

The Association between Hyponatremia and Recurrent Febrile Convulsion

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Abstract

Background: Febrile seizures are a common pediatric problem, yet there is a great deal of disagreement about the appropriate diagnostic evaluation of a child with this disorder. Different predisposing factors have suggested enhancing the susceptibility to febrile seizure and its recurrence. **Objective:** To determine the effect of hyponatremia in recurrent febrile convulsions. **Materials and Methods:** A case-control study was carried out at Al-Zahraa teaching hospital in Al-Najaf city during the period between 1 January and the end of October 2021. One hundred fifty children in the age range between six months and six years old were studied. We classified the patients into three groups: Group (A) included 50 children who presented with fever without seizure; group (B) included 50 children who presented with simple febrile convulsion; and group (C) included 50 children who presented with recurrent febrile convulsions. Group A was considered as the control group. The serum level of sodium Na^+ was estimated in these three groups by Na kits. **Results:** There was no significant difference between males and females, in all age groups. Also, it was shown that a family history of febrile convulsion represented 20%, 50%, and 50% in groups A, B, and C, respectively; a family history of recurrent febrile convulsion represented 4%, 4%, and 10%, in groups A, B, and C, respectively; and a family history of epilepsy represented 0%, 4%, and 0% in groups A, B, and C, respectively. A value of P in family history of febrile convulsion was 0.002, in family history of recurrent febrile convulsion was 0.345, and in family history of epilepsy was 0.132. Therefore, there was no significant difference in all parameters except a family history of febrile convulsion that was significant in all three groups. Also, the study will show no significant difference in age, white blood cell count, and random blood sugar whereas there is a significant difference in temperature. A significant difference in serum sodium level was the lowest in group C. Regarding calcium level, there was a significant difference between groups A and B. **Conclusion:** There is a significant association between recurrent febrile convulsion and lower level of serum sodium, in which serum sodium concentration is lower in those patients with recurrent febrile convulsion.

Keywords: Association, hyponatremia, recurrent febrile convulsion

INTRODUCTION

Febrile seizure is the most common form of childhood seizure that occurs in 2–5% of children.^[1] It represented the most common childhood seizure disorder; however, it existed only in association with an elevated temperature. Evidence suggests, however, that they have a little connection cognitive function, so that the prognosis for normal neurologic function is excellent with children with febrile seizure.^[1] Another definition from the International League Against Epilepsy (ILAE) is a seizure occurring in childhood after 1 month of age associated with a febrile illness, not caused by an infection of the central nervous system (CNS), without previous neonatal seizure or previous unprovoked seizure, and not meeting the criteria

for other acute symptomatic seizure.^[2] A febrile seizure is defined by the ILAE as a seizure occurring in association with febrile illness in the absence of CNS infection or acute electrolyte imbalance in children older than one month without a prior febrile seizure.^[3] According to Berg, a febrile seizure is defined as a seizure occurring between six months and six years of age.^[4] Approximately 30–50% of children have recurrent seizures, with later

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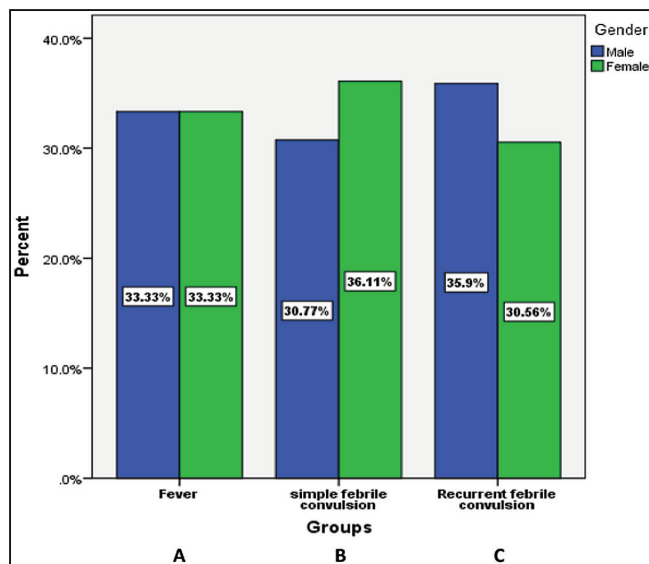


Figure 1: Distribution of fever, simple and recurrent febrile convulsion according to gender

episodes of fever.^[5,6] The American Academy of pediatrics practice parameter does not recommend S. electrolytes to be obtained routinely in the evaluation of a child with first febrile seizure, unless clinically indicated.^[7] Hyponatremia is a condition that occurs when the level of sodium in our blood is abnormally low. Sodium is an electrolyte, and it helps regulate the amount of water that is in and around cells. In hyponatremia, one or more factors ranging from an underlying medical condition for drinking too much water during endurance sports causes the sodium in our body to become diluted. When this happens, our body water levels rise, and our cells begin to swell. This swelling can cause many health problems from mild to life-threatening.^[8] Two studies in Europe have demonstrated a relationship between low serum Na⁺ level and the risk of developing recurrent seizure within the same febrile illness. One study by Paul SP (2015) reported that the Na levels were significantly lower in children with recurrent febrile seizure as compared with simple febrile convulsion, without recurrence.^[8] They concluded that hyponatremia might increase the risk of multiple seizure during the same febrile illness. Moreover, a prospective study published by Khosroshahi *et al.*^[9] concluded that the probability of repeated episodes of seizure may be related to a low level of serum sodium. In another study, S. Na level in patients with febrile convulsion was significantly lower than that obtained in children with fever. The aim of this study was to determine the role of serum sodium level in predicting the recurrence of simple febrile seizure in children aged between six months and six years.

