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A Retrospective Review of First Febrile Convulsion and Its Risk Factors for Recurrence in Hong Kong Children

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Abstract Febrile convulsion is the most common convulsive disorder in childhood. Many parents who had witnessed a child's first convulsion think that their child is going to die or is already dead. Intense parental anxiety and fear for recurrence is observed. Risk factors for recurrence of febrile convulsion is available in overseas studies but only limited local data is available. ***Objective:*** To determine the risk factors for recurrence of patients admitted for first febrile convulsion. ***Methods:*** The records of patients, admitted to Kwong Wah Hospital for first febrile convulsion from January 2002 to December 2004 were reviewed. Demographic data, characters of seizure, family history of febrile convulsion and epilepsy in first-degree relatives, investigations done and aetiology identified were noted. Outcome was measured in January 2007 with follow-up phone call made to re-confirm family history of seizure disorders and outcome of the patient. ***Results:*** One hundred and eighty-one patients were admitted for first febrile convulsion in the period studied. Out of 181 patients, 159 were valid for analysis, 22 failed contact. The most common seizure type was generalised tonic-clonic seizure, occurred in 82 patients (51.6%). Complex febrile seizure was observed in 37 patients (23.3%). Positive family history of febrile convulsion and epilepsy in first-degree relatives was noted in 29 patients (18.2%) and 4 patients (2.5%) respectively. Recurrence of febrile convulsion occurred in 36 patients (22.6%) and development of epilepsy in 2 patients (1.3%). Multivariate logistic regression showed young age was the only significant risk factor for the recurrence of febrile convulsion ($p<0.001$). ***Conclusion:*** For first febrile convulsion, 22.6% recurred and young age was the only significant risk factor for recurrence.

Key words Age; Family history of epilepsy; Family history of febrile convulsion; Febrile convulsion; Recurrence

Introduction

Febrile convulsion (FC) is the most common neurological, as well as seizure disorder in children.[1,2] Population studies in Western Europe and the USA report a cumulative incidence of 2-5%.[3,4] The incidence worldwide varies from 5-10% in India, 8.8% in Japan and 14% in Guam.[2] It was distinguished from other seizures in the mid-19th century.[5] Treatment at that time was directed to the underlying causes of fever rather than the seizure itself. With the introduction of the thermometer at the end of the 1800s, fever was understood to be the primary trigger of convulsion. Current view of FC is based on 2 population-based studies conducted by van den Berg & Yerushalmy[6] and Nelson & Ellenberg:[7] it is common, many of them recur, developmental outcome is not altered and few children later develop epilepsy. Overseas study of risk factors for recurrence of FC were well described by Knudsen[8] and Berg et al[9]: age 15 months or less at the time of the first FC, epilepsy in first-degree relatives, FC in first-degree relatives, a first complex FC, and day nursery care. However, among all these risk factors, age is the single, strongest, and most consistent risk factor.[3,4,9-12] Local data is limited. Chung et al[13]

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identified 3 significant factors for recurrence: early age of onset, family history of febrile seizure and complex febrile seizure. Kong & Ko[14] showed family history of FC in first-degree relatives was the only statistically significant risk factor for recurrence while age was not. We conducted a retrospective study to review all cases of first FC, to identify the characteristics of the FC and the risk factors for recurrence.

