International Journal of Advanced Research in Biological Sciences
ISSN: 2348-8069
www.ijarbs.com
DOI: 10.22192/ijarbs Coden: IJARQG(USA) Volume 5, Issue 8 - 2018

Research Article


DOI: http://dx.doi.org/10.22192/ijarbs.2018.05.08.010

# Risk Factors for recurrent febrile seizure in children Admitted to Sulaimani Pediatric Hospital

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## Abstract

Background and objectives: Febrile seizure is the most common convulsive disorder during childhood. Intense parental anxiety and fear from recurrence is observed.

Materials & Methods: this observational study was undertaken from 1st February to the end of June 2010. One hundred ten children between 6 months and 6 years of age admitted with attack of febrile seizure were recruited. Demographic data including age, sex, type & duration of febrile seizure, family history of febrile seizure and epilepsy, interval between fever onset and occurrence of seizure were recorded & investigations like [Total & differential WBC (lymphocyte & neutrophil) counts] were done for all cases.

Results: Out of 110 patients 54 cases were male (49.1%) & 56 were female (50.9%). Male to female ratio among those with recurrent febrile seizures was 1.4:1. The peak age group for febrile seizure was 13-24 months (49.1%) & the mean age was 22.1 months. Complex febrile seizure was observed in 40 patients (38.2%). Positive family history of febrile seizure was noted in 48 patients (43.6%) and family history of epilepsy in 10 patients (9.1%) was positive. It was found that 52.7% of cases were having respiratory tract infection. 39.1% having gastroenteritis & in 2% no focus of infection were found. Most of cases (82.7%) had normal total WBC count.

Conclusion: It can be concluded from the present study that the first attack of febrile seizure in younger age (≤12 months). Complex febrile seizure & Positive family history of febrile seizure in children <12 months were risk factors for recurrent febrile seizures.

**Keywords:** Febrile Seizure, Age, Risk Factors, Nerurological Examinations

## Introduction

Seizures are the most common cause for referral to pediatrics neurology practice. It is a common neurological disorder in the pediatric age group & occur with a frequency of 2-4% of children between ages 6 months- 6 years (1).

A seizure is a sudden, transient disturbance of brain function. manifested by involuntary motor, sensory, autonomic, or psychic phenomena, alone or in combination. often accompanied by alteration or loss of consciousness(2). Febrile seizure was distinguished from other seizures in the middle of 19" century; treatment at that lime was directed to the underlying cause of fever rather than the seizure itself, with the introduction of thermometer at the end of 1800s, fever was understood to be the primary trigger of seizure (3).

The exact mechanism & aetiology of febrile seizure was not so clear, but now linkage studies in many families have mapped the FS gene to chromosome 19p and 8q 13-21(1).An autosomal dominant inheritance are demonstrated in some familes(1). Viral infections of the upper airways, exanthema subitum, acute otitis media, infection of the urinary tract and febrile reactions after vaccination are considered as the most frequent precipitating factors. It has been recognized that there is significant genetic component for susceptibility to febrile seizures(4). Febrile seizures that occur after immunizations are occurring in response to temperature elevation ( 5)

No investigations are routinely necessary in all children after a febrile seizure. Most population-based studies of febrile seizure have shown the vast majority of children with febrile seizure have an excellent prognosis. Intelligence is not impaired and mortality and neurological sequel are very rare and arc usually due to pre-existing conditions (6).

The three components, age, fever, and a seizure, are critical elements in the definition.

## AGE

Most febrile seizures occur between 6 months and 3 years of age with the peak incidence at 18 months. ([4,5,6]). Approximately 6–15% occur after 4 years, and onset after 6 years is unusual. Regardless of the population, most data support the unique age specificity of the maturing brain's sensitivity to fever([4]).. Although the mechanism of this increased susceptibility is unclear, animal models suggest that there is enhanced neuronal excitability during the normal brain maturation. ([7]).

