

Recurrent Seizure during Hospitalization in Children with the First Febrile Seizure: Incidence and Risk Factors

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Abstract

Background: The present study aimed at evaluating the demographic and laboratory factors associated with the recurrent seizure during hospitalization in the children with the first febrile seizure.

Methods: This cohort study was performed in Ghaem hospital, Mashhad University of Medical Sciences, Mashhad, Iran, from 2018 to 2019. Totally 483 admitted children aged 6-60 months with the first febrile seizure were included. The repetition of seizure during hospitalization was considered as incidence of recurrent seizure.

Results: Among 483 children with the first febrile seizure, recurrent seizure occurred in 57 patients (11.8%). The serum level of potassium, magnesium and calcium in children with recurrent seizure significantly was lower in comparison to the patients without repeated seizure. Complex seizure was the major risk factor for recurrent seizure (relative risk: 377.74, p=0.001). The risk of recurrent seizure decreased with the increase of serum level of potassium, calcium and magnesium. The risk of recurrent seizure increased with the increase of body temperature but not significantly.

Conclusion: The incidence rate of recurrent seizure in children with the first febrile seizure was 118 cases per 1000 population. Complex seizure was the main risk factor for the seizure recurrence. Higher serum levels of potassium, calcium and magnesium may decrease the risk of recurrent seizure.

Key Words: Seizure, Seizure recurrence, Complex seizure, Child, Risk factor, Febrile seizure, Upper respiratory tract disease.

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1- INTRODUCTION

Febrile seizure (FS) is a common disorder among children aged 6-60 month with no neurological conditions and previous history of seizure (1). The prevalence of FS is approximately 2-5% worldwide (2). FS is categorized as partial or generalized and simple or complex according to the duration, number of attacks (usually in 24 hours). FS is simple in 65-90% of patients (3). According to documents relapse may occur in 30-40% of patients. Almost 50-70% of relapses are in the first year and 90% are during 2.5 years after FS occurrence. Gender, age, positive family history, genetic factors and body temperature during seizure are suggested as risk factors (4, 5). Prevention of seizure recurrence is necessary because of probable complications which affect quality of life (6). Identification of risk factors may help prevent recurrent seizure.

There are few studies evaluating the risk of recurrent seizure in children with the first febrile seizure during hospitalization. Therefore, the present study was carried out evaluating the demographic and laboratory factors which may be associated with the recurrence seizure during hospitalization in the children aged 6-60 month with the first febrile seizure.

2- PATIENTS AND METHODS

The present cohort study was performed in Ghaem hospital, Mashhad University of Medical Sciences, Mashhad, Iran, from 2018 to 2019. The study protocol was approved by the Ethics Committee of Mashhad University of Medical Sciences (code: IR.MUMS.fm.REC.1396.689). Totally 483 admitted children aged 6-60 months with first febrile seizures were included. All showed the classic criteria of FS. The diagnosis of FS was documented based on the clinical symptoms by the pediatrician. The axillary body temperature higher than 38°C was considered as fever and was

measured according to the standard protocol. Patients with meningitis, severe malnutrition, chronic renal disease (CRD), hypocalcemia, hypomagnesemia, hypoglycemia, hypo- and hypernatremia were excluded. The seizure recur during hospitalization was considered as incidence of recurrent seizure. Simple febrile seizure was recognized as generalized, when it had duration less than 15 minutes, single episode of seizure and occurred within 24 hours of the onset of fever. A focal, prolonged (≥ 15 minutes), and/or recurrent within 24 hours usually in the same febrile illness was classified as complex febrile seizure (7).

2-1. Data analysis

Statistical analyses were performed using SPSS windows program version 16 (SPSS Institute, Inc., Chicago, IL, USA). All experimental values are presented as mean \pm standard deviation (SD) or frequency percentage. Chi-squared test was used to screen the associations between the qualitative variables. Logistic regression was performed for determination of risk factors. Independent t-test was also applied for comparing the quantitative variables. P-values less than 0.05 were considered statistically significant.

