Original Article

TO IDENTIFY THE FACTORS AFFECTING THE RISK OF RECURRENT FEBRILE SEIZURES IN SAUDI CHILDREN

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ABSTRACT

Objective: To identify the risk factors of recurrent febrile seizures (FS) in Saudi children in a Northern Province of Hail in Saudi Arabia.

Study Design: Descriptive prospective study.

Place and Duration of Study: Pediatric department, King Khalid Hospital Hail, Kingdom of Saudi Arabia from 01 October 2010 to 30 September 2011.

Patients and Methods: A total of 132 children [age ranges from 03 months to 60 months] were included in the study, while they were admitted with the diagnosis of FS during the study period, in the Pediatric department of the King Khalid University Hospital, Hail. A predesigned study proforma was utilized for data collection. All the children included in the study were followed for a period of 01 year after discharge from the pediatric ward for any recurrence of FS.

Results: During the study period 132 children were admitted for FS, the mean age of children in our sample was 16 months. There was a preponderance of male children. Among the causes of fever, mostly 63(47.73%) had symptoms of viral prodrome. Recurrent febrile seizure was found in 46 (34.85%) children.

There was a statistically significant association between low temperature at onset of seizure and recurrent FS in 65.22% cases *p*-value= 0.001). Similarly, the association of duration of fever (≤ 6hour) prior to onset of FS and recurrence was found to be significant in 56.52% (*p*-value= 0.001). Moreover it was found that lower age < 12 months at onset of first FS and complex FS had a statistically significant association with its recurrence in 65.22% and 69.57% cases respectively *p*-value= 0.01 and 0.001). Non significant factors were sex and family history.

Conclusion: FS is a common paediatric problem predominantly seen in males. Almost one third of these children are at risk for recurrence in later dates. The risk factors for these recurrences are modest rise in body temperature at the onset of seizure, younger age at presentation, onset of seizure within 6 hours of fever and atypical presentation. These findings help in terms of control/prophylaxis for FS recurrence, along with appropriate parental education and counseling.

Keywords: Febrile seizures, Recurrence, Risk factor.

INTRODUCTION

Febrile seizures (FS) are the most common seizure disorder during childhood[1]. It generally has an excellent prognosis but may also signify a serious underlying acute infectious disease such as sepsis or bacterial meningitis. Therefore, each child with a seizure associated with fever must be carefully examined and appropriately investigated for the cause of the fever, especially when it is the first seizure[2]. FS are age dependent and are rare before 9 months and after 5 year of age. Some definitions of FS

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have lower and upper age limits (for example, three months to five years. Such limits reflect conventions but are not founded on an etiologic basis and are not universally accepted. The peak age of onset is approximately 14-18 months, and the incidence approaches 3-4% of young children[3]. According to a consensus conference held by the National Institutes of Health, Bethesda, Maryland (1980), FS is described as "an event in infancy or childhood usually occurring between 3 months and five years of age, associated with fever, but without evidence of intra-cranial infection or a defined cause"[4]. This is a unique form of epilepsy that occurs in early childhood and only in association with an elevation of temperature. The underlying pathophysiology is unknown, but genetic predisposition clearly contributes to the occurrence of this disorder[5]. FS are a benign

disorder with an unknown etiology. They can be broadly classified into two groups: (a) Simple FS - generalized, <15 minutes and a total duration of 30 minutes when in series; (b) Complex FS - focal or generalized, >15 minutes; >30 minutes in duration when in series[6]. Recurrence FS in the third world range from 21%-29.3% as indicated by studies conducted in the Middle East and Nigeria[7,8] In the west, however, recurrence rates are much more varied, ranging from 30%-50%[9]. There are many well-established risk factors for recurrence of FS, the major factors are age less than 1 year, duration of fever less than 24 hour, and fever between 38 -39°C[2,3]. Age of onset is one of the most consistent and strongest predictor of recurrence[10]. Another important and well-documented association is one of temperature with recurrence of seizures. A rise in temperature by one degree almost doubled the risk of recurrence. An increased association was found between a shorter duration of fever and an increased risk of recurrence[11]. Several studies have shown that a low degree of fever while in the emergency department was a strong independent predictor of recurrent FS. Offering et al, documented an association between temperature rise and increase in the recurrence rate of FS, but to an extent. Higher temperatures (40°C) were associated with a lower risk of recurrence[12]. Other factors associated with recurrence of both simple and complex FS include a (a) positive family history which was associated with an absolute recurrence risk of 20%[13], (b) a positive correlation with the previous number of recurrences of seizures[11] whereby a greater number of previous recurrences resulted in a greater rate of recurrence of FS and (c) duration of seizure which is another well established risk factor for recurrence. In addition, children who have experienced a complex febrile seizure have been shown to have a greater rate of recurrence[11]. A number of studies were carried in Europe, Middle East, Nigeria and South Asia. In Saudi Arabia we have diversity in environmental, genetic, racial, social and cultural factors along with a rapid urbanization and extensive development of health care program which stretches to outreach areas, this study was conducted to identify the risk factors of recurrent FS Saudi children in a Northern region of Hail province in Saudi Arabia. This will help us to formulate our strategy in terms of control/prophylaxis for FS recurrence, along with appropriate parental education and counseling.