## Fever

By definition there has to be a febrile illness or certainly fever. Many febrile seizures occur early in the illness and may be the presenting feature, but others occur during or after the onset of fever, ([8,9]). Observations that may in part reflect the difficulties in both taking and accurately recording the temperature of young children. There are no data to support the rate of temperature rise as being more important than the peak temperature achieved. ([10,11]). It is also unclear whether there may be a lower limit of fever under which it would be difficult to make a diagnosis of an FS, ([12]). With some studies citing >38°C and others, >38.4°C. It is possible that the peak of the fever may be related to recurrent FS. ([13]). Children with FS with a relatively low fever (<38.9°C) tend to present with an initial seizure that has focal features or is repeated within the same febrile illness. ([14]). Antipyretics have not been shown to reduce the risk of febrile seizures, ([15,16]). Suggesting that it may not be the fever itself that causes an FS. Animal studies suggest a possible role of endogenous pyrogens such as interleukin 1 that, by influencing neuronal excitability, may link fever and seizure activity. ([17]). Preliminary studies in children appear to support the hypothesis that the cytokine network is activated and may have a role in the pathogenesis of FS, ([18,19]). But the precise pathological or clinical significance of these observations is as yet unclear.

## Seizure

Clearly, FS must have a clinical component—a "seizure". The NIH Consensus definition uses the vague term, "event" rather than seizure. ([21]). Other episodes or clinical events that may typically mimic an epileptic (and specifically a tonic-clonic) seizure, including rigors, syncope, reflex anoxic seizures, breath holding spells, impaired consciousness, and apnoea may also be associated with any febrile illness and must be excluded by taking a careful history. It is possible that a number of children with FS reported in the literature may in fact have had one of these other paroxysmal, non-epileptic disorders and not FS. ([21]).

Febrile seizures are typically divided into two types, "simple" and "complex". A simple FS comprises of generalized tonic-clonic activity without focal features, of less than 10 minutes duration, without a recurrence in the subsequent 24 hours and resolving spontaneously. Complex febrile seizures are defined on one or more of the following features: a partial (focal) onset or showing focal features during the seizure, prolonged duration (greater than 10–15 minutes), and recurrent within 24 hours or within same febrile illness ([4,8]). The term "complex" may in the future be replaced by "complicated" in light of the new proposed seizure classification in which the words simple and complex in the ILAE classification of partial seizures may disappear([4]).Arguably, the most appropriate approach would be to replace either term—"complex" or "complicated", with the precise description of the seizure and specify whether the FS was "prolonged", "focal", or "multiple".([4]).

## Risk factors

**What are the risk factors for developing a febrile seizure?**

Febrile seizures occur when a susceptible child of a critical age has a fever. The fever is typically higher than in control children with a similar illness, although the seizure does not always occur at the same time as the peak temperature or necessarily at the onset of fever. ([19]). The most consistently identified risk factor for FS is the presence of a close family history (within first degree relatives) of FS. The more relatives affected, the greater the risk. In cohorts of children with FS, the risk that siblings will have an FS is 10–45 %([20]). Many studies have also found that the risk may be increased by an underlying brain disorder. Premature birth, delayed discharge from the neonatal intensive care unit, and developmental delay are potential markers for suboptimal brain function, but there is conflicting evidence definitively linking these factors and FS ([21]). Which may in part reflect whether the study was hospital or community based. Other studies suggest an increased risk with exposure to infectious illnesses such as human herpesvirus-6([22])..

**What are risk factors for recurrence?**

Most children with FS do not experience further FS, but one third will; age would appear to be the single, strongest, and most consistent risk factor. ([23]). More than half of the risk is realised during the first year after the initial FS and over 90% recur within two years. A family history of febrile seizures (but not epilepsy) in a first degree relative is associated with an increased risk of recurrence. ([23]). Recurrences appear to be more likely in children whose initial FS occurred with a relatively low fever. ([23]). Multiple initial seizures occurring during the same febrile episode also appear to be associated with an increased risk of recurrence. ([24]). Recurrent FS tend to be prolonged if the initial FS was prolonged. ([14]). However, febrile status epilepticus in an otherwise normal child does not appear to significantly increase the risk for further febrile seizures or the development of epilepsy. ([24])

## The Aim of the Study

1. The aim of this study is to evaluate certain risk factors for occurrence of recurrent febrile convulsion.
2. To find some of characteristic feature of FS in our society.