3- RESULTS

3-1. Baseline characteristics

Among 483 admitted children with the first febrile seizure, recurrent seizure occurred in 57 patients (11.8%). The incidence rate was 118 cases per 1000 population. The mean age of children with and without recurrent seizure was 21.64 ± 13.22 and 22.86 ± 12.14 month, respectively ($p = 0.48$). Thirty (52.6%) and 238 patients (55.9%) were male in children with and without recurrent seizure, respectively ($p = 0.67$). Type of seizure was simple in 1 patient (1.8%) with recurrent seizure and 371 (87.1%) patients without recurrent seizure ($p = 0.001$). Body temperature was more than 38.5 °C in 33

patients (57.9%) with recurrent seizure and 195 (45.8%) patients without recurrent seizure ($p = 0.09$). The upper respiratory tract disease (URTI) was the most common underlying disease among

patients (35.1% and 45.1% in children with and without recurrent seizure, respectively ($p = 0.27$). Baseline characteristics are presented in **Table 1**.

Table-1: Demographic and clinical characteristics of febrile children with and without recurrent seizure

Variable		With repeated seizure (n=57)	Without repeated seizure (n=426)	P value
Age (month)		21.64±13.22	22.86±12.14	0.48 *
Gender	Male	30 (52.6%)	238 (55.9%)	0.67 **
	Female	27 (47.4%)	188 (44.1%)	
Type of seizure	Simple	1 (1.8%)	371 (87.1%)	0.001 **
	Complex	56 (98.2%)	55 (12.9%)	
Body temperature	Equal or more than 38.5 ⁰ C	33 (57.9%)	195 (45.8%)	0.09 **
	Less than 38.5 ⁰ C	24 (42.1%)	231 (54.2%)	
Underlying disease	URTI	20 (35.1%)	192 (45.1%)	0.27 **
	LRTI	3 (5.3%)	15 (3.5%)	
	UTI	7 (12.3%)	25 (5.9%)	
	GE	15 (26.35)	95 (22.3%)	
	Others	12 (21.1%)	99 (23.2%)	

URTI: upper respiratory tract disease, LRTI: lower respiratory tract disease, UTI: urinary tract infection, GI: gastroenteritis, * independent t test, ** chi square test

3-2. Laboratory characteristics

Among the included children, hemoglobin concentration was lower than 11 g/dl in 24 patients (42.1%) with recurrent seizure and 128 patients (30%) without recurrent seizure ($p = 0.07$). The mean of white blood cells (WBC) in children with and without recurrent seizure was 10822.81±4473.17 and 11012.21±4090.94 cell/ μ l, respectively ($p = 0.74$). The mean of polymorphonuclear cells (PMN) percent in children with and without recurrent seizure was 60.62±18.06 and 64.90±15.42, respectively ($p = 0.09$). The mean of lymphocytes percent in children with and without recurrent seizure was 33.84±16.89 and 26.93±15.54, respectively ($p = 0.002$). Moreover, there was a significant difference between children with and without recurrent seizure in serum level of

potassium (4.33±0.45 versus 4.55±0.43 mEq/L, $p = 0.001$), magnesium (2.30±0.23 versus 2.41± 0.21 mEq/L, $p = 0.04$) and calcium (9.42±0.53 versus 9.62±0.53 mEq/L, $p = 0.009$), respectively. But there was no significant difference between children with and without recurrent seizure in serum level of platelet, sodium and sugar. The laboratory data are presented in **Table 2**.

3-3. Risk factors

According to the results of the regression analysis, complex seizure was a major risk factor for recurrent seizure (relative risk (RR): 377.74, $p = 0.001$). The risk of recurrent seizure decreased with the increase of serum level of potassium, ca and mg but not significantly ($p = 0.13$, 0.31, and 0.06, respectively). In addition, the risk of recurrent seizure increased with

the increase of body temperature but not significantly (RR=1.62, p = 0.08). The

related data are presented in **Table 3**.

Table-2: Laboratory characteristics of febrile children with and without repeated seizure

Variable		With repeated seizure (n=57)	Without repeated seizure (n=426)	P value
Hb	Lesser than 11 (g/dl)	24 (42.1%)	128 (30%)	0.07**
	More than 11 (g/dl)	33 (57.9%)	298 (70%)	
WBC (cell/ μ l)		10822.81 \pm 4473.17	11012.21 \pm 4090.94	0.74 *
PMN cells (%)		60.62 \pm 18.06	64.90 \pm 15.42	0.09 *
Lymphocyte (%)		33.84 \pm 16.89	26.93 \pm 15.54	0.002 *
Platelet (cell/ μ l)		276.25 \pm 110.49	280.18 \pm 83.52	0.75 *
Sodium (mEq/L)		135.66 \pm 3.15	135.31 \pm 2.21	0.40 *
Potassium (mEq/L)		4.33 \pm 0.45	4.55 \pm 0.43	0.001 *
Magnesium (mEq/L)		2.30 \pm 0.23	2.41 \pm 0.21	0.04 *
Calcium (mg/dL)		9.42 \pm 0.53	9.62 \pm 0.53	0.009 *
Sugar (mg/dl)		105.10 \pm 29.12	108.41 \pm 24.58	0.36 *