MATERIAL AND METHODS

This descriptive prospective study was conducted at Pediatric Department, King Khalid University Hospital Hail, Kingdom of Saudi Arabia from 01 October 2010 to 30 September 2011. All children admitted to the King Khalid Hospital, Pediatric department, between the ages 03 months to 60 months, with the first febrile episode of Febrile Seizures during the study period were included in the study. For the purpose of our study, a febrile seizure was defined as a seizure that occurred while the child had a rectal temperature of at least 101°F (38.3°C) or an axillary temperature of at least 100°F (37.8°C) documented either in the emergency department or in the history and recurrent febrile seizures was defined as subsequent febrile seizures following a previous episode, with a seizure free period of unspecified duration between the two events. The children excluded from the study were (a) those presenting with less than three months of age and more than 60 months of age, (b) those presenting with afebrile seizures, (c) those having seizures with proven CNS infection as meningitis/encephalitis, (d) those with history of prior convulsions secondary to underlying neurological pathology like post-meningitis, post-encephalitis sequel or cerebral palsy etc (e) those with seizures secondary to electrolyte derangement or due to metabolic causes. A total of 132 children [age ranges from 03 months to 60 months] were included in the study, while these children were admitted with the diagnosis of febrile seizures during the study period. A predesigned study proforma was utilized for data collection. Variables used in the study included age, sex, family history of febrile seizures, any family history of seizure disorder, type of seizures, duration of febrile illness prior to onset of seizures, temperature at the time of seizures and duration of seizures. It also

includes the routine investigations, and neuroimaging and EEG as indicated. All the children included in the study were followed for a period of 01 year after discharge from the pediatric ward for any recurrent FS. The data was analyzed by SPSS version 15. Descriptive statistics were used to describe the data. Frequency and percentages were used to describe the categorical variables. Chi-square test was applied to determine significance. p value <0.05 was considered significant. Relative risk of recurrent febrile fits was calculated considering variable, collected during the study.

RESULTS

This study was conducted on 132 children presenting with febrile seizures and followed for one year for any recurrence. The cause of febrile illness was found out to be viral prodrome in 63 (47.73%), non-specific febrile illness in 28(21.21%), gastroenterits in 22 (16.66%), URTI in 12 (9.1%) and UTI in 07 (5.3%) children. There was male predominance with a female to male ratio 1:1.5. The mean age of children was 16 months, ranging from 5 to 56 months.

Family history of febrile seizures was positive in 38 (28.79%) children and family history of seizure disorder was positive in 20 (15.15%) children.

Most of the children presented with simple febrile seizures. The mean temperature at 1st febrile seizure was 39.8°C, ranging from 38.2 to 41.2°C.

Mean duration of fever till 1st febrile seizure was 18 hours, ranging from 2 to 54 hours. All routine investigations were either found within normal limits or suggest the underlying etiology. Lumbar puncture was done in 33(25%) children but none had meningitis or encephalitis. Neuroimaging was done in same children as a prerequisite for lumber puncture, to rule out raised intracranial pressure, cerebral edema or any underlying CNS pathology, which was normal. EEG was also done in 12(9.1%) children which was also normal.

Recurrent FS was found in 46(34.85%) children. The relative risk (RR) of recurrency was calculated for age, gender, family history, temperature, duration of illness, and duration of fits as shown in Table.

