Original Article

Recurrent Rates and Risk Factors of Febrile Seizures in the Subsequent Illness Following the First Febrile Seizures in Thai Children

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Objective: To determine risk and risk factors of recurrent febrile seizures after first febrile seizures.

Materials and Methods: This was an observational prospective cohort study on children 6 months to 5 years of age who presented with the first febrile seizures between January 2007 to June 2013. The data was collected from medical records and interviews with parents.

Results: 357 children were enrolled with the first febrile seizures with a mean (SD) age of 20.9 (12.4) months. 19.3% of these had recurrent febrile seizures and a cumulative risk of recurrence was 13%, 19% and 19.3% at 12, 24 and 50 months after first febrile seizures, respectively. By multivariate analysis, family history of febrile seizures was the significant risk factor for recurrence of febrile seizures (p<0.05). Age, gender, duration of fever before seizures, the temperature at initial seizures, complex febrile seizures, type of seizures and family history of epilepsy were not associated with risk of recurrent febrile seizures.

Conclusion: The recurrent febrile seizures was more frequent at 12 to 24 months after the first febrile seizures and the positive family history of febrile seizure was increasing risk of recurrent febrile seizures in subsequent illness.

Keywords: Febrile seizures, Recurrent febrile seizures, Risk of recurrence, Risk

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Febrile seizures are the most common disorder in children with occur in 2 to 5% of all children[1-4]. Approximately one-third of children who have had a febrile seizures would experience recurrent seizures, while 10% of those would develop three or more recurrences[1-10]. The risk factors for recurrence were identified in previous studies and the strongest risk factors were a family history of febrile seizures and a young age (younger than 12, 15 or 18 months) at the first febrile seizures[1,2,4-8,11,12]. Moreover, some studies have reported the duration of the fever before seizures, temperature at seizures, type of seizures, complex febrile seizures, neurodevelopment status and a family history of epilepsy were associated with risk factors of recurrent febrile seizures[1-5,8,11-16]. There was only one study regarding risk and risk factors of recurrent febrile seizures in Thai children from Chiang Mai[17].

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However, the difference of race, ethnicity or location may effect to risk of recurrent febrile seizure. Therefore, the correlation between risk factors and recurrence of febrile seizures remains unclear especially in Thai population.

The aim of this observational prospective cohort study was to determine risk and risk factors of recurrent febrile seizures after the first febrile seizures.

Materials and Methods

Children 6 months to 5 years of age presented with a clinically diagnosis of the first febrile seizures at HRH Princess Mahachakri Sirindhorn Medical Center were enrolled and followed-up every 6 to 12 months between January 2007 to June 2013. Children with intracranial causes, afebrile seizures and seizures treatment with long term of anticonvulsive drugs including intermittent diazepam were excluded. The parents were informed consent (SWUEC/Ex16/2555).

The information of children with the first febrile seizures between January 2007 to December 2011 was collected from medical records. In case of incomplete information from medical records, we interviewed their parents by phone call. The information from January 2012

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to June 2013 was collected from medical records and direct interviewing with parents including the information while children were followed-up every 6 to 12 months in order to evaluate the recurrence of febrile seizures.

The collected information included age at the first febrile seizures, gender, first or second degree relative with history of febrile seizures and epilepsy, neurodevelopment status, duration of fever before seizures (less than or equal 24 hours, and more than 24 hours), body temperature at seizures (less than 39°C, and more than or equal 39°C) and description of seizure types (complex febrile seizures consist of focal feature, seizures prolonged more than or equal 15 minutes and recurrent seizures within 24 hours). Description of seizure types was classified by the pediatric neurologist.

Sample size and statistical analysis

The sample size of this group was estimated to be 125. This provided a 95% CI for prevalence of recurrent febrile seizures of 0.33±0.05.

The information was analyzed by SPSS 15.0. The results were displayed as Kaplan-Meier survival curves with the cumulative probability of recurrent febrile seizures plotted as a function of time from the first febrile seizures. Student's t-test and Chi-square test were used to compare continuous and categorical variables, respectively. Multivariate analysis was performed using a logistic regression model $p<0.05$ was considered to be significant.

Results

Of 357 children with mean (SD) age of 20.9 (12.4) months were diagnosed of the first febrile seizures. Among of them, 210 (58.5%) were males and 69 (19.3%) had recurrent febrile seizures. The risk of recurrence in patients who had 3 and 4 episodes of febrile seizures were 3.9% (14/357) and 0.8% (3/357), respectively.

The overall recurrence rate was 19.3%. The cumulative recurrence rate was 13 %, 19% and 19.3% at 12, 24 and 50 months after first febrile seizures, respectively. This study showed that there was no more rising of recurrent rate after 50 months (Figure 1). Of patients with recurrent febrile seizures, 33.3% (23/69) had family history of febrile seizures. The positive first or second degree relative with history of febrile seizures was the significant predictor of recurrent febrile seizures ($p<0.05$) and multivariate analysis showed that the positive first or second degree relative with history of febrile seizures still was the significant predictive risk factor of recurrent febrile seizures ($p = 0.02$) (Table 1). The recurrence rate at 13 months after initial febrile seizures was 21% for patients with family history of febrile seizures and 11% for patients without family history of febrile seizures (Figure 2).

Age at the first febrile seizures, gender, family history of epilepsy, neurodevelopment status, duration of fever before seizures, temperature at seizures, type of seizures and complex febrile seizures were not significant risk factors to predict recurrence of febrile seizures (Table 1).

