

Predictive Factors for Complex Versus Simple Febrile Convulsion In Children

Najdat Shukur Mahmood (MChB, FICMS) ¹

Abstract

Background: Febrile seizure has a good prognosis, but may be presented with status epilepticus and may raise the possibility of acquiring epilepsy later in life. These consequences are highly related to many features, including complex criteria.

Objective: To investigate for factors which may be associated with increased incidence of complex febrile seizure.

Patients and Methods: This is a cross-sectional comparative study done within 2013- 2014. The associations of febrile convulsion and its criteria with demographic and other characters of the patients were evaluated. Chi square was applied for statistical analysis.

Results: Seventy six children were enrolled, male gender was 56.6% (n=43) and 39 (51.3%) of them were having complex febrile convulsion. There was no significant effect of age and sex on the type of febrile seizure; criteria of complex febrile seizure (prolonged, repetitive, and focal seizures) were unrelated among each other. Consanguinity marriage has a clear relationship with simple type (p value=.008), vaginal delivery was significantly associated with complex seizure (p value=0.047), non- respiratory causes of fever are associated with prolonged febrile seizure (p value= .024), while no differences between the types of febrile seizure regarding many other criteria, including anemia, body weight variations, previous febrile seizure, family history of febrile seizure, and others.

Conclusion: There were only a few criteria predispose the child for complex febrile seizure, including non- respiratory causes of fever, vaginal delivery, non-consanguineous parents, and possibly prematurity; therefore complex febrile convulsion cannot be entirely predicted, but a trend can be expected if these mentioned factors were experienced.

Key words: Predictive factor, febrile seizure, children .

Corresponding Author: najdat77@yahoo.com.

Received: 13th April 2017

Accepted: 14th May 2017

¹ Department of Pediatrics- College of Medicine-Diyala University-Diyala, Iraq.

Introduction

Febrile convulsion is defined as seizure that arise in children between one month and 6 years old, related to fever without intracranial infections or a clear causes. It is the most common seizure disorder in children and a frequent reason of emergency admissions in pediatrics hospitals. The peak age of onset is \approx 14–18 mo of age. They occur in about 2% to 4% of young children in the

South America, United States, and Western Europe; they are stated to be even more frequent in Asian peoples [1-3].

In the majority of cases, the disorder seems to be polygenic, the genetic contribution to the incidence of febrile seizures is displayed by a positive family history of febrile convulsion. In several families, autosomal dominant inheritance is

prominent, and many implicated genes have been identified. Identified single genes include FEB 1, 2, 3, 4, 5, 6, and 7 genes on chromosomes 8q13-q21, 19p13.3, 2q24, 5q14-q15, 6q22-24, 18p11.2, and 21q22. Only the function of FEB 2 is known: it is a sodium channel gene, SCN1A [4].

Febrile seizures (FS) are classified into simple (typical) and complex (atypical) and children in either of these subgroups may have a family history of febrile or afebrile seizures or a pre-existing neurologic abnormality [2][3]. The majority of febrile convulsions are typical, whereas 9-35% of febrile seizures are atypical (complex) [5].

Febrile seizures have an excellent prognosis but it may also denote a serious underlying acute infectious illness such as bacterial meningitis or sepsis [2][6]. After the first febrile seizure, around 33% of affected children will have one or more recurrences, and approximately 9% of them will experience three or more [2]. Increased recurrence risk is associated with many factors, include complex features, age <12 mo, lower temperature before convulsion, and a positive family history of febrile seizures [3]. Accumulative epidemiological facts indicates that febrile seizures are the most common established antecedent for epilepsy in children, though the precise risk for unprovoked seizures (epilepsy) after FS is unclear [5]. Factors that consistently augment the risk for developing epilepsy following febrile seizures, include a complex features, family history of epilepsy, and an early onset neurodevelopmental abnormalities [3][7][8]. The risk for developing epilepsy from a simple febrile seizures is 1.0–2.4%, and in a complex one is 4.1– 6.0% [9]. Simple febrile seizures do not increase risk of mortality even though they are understandably, concerning to the parents when they observe them firstly. Complex febrile seizures may have an about two fold long-term raising in mortality over the succeeding 2 years, when

compared to the general population, possibly due to the primary pathology [3].

