

# ORIGINAL ARTICLE

## The first febrile seizure; predisposing factors and recurrence rate

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## Abstract

### Objective

Febrile seizure is the most common worrisome neurologic disorder in children in terms of parental point of view. The purpose of this study was to answer distressing parents' questions about the prevalence and possibility of febrile seizure recurrence.

### Materials & Methods

140 patients who were admitted due to the first febrile seizure in the six months (March up to September) of the year 2015 were enrolled to this study. Exclusion criteria include central nervous system infection, non-confirmed febrile seizure and lack of parental acceptance for long-term inclusion in this study. All children were followed in terms of second febrile seizure during one year follow-up from the time of first febrile seizure. (3 sentences were deleted).

### Results

Recurrence of febrile seizure was 25.7 % during one-year follow-up. Significant risk factors for recurrence include: age less than one year old, male gender, seizure with low level of fever, family history of epilepsy, family history of febrile seizure, complex febrile seizure (focal and repeated in 24 hours), seizure duration more than 15 minutes and parental indifference to the onset of fever in their children before seizure occurrence. Although duration of fever before seizure, failure to thrive, positive history of admission in neonatal period, dystocia at birth delivery and children with day care staying were associated with greater febrile seizure recurrence; but, they did not have significant relationship with recurrence rate. Prophylaxis with benzodiazepine reduced the recurrence rate.

## Conclusion

Chance of febrile seizure recurrence in one-year follow-up increased in presence of risk factors expressed in finding part. parental indifference to the onset of fever in their children that is starting before seizure was a considerable risk factor in terms of recurrence prevalence. We recommended to emphasis on parental education about this new finding as a risk factor for febrile seizure in order to prevent its future recurrence.

**Keywords:** Risk factors; Febrile seizure; Recurrence.

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## Introduction

Seizures associated with fever may be induced by central nervous system infection, unknown epilepsy or simple febrile seizures (1). Febrile seizure refers to seizures that occur with a central temperature of 38 degree centigrade or higher, that are not the result of central nervous system infection or any metabolic imbalance, and that occur in the absence of a history of prior afebrile seizure (2). Treatment with intermittent oral diazepam only during febrile illness and prolonged treatment with phenobarbital; witch both methods have special limitations and advantages (3, 4). It is preferable to use oral Benzodiazepines (Diazepam and Clobazam) in children who are high risk for recurrences in order to reassure worried parents (5). Nowadays, it is recommended not to start anticonvulsant treatment for febrile seizure until seizure attacks could be life-threatening to child (6). Medical treatment is not proposed with the aim of epilepsy prevention (7).

New posed risk factors to increase febrile seizure recurrence include: neonatal discharge in 28<sup>th</sup> days of life or later, parental complaint of delayed growth and development in child and child's day care staying due to working parents (8). Moreover, iron

deficiency is strongly recommended as a risk factor in the first febrile seizure occurrence (9, 10, 11). If the patient is receiving long term anticonvulsant treatment, it is preferable to consider physical exam and risk factors associated with recurrence more than etiologic factors and laboratory findings (12). Many researches were conducted in Iran and other countries regarding febrile seizure in children (13, 14). Factors that effective in recurrence prevalence have been reported variously in different studies (15, 16).

The purpose of this study was to express findings in our neurologic center. Our objective was to determine important risk factors and prevalence of febrile seizure recurrence in children admitted in Mousavi Hospital in Zanzan during one-year after the first febrile seizure.

## Materials & Methods

This cohort study has been conducted on more than 90% of children admitted for first Febrile seizure (140 patients totally) in Mousavi Hospital. All 9 months to 5 years-old children with first febrile seizure occurred in the six months (March up to September) of the year 2015 were included in our study. The diagnosis of febrile seizure

was confirmed in all cases. The most important limitation in this study was missing the all patients admitted in hospital with this diagnosis. This limitation was reduced to less than 10% (in all admission) with great cooperation of medical interns, residents and pediatric ward secretary. seven patients were excluded from study due to suspected central nervous system infection, non-confirmed febrile seizure and lack of parental acceptance for long-term inclusion in this study. Questionnaire was filled for all children after obtaining written informed consent. We recorded all patient information, address and phone numbers and followed them during one-year period from the time of first admission.

Seizure was recurred in 36 patients during one-year follow-up. These patients were invited for face to face conversation, physical and neurological examination. Fortunately, all children returned for visit. All mentioned risk factors were evaluated and registered in the questionnaire. Data gathered in questionnaire were analyzed by an expert statistician with Chi-square Fisher method. value less than 0.05 was significant. All results in this study were published statistically and all personal information were preserved privately.