MATERIALS AND METHODS

This study was carried out at Al-Zahraa teaching hospital in Al-Najaf city during a period between 1 January and

the end of October 2015. The study was conducted on 150 children: 50 of them had fever, 50 had simple febrile convulsion, and the remaining 50 children had recurrent febrile convulsion. The ages of the studied groups ranged between 6 and 60 months old. The studied patients were divided into three groups.

- Group A: Included 50 children who presented with fever only, no other sign.
- Group B: Included 50 other children who presented with simple febrile convulsion.
- Group C: Included 50 children who presented with recurrent febrile convulsion.

Blood samples, about 2 cc, were aspirated under the aseptic technique for measurement of the serum level of Na⁺. All consecutive children admitted in the pediatrics hospital in E.U. or outpatient or pediatrics ward fulfilled the following criteria:^[9]

Inclusion criteria

- Children aged between 6 and 60 months, with febrile seizure (defined as a seizure that occurs in association with a febrile illness). The setting is fever in a child aged six months to five years.
- The single seizure is generalized and lasts less than 15 min.
- The child is otherwise neurologically healthy and without neurologic abnormality by examination or by developmental history.
- Fever (and seizure) is not caused by meningitis, encephalitis, or any other illness affecting the brain.

In the absence of CNS infection or any other defined causes of seizure.

Exclusion criteria

- Children with unprovoked seizure.
- Complex febrile convulsion.
- Neurological infection.
- Developmental delay.
- Children with a history of birth asphyxia.
- Persistent neurological deficit.
- Children with gastroenteritis or pneumonia.

All children included in the study will be subjected to the following: Demographic data, seizure details, nature of febrile illness, a family history of epilepsy, febrile seizure, temperature at admission, and nutrition status will be recorded. Estimation of S. Na, Ca, and random blood sugar was also done.

Study measurements

- Take 2 cc of blood from each of the 150 children, to measure the serum level of sodium,
- And by using the below formula:

Black tube-Test tube
Black tube-Standard

= S. Na mmol/L

Statistical analysis was done by using SPSS (statistical package for social sciences) version 20 in which we use the chi-square test for categorical data and ANOVA test with LSD for numerical data. We set $P \leq 0.05$ as significant.

Ethical approval

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients verbal and analytical approval before sample was taken. The study protocol and the subject information and consent form were reviewed and approved by a local ethics committee according to the document number 18 (including the number and the date in 17/4/2014) to get this approval.

RESULTS

Data collected from 150 patients (78 males and 72 females) were analyzed. Overall, 50 (33.3%) had fever without convulsion, 50 (33.3%) had simple febrile convulsion, and

50 (33.3%) had recurrent febrile convulsion as in Figure 1. In Table 1, there was no significant difference in all parameters except a family history of febrile convulsion, which was significantly less in children with fever only.

Table 2 shows no significant difference in age, WBC count, and RBS. There is a significant difference in temperature between group B and both groups A and C, which is lower in group B. Also, there is a significant difference in serum sodium level, which is lowest in group C. Regarding the calcium level, there is a significant difference between groups A and B.

As observed in Table 3, a comparison of F.C. in groups B and C with control group A showed that there was no significant difference between case and control group.

As depicted in Tables 4 and 5, those who had a low Na level were six times more likely to develop recurrent febrile convulsion. A comparison of R.F.C with fever without convulsion, in S. Na. level, revealed that there was a significant difference between them.

DISCUSSION

Febrile convulsion is a terrifying event for parents, and it seeks emergent medical attention. Attempts have made to

Table 1: Comparison between groups in some demographic parameters

Variable	Fever (A)	Simple febrile convulsion (B)	Recurrent febrile convulsion (C)	P Value
Gender				
Male	26(52%)	24(48%)	28(56%)	0.726
Female	24(48%)	26(52%)	22(44%)	
Family history of febrile convulsion	10(20%)	25(50%)	25(50%)	0.002
Family history of recurrent febrile convulsion	2(4%)	2(4%)	5(10%)	0.345
Family history of epilepsy	0(0%)	2(4%)	0(0%)	0.132