Age was classified into three groups of <12 months (G-A), 12 – 24 months (G-B) and >24 months (G-C). Relative risk of recurrency in G-A was nearly twice than G-B and was statistically significant (p-value=0.01 and Chi square=6.57). The relative risk between G-B to G-C 1.68 times but showed non-significant results (p-value=0.27 and Chi-square=1.20). The relative risk was 3.3 times more in children of G-A compared to G-C (p-value=0.001, Chi-square=11.31). Recurrent FS showed overall significant association with age groups (p-value=0.001, Chi-square=13.87) and showed declined trend in recurrency with increasing age.

The risk of recurrency did not show any significant association with gender (p-value=0.66, Chi-square=0.19).

Family history of FS did not show any association with recurrency (p-value=0.26, Chi-square=1.24). However in our study it described as 0.76 times more in children with no family history compared to those having family history of FS. risk (RR) of Recurrent FS for complex fits: Recurrent FS showed high dependency on complex fits. The chance of having recurrency is 5.45 times more in complex as compared to simple , p-value=0.001 and Chi-square=54.32.

Temperature is classified into three groups as 38°C - 39°C (G-A), 39°C - 40°C (G-B) and > 40°C (G-C). The G-A showed significant risk of recurrency as compared to G-B with RR=4.17 times more in G-A as in G-B. (p-value=0.001, Chi-square=33.75). There was no significant difference found in G-B to G-C (p-value=0.36, Chi-square=0.83). When G-C was compared to G-A it was found highly significant with p=0.001, Chi-square=40.51 and R.R=6.39 times.

Duration of illness was also grouped as: G-A as <6 hours, G-B between 6 – 24 hours and G-C of >24 hours. From G-A to G-B of illness, it did not show any significant difference with

RR=1.56, *p*=0.06 and Chi-square=3.48. However, when G-A compared to G-C it was

Relative risk (RR) of recurrent febrile seizures for duration is classified into: > 30

Table-: Relative risk (RR) of recurrent febrile seizures for relevant variables.

Varaibles	Febrile Seizures		Total	Comparative Groups	RR	95% CI of RR	Chi-square	*p*-value
	Recurrent	Non-recurrent						
Age groups (months)								
<12 months (G-A)	30	28	58	G-A vs G-B	1.97	1.12-3.48	6.57	0.01*
12-24 months(G-B)	11	31	42	G-B vs G-C	1.68	0.65-4.34	1.2	0.27
> 24 months (G-C)	5	27	32	G-A vs G-C	3.31	1.43-7.69	11.31	0.001*
Total	46	86	132	Over all	xx	xx	13.87	0.001*
Gender								
Male	26	52	78	Female vs Male	0.9	0.56-1.44	0.19	0.66
Female	20	34	54					
Total	46	86	132					
Family History								
Negative	30	64	94	Negative vs Positive	0.76	0.47-1.22	1.24	0.26
Postive	16	22	38					
Total	46	86	132					
Fits								
Complex	32	7	39	Complexvs Simple	5.45	3.29-9.03	54.32	0.001*
Simple	14	79	93					
Total	46	86	132					
Relation to temperature (°C)								
38-39 (Co) (G-A)	30	6	36	G-A to G-B	4.17	2.35-7.39	33.75	0.001*
39-40 (Co) (G-B)	10	40	50	G-B to G-C	1.53	0.61-3.88	0.83	0.36
>40 (Co) (G-C)	6	40	46	G-A to G-C	6.39	2.99-13.67	40.51	0.001*
Total	46	86	132	Over all	xx	xx	51.7	0.001*
Duration of illness (hours)								
<6 hrs (G-A)	26	24	50	G-A to G-B	1.56	0.96-2.52	3.48	0.06
6 - 24 hrs (G-B)	16	32	48	G-B to G-C	2.83	1.04-7.73	5.02	0.03*
> 24 hrs (G-C)	4	30	34	G-A to G-C	4.42	1.7-11.52	14.27	0.001*
Total	46	86	132	Over all	xx	xx	14.5	0.001*
Duration of fits (minutes)								
> 30 minutes (G-A)	19	8	27	G-A to G-B	1.13	0.76-1.67	0.35	0.55
15-30 minutes (G-B)	15	9	24	G-B to G-C	4.22	2.30-7.74	22.04	0.001*
<15minute (G-C)	12	69	81	G-A to G-C	4.75	2.67-8.46	30.54	0.001*
Total	46	86	132	Over all	xx	xx	37.4	0.001*

G:- Group; CI:- Confidence interval, *:- Significant results

highly significant with RR=4.42, *p*-value=0.001, Chi-square=14.27.

minutes (G-A), 15 -30 minutes (G-B) and <15 minutes (G-C), for G-B showed significant difference as compared to G-C (R.R=4.22, Chi-

square=22.04 and *p*=0.001). Similar trend of recurrence was observed in G-A when compared with G-C and the relative risk was 4.75 more in G-A as compared to G-C (Chi-square=30.54 and *p*-value=0.001).