## Patients and Method

This study was conducted among 110 children taken randomly aged 6-72 months from both genders admitted to Sulaimani pediatric teaching hospital presenting with seizure & fever (1st or recurrent attacks) during the period from 1st February to end of June 2010.

Cases of trauma, meningitis, neurologically handicapped, congenital malformation of the CNS, epilepsy, history of drug ingestion and those with suspected metabolic disorders were excluded from the study after taking detailed history & performing clinical examination. For the purpose of study, the case definition of febrile seizure was a convulsive seizure in infant & children aged 6-72 months in association with temperature of 38c° or higher.

A seizure was defined as simple if it was generalized, lasting for less than 15 minutes and not recurred with in 24 hours, while seizure regarded complex if it has lasted 15 minutes or more and'-or if it recurred more than one time with in 24 hours and/or if the seizure had focal onset(1).

Neurological examination(like menengial signs, conscious level and others) was done ,also CSF in suspected cases of meningitis was done. Core temperature was taken for all patients at time of examination.

Total &. differential white blood cell count including absolute neutrophil & lymphocyte count were done for all cases.

Blood sugar ,Serum calcium ,GSE ,Stool culture, GUE and urine culture was done according to provisional diagnosis.

Parametric tests (Chi square) were used for normally distributed and non parametric tests for other. data. P value of less than 0.05 was considered significant, while odd ratio of more than 1 considered significant.

## Results

One hundred ten cases were studied, their ages were between 6 - 72 months.

Table (1) showed that 81 cases (73.6) were under 2 years of age, 27cases(24.5%) were in age group of 6-12 months & 54 cases (49.1%) were between 13-24 months [36 cases (46.2 %) with first attack & 18 cases (56.25%) with recurrent attacks.

In table (2) revealed that male gender accounts for 49.1% (54 cases) with male to female ratio is the same but among those with recurrent attacks there was male predominance with male to female ratio of 1.4:1. This table also reveals relation between febrile seizure (FS) & family history of FS ;48 cases (43.6%) had positive family history of febrile seizure. Those with first attack 38.5% of them had positive family history (11.5% in 1st degree relatives) while among those with recurrent attacks 56.3% had positive family history (15.6% in 1st degree relatives). Only 10 cases (9.1%) had family history of epilepsy, 6 of them (60%) developed frequent attacks of seizure during the same illness (complex seizure).

Table(3) shows recurrence rate in those cases who had positive family history of FS & they got the first attack of FS in young age (<1 year old)

In table (4),forty five cases (40.9%) had fever for more than 24hours before developing seizure & only 21 cases (19,1%) had fever for 1-6 hours, from those 19.3% of cases, 52.4% developed more than 1 attack of febrile seizure during the same illness.

Figure (1) showed that about 78.2 % of cases who presented with recurrent attack had history of first febrile seizure at I year old of age or younger (p-value =0.000).

Simple FS were more common in those cases with 1st attack of FS (69.2%), while complex FS were common (59.4%) in those with recurrent attacks (p-value= 0.009) as shown in figure( 2).

Figure (3) shows the possible cause of fever in which 58 cases (52.7%) had RT, 43 cases (39.1%) had acute gastroenteritis & in 2 cases (2%) no focus of infection found.

Table( 5) shows the association between total white blood cell (WBC) count & FS; from total 110 cases 9l cases (82.7%) had normal WBC count.