Methods

The hospital records of patients admitted for first FC to Kwong Wah Hospital, a regional hospital in Hong Kong, from January 2002 to December 2004 were reviewed. Inclusion criteria were convulsion occurring in a child, aged 6 months to 5 years, associated with fever (>38°C) but without evidence of intracranial infection or defined cause (metabolic dysfunction), who is otherwise neurologically normal.[10] Convulsions with fever in children who have abnormal neurological status or previous afebrile convulsion or previous febrile convulsion were excluded. Simple FC is defined as primary generalised convulsion lasting less than 15 minutes and not recurring within 24 hours. Complex FC is defined as focal or prolonged (>15 minutes) convulsion, and/or more than one convulsion in 24 hours.[10] Demographic data, characters of convulsion, family history of FC and epilepsy in first-degree relatives, investigations performed, aetiology, subsequent outcome and time interval between the first attack and its recurrence were collected from the hospital records. Investigations including electroencephalography (EEG), computed tomography (CT) or magnetic resonance imaging (MRI) of brain, lumbar puncture (LP) and blood culture were done in some cases. Aetiology was divided into 9 groups: upper respiratory tract infection, otitis media, pneumonia, gastroenteritis, roseola infantum, viral illness, urinary tract infection, bronchiolitis and other. Outcome was divided into 5 groups: normal development without any recurrence of FC, normal development with recurrent FC, epilepsy, developmental delay and other. Follow-up phone call conducted for all patients in January 2007, to re-confirm the status of family history of FC and epilepsy, and the latest outcome of the patient.

Statistics

The data obtained from first FC event in children with or without recurrent FC were compared. The differences in age, temperature at onset or first known temperature, duration of FC between two groups were tested by Student's t-test. If the data was not normally distributed, as evidenced by Kolomogrov-Smirnov test, the differences were tested by Mann-Whitney U test. Categorical variables such as gender, type of seizure, type of FC, family history of FC and epilepsy etc. were compared by Fisher's exact test or chi-square test.

Parameters with $p<0.5$ in univariate analysis were subjected to multivariate logistic regression analysis without any automatic elimination process.

SPSS 11 for Mac OS X was used for all analysis. $p<0.05$ was considered as statistically significant.

Results

One hundred and eighty-one patients were admitted for first febrile convulsion during January 2002 to December 2004. Twenty-two patients were excluded from study because of failed contact via phone. The mean follow up time was 38 months (range: 24 to 48 months). In the remaining of 159 patients, the summary is presented in Table 1. Thirty-seven patients (23.3%) had complex FC and 29 patients (18.2%) had family history of FC in first-degree relatives. Distribution of age of seizure onset is described in Figure 1, 82 patients (52%) had seizure onset below 2 years of age (24 patients in the group of 6-12 months, 31 patients in the group of 13-18 months and 27 patients in the group of 19-24 months). One hundred and thirty-four patients (84.8%) had seizure less than 5 minutes (Figure 2). Regarding investigations, 15 of them had EEG, 12 of them had CT, none had MRI, 13 of them had LP and 38 of them had blood culture. Out of these 159 patients, 36 had recurrent FC within 2 years. For the recurrence of FC, 15 patients (42%) had the attack in the next 6 months, 27 patients (75%) had the attack in one year and all had the recurrence within 2 years. By comparing those with recurrent FC and those without recurrent FC, as shown in Table 2, age at onset was significantly lower in patients with recurrent FC. Multivariate logistic regression was constructed with recurrent FC as the dependent variable. Age, gender, type of seizure, status epilepticus and FC in first-degree relatives were used as independent variables (Table 3). The only significant risk factor for recurrent FC was young age at onset.

Table 1 Summary statistics of all patients with FC

Variables	Number=159 (%)
M/F	94/65
Age (months)	
Mean	26.2
SD	13.0
Temperature at onset/first known temperature (Degree Celcius)	
Mean	39.4
SD	0.69
Duration of FC (minutes)	
Median	2
Interquartile range	1 to 5
Type of seizure	
GTC	82 (51.6)
Tonic	51 (32.1)
Clonic	14 (8.8)
Atonic	4 (2.5)
Unclassified	8 (5.0)
Type of FC	
Simple	121 (76.1)
Complex	37 (23.3)
Unclassified	1 (0.6)
Status epilepticus	2 (1.3)
Aetiology	
URTI	63 (39.6)
OM	10 (6.3)
Pneumonia	13 (8.2)
GE	7 (4.4)
Viral illness	48 (30.2)
UTI	5 (3.1)
Bronchiolitis	5 (3.1)
Other	8 (5.0)
Roseola infantum	0 (0)
FC in 1st degree relatives	29 (18.2)
Epilepsy in 1st degree relatives	4 (2.5)