## Results

In this study, febrile seizure recurrence during one-year follow-up was 25.7 % (in 36 patients). Seizure recurred in 47.6 % of children less than one-year old and 21.8 % in children with the age of 1 to 5 years-old. Recurrence was more common in children less than one-year old (P value = 0.013). Seizure recurred in 40.3 % of males and 14.1 % of females. Febrile seizure recurrence was more common in boys (P value = 0.000). Seizure recurred in 37% of children who had fever

less than 38.5 during febrile seizure and 23% of children with fever equal or more than 38.5 degree centigrade. Occurrence rate in children with low level of fever were more than patients with high fever (P value =0.134). 47.6 % of children with positive family history of epilepsy and 21.8 % of children with negative family history of epilepsy had recurrences. Children with positive family history of epilepsy experienced more recurrences (p value = 0.013).

48.4 % of Children with positive family history and 19.3 % of children with negative family history of febrile seizure experienced recurrence. Children with positive family history had more recurrence compared to patients with negative family history of febrile seizure. (p value = 0.001)

Recurrence occurred in 45.5 % of children with complex febrile seizure (focal and repeated in 24 hours) and 22% of children with simple febrile seizure. Children with complex febrile seizure (focal and repeated in 24 hours) suffered more recurrences compared to simple Febrile seizure (P value = 0.021). 24.4 % of children with seizure duration shorter than 15 minutes and 41.7 % of children with seizure duration longer than 15 minutes experienced recurrence (P value = 0.049). Recurrences occurred in 43.5 % of children with parental indifference to the onset of fever in their children before seizure occurrence and 22.2 % of children with parental attention to the onset of fever before seizure occurrence. Children with parental indifference to the onset of fever in their children before seizure occurrence had more recurrences (P value = 0.033). 36.6 % of patients with fever less than one hour before febrile seizure and 21.2 % of children with fever more than one hour had recurrences. Recurrence rate in children with fever less than one hour was higher than other group but

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this difference was not significant statistically (P value = 0.058). 38.5 % of cases with growth failure and 22.8 % of cases without growth failure had recurrences. Although recurrence rate was higher in children with growth failure but statistical gap between them was not considerable (P value = 0.099)

Recurrence happened in 28.2 % of children who had being sent to day care and 24.8 % of children who were remained at home. Recurrence incidence in children keeping in day care was higher in

comparison with another group. This statistical difference was not significant (P value = 0.675). 27.8 % of children with dystocia and respiratory support in birth time and 25% of children without dystocia and respiratory support at birth experienced recurrences. This statistics was not significant (P value = 0.742). 13.9 % of patients with use of Benzodiazepines prophylaxis and 41% of patients without use of Benzodiazepines prophylaxis had recurrence. This data was statistically significant (P value = 0.000). (Table 1)

**Table 1:** Correlation between recurrence rate and risk factors in first febrile seizure

Risk Factors	Total	Positive Recurrence		Negative Recurrence		P Value
		Percent	Number	Percent	Number	
Age 9-12 Months	21	47/6	10	52/4	11	0.013
Age 1-5 years	119	21/8	26	78/2	93	0.013
Boys	62	40/3	25	59/7	37	0.000
Girls	78	14/1	11	85/9	67	0.000
Positive Family History of FC	31	48/4	15	51/6	16	0.001
Negative Family History of FC	109	19/3	21	80/7	88	0.001
Patient Indifference to the fever in child	23	43/5	10	56/5	13	0.033
Patient attention to the fever in child	117	22/2	26	77/8	91	0.033
Fever < 38.5	27	37/0	10	63/0	17	0.134
Fever >= 38.5	113	23/0	26	77/0	87	0.134
Positive Family History of Epilepsy	21	47/6	10	52/4	11	0.013
Negative Family History of Epilepsy	119	21/8	26	78/2	93	0.013
Complex FC (focal and repeated in 24 hours)	22	45/5	10	54/5	12	0.021
Simple FC	118	22/0	26	78/0	92	0.021
Positive Failure to Thrive	26	38/5	10	61/5	16	0.099
Negative Failure to Thrive	114	22/8	26	77/2	88	0.099
Positive Day Care	39	28/2	11	71/8	28	0.675