Table 1: Age distribution in febrile seizures

| Age in months | 1st attack | 2nd attack | >2 attacks | Total |
|---|---|---|---|---|
| 6-12 | 19(24.4%) | 5 (27.8%) | 3(21.4%) | 27 (24.5%) |
| 13-24 | 36 (46.2%) | 11 (61.1%) | 7 (50.0%) | 54(49.1%) |
| 25-49 | 20(25.6%) | 0 (0%) | 4 (28.6%) | 24(21.8%) |
| 50-72 | 3 (3.8%) | 2(11.1%) | 0 (0%) | 5 (4.5%) |
| Total | 78(100%) | 18(100%) | 14(100%) | 110(100%) |

Table 2; Febrile seizure & its relation with gender, family history of FS & epilepsy

| Risk factors | 1st attack | 2nd attack | >2 attacks | Total | P-value | OR |
|---|---|---|---|---|---|---|
| 1 .Gender | | | | | 0.34 | 0.57 |
| Male | 35(44.9%) | 10(55.6%) | 9 (64.3%) | 54(49.1%) | | |
| Female | 43(55.1%) | 8 (44.4%) | 5 (35.7%) | 56(50.9%) | | |
| 2. Family history of FS | 30(38.5%) | 10(55.6%) | 8(57.1%) | 48(43.6%) | 0.231 | 0.47 |
| 3. Family history of | 7 (9.0%) | 0 (0%) | 3(21.4%) | 10(9.1%) | ,0.112 | 0.9 |

OR= Odd Ratio

Table 3: family history of FS in cases with younger age of initial attack (<12 months) & their relation with recurrent attacks.

| Family history of FS | 2nd attack | >2 attacks | Total | P- value |
|---|---|---|---|---|
| Yes | 9 (36%) | 6 (24%) | 15(60%) | 0.03 |
| No | 6 (24%) | 4(16%) | 10(40%) | |
| Total | 15(60%) | 10(40%) | 25 (100%) | |

( P _value) significant

Table 4: duration of fever before the attack of febrile seizure with its effect on frequency of attacks

| Duration of fever hours | 1 attack | 2nd attack | > 2 attacks | Total | P-value |
|---|---|---|---|---|---|
| 1-6 hr | 10(13.2%) | 5(27.8%) | 6(37.5%) | 21(19.1%) | |
| 7-12 hr | 26 (34.2%) | 2(11.1%) | 1 (6.3%) | 29 (26.4%) | |
| 13-24 hr | 12(15.8%) | 3(16.7%) | 0 (0%) | 15(13.6%) | 0.023 |
| >24 | 28 (36.8%) | 8(44.4%) | 9 (56.3%) | 45 (40.9%) | |
| Total | 76(100%) | 18(100%) | 16(100%) | 110(100%) | |

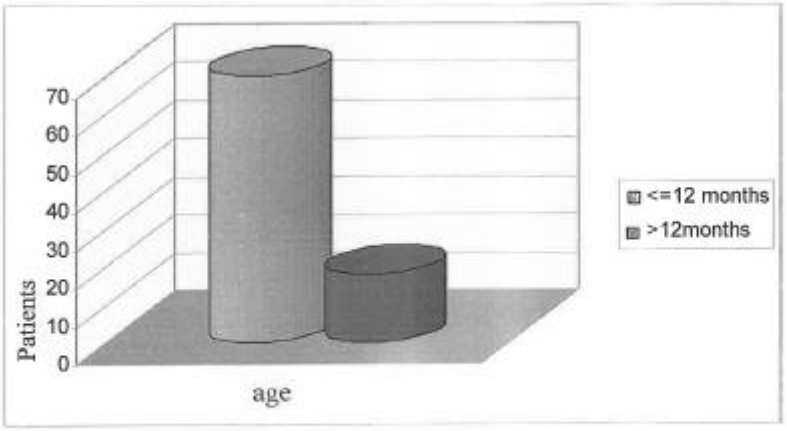
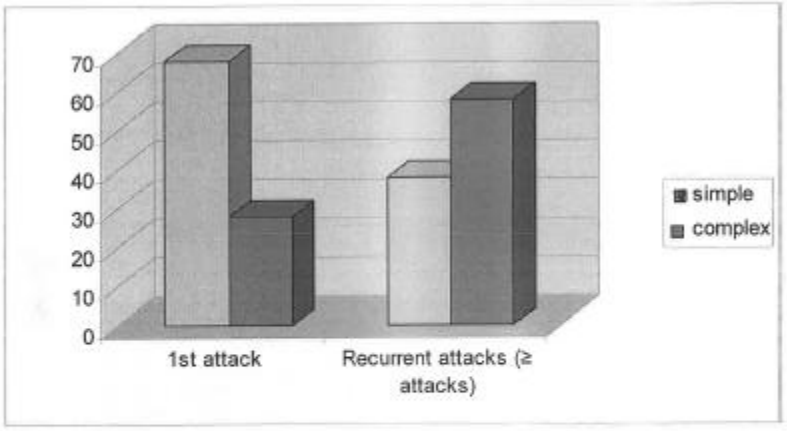