Several comprehensive studies were done world widely concerning the risk for febrile convulsion recurrence & epilepsy, but few observations were talking about the risk of having a CFS. This study aimed to look for factors that can assist to predict who children are more liable to experience CFS to arrange for precautions, management, and future prognosis.

Materials and Methods

The study was a comparative cross-sectional study; it was done at Al Batool Teaching Hospital for Maternity and Children at Baquba- Diyala province/ Iraq from August 2013 to March 2014. We got an informed consent from the patients/ their relatives gave prior to the participation in the study.

Inclusion/ exclusion criteria

This study include children who presented with febrile convulsion as defined by International League Against Epilepsy (ILAE) (they are defined febrile convulsion as “a seizure occurring in childhood after one month of age, associated with febrile illnesses not caused by an infection of the central nervous system, without previous neonatal seizures or a previous unprovoked seizure, and not meeting criteria for other acute symptomatic seizures”[1] therefore, the inclusion criteria were babies from completed one month - 6 years old who have convulsion associated with fever with exclusion of children had an infection of the central nervous system (they were excluded by cerebrospinal fluid analysis in suspected cases) and children have previous neonatal seizures or a previous unprovoked seizure, and the seizure must not be meeting criteria for other acute symptomatic seizures.

The children who have neurological deficits such as cerebral palsy or developmental delay have been excluded.

Denver II development screening test was applied to assess neurodevelopment function. Simple versus complex febrile convulsions

Febrile seizures were subdivided into simple "typical" (generalized, duration 15 minutes or less, and without recurrence within the next 24 hours) or complex "atypical" when the convulsion met one or more of the following features: the duration is >15 min, repeated convulsions occur within 24 hours, and focal seizure [2][3][10].

Studied variables

Interview with the patients' parents or near relatives was carried out by a well trained personnel; they were using a self-administered questionnaire which includes information regarding age, sex, the febrile illness (the etiology and the duration of fever before convulsion), using of antibiotics before convulsion, body weight, anemia, previous FS, birth history (gestational age, mode of delivery, and crying after birth), family history of febrile convulsion, and consanguineous parents. In addition to full description of the convulsion attack (duration, distribution, and repetition).

The etiology of the seizure was divided into either respiratory or non-respiratory cause, non-respiratory causes include any causative factor that involve a system other than respiratory tract, including fever and skin rash. The weight was measured by a weight scale called Kubota for children less than 2 yr old and Rossmax scale for children 2 years old or more, then plotted on the World Health Organization (WHO) growth charts of weight per age; the children

were classified into either underweight (below minus two standard deviations from median weight for age) or normal body weight [11]. Anemia was determined by measuring packed cell volume (PCV), lowest normal PCV was taken at 31% for babies less than 6 months old and at 33% for 6 mo-6 yr; if the value was less than that level, it was considered anemic state [12].

Statistical analysis

Chi-square test was used to assess the associations and the level of significance was set at 0.05 level. Data were analyzed by Statistical Package for Social Sciences (SPSS) software (version 16). To investigate the effect of the study variables, we compared the group of patients having simple FS firstly with the whole complex FS patients, then with the patients who have single criteria of complex FS (prolonged, focal, and repetitive within 24 hours) separately.

Result

During the period of the study, 80 children without neurological or developmental problems were admitted to the hospital due to febrile convulsion, 4 children of them were excluded due to missing data and 76 children were enrolled in the study. Most (63.1%) of the recruited children were younger than 2 years (p value .022); 5 babies (6.6%) of them were under 6 months, the remaining (36.9%) were 2-6 years old. Male gender comprises 56.6%; there was no gender effect on distribution of the study group (p value= .251), table (1).

Table (1): Distribution of the study group to age and gender.