SD=standard deviation, GTC=generalised tonic-clonic, URTI=upper respiratory tract infection, OM=otitis media, GE=gastroenteritis, UTI=urinary tract infection

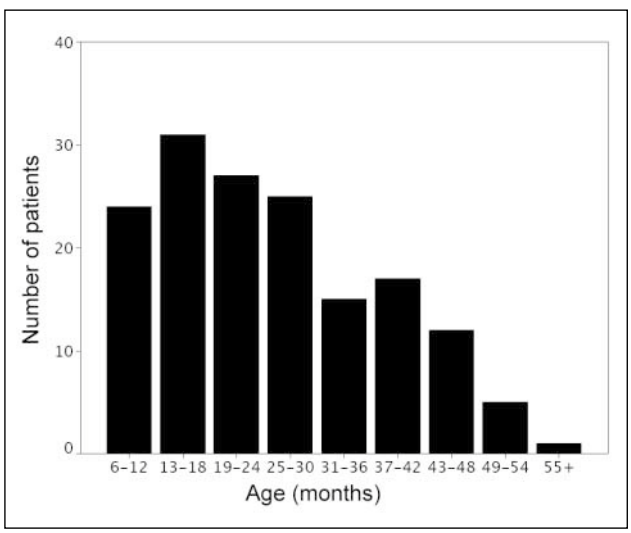

Figure 1 Age of first febrile convulsion.

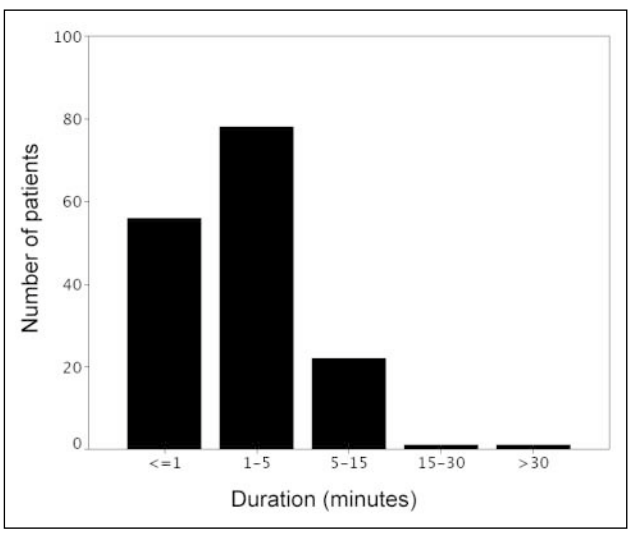

Figure 2 Duration of first febrile convulsion.

Table 2 Comparison of patients with and without recurrent FC

	Patients with recurrent FC Number=36 (%)	**Patients without recurrent FC Number=123 (%)**	**P-value**
Male / Female	19 / 17	75 / 48	0.442
Age (months)			
Mean	19.2	28.2	<0.001
SD	10.3	13.0	
Temperature at onset/first known temperature			
Mean	39.4	39.4	0.804
SD	0.7	0.7	
Duration of FC			
Median	2.5	2.0	0.670
Interquartile range	1.0-5.0	1.0-5.0	
Type of seizure			
GTC	21 (58.3)	61 (49.6)	
Tonic	12 (33.3)	39 (31.7)	
Clonic	0 (0)	14 (11.4)	0.334
Atonic	1 (2.7)	3 (2.4)	
Unclassified	2 (5.4)	6 (4.9)	
Type of FC			
Simple	28 (77.8)	93 (75.6)	
Complex	8 (22.2)	29 (23.6)	1.000
Unclassified	0 (0)	1 (0.8)	
Status epilepticus	1 (2.8)	1 (0.8)	0.405
Aetiology			
URTI	13 (36.1)	50 (40.7)	
OM	2 (5.6)	8 (6.5)	
Pneumonia	2 (5.6)	11 (8.9)	
GE	2 (5.6)	5 (4.1)	
Viral illness	13 (36.1)	35 (28.4)	0.919
UTI	1 (2.8)	4 (3.3)	
Bronchiolitis	2 (5.6)	3 (2.4)	
Other	1 (2.8)	7 (5.7)	
Roseola infantum	0 (0)	0 (0)	
FC in 1st degree relatives	8 (22.2)	21 (17.1)	0.473
Epilepsy in 1st degree relatives	0 (0)	4 (3.3)	0.575