Figure 1: relation between age of initial febrile seizure & recurrent attack




Recurrent attacks (>2 attacks)

Figure 2: types of febrile seizure in both 1st & recurrent attack

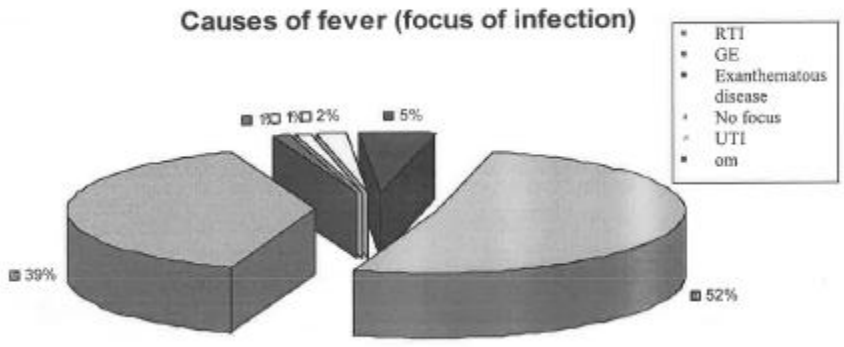



Figure 3: Causes of fever (focus of infection) in febrile seizure

RTI=Respiratory tract infection

GE= gastroenteritis

UTI=urinary tract infection

OM=otitis media

Table 5: White blood cell counts in febrile seizures

| White blood cell count | Normal | Increased | Decreased | Total | P-value |
|---|---|---|---|---|---|
| Total WBC count | 91 (82.7%) | 11 (10%) | 8 (7.3%) | 110 (100%) | 0.04 |

## Discussion

In this study 110 cases were studied, there age were between 6 and 72 months, most cases were under 2 years of age, mainly between 1-2 years of age. This coincide with Chan et al(3) in which 52% of patients had seizure onset below 2nd year of age.

It has been reported that the younger the age at the first FS the higher the incidence of recurrence. 78.2 % of cases who presented with recurrent attack had history of first febrile seizure at 1 year of age or younger, similar findings were demonstrated by Al-Zwaini(9).

It was suggested that male is a risk factor for recurrence(3 and 9). In this study male gender was predominant among those with recurrent attacks with male to female ratio was 1.4:1.

In this study only (19.1%) had fever for 1-6 hours and 52.4% of them developed more than 1 attack of febrile seizure during the same illness. Al-Ossaimi (10), which mention that shorter duration of fever is risky for further recurrent attacks.

This study revealed that simple FS were more common in those cases with 1st attack of FS (69.2%). while complex FS were common (59.4%) in those with recurrent attacks, this is disagree with Chan et al(3) which found that simple FS were ~~more~~ common in both 1st & recurrent attacks & this may be due to that our age limit was wider than that included by Chan et al(3).

This study has showed that most cases with recurrent FS had positive family history of febrile seizure ( 56.3% ) as shown in many studies(3,5 and 11).

In this study only (9.1%) had family history of epilepsy, (60%) of them had developed frequent attacks of seizure during the same illness (complex seizure), this agree with Al-Eissa et(12) , which found that history of FS and epilepsy in parents or siblings was marginally more common among children with complex FS than those with simple FS.

