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Research Article

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Assessment The Risk Factors Of Recurrent Febrile Convulsion In Children

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Abstract

Background:-Febrile convulsion is the most frequent type of seizures in children under 6 years of age. Significant number of these children will later suffer from recurrence of febrile convulsion.
Objectives:- is to identify the main risk factors that imply for recurrent febrile convulsions in children & study febrile convulsion according the sex, age, type of seizure.
Patients and Methods: -This prospective study done in the central teaching hospital of pediatrics in Baghdad from 1st of October 2009 to the 1st of October 2010. We have carried out a case control study and arrange it on chi square.
This study include 190 patient at age between 6months - 6 years. 94 of them had recurrent febrile convulsion (two or more) (case) and 96 of them had single febrile convulsion (control). The following factors is dependent is the study:- Age of first FC, sex, family history of febrile convulsion in the 1st and 2nd degree relatives and family history of the epilepsy, severity of fever at onset of FC, duration between the onset of fever and the onset of FC, type of convulsion and cause of fever.
Results:- The following findings for risk factors in the Children with recurrent seizures for case and control were the age at onset 6-12months (63.8% vs 54%), male sex (70.6% vs 56.25%) and who had positive family history of FC in first degree relative (58.6% vs 47.9%) and family history of FC 2nd degree relatives (42.3%va35.4%) and family history of epilepsy (38% vs 19.7%), low degree of temperature (<=39) were (58.5% vas 26%), the duration between the onset of fever and the attack of fit, complex type of convulsion(52.2% vs 33.3%) and finally the cause of fever.
Conclusion;-The factors that increase the risk of recurrence of febrile FC:-the onset of FC at the age below 12 months, male sex, positive family history of FC in the first degree relatives, low temperature for the development of FC below 39 degree centigrade, positive family history of epilepsy, complex type of the FC. While the family history of FC in the 2nd degree relatives, the duration between the onset of fever and the occurrence of FC and the cause of fever considered **not** the risk factors for the recurrence of FC.

Keywords: febrile convulsion, risk factors, recurrent febrile convulsion, complex fit.

Introduction

Background:- definition of febrile convulsion:- It is defined as an abnormal neurological functional events in neurologically healthy infant/children between 6 months and 5 years of age associated with fever>38 ºC (rectal temperature) but without evidence of intracranial infection as defined cause and no history of prior a febrile seizures [(1)].

FC is most frequently occurring epilepsy Syndrome and 2-4% of all children experience at least one FC**,** They are slightly more common in boys and black (4.2%) versus white children (3.5%) [(2)].

Etiology:- Three features interact to bring on a febrile seizure: **immature brain**, **fever** and **genetic predisposition** They are believed FC triggered by fever induced by the vaccine. Their subsequent clinical course is identical to other FCs, and does not increase the risk for subsequent a febrile seizures or abnormal neurologic development[(3)]. Although the mode of inheritance is unknown, **genetic factors** are clearly important. Autosomal recessive inheritance is unlikely, as there is an excess of parents affected and the risk to siblings is approximately 25% [(4)].

Pathogenesis and pathophysiology: - The pathophysiology of FC is unknown. The role of cytokine network activation is presently being studied along with an increased susceptibility to febrile convulsion associated with specific interleukin alleles [(5,6)]. Circulating toxins, immune reaction products, and viral or bacterial invasion of the central nervous system have been implicated, together with relative lack of myelination in the immature brain and increased oxygen consumption during the febrile episode[(7)]. Immaturity of thermoregulatory mechanisms [(34)] and a limited capacity to increase cellular energy metabolism at elevated temperatures have been suggested as contributory factors [(8)].

Clinical manifestation:- A simple FC is may be associated with a core temperature that increases rapidly to 39ºC or greater [(9)] . Simple FC is generalized seizure, lasting less than 15 minutes, not recurring within 24 hours, and with no postictal neurological abnormalities. Complex FC is focal, prolonged or recurrent within 24 hours or associated with postictal neurological abnormalities such as Todd's Paresis. These seizures constitute around 15% of febrile seizures [(10)].

Febrile status epilepticus (seizure duration of 30 minutes or more, either one long lasting or a series of shorter seizures without regaining consciousness intricately) sometime develop [(10)].

Managements of febrile convulsion:- The initial workup of a FCs should include a thorough history from a reliable witness and complete pediatric and neurologic examination [(35)]. If the cause of fever can be identified and if the child presents no disturbance of consciousness, it is usually not necessary to obtain further laboratory evaluation [(11)].

Determination of serum electrolytes (particularly sodium), glucose, blood urea nitrogen, calcium, and phosphorus levels should be reserved for when there is a reasonable suspicion that one or more may be abnormal, lumbar puncture should be performed only when there is clinical evidence of possible meningitis[(10)].