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Negative Day Care	101	24/8	25	75/2	76	0.675
Seizure Happened before Start of Fever	23	43/5	10	56/5	13	0.033
Seizure Happened after Start of Fever	117	22/2	26	77/8	91	0.033
Duration < 15 Min	116	22/4	26	77/6	90	0.049
Duration >= 15 Min	24	41/7	10	58/3	14	0.049
Positive Dystocia	36	27/8	10	72/2	26	0.742
Negative Dystocia	104	25/0	26	75/0	78	0.742
Positive Use of Diazepam	79	13/9	11	86/1	68	0.000
Negative Use of Diazepam	61	41/0	25	59/0	36	0.000
Time between Starting of Fever and Seizure < 1 Hours	41	36/6	15	63/4	26	0.058
Time between Starting of Fever and Seizure > 1 Hours	99	21/2	21	78/8	78	0.058
Positive History of Neonatal Admission	26	38/5	10	61/5	16	0.099
Negative History of Neonatal Admission	114	22/8	26	77/2	88	0.099

## Discussion

Recurrence rate in this study with 140 children aged 9 months to 5 years-old, after the first febrile seizure was 25.7 % during one-year follow-up. Recurrence incidence in children less than one-year old age was 47.6 %. According to Nelson Essential of Pediatrics, incidence rate of febrile seizure in children older than one year of age is 28% and in children younger than one year old is 50%. Febrile seizure recurred in 30% of children and 50% of children younger than one year old based on statistics in Nelson text book of pediatrics. Our findings were consistent with statistics in Nelson textbook and Nelson Essential of pediatrics which are authentic referral textbook of pediatric.

In a study in 2012, total recurrence rate in children 1-5 years old reported 11.7 % (17).

In another study in 2012, relapse incidence of

febrile seizure was 15-70 % in first 2 years after the first febrile seizure (18). In a study in 2014, recurrence rate was 17.5 % (19). Approximately, findings of these studies were consistent with our results. The most common point in reviewed studies was the higher relapse rate in children younger than one year old.

According to our study, significant recurrence risk factors include: age younger than one year old, male gender, seizure with low fever, positive family history of epilepsy, Positive family history of febrile seizure, complex febrile seizure (focal and repeated in 24 hours), seizure duration more than 15 minutes and parental indifference to the onset of fever in their children before seizure occurrence. All these factors except daily child-keeping in daycare and parental indifference to the onset of fever in their children before seizure

occurrence are according to Nelson textbook of pediatric.

If we compare the main risk factors in this study with risk factors in other references (20), it is obvious that they were similar to each other. But, parental indifference to the onset of fever in their children before seizure occurrence as a risk factor in our study was a new risk factor and have not been evaluated in other studies. This risk factor was significant in terms of recurrence rate.

The cause of this finding could be the lack of sufficient parental attention in detecting of fever, so it is better to inform parents about recurrence prevention by early detection of child's fever.

In our study, fever duration before seizure, child's growth failure, admission history during neonatal period, keeping child in daycare and history of dystocia and ventilation support at birth time were associated with higher level of recurrences. But, there were no considerable relation between these risk factors. Some of following risk factors are significant in occurrence of first febrile seizure (not recurrence). They include hyponatremia, Iron deficiency anemia and zinc deficiency (21).

## **In Conclusion**

Recurrence rate of febrile seizure in presence of mentioned risk factors increased which was similar in prevalence to many other studies. But, parental indifference to the onset of fever in their children was a significant risk factor for recurrence of seizure in this study. As we mentioned in our results, recurrence of febrile seizure occurred in 43.5 % of children with parental indifference to the onset of fever in their children before seizure occurrence and 22.2 % of children with seizure after fever detection by parents and fever management. This febrile seizure recurrence statistical data due

to this mentioned risk factor (43.5%) is significant enough to be considered. This risk factor has not been assessed before in other authentic studies around the world. So, it could be posed as a new risk factor if more clinical trials in future evaluate its significance as a risk factor for febrile seizure that could easily be managed by parents. Therefore, it is recommended to warn parents about paying more attention to their child s' fever during febrile illnesses in terms of recurrence prevention.

It is recommended that to find the relationship between parental indifference to the onset of fever before seizure occurrence and recurrence rate, a complementary study with a larger sample size is beneficial in order to discover more detailed results about this subject.

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## **Author's Contribution**

Alinaghi Kazemi, Mohammad Vafae-Shahi and Reza Sharvin Badv designed and managed the study. Ali Piri and Ramazan Fallah analyzed and interpreted the patients' data and performed follow-up of the patients. Leila Tahernia was major contributors in writing the manuscript.

All of the authors read and approved the final manuscript.

## **Conflict of Interest**

The authors declare that there is no conflict of interest

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