SD=standard deviation, GTC=generalised tonic-clonic, URTI=upper respiratory tract infection, OM=otitis media, GE=gastroenteritis, UTI=urinary tract infection

Table 3 Multivariate logistic regression analysis of risk factors associated with febrile convulsion recurrence

	B (SE)	**Adjusted odds ratio (95% CI)**	**P-value**
Age	-0.072 (0.021)	0.931 (0.893 to 0.970)	0.001
Female gender	0.240 (0.424)	1.271 (0.554 to 2.919)	0.572
Status epilepticus	6.59 (22.00)	729.55 (0 to >1000)	0.764
FC in 1st degree relatives	-0.113 (0.529)	0.893 (0.317 to 2.518)	0.831
Type of seizure			
GTC	0.271 (0.923)	1.311 (0.215 to 8.005)	0.769
Tonic	-0.068 (0.945)	0.934 (0.147 to 5.955)	0.943
Clonic	-11.73 (30.77)	0.001 (0 to >1000)	0.703
Atonic	0.326 (1.482)	1.386 (0.076 to 25.30)	0.826
Unclassified	Referents		

B=regression coefficient, GTC=generalised tonic-clonic

Discussion

Type of seizure could not be classified in 8 patients (3 of them had up-rolling of eyes only, 2 had jerky movement of 4 limbs for 1-2 seconds and the other 3 just had convulsion mentioned in the case notes). The type of febrile convulsion could not be classified in 1 patient, as the witness could not tell the duration of the seizure. In our study, male to female (M/F) ratio was 1.45, the age group of peak incidence was 13-18 months, 78 patients (49%) had the seizure lasted for 1-5 minutes.

Overseas studies showed between 9-35% of all first FC are complex,[4,15,16] a positive family history of febrile convulsion can be elicited in 25-40% of patients with FC,[17] recurrence of FC occurs in 30-40% of patients.[15,18] Locally, Kong & Ko[14] showed 23% of his patients had complex FC, positive family history of FC and recurrence of FC was 21% and 27% respectively. According to Kwong et al,[19] 15% of FC were complex, 20% had positive family history of FC and recurrence occurred in 39%, a relatively high portion of patients. Chung et al[13] showed similar results except only 18% of his patients had recurrence of FC. A comparison of findings of local studies is summarised in Table 4. The main differences among 4 studies were relatively high recurrence of FC by Kwong et al, relatively low recurrence of FC and development of afebrile seizure by Chung et al. The latter may be explained by the relatively short follow-up period. There may be other factors present in Kwong's patients to account for its high recurrence. The present study showed similar results with overseas data and Kong & Ko's series. Interestingly, Kong & Ko and our series studied the population of Kowloon side while the populations studied by Chung et al and Kwong et al came from the other 2 geographic divisions in Hong Kong. There may be some unidentified risk factors present among the populations studied. Thus a large-scale study involving all major hospitals throughout Hong Kong is warranted.

The 2 commonest types of seizure were: generalised tonic-clonic seizure in 82 patients (51.6%) and generalised tonic seizure in 51 patients (32.1%). For the complex seizure group, none had focal seizure, 7 patients (4% of total) had seizure longer than 15 minutes and the remaining 30 patients (19% of total) had cluster of attacks within 24 hours. For the aetiology of fever, nearly 70% of patients were explained either by URTI or viral illness, similar findings were demonstrated by Nelson & Ellenberg and Lewis et al.[7,20] It is well known that FC is common during the course of roseola infantum.[21] It was reported that HHV-6 accounts for 26-35% of children with febrile convulsions.[22-24] We have particularly looked for roseola infantum clinically, but not a single case was noted in our series. This is probably due to the fact that viral study was not performed routinely in the investigation of FC in our department. Out of 159 patients, one had Streptococcus pneumoniae bacteremia as the aetiology of fever. His chest X-ray and cerebrospinal fluid were normal.

