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## **Risk Factors For First Attack Of Febrile Convulsion: Case Control Study**

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## Abstract

**Background:** Febrile seizures are the most common cause of convulsions in children. Most are simple in nature, although those with focal type, prolonged duration more than (15 min) or those that recur within 24 hours or within the same febrile illness are considered complex.

**Objective:** This is case- control study was carried out to :-Analyze the risk factors associated with first febrile convulsion in comparison to control group of the same age.Analyze the risk factors associated with complex febrile convulsions.

**Subjects and Methods: Patients:** A case –control study had been done at Basrah peadiatric teaching hospital in pediatric medical department on 115 patients admitted with first attack of convulsion and fever, their ages ranged from six months to six years. They had been admitted during the time from January2015 to the end of August 2015. Sixty - nine were males and 46 were females. Cases were matched with control group of 130 children without fever or fit in relation to age (6 months -6 years).

**Results:** The significant risk factors were positive family history of febrile convulsion P-value < 0.001, positive family history of developmental delay P-value < 0.01 patient s, history of preterm gestational age P-value < 0.01. Other risk factors were not found to be significantly correlated with first febrile convulsion .The study has revealed that there is a significant correlation between first complex febrile convulsion and young age of patients ( $\leq 15$  months), P-value < 0.05. The common infections leading to febrile

convulsions were upper respiratory infections (40 % of the all causes), which was significantly associated with simple febrile convulsions.

**Conclusoin:** From this study three risk factors for first attack febrile seizure were identified ,which may help in the prevention include positive history of febrile seizures in the family and developmental delay and history of the prematurity .Complex type was found in 49.6 % of patients with febrile seizure and was related to young age ( $\leq 15$  months) .Upper respiratory tract infections were the most common factor related to increase temperture in children with febrile convulsion & related to the simple type of febrile convulsions.

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## **Introduction:**

Febrile convulsions are the most common type of convulsions in pediatric age. Most are simple type, although those with localized type , duration more than (15 min) or those that recur within 24 hours or within the same febrile illness are regarded complex. Diagnosis of this convulsions is essentially clinical and based on its description provided by care givers.It is very important to exclude underlying meningitis, either by clinical features or, if any doubt presents, by cerebrospinal fluid analysis<sup>(1,2)</sup>.

**Epidemiology:** By seven years of age, nearly 3% to 4% of children have at least one or more febrile convulsions. They are more in black children(4.2%)versus white  $(3.5\%)^{(3,4)}$ . Regarding the sex distribution males and females are equally affected<sup>(5)</sup>.

However the prevalence in boys is slightly higher than in girls <sup>(6)</sup>. Febrile convulsions are age dependent and are less common before nine month and after six year of age. The peak age of occurance is  $\approx 14-18$  mo of age <sup>(1,5)</sup>.

**Etiology:** Three things interact to bring on a febrile convulsions : immature brain,

fever and genetic predisposition. Febrile seizures rarely occur before age 6 months or after ages 4 years to 5 years, so there is a obvious association with brain development. The nature of this development. process is unclear and could be related to increasing myelination, "dying back" of excessive neurons or increasing synaptic complexity <sup>(7)</sup>.

Viral infections of the respiratory tract, roseola and acute otitis media are most frequently the causes of febrile seizure <sup>(1)</sup>. Shigella dysentery are said to be associated with a particularly high risk of febrile seizures<sup>(6)</sup>.