Table 2: Comparison between groups in different parameters

Variable	Fever (A) (n = 50)	Simple febrile convulsion (B) (n = 50)	Recurrent febrile convulsion (C) (n = 50)	P Value		
	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD	A versus B	A versus C	B versus C
Age/months	30.82 $\pm$ 18.037	31.38 $\pm$ 15.306	35.43 $\pm$ 14.895	0.862	0.153	0.209
Temperature	38.72 $\pm$ 0.427	38.45 $\pm$ 0.377	38.76 $\pm$ 0.477	0.002	0.634	<0.001
WBC	10640 $\pm$ 2601.09	10534 $\pm$ 3054.71	11080 $\pm$ 3560.1	0.864	0.479	0.379
S.Na	135.18 $\pm$ 1.803	135.10 $\pm$ 2.702	131.76 $\pm$ 3.750	0.893	<0.001	<0.001
S.Ca	8.62 $\pm$ 0.430	8.81 $\pm$ 0.467	8.79 $\pm$ 0.518	0.040	0.068	0.817
RBS	106.98 $\pm$ 11.901	103.90 $\pm$ 12.221	108.38 $\pm$ 12.98	0.215	0.573	0.072

Table 3: Relationship between serum Na level and convulsion

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	Fever with convulsion (n = 100)	Fever without convulsion (n = 50)	P Value
Hyponatremia	59(59%)	24(48%)	0.201
Normal Na level	41(41%)	26(52%)	
Odds ratio = 1.559 95%CI = 0.745–3.269			

Table 4: Association between serum Na level and simple febrile convulsion

			Groups	P Value
Serum Na	Hyponatremia	Simple febrile convulsion	Fever	0.102
	Normal Na level	16	24	
Total		32.0%	48.0%	
		34	26	
		68.0%	52.0%	
			50	
			100.0%	

Odds ratio = 0.51 95%CI (0.208–1.241)

Table 5: Significant association between low serum Na level and recurrent febrile convulsion

	Recurrent febrile convulsion (n = 50)	Fever without convulsion (n = 50)	P Value
Hyponatremia	43(86%)	24(48%)	<0.001
Normal Na level	7(14%)	26(52%)	

Odds ratio = 6.65 95%CI(2.3–19.9)

identify predisposing risk factors and predictors of recurrent seizure. This knowledge has a practical value as to whether to admit the child and advising parents of a repeated convulsion.^[5] In the current study, we used 150 children, with mean age (30.82 ± 18.037) in group A, ($31.38 \pm 15.3.306$) in group B, and (35.43 ± 14.895) in group C, with no significant difference between males and females. However, we found that there is a relationship between hyponatremia and recurrent febrile convulsion, that is, hyponatremia plays the role of a risk factor for recurrent febrile convulsion, P value in A/C <0.001, B/C <0.001, which is significant. Our study was supported by Khosroshahi *et al.*'s^[9] study, consisting of age-matched children who presented to the E.U. with fever, without seizure, and a group of healthy afebrile children; this demonstrated a relationship between lower S. Na level and the incidence of developing recurrent seizure within the same febrile illness.^[8,9] However, the study by Paul SP included no control group.^[8] It was also reported that low S. Na levels played a significant role in recurrent simple febrile seizure. Contradictory to earlier European studies, Carapetian *et al.*^[7] In which (175) children ages (6month- 5year) old. (136) febrile child presented to the EU, with generalize seizure, lasting less than 15 min, (34) a febrile children used as a control group and measured the mean S.Na for all, they found that the mean S.Na for (27) children with febrile seizure was (135.48) mmol/L during 24 h did not differ from those (109) children with recurrent febrile convulsion. This finding may be due to mildly raised antidiuretic hormone (ADH) during acute febrile illness and, as a result of fluid retention; this will lead to relative hyponatremia and may decrease the threshold of fluids that can aggravate hyponatremia and promote febrile seizure.^[10] And the mean S.Na for 109 children with simple febrile seizure. As well as the mean S.Na for a febrile children used as control group were higher than the other children in other groups. However, the study was similar to the finding of Maksikharin and Prommalikit's.^[11] study.^[12]

Other studies wherein a febrile seizure was viewed as a control found that both febrile groups had relative hyponatremia, but with no statistically significant difference between afebrile seizure and febrile seizure. This is similar to the current study, where we compare between the fever without convulsion and fever with convulsion, whether simple or recurrent; we found that it is not significant with $P = 0.201$. When we compared between the fever without convulsion and fever with recurrent febrile convulsion, it was significant with $P < 0.001$. However, Iran study was similar to the finding of Thoman *et al.*'s^[11] study. This study was undertaken in children with febrile seizure with retrospective data collected from medical records; they used 315 children with febrile seizure, with a mean age of 12.5 months, which more than our study 181(57.5%) male, (47) episodes of recurrent febrile seizure within 24hour occurred in 39 children (12.4%) – 276 pt. with single febrile seizure the serum of Na. was [134.94 mmol/L] and those in whom febrile seizure recurrent within 24h (134.99) mmol/L so they found that there were no significant different.^[13] While in our study, there was significant different between simple febrile convulsion and recurrent febrile seizure.

CONCLUSION

Many factors affect febrile convulsion. The current study demonstrated that a decrease in the level of Serum Na+ or relative hyponatremia may play a role as a risk factor for recurrent febrile convulsion. There is a significant association between recurrent febrile convulsion and a lower level of serum sodium, in which serum sodium concentration is lowest in that patient with recurrent febrile convulsion.

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Conflicts of interest

There are no conflicts of interest.

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