Age/ Gender	Male number (%)	Female number (%)	Total number (%)
1 mo- 2 yr	26 (34.2)	22 (28.9)	48 (63.1)*
< 2- 6 yr	17 (22.4)	11 (14.5)	28 (36.9)
Total	43 (56.6)	33 (43.4)	76 (100)

* p value= .022

Thirty seven children of the enrolled patients were having simple febrile convulsion (48.7%) and 39 (51.3%) children have complex febrile convulsion (those children were distributed as follows: 23 (59%) repetitive, 14 (36%) prolonged, and 13 (33%) focal, 11 children had more than one complex feature. Previous febrile seizures were experienced in 13 children (17.1%), complex FC is now presenting in 5 (38.5%) of them.

Focal febrile convulsion was more related to repetitive than single FS but this association was statistically not significant. Prolonged FS was near evenly distributed between focal and generalized FS and also between repetitive and single FS. In summary, the criteria of CFS were unrelated between each other (table 2).

It was clear that both the age and gender of the children didn't affect the type of

febrile convulsion. Vaginal delivered babies were having CFS more than those delivered by cesarean section and this association was statistically significant. Non- respiratory causes of febrile illness were statistically associated with prolonged FS. History of consanguinity marriage had highly significant association with non- prolonged FS. Children who previously have FS appear to be more prone for simple FS than children who were presenting the 1st attack, but this relationship was not significant statistically. Some variables were deranged in small proportions, e.g. body weight and gestational age, so their statistical analysis of association cannot be reliable. Most of the other considered variables showed no consequences on the characteristics of FS (tables 3- 6).

Table (2): Relationship between criteria (distribution, duration, and recurrences within 24 hours) of the febrile seizure of the enrolled children.

	Distribution of seizure			Duration of seizure		
	Focal number (%)	Generalized number (%)	p value	≤ 15 min. number (%)	> 15 min. number (%)	p value
Repetition of seizure within 24 hours						
-Yes	6 (26.1)	17 (73.9)	.171	19 (82.6)	4 (17.4)	.879
- No	7 (13.2)	46 (86.8)		43 (81.1)	10 (18.9)	
Total	13 (17.1)	63 (82.9)		62 (81.6)	14 (18.4)	
Duration of seizure						
- ≤ 15 min.	11 (17.7)	51 (82.3)	.756			
- > 15 min.	2 (14.3)	12 (85.7)				
Total	13 (17.1)	63 (82.9)				

Table (3): Significance of the effect of patients' characters and variables on the type of febrile seizure.

Variable		Type of febrile seizure		p value
		Simple number (%)	Complex number (%)	
Age	- 1 mo- < 2 yr	23 (47.9)	25 (52.1)	.861
	- 2 yr- 5yr	14 (50)	14 (50)	
Sex	- Male	19 (44.2)	24 (55.8)	.370
	- Female	18 (54.5)	15 (45.5)	
Cause of fever	- Respiratory	26 (56.5)	20 (43.5)	0.091
	- non- respiratory	11 (36.7)	19 (63.3)	
Duration of fever before seizure	- Equal or less than hour	9 (50)	9 (50)	0.898
	- More than 1 hour	28 (48.3)	30 (51.7)	
Pretreatment with antibiotics	- Yes	8 (57.1)	6 (42.9)	.483
	- No	29 (64.8)	33 (53.2)	
Body weight	- Normal	35 (48.6)	37 (51.4)	.600
	- Underweight	2 (50)	2 (50)	
Anemia	- Positive	6 (42.9)	8 (57.1)	.629
	- Negative	31 (50)	31 (50)	
Previous febrile convulsion	- Yes	8 (61.5)	5 (38.5)	.308
	- No	29 (46)	34 (54)	
Gestational age	- Preterm	1 (33.3)	2 (66.7)	.587
	- Full term	36 (49.3)	37 (50.7)	
Mode of delivery	- Vaginal delivery	24 (42.1)	33 (57.9)	0.047*
	- Caesarean section	13 (68.4)	6 (31.6)	
Crying at birth	- Cried immediately	34 (47.2)	38 (52.8)	0.279
	- Not cried immediately	3 (75)	1 (25)	
Family history of febrile seizure	- Yes	15 (46.9)	17 (53.1)	.788
	- No	22 (50)	22 (50)	
Consanguinity marriage	- Yes	28 (52.8)	25 (47.2)	.272
	- No	9 (39.1)	14 (60.2)	
Total		37 (48.7)	39 (51.3)	

* significant association.