The overall association of duration of fits with recurrence of FS was found statistically significant.

DISCUSSION

In our study majority of the children admitted for FS had simple FS (70.45%). Mustafic N et al, also found higher frequency of simple FS in their study[14]. Male sex accounted for slightly higher 59% and female were 41% among the children with recurrent FS. Trainor JL et al,[15] in their study had shown that 64% of study population was males, whereas in another study by Ojha AR et al,[16] also shown that male children were predominantly affected. In contrast, Rantala et al,[17] found the female gender to be at a 1.32 times greater risk of having a recurrenct FS. In our study 46 (34.85%) children had recurrent FS during one year period of follow up. In general, a range of (21% -47%) have been quoted for recurrence rate/risk in literature from several studies[6,9]. Our study shows a slightly higher recurrence risk of 34.85%, Nelson et al[18] similarly documented a cumulative recurrence risk of 34.9%. In a study by Ojha AR et al,[16] 51% of children with FS had recurrence, and it is comparable to another study done by Pavlidou E et al who had showed the recurrence rate of 48% in their[19]. However, this could be due to the age range the authors followed (18 - 38 months), since it is known that the risk of FS is highest during the first two years of life. These studies suggest that the recurrence rate declines with increasing age.

Majority of our cohort were <12 months, although we looked at a wide age range (3 months - 60 months) to study FS recurrence in Saudi children. Several other studies[7,13] have also evaluated FS recurrence beyond five years of age. Age at the time of first FS is perhaps the single most consistent predictor of recurrent FS[20].

Of the 46(34.85%) children who had recurrence of FS in our study, 65.22% had temperature in 38°C to 39°C range, and 21.74% occurred in 39°C to 40°C temperature and just 13.04% occurred > 40°C. Western based studies have proven time and again that the risk of recurrence decreases with higher temperatures (>40 degrees Celsius) and that it is at lower temperatures when the risk of recurrence increases[9,13,21]. Airedi Al,[8] found a ten times higher risk of recurrence in children with a temperature of <40 degrees. As evident in our study that almost 2/3rd children with recurrent FS are having temperature < 39°C, and it was also stated by Offringa et al,[12] in a review of five studies, showing a pooled increase of 12% recurrence in children with a temperature of <40 degrees Celsius as opposed to those with a temperature of >40 degrees Celsius at the time of FS. However the study by Tarkka R et al. has shown no association of recurrent FS with low grade fever[11]. As with sex, family history of FS was not statistically significant in our study as a risk factor for recurrent FS. Several studies have evaluated the association between family history (basically first degree relative) and recurrence of FS. In a meta analysis, Offring a et al[12] found an overall recurrence of 43% in children who had a positive family history as opposed to a 32% in those without a positive family history. However contrary to this in our study 65.22% children with recurrent FS are without a positive family history. This was also similarly observed by Ojha AR et al[16].

This study also has shown that children were more likely to have recurrence if they had a shorter duration of fever before onset of seizure. Other studies have also shown similar findings[15,19]. In addition, our study has also shown an increased risk of recurrence among those who had an atypical presentation. Study by Al-Eissa YA also reported a similar finding[22].

The most common cause of fever in the study population was viral fever (47.73%) followed by non specific febrile illness, gastroenteritis, URTI and UTI. Millichap JJ et al, in their study had shown that 35% of cases had fever of viral origin[23]. Whereas 53% of the children had URTI in a study done by

Abuekteish F et al[24]. In our study we used clinical signs and symptoms to diagnose a child with viral fever. This may be the reason for overestimation of the cases that had viral fever.

CONCLUSION

The FS is one of the common causes of paediatric hospital admissions. Male children and simple FS account for the majority of cases. Those children who only had a modest rise in body temperature at the onset of FS, those who had atypical FS, had first FS at younger age and those who had an onset of FS within 06 hours of fever are at high risk of recurrent FS on later dates. These findings need further validation with auxiliary studies involving large sample size. This also has implications in terms of control/prophylaxis for FS recurrence, suggesting timely anti-pyretic, and treatment of febrile illnesses along with appropriate parental education and counseling.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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