By comparing those with recurrent FC and those without recurrent FC, among all parameters, sex, age, type of seizure, status epilepticus and family history of FC in first-degree relatives were eligible to be further analysed by multivariate logistic regression as their P value all <0.5. The other parameters including family history of epilepsy in first-degree relatives, temperature at onset/first known temperature, type of FC and the aetiology of fever were excluded. Multivariate logistic regression analysis was performed and it confirmed young age was the only significant risk factor for recurrent FC with a P value of 0.001, as shown in Table 3. The mean value of temperature of the groups was exactly the same, it might be explained by the small number of patients with recurrence and temperature is not a strong risk factor for recurrence. Family history of FC in first-degree relatives was not shown to be a risk factor for recurrence, though both Knudsen[8] and Berg et al[9] had the opposite finding. It might be due to our relatively low percentage of positive family history of FC and relatively low recurrent rate.

Table 4 Comparison of findings of the local studies

Author	Year	Complex seizure (%)	Family history of FC (%)	Recurrence of FC (%)	Development of afebrile seizure (%)
Kong & Ko[14]	2000	23.0*	21.0	27.0	0.9
Kwong et al[19]	2003	15.0	20.0	39.0	-
Chung et al[13]	2006	16.0	17.5	18.0	0.4
Present study	2007	23.3	18.2	22.6	1.3

*Kong mentioned 23% of patients had atypical febrile convulsion which defined by >15 minutes of duration, focal seizure, multiple seizures, younger than 6 months or older than 6 years.

The proportion of various investigations done for the first febrile convulsion was also recorded. EEG was done in 15 patients (9.4%) for their first attack of FC, 7 were ordered because of prolonged convulsion, the other 8 were either because of cluster of attacks with or without strong family history. None of the EEG showed specific abnormality that affected the management of the patient. On the other hand, 2 patients developed epilepsy later on, both of them did not have the EEG ordered during the first FC admission as they had simple FC. One of them had positive family history of febrile convulsion in his father. There is no evidence suggesting that abnormal EEGs after the first FC are predictive for the risk of recurrence or development of epilepsy.[25,26] The American Academy of Pediatrics (AAP) recommends EEG should not be performed in the evaluation of a neurologically healthy child with a first simple FC.[27] Based on our data, we even have reservation on obtaining EEG for children with complex FC, this is supported by Maytal et al[28] and Kuturec et al.[29] Interestingly, Chamberlain & Gorman[30] showed the risk of bacteremia would appear to be the same in children with fever with or without simple FC. In our series, blood culture was done in 38 patients (23.9%), only one was positive for bacteremia. Thus blood culture should be only be done after individual evaluation for signs of sepsis, rather than as one of the routine investigation of FC.

It is a frightening experience for parents to witness their own child having a seizure attack. So far, the best medicine for FC is reassurance to the family.[3,31] The following information should be given to the parents: FC is common in children, recurrence will occur in about one third of them, the risk of brain damage and later epilepsy are very rare[32] and no evidence that any child has ever died as a result of FC.[33,34] Both Uhari et al[35] and van Stuijvenberg et al[36] showed that antipyretics, acetaminophen and ibuprofen, were not effective to prevent recurrence. Thus the use of antipyretics is for alleviation of the child's discomfort rather than the prevention of recurrence.

There are several limitations in our study. First of all, it was a retrospective study. The follow up period was relatively short. The recurrence of FC was relatively lower when compared to other studies. We did not assess whether day nursery care is a risk factor for recurrence because this question was usually not asked during the assessment of FC. There is room for improvement in our documentation of the pattern of seizure as we could not classify the seizure in 5% of our patients. For the family history of FC and epilepsy, the status can only be confirmed after repetitive asking to the parents or even to the grandparents.

Conclusion

The present study showed that children who had first febrile convulsion, 22.6% recurred and young age was the only significant risk factor for its recurrence. A large-scale study with collaboration with other hospitals is helpful to delineate the real picture of FC in Hong Kong.

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