RTI found to be the most common precipitating factor for FS & gastroenteritis as the second common precipitating factor, this is in agreement with Chan et al(3) ; which revealed that RTI accounts for 50.9% but it disagrees with this study about GE as 2nd common cause, in this point it coincide with Omeran et al(13) , in which gastroenteritis account for 27.3% & this is depend on the season in which the study is undertaken and on general prevalence of diarrhea among children.

WBC count is normal in almost most of cases of FS, this in coincide with Kent (8)found no association between febrile seizure & total blood leukocyte.

## Conclusion

Younger age (<12 months) of the initial febrile seizure was highly significant risk factor for recurrent febrile seizures in the future. Also male gender and Cases with positive family history of febrile seizure in 1st degree relatives are risky for developing recurrent attacks & those with complex febrile seizure tend to recur.

Short duration of fever before developing febrile seizure (<6 hours) has risk of frequent attacks during the same illness.

Investigations such as WBC count not routinely recommended as most of cases had normal leukocyte count.

## Recommendations

1. **The early use of antipyretics and anticonvulsants like diazepam when temperature elevated especially in those with younger age at presentation, complex FS and family history of FS.**
2. **Family education about risk factors for recurrent FS.**

## Acknowledgments

I would like to express my deepest graduate and respect to Dr. Jamal. A. Rashied and Dr. Adnan. M. Hamawand for their helpful advises, meticulous supervision , and guidance throughout the process of this study , also I am very grateful to every had helped me in this study.

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# الخلاصة

الاختلاجات الحرارية هي أكثر أنواع الاختلاجات في الأطفال أعمارهم اقل من٦ سنوات هدفنا من هذه الدراسة هو بيان العوامل الرئيسية التي تلعب دور في تكرار الاختلاجات الحرارية.أجريت هذه الدراسة الاستطلاعية في مستشفى الاطفال التعليمى في السليمانية للفترة من الأول من شباط٢٠١٠ لغاية تموز٢٠١٠. ضمت الدراسة ١١٠ طفل يعاني من اختلاجات حرارية أعمارهم تتراوح ما بين ٦ اشهر الى ٦ سنوات . تم اعتماد عوامل الخطورة التالية: العمر الحالي للمريض والعمر الذي بدأ به أول اختلاج حراري ، الجنس ، عدد مرات الاختلاجات الحرارية ، وجود تاريخ عائلي ( قرابة من الدرجة الأولى أو الثانية ) للاختلاجات الحرارية أو الصرع، نوع الاختلاج الحراري بسيط أو معقد، درجة الحرارة والوقت الفاصل بين ارتفاع الحرارة وحدوث الاختلاج.

## الاستنتاج :

العوامل التي تؤدي الى زيادة خطر تكرار الاختلاجات الحرارية هي :

١. عمر الطفل اقل من ١٢ شهر عند حدوث أول اختلاج حراري.

٢. جنس الطفل الذكور أكثر من الإناث.

٣. وجود تاريخ عائلي للاختلاجات الحرارية.

٤. قصر فترة ارتفاع درجة الحرارة قبل حدوث الاختلاجات.

٥. وجود اختلاجات حرارية معقدة.

٦. وجود تاريخ عائلي للصرع .

وزارة الصحة
دائرة الصحة في السليمانية
قسم الدراسات العليا والبحث العلمي

# تقييم عوامل الخطورة للاختلاجات الحرارية المتكررة في الأطفال

أطروحة

مقدمة إلى دائرة الصحة في السليمانية / قسم الدراسات العليا

كجزء من متطلبات نيل درجة الدبلوم العالي في طب الأطفال

من قبل الطلاب

د. أحمد حسن علوان
د. علي جاسم محمد
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How to cite this article:
Ahmed Hasan Alwan, Ali Jassim Mohamed, Jamal Ahmed Rashid. (2018). Risk Factors for recurrent febrile seizure in children Admitted to Sulaimani Pediatric Hospital. Int. J. Adv. Res. Biol. Sci. 5(8): 80-96.
DOI: http://dx.doi.org/10.22192/ijarbs.2018.05.08.010