionally, there appears to be a genetic predisposition, as FC can run in families.[14]

According to (Figure 1), we observe that the most frequently associated diseases with febrile convulsions were upper respiratory infections, which are common in winter and autumn when febrile convulsions typically increase.[15] This was followed by tonsillitis and urinary tract infections. We also found that the majority of our sample were boys, which aligns with the results of Hoque et al.[16] However, we did not find a statistically significant correlation between gender and the recurrence of febrile convulsions.

The results of this study have significant clinical implications, including the potential to identify high-risk children during initial presentations by measuring serum

sodium levels. This could lead to closer follow-up and parental education in cases of hyponatremia. Furthermore, it is important to manage fever distinctly, monitor vital signs, and consider fluid and electrolyte management strategies in recurrent cases.

However, several limitations must be acknowledged. Serum sodium levels can fluctuate based on hydration status, recent fluid intake, and laboratory timing. The presence of fever itself can influence electrolyte balance through mechanisms such as dehydration or ADH release. While we correlated repeated febrile convulsions with low serum sodium levels, we wonder if other factors, such as hypomagnesemia or additional genetic causes, may also contribute to recurrent convulsions.

CONCLUSIONS

We suggest that future studies be conducted to compare results and aggregate recommendations. In conclusion, this study explores the potential predictive value of low serum sodium in the recurrence of simple febrile convulsions. We advocate for further prospective studies to compare results and aggregate recommendations. Until then, routine monitoring of electrolytes may still be advisable in children presenting with febrile convulsions.

Declarations

Ethical Approval and Consent to participate: Ethical approval to study was obtained from the Scientific Research Ethics Committee at Latakia University in accordance with the Declaration of Helsinki.

Consent for publication: Not applicable.

Availability of Data and Materials: All the data generated or analyzed during this study are included in this published article. The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests: None.

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Author contribution: Bushra Jamahiri, collected the data, checked the quality of the data collection, analyzed and interpreted the data, designed and coordinated the study, undertook and checked the quality assessment, produced the first draft of the manuscript, wrote and edited the manuscript and approved the final manuscript before submission. Mazen Ghalia and Ahmad Chreitah were the supervisor of the project; undertook and checked to the quality assessment, checked the quality of the collected data; analyzed and interpreted the data; checked the quality assessment; edited the manuscript and approved the final manuscript before submission.

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