## The risk factors for developing a febrile convulsions:

(1) **Family history :** A strong family history of febrile convulsions in siblings and parents

suggests a genetic predisposition and represents the most consistently identified risk factor for FS. The more relatives affected , the greater the risk<sup>(1,7,8)</sup>.Fist febrile convulsions of simple type are more common in children with family history of febrile convulsion<sup>(9)</sup>. Positive family history of epilepsy was reported as risk factor of febrile seizure.<sup>(10,11)</sup>

(2) **Development delay** :The hallmark of a neurodegenerative disease is increasing disturbance of neurologic function with loss of speech, vision, hearing, or locomotion, often associated with seizure .Convulsions, intellectual, and visual disturbance are obvious in the gray matter diseases <sup>(1)</sup>. Parental report of slow development is considered as a risk factor for a first febrile convulsion<sup>(5,12,13)</sup>

(3) Infections: Viral infections of the respiratory tract and acute otitis media are most frequently the causes of febrile convulsions <sup>(14)</sup>. Recent studies have shown an relationship between primary infection with HHV-6 infection and 31% of FS in infants and small age children, which often results in the development of a complex FS and might be a risk factor for subsequent development of epilepsy<sup>(5,15)</sup>.

**Treatment** and prevention: Routine management of a normal infant with simple brief febrile convulsions includes a careful search for the cause of the fever and reassurance and education of the parents. Active measures to control the fever, including the use of antipyretics, may reduce discomfort and are reassuring. Diazepam is the most widely used drug for the acute management of all types of seizures in both adults and children. Prolonged anticonvulsant prophylaxis for preventing recurrent febrile convulsions is controversial and no longer recommended for most children<sup>(1)</sup>.

**Aim of the study:** This is case- control study was carried out :-To study the risk factors that

were associated with first febrile convulsion in comparison to control group of the same age and to study the risk factors that were related to the complex febrile comvulsions.

**Subjects and Methods : Subjects , Patients:** A case –control study had been done at Basrah Maternity and Children Hospital in pediatric medical department on 115 patients admitted with first attack of convulsion and fever,their ages ranged from six months to six years.They had been admitted during the time from January2015 to the end of August 2015. Sixty - nine were males and 46 were females.

**Control group:** Control group included 130 children (6 months - 6 years of age) ,71 were males and 59 were females had visited AL-Razi health center and AL-Tanoma health center during same time of the study, all had no fever or convulsion,they attended health centers for vaccination or minor illnesses.

**Data collection:** A special questionnaire had been formed to collect informations about the following :

**Patients:** Information regarding the history : Name, sex, age, residence, date of admission, date of discharge, number of fits, type of fit, duration of fit,duration of fever,rigor, sweating,fit onset after fever, related symptoms, family history (in the first & second degree relatives) of febrile convulsion ,epilepsy and developmental delay, administration of the vaccines and their types within 2 weeks, day care attendance, history of admission to NCU and its duration, history of chronic diseases, birth weight , gestational age .Information regarding the examination:All were examined patients generally systematically and neurologically including measurement of their temperature and body weight. Investigation:Investigation were done in relation patients to the like CXR,GUE,GSE,CBP,others. Mostly all the variables that had been taken by history and

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examination were compared between cases &control.

Classification of cases: (1)According to the type of fit:The cases of febrile convulsion were divided into 2 types(simple, complex) .A case was considered as a complex if one or more of the following criteria were present :

(1) Seizure time is >15 min.

(2) Recurrent seizures occur within 24 hr

(3) Focal seizure activity or focal findings are present <sup>(1)</sup>. The type of FS was studied in relation to age ,sex ,family history of FS, epilepsy & developmental delay, birth weight, gestational age, degree of temperature, duration of fever&onset of fit after fever.(2) According >to the age:Two age groups:  $\leq 15$  months & 15 months. The age groups were studied in relation to family history of FS,epilepsy&developmental delay. Classification of some variables :Birth weight 2.5 kg ) <sup>(1)</sup>.  $\langle$ (Averge $\geq$ 2.5 kg , Below averge 38.5 °C ) >Degree of temperature ( $\leq$  38.5 °C , 3 days) (1,5). > (8). Duration of fever ( $\leq$  3 days , 12 hr) > Onset of fit after fever onset (< 12 hr, (13)

**Control:** Data related to the control group were obtained included: Name,sex,age,residence,family history(in the first &second degree relatives) of febrile convulsion,epilepsy and developmental delay , administration of the vaccines and their types within 2 weeks,day care attendance,history of admission to NCU and its duration, history of chronic diseases,birth weight ,gestational age and current body weight.