Table (4): Significance of the effect of patients' characters and variables on the duration of febrile convulsion.

Variable		Duration of febrile seizure ^a		p value
		Non-prolonged number (%)	Prolonged number (%)	
Age	- 1 mo- < 2 yr	23 (71.9)	9 (28.1)	.889
	- 2 yr- 5yr	14 (73.7)	5 (26.3)	
Sex	- Male	19 (76)	6 (24)	.588
	- Female	18 (69.2)	8(30.8)	
Cause of fever	- Respiratory	26 (83.9)	5(16.1)	.024*
	- non- respiratory	11 (55)	9(45)	
Duration of fever before seizure	- Equal or less than hour	9 (75)	3(25)	.828
	- More than 1 hour	28 (71.8)	11(28.2)	
Pretreatment with antibiotics	- Yes	8 (88.9)	1(11.1)	.226
	- No	29 (69)	13(31)	
Body weight	- Normal	35 (71.4)	14(28.6)	.552
	- Underweight	2 (100)	0	
Anemia	- Positive	6 (60)	4(40)	.321
	- Negative	31 (75.6)	10(24.4)	
Previous febrile convulsion	- Yes	8 (80)	2(20)	.556
	- No	29 (70.7)	12(29.3)	
Gestational age	- Preterm	1 (100)	0	.534
	- Full term	36 (72)	14(28)	
Mode of delivery	- Vaginal delivery	24 (66.7)	12(33.3)	.145
	- Caesarean section	13 (86.7)	2(13.3)	
Crying at birth	- Cried immediately	34 (70.8)	14(29.2)	.552
	- Not cried immediately	3 (100)	0	
Family history of febrile seizure	- Yes	15 (71.4)	6(28.6)	.881
	- No	22 (73.3)	8(26.7)	
Consanguinity marriage	- Yes	28 (84.8)	5 (15.2)	.008*
	- No	9 (50)	9 (50)	
Total		37 (72.5)	14 (27.5)	

* Significant association, **Highly significant association.

^a In this table, prolonged seizure (more than 15 minutes) had compared with simple febrile seizure (FC) which is non-prolonged (15 min or less). Those who had other features of complex FC (i.e. focal and repetitive features) had been excluded from this table to avoid their bias effect on variables, so the number of all included patients were 51.

Table (5): Significance of the effect of patients' characters and variables on the repetition of febrile convulsion within 24 hours.

Variable		Seizure's repetition within 24 hours ^a		p value
		Non repetitive number (%)	Repetitive number (%)	
Age	- 1 mo- < 2 yr	23 (57.5)	17(42.5)	.348
	- 2 yr- 5yr	14 (70)	6(30)	
Sex	- Male	19 (59.4)	13 (40.6)	.696
	- Female	18 (64.3)	10(35.7)	
Cause of fever	- Respiratory	26 (70.3)	11(29.7)	.082
	- non- respiratory	11 (47.8)	12(52.2)	
Duration of fever before seizure	- Equal or less than hour	9 (60)	6 (40)	.878
	- More than 1 hour	28 (62.2)	17 (37.8)	
Pretreatment with antibiotics	- Yes	8 (66.7)	4 (33.3)	.690
	- No	29 (60.4)	19 (39.6)	
Body weight	- Normal	35 (61.4)	22 (38.6)	.570
	- Underweight	2 (66.7)	1 (33.3)	
Anemia	- Positive	6 (50)	6 (50)	.353
	- Negative	31 (64.6)	17 (35.4)	
Previous febrile convulsion	- Yes	8 (66.7)	4 (33.3)	.690
	- No	29 (60.4)	19 (39.6)	
Gestational age	- Preterm	1 (33.3)	2 (66.7)	.300
	- Full term	36 (63.2)	21(36.8)	
Mode of delivery	- Vaginal delivery	24 (55.8)	19 (44.2)	.138
	- Caesarean section	13 (76.5)	4 (23.5)	
Crying at birth	- Cried immediately	34 (60.7)	22 (39.3)	.570
	- Not cried immediately	3 (75)	1 (25)	
Family history of febrile seizure	- Yes	15 (60)	10 (40)	.822
	- No	22 (62.9)	13 (37.1)	
Consanguinity marriage	- Yes	28 (65.1)	15 (34.9)	.382
	- No	9 (52.9)	8 (47.1)	
Total		37 (61.7)	23 (38.3)	