Hb: hemoglobin, WBC: white blood cell, PMN: polymorph nuclear, μ g: microgram, dl: deciliter, μ l: microliter, mEq: mill equivalent, L; liter, * independent t test, ** chi square test

Table-3: Risk factors for repeated seizure in children with febrile seizure

Variable	Relative risk	CI (95%)	P value*
Hb (\geq 11 μ g/dl)	0.59	(0.34,1.04)	0.60
Body temperature (more than 38.5 0C)	1.62	(0.93,2. 85)	0.08
PMN (%)	1.081	(0.942,1.240)	0.27
Lymphocyte (%)	1.11	(0.967,1.282)	0.13
Potassium (mEq/L)	0.32	(0.75,1.41)	0.13
Magnesium (mEq/L)	0.26	(0.20, 3.50)	0.31
Calcium (mg/dL)	0.37	(0.13, 1.062)	0.06
Complex seizure	377.74	(51.25, 2784.39)	0.001

Hb: hemoglobin, PMN: polymorph nuclear, μ g: microgram, dl: deciliter, mEq: mill equivalent, L; liter, CI: confidence interval * logistic regression

4- DISCUSSION

In this cohort study, 483 children aged 6-60 month with the first febrile seizure were studied during hospitalization to evaluate the incidence of recurrent seizure and its risk factors. The incidence of recurrent seizure was 118 cases per 1000 population. Complex seizure was the main risk factor for seizure recurrence.

FS is a life-changing event. It may have physical and psychological outcomes. In a

patient with the first FS, the clinician must decide whether the risk factors of recurrent seizure exist or not. This is very important in the management of patients with FS (8). Seizure carries significant morbidities ranging from self-injury to severe complications. Furthermore, febrile seizure seriously affects the patient's quality of life (9). During the past decade, several risk factors of the recurrent seizure in children with the first febrile seizure have been defined. These include laboratory,

clinical and demographic related factors (2, 4, 10, 11).

There are several studies evaluating the incidence and risk factors of recurrent seizure in children. But studies evaluating the risk factors during hospitalization are very few. In a study by Jamal et al. on 132 children with febrile seizure, recurrent seizure was reported in 34.85% of children. They reported that modest rise in body temperature at the onset of seizure, younger age at presentation, onset of seizure within 6 hours of fever, and complex seizure are the main risk factors for the recurrent seizure (12). Contrary to Jamal, in our study, the body temperature more than 38.5°C increased the risk of recurrent seizure, though the increase was not significant (RR=1.62, p =0.08). Additionally, in our study no demographic related risk factors were recognized in the population. But in agreement with Jamal, complex seizure was recognized as a major risk factor in our study. In another study on children with FS, family history of seizure and body temperature less than 38°C were identified as risk factors for seizure recurrence (13).

Berg et al. proposed that seizure recurrence is more in febrile children with a complex seizure (14). In line with Berg, the present study showed that complex seizure was the main risk factor for seizure recurrence with a relative risk of 377.74. Nonetheless, some studies suggest that there is no relationship between complex seizure and risk of seizure repetition (5).

Laboratory risk factors have been verified in several studies but the results are inconsistent. In a study on children with febrile seizure, it was reported that serum level of sodium did not differ in febrile children with and without recurrent seizure but their serum level of sodium was significantly lower in comparison to febrile children (15). This finding was confirmed in our study. According to another report, serum levels of iron, zinc,

magnesium and calcium did not differ between febrile children with and without seizure (16). But in our study higher serum levels of magnesium, calcium and potassium decreased the risk of recurrent seizure (RR<1) but not significantly (p>0.05). Maybe a larger sample size can reaffirm our results statistically.

5- CONCLUSION

The incidence rate of recurrent seizure in children with the first febrile seizure was 118 cases per 1000 population. Complex seizure was the main risk factor for the seizure recurrence. The serum level of Potassium (K), Magnesium (Mg) and Calcium (Ca) in children with repeated seizure was significantly lower, in comparison to no repeated seizure patients.

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7- CONFLICT OF INTEREST

None.

8- REFERENCES

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