Neuroimaging should not be performed in the routine evaluation of child with a first simple FC. CT or MRI should be performed only when an underlying structural lesion, An EEG should not be routinely performed in the evaluation of a neurologically healthy child with a first simple febrile convulsion, either at the time of presentation or within the following month. Because abnormal EEGs do not reliably predict the development of epilepsy or recurrent febrile seizures [(12)].

Outcome of febrile convulsions:- Children with FC usually have a good prognosis. Most children with FC do not experience further FC, but approximately 30% of patients with one FC will have a recurrence. The risk of recurrence decrease with increasing patient's age. [(13,14)]

A-Epilepsy:-The risk of subsequent epilepsy is rare but increases with each of the following factors:

1· Neurological abnormalities or developmental delay before the onset of FC.
2· Age of less than 9 months at first FC.
3· Family history of epilepsy.
4· Complex convulsions.

In the absence of these risk factors 1 % of children go on to develop epilepsy (compared with 0.4% of children without a history of FC),the incidence epilepsy increase to 9%, when several risk factors are present. [(13)]

B-Neurodevelopment:

Most studies have shown no obvious association between simple or complex FC. and the later development of neurological deficits (for example hemiplegia), overall cognitive functioning, or specific memory impairment. [(14)].

Patient and Method

CSF examination as well as serum calcium, blood sugar, blood urea, serum creatinine, G.S.E, stool culture, GUE, urine culture, CXR, EEG. This is a prospective, hospital based, case –control study conducted from 1st of October 2009 to the 1st of October 2010 all patients with FC referred to the emergency department of Central Pediatric teaching Hospital in Iskan were examined after taken full history (age, sex –etc), assessment &full investigation. Development assessment has been done for each patient.

Convulsions were labeled as febrile by excluding infections of central nervous system in developmentally normal children on basis of history, examination including neurological examination & relevant laboratory investigation according to the provisional diagnosis for e.g. A total number of patients are 190 divided in to two groups, 94 patients with recurrent attack of FC (cases) & 96 patients with 1st attack of FC(control).

Any patients with history of neonatal seizure or a febrile convulsion at any age were excluded from the study.

Both groups of patients (case &control) were select as patients with first attack group (control) & recurrent attack of febrile convulsion group (cases) and to find out the association between occurrence of second or third attack of FC and other factors as a risk factors compared for possible risk factors (age, sex, family history of febrile convulsion in 1st &second degree relative , family history of epilepsy ,duration between the onset of fever and the onset of convulsion , degree of temperature at onset of FC, type of FC and cause F (fever) for patient of FC information were taken about their :age of 1st FC (6-12 months,12-24 months, 24-36 months and <36 month),sex (male & female),family history of FC in 1st degree relatives (parents or siblings),family history of FC in 2nd degree relatives (grandparents, uncles, aunts or cousins),family history of epilepsy .Duration between the onset of fever and onset of FC (<2 hr,2-24hr, >2 hr),Height of temperature at onset FC(<39 cent,>39 cent.),Types of the FC (simple or complex) and the real cause of fever. the information was obtained directly from mothers of patients (case & control).

Our patients with recurrent FC (cases) were admitted to the hospital while those with single FC (control) some of them admitted to the hospital for other medical non relevant problem and other were taken from out patients department. Data was analyzed using chi square and P value considering value of <0.05 significant.

Results

The result of the most patient with recurrent FC occurs at the age between 6-12 months of age (63.8%) while the half of 1st FC(control) (54%) were at these age group with P value=0.01 which is statistically significant as shown in table (1)

Table(1): Distribution of the patients (cases & controls) according to the age of the 1st attack.

Age /Months	Cases	%	Controls	%
6-12mo	60	63.8	52	**54**
12-24mo	21	22.3	30	**31.2**
24-36mo	8	8.5	10	**10.4**
>36mo	3	3.1	4	**4.16**
Total no	**94**	**100**	**96**	**100**

2 א =9.25 df=1 p value= 0.011

Distribution of patients according to sex show two third of cases & more than half control group were male with 70.6 % & 56.25% respectively while the female case and control findings are 29.4%&43.75% respectively with male: female ratio is 2.35:1 &1.28:1 for the cases and control respectively with p value =0.0466 which is statically significant as shown in table (2).

Table (2) Distribution of the patients (cases & controls) according to the sex

Risk factor Sex	Cases	%	Controls	%
Male	**66**	**70.6**	**54**	56.25
Female	**28**	**29.4**	**42**	43.75
Total no.	94	100	96	100

ϰ2=3.4 df=1 p value= 0.0466

The family history of FC in 1st degree relative show good correlation with recurrence FC (cases group) 68% in compare with control group 41.6% while the negative family history is 32%&58.4% for the case and control respectively, with P value =0.0004 which is statistically significant as shown in table (3).