**Exclusion criterias:** Past history of febrile convulsion .Past history of any afebrile seizure .History of maturation delay . Age below six months & above six years .Cases of CNS infection:They were excluded depending on clinical manifestations (lethargy, irritability, vomiting, nuchal rigidity, bulging fontanel,

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headache, drowsiness, toxicity, coma, and prior antibiotic use). And /or positive labrotary investigation.

**Ethical consideration:** formal permission was taken from health and education directorates, also permission was taken from each family about taking the informations of their children in cases and control group.

**Stastical analysis:** Statistical analysis was carried out using Statistical Packages for Social Sciences(SPSS) software version 18,data were expressed and comparisons of proportions was done using chi square, Fisher exact test, P-value of < 0.05 was considered statistically significant, P-value of <0.01 as highly significant and P-value of <0.001 as extremely significant. For each variable the odd s' ratio (OR) and 95% confidence interval (CI) were

assessed for the study of different potential risk factors .

**Results**:Distribution of cases &control in relation to age &sex .The total number of children included in the study were (245); 115 children with first febrile convulsion and (130) children as a control group. The mean age of cases was  $22.34 \pm 16.42$  months , while in control group the mean age was  $22.70 \pm 18.09$ months . The number of children with age <15 months was 64 (55.7%) for patients 63 (48.5%) for control, while the number of children with age > 15 months was 51(44.3%)for patients 67(51.5%) for control with a male: female ratio of 1.5:1 in cases and 1.2:1 in control, Table (1). This table reveals that there was no significant differences between cases and control in relation to the age & sex of the children.

Age and sex	Cases No. %	Control No. %	P-value
Age ≤ 15 months >15 months	64 (55.7%) 51 (44.3%)	63 (48.5%) 67 (51.5%)	>0.05
Total	115	130	
Sex Male Female	69 (60.0%) 46 (40.0%)	71 (54.6%) 59 (45.4%)	>0.05
Total	115	130	

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## Characterstic features of febrile convulsion cases versus control group in relation to family history of febrile convulsion,epilepsy &developmental delay

Risk factors including family history of febrile convulsion, epilepsy & developmental delay were studied in both cases and control and presented in Table (2). This table reveals that family history of febrile convulsion was positive in 51 (44.3%) of cases, while in control was positive in 18 (13.8%), the difference was statistically significant, **P-value** (<0.001). Also this table shows that the family history of developmental delay was positive in 19 (16.5%) of cases , while in controls was positive in 8(6.2%), the difference was statistically significant, **P-value** (<0.01). This table shows that the family

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history of epilepsy was positive in 6 (5.2%) of cases, while in control was positive in 15 (11.5%), the difference was statistically not significant , **P-value** (>0.05).

Table (2)Distribution of cases & controls in relation to family history of febrileconvulsion,epilepsy and developmentaldelay

Family history	Cases No. %	Control No. %	P-value
Febrile convulsion: Positive Negative	51 (44.3%) 64 (55.7%)	18 (13.8%) 112 (86.2%	< 0.001
Total	115	130	
Epilepsy: Positive Negative	6 (5.2%) 109 (94.8%)	15 (11.5%) 115 (88.5%)	>0.05
Total	115	130	
Developmental delay: Positive Negative	19 (16.5%) 96 (83.5%)	8 (6.2%) 122 (93.8%)	< 0.01
Total	115	130	

**Complex features in febrile convulsion** The complex features of seizure were studied ;number of seizure & duration of seizure in relation to type of seizure ,Table (3-A) & number of seizure in relation to duration of seizure, Table (3-B). The all result was statistically not significant **P- value** (>0.05).