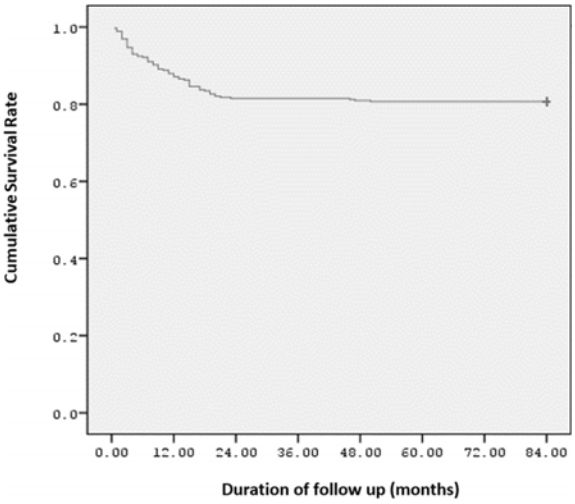

Figure 1. Probability of recurrence after the first febrile seizures by Kaplan Meier curve.

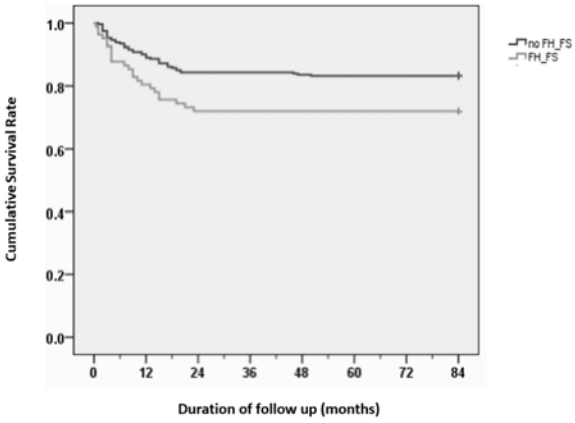

Figure 2. Probability of recurrence after the first febrile seizures as a function of the family history of febrile seizures by Kaplan Meier curve; FH_FS = family history of febrile seizures.

Discussion

In the present study, the risk of recurrence was approximately 19.3%, most of the recurrence occurred within 24 months after first febrile seizures, which was similar to the previous studies[18-20]. The present study showed that the recurrent rate of febrile seizures was lower than the other studies in Western countries which have demonstrated risk of recurrence is about 30 to 40%[16,21,22]. Possible reasons for this may be due to the different ethnicities, sample size and the methodology design of these studies.

Family history of febrile seizures was the significant predictive risk factor of recurrent febrile seizures in this study which was similar to the other literatures[1,2,4-8,10,11,17,18,20,22,23]. Furthermore, this result

Table 1. Correlation of risk factors and febrile seizures recurrence

Factors	No recurrent febrile seizures, n (%)	Recurrent febrile seizures, n (%)	*p*-value
Gender			0.772
Male	170 (59)	40 (58)	
Female	118 (41.0)	29 (42.0)	
Age, months			0.235
<18	132 (45.8)	37 (53.6)	
≥18	156 (54.2)	32 (46.4)	
Neurodevelopment status			0.824
Normal	283 (98.3)	68 (98.6)	
Abnormal	5 (1.7)	1 (1.4)	
Family history of febrile seizures			0.021
Yes	59 (20.5)	23 (33.3)	
No	229 (79.5)	46 (66.7)	
Family history of epilepsy			0.139
Yes	16 (5.6)	7 (10.1)	
No	272 (94.4)	62 (89.9)	
Temperature, °C			0.229
<39	119 (41.3)	23 (33.3)	
≥39	169 (58.7)	46 (66.7)	
Duration of fever before seizures, hours			0.356
≤ 24	228 (79.2)	59 (85.5)	
>24	60 (20.8)	10 (14.5)	
Type of seizures			0.999
Generalized	286 (99.3)	69 (100)	
Focal	2 (0.7)	0 (0)	
Type of febrile seizures			0.340
Simple	246 (85.4)	62 (89.9)	
Complex	42 (14.6)	7 (10.1)	

supports the findings of the recent studies about genetic predisposing factor to febrile seizures such as gene association with sodium channel, GABA receptor, Voltage-gated potassium channel, neuronal nicotinic cholinergic receptor and interleukin receptors[2,4,24-31]. Other factors including gender, age at onset of the first febrile seizures, duration of fever before seizures, temperature at seizures, family history of epilepsy, complex febrile seizures, type of seizures and neurodevelopment delay are not increasing risks for recurrence of febrile seizures in our study.

Based on previous studies, age at onset of the first febrile seizures was the strongest risk factor for seizure recurrence[1,5-8]. The younger age at onset of the first febrile seizures is increasing risk of recurrent febrile seizures that this factor may be associated with lower threshold for febrile seizures[9,17,18,23,32]. Conversely, our study and the study of Tosun et al[22] showed that there was no association between age at onset of the first febrile seizures and seizure recurrence. For the duration of fever before seizures and temperature at seizures, previous studies reported that these factors were associated with recurrent febrile seizures. However, Chung et al[18], Tosun et al[22], Kantamalee et al[17] and the present study showed the duration of fever before seizures and temperature at seizures was not the increasing risk of recurrent febrile seizures. These could be from the difference of ethnicities and the accurate history of onset of fever and level of body temperature from the parents.

Conclusion

Febrile seizures are the most common seizures disorder in childhood and the recurrent febrile seizures are more frequent within 24 months after the first febrile seizures. The positive of family history of febrile seizures will help us to recognize the seizure recurrence in the subsequent illness.

What is already known on this topic?

Risk factors for recurrent febrile seizures in foreign studies are a positive family history of febrile seizures, a young age (younger than 18 months) at the first febrile seizures, the short duration of the fever before seizures and lower temperature at seizures.

What this study adds?

A positive first or second degree relative with history of febrile seizures was significant risk factor of febrile seizures recurrence in Thai population.

Acknowledgements

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Potential conflicts of interest

The authors declare no conflict of interest.

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