^a In this table, repetitive seizure had compared with simple febrile seizure (FC) which is non-repetitive. Those who had other features of complex FC (i.e. prolonged and generalized features) had been excluded from this table to avoid their bias effect on variables, so the number of all included patients were 60.

Table (6): Significance of the effect of patients' characters and variables on the distribution of febrile convulsion.

Variable		Distribution of febrile seizure ^a		p Value
		Generalized number (%)	Focal number (%)	
Age	- 1 mo- < 2 yr	23 (74.2)	8 (25.8)	.968
	- 2 yr- 5yr	14 (73.7)	5 (26.3)	
Sex	- Male	19 (65.5)	10 (34.5)	.108
	- Female	18 (85.7)	3 (14.3)	
Cause of fever	- Respiratory	26 (81.3)	6 (18.7)	.119
	- non- respiratory	11 (61.1)	7 (38.9)	
Duration of fever before seizure	- Equal or less than hour	9 (81.8)	2 (18.2)	.503
	- More than 1 hour	28 (71.8)	11 (28.2)	
Pretreatment with antibiotics	- Yes	8 (66.7)	4 (33.3)	.506
	- No	29 (76.3)	9 (23.7)	
Body weight	- Normal	35 (74.5)	12 (25.5)	.962
	- Underweight	2 (66.7)	1 (33.3)	
Anemia	- Positive	6 (66.7)	3 (33.3)	.580
	- Negative	31 (75.6)	10 (24.4)	
Previous febrile convulsion	- Yes	8 (72.7)	3 (27.3)	.913
	- No	29 (74.4)	10 (25.6)	
Gestational age	- Preterm	1 (100)	0	.549
	- Full term	36 (73.5)	13 (26.5)	
Mode of delivery	- Vaginal delivery	24 (66.7)	12 (33.3)	.058
	- Caesarean section	13 (92.9)	1 (7.1)	
Crying at birth	- Cried immediately	34 (72.3)	13 (27.7)	.290
	- Not cried immediately	3 (100)	0	
Family history of febrile seizure	- Yes	15 (71.4)	6 (28.6)	.724
	- No	22 (75.9)	7 (24.1)	
Consanguinity marriage	- Yes	28 (80)	7 (20)	.140
	- No	9 (60)	6 (40)	
Total		37 (74)	13 (26)	

^a In this table, focal seizure had compared with simple febrile seizure (FC) which is generalized. Those who had other features of complex FC (i.e. prolonged and repetitive features) had been excluded from this table to avoid their bias effect on variables, so the number of all included patients were 51.

Discussion

This study takes care for the commonest cause of seizure in pediatric age group, febrile seizures. Although it has a good prognosis, many problems may be related, including status epilepticus, recurrences and epilepsy later on. This study is a trial to determine who is the child more prone to experience a complex febrile seizure (in particular, prolonged febrile seizure) and will be at a risk for their consequences.

Within seven months of the study, 76 neurologically normal children with febrile convulsion had admitted to the emergency unit of the hospital, completed the interview and enrolled in the study, 4 patients were excluded due to missed data and a significant number of febrile convulsive children were not enrolled in the study because of having cerebral palsy or other neurological insult.