Table(3-A) Type of seizure in relation to number & duration of seizure

Characters of seizure	Generalized tonic clonic seizure No. %	Focal seizure No. %	P-value
No. of seizure Single $\geq 2$	64 (63.4%) 37 (36.6%)	8 (57.1%) 6 (42.9%)	>0.05
Total	101 (87.8%)	14 (12.2%)	
Duration of seizure ≤15 min. >15 min.	93 (92.1%) 8 (7.9%)	14 (100%) 0 (0.00%) <sup>*</sup>	>0.05
Total	101 (87.8%)	14 (12.2%)	

\* fisher s' exact test

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Duration of seizure	Single seizure No. %	≥2 seizures No. %	P-value
≤15 min. >15 min.	66 (91.7%) 6 (8.3%)	41 (95.3%) 2 (4.7%)	>0.05
Total	72 (62.6%)	43 (37.4%)	

#### Table (3-B) Number of seizure in relation to duration of seizure

The causes of fever according to the type of febrile convulsion

The type of convulsion was studied in relation to the causes of the fever. URTIs were found in 27 (46.6%) of patients with simple convulsion & in 19 (33.4%) of complex convulsion. The result was statistically significant **P- value** (<**0.05**). So the URTIs were statistically related to the simple type .

#### Table (4) Causes of fever in relation to the type of febrile convulsion

ETIOLOGY	Simple febrile convulsion No. %	Complex febrile convulsion No. %	Total No. %	P-value
URTI	27 (46.6%)	19 (33.4%)	46 (40%)	<0.05
Otitis media	9 (15.5%)	5 (8.7%)	14 (12.2%)	>0.05
Pneumonia	11 (19.0%)	19 (33.3%)	30 (26%)	>0.05
Bronchiolitis	3 (5.2%)	3 (5.3%)	6 (5.2%)	>0.05
Gastrointerit is	4 (6.9%)	7 (12.3%)	11 (9.6%)	>0.05
Urinary tract infections	4 (6.9%)	4 (7.0%)	8 (7.0%)	>0.05
Total	58 (50.4%)	57(49,6%)	115 (100%)	

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**The frequency of causes of fever in all the cases of febrile convulsion** The more frequent causes of fever were (from up to down):URTI 46 (40%), Pneumonia 30 (26%), Otitis media 14 (12.2%) & Gastrointeritis 11 (9.6%), Urinary tract infections 8 (7.0%), Bronchiolitis 6 (5.2%).

Odd s, ratio (OR) and 95% confidence interval (CI) analysis of risk factors for febrile convulsion For each variable the odd s' ratio (OR) and 95% confidence interval (CI) were assessed for the study of different potential risk factors. The whole variables included in the study were subjected to odd s' ratio (OR) and 95% confidence interval (CI) analysis to know which variables are significantly correlated with first attack of febrile convulsion. Family history of febrile convulsion, family history of developmental delay and patient s, history of prematurity were found to be an independent significant risk factors for first attack of febrile convulsion, (P < 0.05).

## Table (5) the odd s' ratio (OR) and 95% confidence interval (CI) analysis of significant risk factors for febrile convulsion

Variable	Odd s 'Ratio	95% confidance intervals	P-value
Family history of febrile convulsion	4.718	(2.501 -8.901)	< 0.001
Family history of developmental delay	3.263	(1.304 -8.168)	< 0.05
History of prematurity	4.373	(1.128 - 16.962)	< 0.05