Table (3) Distribution of the patients (cases & controls) according to the family history of FC in 1st degree relative.

Risk factor FH of FC	Cases	%	Controls	%
Positive family history of FC in 1st degree relative	**64**	**68.0**	**40**	41.6
Negative family history of FC in 1stdegree relative	**30**	**32**	**56**	58.4
Total no.	94	100	96	100

ϰ2 =12.33 df=1 p value= 0.0044

Patients with positive family history of FC in 2nd degree relative for both cases and control groups show low percentage with 42.3% & 35.4% respectively, while the negative family history of 2nd degree relatives is 57.8%&64.6% for the case & control respectively with P value =0.476 which is statistically not significant as shown in table (4) .

Table (4) Distribution of the patients (cases & controls) according to the family history of FC in second degree relative

Risk factor FH of FC	Cases	%	Controls	%
Positive family history of FC in 2nd degree relative	**39**	**42.3**	**34**	35.4
Negative family history of FC in 2nd degree relative	**55**	**57.8**	**62**	64.6
Total no.	94	100	96	100

ϰ2 = 0.51 df=1 p value= 0.474

Finding of positive family history of epilepsy in cases & control groups show 38% &19.7%respctively, while the negative family history of the epilepsy are 62% for the cases and 80.2% for the controls with P value=0.0079 which is statistically significant as shown in table (5).

Table (5) Distribution of the patients (cases & controls) according to the family history of epilepsy

Risk factor	Cases	%	Controls	%
Positive family history of epilepsy	**36**	**38**	**19**	19.7
Negative family history of epilepsy	**58**	**62**	**77**	80.2
Total no	94	100	96	100

ϰ2 =7.3 df=1 p value= 0.0079

The degree of elevated temperature at onset of FC show that 58.5% of cases group were <= 39C & about one quarter of control group (26%) were <=39C with while the temperature >39 is 41.5% for the cases and 71% for the control with p value= 0.000011 which statistically significant as shown in table (6)

Table (6) Distribution of the patients (cases & controls) according to the degree of temperature

Risk factor	cases	%	Controls	%
Temp.≤39c at onset of 1st FC	**55**	**58.5**	**25**	26
Temp.>39c at onset of 1st FC	**39**	**41.5**	**71**	74
Total no.	94	100	96	100

ϰ2 =19.23 df=1 p value= 0.000011

More than one half of attacks of FC in cases and in control group occur between 2- 24 hour of occurrence of fever with 56.3%&63.2% respectively with P value =0.628 which is statistically not significant as shown in table (7).

Table (7): Distribution of the patients (cases & controls) according to the onset of FC with regard to onset of fever

Risk factor	Cases	%	Controls	%
<2 hours of fever before onset of FC	**20**	**21.2**	**24**	25
2-24 hr before onset of the FC	**53**	**56.3**	**61**	63.5
>2 hours of fever before onset of FC	**21**	**22.34**	**12**	12.5
Total no	94	100	96	100

ϰ2 =0.23 df=1 p value= 0.6278

The type of convulsion which occur during 1st attack of FC are slightly different between cases and control group and show simple type of convulsion in cases group 47.8% & complex type in cases group 52.2% & in control group there is 67.7%&33.3% as simple and complex type of convulsion respectively with P value =0.013 which statistically significant as shown in table (8).

Table (8): Distribution of the patients (cases & controls) according to the type of convulsion

Risk factor	Cases	%	Controls	%
Simple FC	**45**	**47.8%**	**64**	67.7%
Complex FC	**49**	**52.2%**	**32**	33.3%
Total no.	94	100%	96	100%

ϰ2 =6.11 df=1 p value= 0.013

The cause of the fever occurring during the 1st attack of the FC show no difference between the case and control with P value=0.755 which is statistically not significant as shown in table (9).

Table (9) The cause of fever in case and control study

Cause of fever	Case	%	Control	%
Upper respiratory tract infection	**55**	**58.5**	**52**	54.16
Pneumonia	**25**	**26.5**	**24**	25
Gastroenteritis (Bloody &watery diarrhea)	**6**	**6.3**	**10**	10.4
UTI	**5**	**5.3**	**6**	6.25
Post-vaccination (DTP)	**3**	**3.3**	**4**	4.2
Total	94	100	96	100

ϰ2 =1.19 df=1 p value= 0.755

Discussion

Febrile convulsions are the commonest cause of convulsions in children under six years of age. Parents are concerned by the risk of recurrence. Parental anxiety and apprehension is related to inadequate knowledge about fever and febrile convulsions.