The included patients were distributed between simple FS 37 (48.7%) and complex type 39 (51.3%), these proportions were inconsistent with other studies. In Iran,

Gourabi and Bidabadi *et al.* (2012) found 81.8% of the patients had simple febrile seizure and 18.2% with CFS and Hosseini and Daipariz *et al.* (2006) reported that simple and complex types of febrile convulsions were 76.4% and 23.6%, respectively, whereas Waruiru, Appleton, Deng and Zulkifli *et al.* (2004, 1994) revealed that atypical criteria reached to 33.3% and 35% of children [5,13-15]. A significant ratio of seizures in the present study were complex may be due to that all enrolled patients were admitted and then recruited from the emergency unite, resulting in recognizing children with more severe convulsions and led to under-presentation of children with simple seizures who were managed in a pediatrician's clinics and sent home.

Of those 39 children having CFS, the complex features were distributed as follows: 23 (59%) repetitive, 14 (36%) prolonged, and 13 (33%) focal (some patients had more than one complex criteria), so multiple seizure attacks within 24 hours is the most frequent feature of CFS and this was comparative with other studies. In the CHES cohort study (Verity 2015), 95 children have CFS, distributed into: 55 (58%) repetitive, 32 (34%) prolonged, and 17 (18%) focal and also some had more than one complex feature and Gourabi *et al.* (2012) found 59% had the repetitive type, 20.5% had the focal type and 20.5% prolonged seizure [13][16]. In this study, the complex criteria were unrelated among each other, this mean that displaying of one feature don't necessarily increase the chance of having another one, in other words, certain complex feature will not predispose the child to have another one. Farwell & Blackner *et al.* (1994) found that focal seizures were much more likely to be of long duration ($p < .001$), the different conditions of the current study, including exclusion of neurologically abnormal children, may be

implicated to exhibit this an altered results [17].

Thirty (39%) children of the enrolled sample were under 1 year and 48 (63.1%) below 2 years and these represent the most affected age groups as reported in Gourabi *et al.* [13]. CFS was approximately evenly distributed above and below 2 years old, making the age unrelated to CFS or its criteria separated (repetitive, prolonged, and focal). These findings were supported by many studies, but Gourabi *et al.* has observed a significant relationship of repetitive febrile seizure with children younger than 2 years [13][18][19]. Most of the repetitive seizures in the current study were also below 2 years old, but the small sample size of these seizures may produce insignificant relationship. In another study (Farwell *et al.*, 1994), febrile seizures in children aged 8 to 11 months were more than twice as likely to be longer than 15 minutes ($p = .015$) [17].

Male gender comprises 56.6% of the enrolled patients, this slight predominance of febrile seizure in males was supported by Gourabi *et al.* and Farwell *et al.* whereas it was more presented in another study, 1.5:1 [13][15][17]. However, the male to female ratio is irrelevant because it must be counted along with the ratio of the population of the study. Focal FS was more prevalent among the male gender. Nevertheless, this association was statistically not significant and this was supported by another studies [13][18][19].

Simple febrile seizures of most patients in the current study were significantly associated with respiratory causes of fever, whereas a non-respiratory causes are most likely predominant in prolonged FS. This may reveal the extreme risk of FS when it is associated with non-respiratory causes and this may be due to the degree of associated fever or due to an unexplained reason related

to the febrile illness itself. Regarding the duration of fever before convulsion, it was clear that most of the children had a fever more than one hour before convulsion and there were no differences between SFS and CFS, as well as their features separated. Pre-treatment with antibiotics before convulsion didn't affect the type of FS. It is noteworthy that the use of antibiotics in most enrolled children was arbitrarily and was not directed to the bacterial cause of the febrile illness, so it was assumed that it has no role in changing the behavior of FS.

This study showed that the previous febrile convulsion is not associated with either single or combination of complex features, this was supported by other studies which exhibit an inconsistent relationship between CFS and recurrence [16][20][21].