## **Discussion**

This study was carried out to assesss the risk factors for first attack of febrile convulsion & to determine the features of children to help in assessment of risk factors for complex type, it was a case-control study both cases &control were matched for ages. The number of the males was found to be more than females(1.5:1) in the cases &(1.2:1) in the control, although the result was not statistically significant, also other studies had showed that males were more likely to be affected by FS for unknown reasons<sup>(16,17)</sup>. Other study showed that male &female were equally affected<sup>(5)</sup>.Regarding genetic factors,this study had shown that positive family history of

febrile convulsion was statistically significant risk factor for developing febrile convulsion ,this result was found by other researches carried out by Anne et al in USA<sup>(18)</sup>, Murat et Turkey<sup>(16)</sup>. al in Talebian et al in Kashan,Iran<sup>(10)</sup>. This is explained by a genetic connection studies in several large families have connected the febrile seizure gene to chromosomes 19p and 8q13-21.An autosomal dominant inheritance pattern is found in some families<sup>(1,2)</sup>. A positive family history of febrile gives the idea about convulsion the importance of gentic factors & shared external condition <sup>(9)</sup>. The study showed also that

positive family history of developmental delay was statistically significant risk factor of developing febrile convulsion. This is explained by the fact that any genetic neurological defect in the family increases the risk of having the family history seizures like of neurodegenerative disorders and demyelinating disorders of theCNS<sup>(1)</sup>. This study had shown that positive family history of epilepsy was not found to be associated with FS,in contrast to other studies which reported that close relative history of epileptic diseases was appear to be a risk factors for  $FS^{(10,11)}$ , this may be explained that families with convulsive by the fact disorders are more likely to have FS due to linkage to several genetic loci<sup>(3)</sup>. The relation of FS with family history of epilepsy was studied because patients with FS & family history of epilepsy are more liable to develop epilepsy later on<sup>(1)</sup>. The study had demonstrated that premature infants were more likely to have FS ,this is similar to the results of other study that reported by Eila et al in Finland<sup>(19)</sup>. This is explained by the fact that prematurity has many risk factors for the perfect maturation of the CNS & for the maturation prenatally &during early period of life due to under development of many organ systems. Developing cortex is more sensitive to provoked seizure.Premature infants were more likely to experience hypoxia or other adverse perinatal events $^{(9,13)}$ . The gestational age was not found to be related to the type of FS, while other study reported that there was association between the prematurity & complex FS<sup>(13)</sup>.

As children with complex features of FS are more liable to have recurrence of FS& later on epilepsy<sup>(1)</sup>, the risk factors for a complex first FS were studied &it was found that 49.57% of admitted patients had complex features. Children  $\leq 15$  months of age were more likely to have complex type of seizure. This result is similar to other results

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that had been reported by Ling et al in Malaysia<sup>(13)</sup>, Tahir in Pakistan <sup>(9)</sup>and Shinnar et al in USA <sup>(20)</sup>, this can be understanded by the fact that immatured cortex is very sensitive to the induced seizures other than tonic clonic type <sup>(9)</sup>. Family history of febrile

convulsion, epilepsy & developmental delay were not found to be related to the type of FS other studies had shown that family history of these genetic problems were more likely to be associated with FS(regardless of the type) which is explained by linkage to certain chromosomes<sup>(10,11)</sup>.Regarding fever.its peak,duration&onset of fit after fever were not found to be related to the type of FS, while in some studies it was found that the relatively low temperature( < 38.5 c) related to recurrent FS with focal features<sup>(8)</sup>. Also other study demonstrated that the height of temperature was significant independent risk factor for FS regardless the type of  $FS^{(18)}$ . The causes of fever were studied , it was found that the URTIs were the fist common factor related to increase temperture, this is similar to the result that was reported by Tahir in Pakistan<sup>(9)</sup>. This may reflect that these infections are one of the common diseases in our country especially the first period of the study included the time at which respiratory tract infections were more related to simple FS, while no difference in other causes was observed.

**Conclusions :** From this study three risk factors for first attack febrile seizure were identified , which may help in the prevention include positive history of febrile seizures in the family and developmental delay and history of the prematurity .Complex type was found in 49.6 % of patients with febrile seizure and was related to young age ( $\leq 15$  months) .Upper respiratory tract infections were the most common factor related to increase temperture in children with febrile convulsion & related to the simple type of febrile convulsions.