Febrile convulsion is benign process, yet diverse factors have been identified to increase risk of relapses. In this study we found that there are several risk factors that predicting the possibility the recurrent of febrile convulsion includes:-

1-age:- **.** Age of less than 12 months at the onset of the first FC is associated with increase incidence for recurrence of FC(with case and control percent is 63.8% vs 54%) this result goes with following studies (Knudsen FU[15] with case and control findings is 71% vs 39% respectively) and, (Tarkkar et al [48] with case and control findings 65.4% vs 44.6% findings)**.**

2-Sex:- sex of the patients was found that male are more liable to have recurrent of FC(with case and control finding is 70.6% vs 56.25%) with two third of cases In compare to one half in control group . with case control ratio 1.4:1 and this was noticed by (Bessisso MS et al[16] with case and control findings are 68.3% vs 53.4%) and (Airede AI studies[17] with case and control findings 72% vs 49.4%)**,** but this result is not compatible to what is found by al Eissa YA[18] study who found that gender had no role in occurrence of recurrence of FC (with case and control findings 56% vs 48.43%)**.**

3-Family history of FC in 1st degree relatives of FC in a first degree relative is a risk factor for recurrence of FC (with case and control findings 58.6% vs 47.9%), and this result goes with studies: (Martin-Fernandez JJ et al[19] with case and control findings 62.5% vs 41.3%) also this findings go with(Offringa M et al [20], with case and control findings 59% vs 39%), (Berg AT et al**(51)**,with case and control findings are 66.5% vs 43.4%)&(Van Esch A et al[21] with case and control findings 57.9% vs 44.2%)

4-family history of FC in 2nd degree relative:- is not a risk factor for recurrence of FC (with case and control findings 39% vs 34%) and this finding is consistent with finding Van Esch A et al**.**[21] with case and control findings 29.6% vs 31.5%.

5-Family history of epilepsy:- in this study seen to be a risk factor for recurrence of FC(with case and control findings is 38% vs 19.7%) and this finding goes with (Martin- Fernandez JJ et al[19] ,with case and control findings is 39.6% vs 20.8%). (Offringa M et al [20],with case and control findings 43.4% vs 18.9%) & (Kundsen F,U studies**,** [47] with case and control findings 33.3% vs 21.4%). but the result did not compatible to what is found by Berg AT et al[40], studies who founds that a family history of epilepsy did not increase the risk factor of recurrence of FC with case and control study 25.4% vs 21.87%.

6-Severity of fever:-Low grade fever i.e.(<=39 cent.) at the onset of first FC is a risk factor for recurrence of FC(with case and control findings 58.5% vs 26%) and this result goes with(Berg AT et al[40] with case ad control study shows 60% vs 37.9%) ,(Offringa et al [24], with case and control study shows 52.6% vs 30.8%) &(El-Radhi studies [54] with case ad control findings shows 42.34% vs 28.34%) but this result is not compatible with (Al- Eissa YA[57] with case and control findings 43.56% vs 38.6%) & (Van Stuijvenberg M et al[20] with case and control findings are 32.2% vs 39.4%) who found low temperature not contributing factor with recurrence of febrile convulsion.

7-Duration of fever:- before the onset of first FC is not a risk factor for recurrence of FC and this finding is not in agreement with the result of Berg AT et al[22] who founds that short duration(less than 2 hours) of fever before onset of first FC is a risk factor for recurrence FC(with case and control findings is 34.4% vs 12.89%) **.**

8-type of convulsion:- Complex first FC is a risk factor for recurrence of FC (with case and control study 52.2 vas 33.3%) in this study group this result compatible to what is found by **(**Knudsen FU[15] with case and control findings is 48.9% vs 23%)&(al Eissa results**,**[18] with case and control findings is 56.6% vs 23.48%) but not compatible with Berg AT et al[22] who found that complex febrile seizures did not increase the risk of recurrence FC. (with case and control findings is 26.7% vs 29.6%)**.**

9-cause of fever:- in this study the cause of fever not consider the risk factor for the recurrence of FC in the children and this result is compatible with Berg AT et al [22], Offringa et al[10].

Conclusion

1-The risk factors associated with increased incidence of recurrence FC are: age less than 12 months at the onset of the first FC, male sex, family history of FC in a first degree relative, family history of epilepsy, low temperature(<= 39 cent.) at the onset of the first FC, type of convulsion(complex type).

2-Family history of FC in a second degree relative and duration of fever (neither long nor short) before the onset of the first FC and cause of fever not considered as the risk factors of the recurrent febrile convulsion.

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