Regarding body weight, Fallah and Tirandazi *et al.* (2013) showed no significant differences between CFS and SFS [19]. This was concordant with our results which showed a trivial weight variation in both groups.

Febrile convulsion is inherited in certain families by autosomal dominant pattern, however, it had no significant mode of inheritance in most families [4]. In this study, history of consanguinity marriage had high significant association with non- prolonged FS when compared with prolonged FS, so most of the prolonged FS associated with non-consanguineous parents. This was disagreed by Ozaydin and Arhan *et al.* (2012) who found that consanguinity marriage is statistically related to CFS [18]. This dissimilarity may be due to differences in the inherited genes causing the disorder. However, consanguineous marriage has a clear impact on the autosomal recessive disorder, so this mode of inheritance, although previously not mentioned, may be related to FS.

Many studies (Habibian and Alipour *et al* and Johnston, 2014, 2012) identified anemia as a risk factor for FS, it was postulated that iron deficiency anemia (IDA) has been associated with alterations in synaptic neurotransmitter systems, including gamma-aminobutyric acid (GABA), norepinephrine, dopamine, glutamate, and serotonin [22][23]. A previous studies found a significant relationship between iron deficiency anemia and CFS, in the present study, anemia was also more prevalent among CFS patients, but this relationship was statistically not significant, this may be due to the involvement of various causes of anemia in the current study other than IDA [18][19].

Family history of FS in the present study was unrelated to the type of convulsion. This was consistent with Ozaydin *et al.* who noted that family history of FS was not different between SFS and CFS [18].

Although vaginal delivery is the natural mode of delivery, it was found that it is statistically related to CFS, hypoxic- ischemic disorders seem to be unlikely related because most of the enrolled children cried immediately after birth and they didn't be admitted to the neonatal care unit. This association may be due to unrecognized factors favor cesarean section as a protective against CFS.

In previous studies (Deng and Zulkifli *et al.*, 1994), the rate of prematurity among children with febrile seizures varied from 0.9 % to 12.6% [24]. In this study 3 children (3.9 %) were delivered prematurely, 2 of them were having CFS, but not significantly associated. Ozaydin *et al.* found a significant relationship between CFS and gestational age and birth weight [18]. However, the statistical analysis of the small sample size cannot be tested efficiently.

In summary, a few criteria have an effect on the features of febrile seizures, others were

unrelated, whereas some factors need another wide study because they were not assessed effectively due to small sample size, which can be considered a limitation of this work.

In conclusion, there were only a few criteria predispose the child for complex febrile seizure, including non- respiratory causes of febrile illnesses, vaginal delivery, non-consanguineous parents, and possibly prematurity; therefore complex febrile seizures cannot be entirely predicted, but a trend can be expected if these mentioned factors were associated.

We suggest to do another study taking in consideration the genetic analysis of patients of both groups "simple and complex febrile seizures.