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دراسة حول عوامل الخطورة المؤدية لحدوث النوبة الاولى للاختلاج الحراري في الاطفال في مستشفى البصرة للنسائية والاطفال

> د. احمد محسن عزیز د.عائدة عبد الکریم منثر

مستشفى الشهيد محمد الموسوي للاطفال . كلية الطب ،جامعة البصرة .

## الخلاصة

المقدمة :- الاختلاجات الحرارية من اكثر اسباب الاختلاجات شيوعا عند الاطفال الاكثر هو النوع البسيط ،على الرغم من ان الاختلاجات الموضعية ،الاختلاجات التي تستمر اكثر من ١٥دقيقة او التي تكون متكررة ضمن ٢٤ساعة يعتبر من النوع المعقد

الهدف :- هذه الدراسة تم تنفيذها لغرض :-تحليل ودراسة عوامل الخطورة المتعلقة بحدوث النوبة الاولى من الاختلاج الحراري بالمقارنة مع العينة الضابطة من نفس العمر، كذلك لغرض تحليل و دراسة عوامل الخطورة المتعلقة بالاختلاج الحراري من النوع المعقد

الطريقة :- أجريت هذه الدراسة المقارنة باستخدام العينة الضابطة لتحديد العوامل المسببة لنوبات الاختلاج الحراري الاولى التي تم ادخالها الى وحدة الطوارئ وردهات الاطفال في مستشفى البصرة للنسائية والاطفال لمدة ٨ اشهر (من بداية كانون الثاني الى نهاية اب ٢٠٠٩ ) على ١١٥ طفل(من عمر ٦ اشهر الى عمر ٦ سنوات) مع النوبة الاولى للاختلاج الحراري تمت المقارنة مع العينة الضابطة المكونة من ١٣٠ طفل (من عمر ٦ اشهر الى عمر ٦ سنوات) بدون حمى اواختلاج حراري.

النتائج :- أثبتت هذه الدراسة أن العوامل المؤثرة و المعتدة إحصائيا على حدوث نوبات الاختلاج الحراري الاولى لدى ألأطفال هي وجود تاريخ عائلي للإصابة بالاختلاج الحراري ، وجود تاريخ عائلي لتأخر التطور و وجود تاريخ الولادة المبكرة لدى مرضى الصرع الحراري، قيمة الاحتمالية اقل من ١٠ ٢٠ كما بينت هذه الدراسة وجود ترابط معتد إحصائيا بين حدوث حالات الاختلاج الحراري من النوع المعقد وبين عمر الاطفال من فئة خمسة عشر شهراو اقل بينت هذه الدراسة ان التهابات المسالك التنفسية العليا الحادة هي من اكثر اسباب الحمى المسببة للاختلاج الحراري (٤٠ بالمئة من مجموع الاسباب ) مع وجود ترابط معتد إحصائيا مع حدوث حالات الاختلاج الحراري من النوع المعتد إعار الاختلاج الحراري الولاة الاحتمالية اقل من .

الاستنتاج :- من خلال هذه الدراسة تم تحديد ٣ عوامل خطورة لنوبة الاختلاج الحراري الاولى و التي يمكن ان تساعد بالوقاية وتشمل وجود تاريخ عائلي للإصابة بالاختلاج الحراري ، وجود تاريخ عائلي لتأخر التطور و وجود تاريخ الولادة المبكرة لدى مرضى الصرع الحراري . نسبة الاختلاجات الحرارية من النوع المعقد في هذه الدراسة كانت ٤٩,٦٪ من المرضى و كانت مرتبطة بالاعمار ≤١٥شهر التهابات المسالك التنفسية العليا الحادة هي من اكثر اسباب الحمى عند الاطفال الذين لديهم اختلاج حراري مع وجود ترابط مع حدوث حالات الاختلاج الحراري من النوع البسيط.