References

- [1] International League Against Epilepsy (ILAE). Guidelines for epidemiologic studies on epilepsy. *Epilepsia*. 1993; 34(4):592–6.
- [2] Hirtz DG. Febrile seizures. *Pediatrics in Review*. 1997; 18(1):5–9.
- [3] Mikati MA, Hani AJ. Febrile Seizures. In: Robert M. Kligman, Bonita F. Stanton, Joseph W. St Geme, Nina F. Schor, editors. *Nelson textbook of pediatrics*. 20th ed. Philadelphia: Elsevier, Inc.; 2016 p. 2829-31.
- [4] Mikati MA, Rahi A. Febrile seizures: from molecular biology to clinical practice. *Neurosciences*. 2004; 10:14–22.
- [5] Waruiru C, Appleton R. Febrile seizures: an update. *Arch Dis Child*. 2004; 89:751-56.
- [6] Huang MC, Huang CC, Thomas K. Febrile convulsions: development and validation of a questionnaire to measure parental knowledge, attitudes, concerns practices. *J. Formos Med Assoc*. 2006;105(1):38–45.
- [7] Annegers JF, Hauser WA, Shirts SB, Kurland LT. Factors prognostic of unprovoked seizures after febrile convulsions. *N Engl J Med*. 1987;316(9):493–8.
- [8] Trinkaus E, Unterrainer J, Haberlandt E, Luef G, Unterberger I, Niedermüller U, *et al*. Childhood febrile convulsions-which factors determine the subsequent epilepsy syndrome? A retrospective study. *Epilepsy Res*. 2002; 50(3):283-92.
- [9] - Baumer JH. Evidence based guideline for post-seizure management in children presenting acutely to secondary care. *Arch Dis Child*. 2004; 89:278–80.
- [10] Farrell K , Goldman RD. The management of febrile seizures. *BCM J*. 2011; 53(6):279-85.
- [11] WHO Child Growth Standard (<http://www.who.int/childgrowth/en>) .
- [12] Brugnara C, Oski FJ, Nathan DG. Normal Mean and Lower Limits of Normal for Hemoglobin, Hematocrit, and Mean Corpuscular Volume. In: Nathan and Oski's hematology of infancy and childhood. 7th ed. Philadelphia; WB Saunders; 2009 p. 456.
- [13] Gourabi HE, Bidabadi E , Cheraghali-pour F, Aarabi Y, Salamat F. Febrile Seizure: Demographic Features and Causative Factors. *Iran J Child Neurol*. 2012. 6(4): 33-7 .
- [14] Hosseini NA, Daipariz M, Alidousti K. Demographic characteristics and predisposing factors of febrile seizures in children admitted to Hospital No. 1 of Kerman University of Medical Sciences. *J Med Counc Islam Repub Iran*. 2006;24(2):107–12.
- [15] Deng CT, Zulkifli HI, Azizi BH. Febrile seizures in Malaysian children: epidemiology and clinical features. *Med J Malaysia*. 1994 ;49(4):341-7.
- [16] Verity CM. Febrile convulsions a practical guide. In: ILAE Lecture Notes in Epilepsy. 15th ed. 2015. Chapter 8 p. 75- 88.
- [17] Farwell JR, Blackner G, Sulzbacher S, Adelman L, Voeller M. First febrile seizures. Characteristics of the child, the seizure, and the illness. *Clin Pediatr (Phila)*. 1994; 33(5):263-7.
- [18] Ozaydin E, Arhan E, Cetinkaya B, Ozdel S, Değerliyurt A, Güven A, *et al*. Differences in iron deficiency anemia and mean platelet volume between children with simple and complex febrile seizures. *Seizure*. 2012; 21(3):211-4.
- [19] Fallah R, Tirandazi B, Akhavan Karbasi S, Golestan M. Iron Deficiency and Iron Deficiency Anemia in Children with Febrile Seizure. *Iran J Ped Hematol Oncol*. 2013; 3(1): 200–3.
- [20] Berg AT, Shinnar S, Hauser WA, Alemany M, Shapiro ED, Salomon ME, *et al*. A



Prospective Study of Recurrent Febrile Seizures.

N Engl J Med. 1992; 327(16):1122-7.

[21] Reese C. Graves, Karen Oehler, Leslie E Tingle. Febrile Seizures: Risks, Evaluation, and Prognosis. Am Fam Physician. 2012; 85(2):149-153.

[22] Habibian N, Alipour A, Rezaianzadeh A. Association between Iron Deficiency Anemia and Febrile Convulsion in 3- to 60-Month-Old Children: A Systematic Review and Meta-Analysis. Iran J Med Sci. 2014; 39(6): 496–505.

[23] Johnston MV. Iron deficiency, febrile seizures and brain development. Indian Pediatr. 2012;49(1):13-14.

[24] Deng CT, Zulkifli HI, Azizi BH. Febrile Seizures in Malaysian Children: Epidemiology and Clinical Features. Med J Malaysia. 1994; 49(4):341.-741.