

## Characteristics of Febrile Convulsions and The Association Between Ketonuria and Febrile Convulsions

Najdat Sh Mahmood (PhD)<sup>1</sup>, Oday Abood Khalil (PhD)<sup>2</sup>, Jalil Ibrahim Alezzi  
(PhD)<sup>3</sup>

<sup>1</sup> College of Medicine, University of Diyala, Diyala, Iraq

<sup>2</sup> Al-Batool Teaching Hospital ,Baqubah, Diyala, Iraq

<sup>3</sup> College of Medicine, University of Diyala, Diyala, Iraq

Correspondence Address:

Dr. Jalil Ibrahim Alezzi

College of Medicine, University of Diyala, Baqubah, Iraq

email: [jalilkadim@gmail.com](mailto:jalilkadim@gmail.com) mobile 009647734132897

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### Abstract

**Background:** Febrile seizures are common and mostly benign. There is growing evidence that ketone bodies derived from fatty acid oxidation during fasting or consumption of high-fat diets can exert broad neuroprotective effects, including anti-convulsant effects.

**Objective:** To determine the characteristics of febrile convulsions and the relationship between ketonuria and febrile convulsions.

**Patients and Methods:** A cross-sectional comparative study was done between May 2018 – December 2019 at Al-Batool teaching hospital. The data included 100 children aged between (6- 60 months) admitted to the emergency unit, 50 % of them were having a febrile convulsion, while the others were presented with fever without a seizure. Blood samples were measured for serum glucose and urine samples were taken for level of ketone bodies (KB) and analyzed by reagent strip test. Statistical analysis was done by using SPSS version 21, level of association between variables was tested by Chi-square at 0.05.

**Results:** Febrile convulsions occur equally in males and females and more likely in children less than 18 months of age (P value=0.157). Causes of fever in children with febrile convulsion were mostly respiratory causes (p value=0. 000). The incidence of hypoglycemia and ketonuria were slightly more common in the non-convulsive group of the study to be statistically insignificant (p- values were 0.169 and 0.275, respectively).

**Conclusion:** The febrile convulsions affect equally males and females and the major cause of fever was respiratory infections. There is no significant relationship between ketonuria and the occurrence of febrile convulsions.

**Keywords:** Febrile convulsion; Ketonuria; Children

## Introduction

Febrile seizures (FS) are the single most common seizure type and occur in 2 to 5% of children younger than 5 years of age with a peak incidence in the second year of life [1]. Neurological sequelae rarely result from either simple or complex febrile seizures [2-5]. Ketone bodies (acetoacetic acid, beta-hydroxybutyric acid, and acetone) are low in the blood and urine of normal individuals in the postprandial or overnight-fasted state. However, these ketoacids become important sources of metabolic energy in circumstances in which the availability of glucose is restricted [6]. The ketogenic diet (KD) is particularly aimed at treating children and adolescents with refractory epilepsy, regardless of the etiology [7]. The KD was developed in 1920 by Wilder and many studies have shown its positive effects, including an over 50% reduction in seizures, which is considered to be clinically relevant [8,9]. During KD, long-chain fatty acids are metabolized in the liver and converted into KBs. These fatty acids are oxidized in the mitochondria, producing high levels of acetyl-CoA, which cannot be oxidized in the Krebs cycle. The excess acetyl-CoA is converted to acetoacetate and subsequently to acetone and  $\beta$ -hydroxybutyrate ( $\beta$ OHB). The KBs cross the blood-brain barrier and are transported by monocarboxylic acid transporters to the brain interstitial space, the glia, and the neurons. In these sites, the KBs act as substrates in the Krebs cycle and respiratory chain, contributing to brain energy metabolism [10]. Long viewed as a simple carrier of energy from the liver to

peripheral tissues during prolonged fasting or exercise [11]. Ketonuria ensues in actual or functional carbohydrate-deficient states when metabolism switches from using carbohydrates to fat to produce energy [12]. The aim of this study is to determine the characteristics of febrile convulsions and the association between ketonuria and febrile convulsions.

## Patients and Methods

This is a cross-sectional comparative study, done within the period of 19th of December 2018 - 6th of March 2019 at the Pediatric Department in Al-Batool Teaching Hospital for Maternity and Children. A self-administered questionnaire was used for data collection.

## Data and definitions

The data included 100 children aged between 6- 60 months, 50 of them were febrile children without convulsions or previous history of convulsions (called as a febrile non- convulsive group), the other 50 children were presented with fever and convulsions (diagnosed as febrile convulsion, called a febrile convulsive group). Diagnosis of febrile convulsion was done after exclusion of central nervous system infection, epilepsy, metabolic disorders, electrolyte changes, and head trauma or malformations [1-3].

## Laboratory analysis

Blood samples of about (5) ml were aspirated and tested for complete blood picture, C-reactive protein level, serum glucose level. KB in urine, the results were

shown as the following: negative, one plus (+) equal to 5mg/dl, and two pluses (++) equal to 15 mg/dl [4].

### Statistical analysis

It was done by using Statistical Package of Social Sciences (SPSS) version 21, data was presented by frequencies, level of association was tested by Chi-square, P value was taken at the level of (0.05) to be significant.

### Results

**Table (1):** Demographic and physical criteria of febrile convulsions group

Characteristics	No. (%)	p-value
Age		
<18mon.	30 (60%)	0.157
>18mon.	20 (40%)	
Gender		
Male	25 (50%)	-
Female	25 (50%)	
Body weight		
Normal	42 (84%)	0.000
Underweight	8 (16%)	
Height		
Normal	46 (92%)	0.000
Below normal	4 (8%)	

The causes of fever in most of the febrile convulsive group of children were respiratory causes (n=37, 74%, P value= 0.000), including URTI, tonsillitis, otitis media, while the others developed fever due to other causes, including gastroenteritis. Regarding criteria of febrile convulsions, simple febrile convulsion criteria were more identified in

It was found that febrile convulsions occur equally in both males and females; it was insignificantly more developed in children less than 18 months of age (n= 30, 60 %). Regarding growth parameters, most of the cases of febrile convulsive children (84%) had normal weight and 16 % were underweight; 92% of them had normal height and 8% were below normal height, as shown in the Table (1).

this study, it showed that 76% of children having a convulsion with a duration  $\leq$  than 15 minute, two-third of them had no recurrence of convulsion within 24 hours, and the most predominant type of convulsions was generalized tonic-clonic type (94%), Table (2).

**Table (2):** Criteria of convulsions in febrile conclusive group

Character	No. (%)	p-value
Duration		
$\leq$ 15 minutes	38(76%)	0.000
>15minutes	12(24%)	
Recurrent in 24 hour		
Recurrence	17(34%)	0.024
No recurrence	33(66%)	
Type		
Generalized	47(94%)	0.000
Focal	3(6%)	

In this study, it had been found that hypoglycemia was more detected in the non-convulsive group of the study (8%) while in the convulsive group it happened in 2%, at the same time, more ketonuria detected in the non-convulsive group with one plus in 8 patients 16% and two pluses in 2 patients 4% while in a convulsive group it was detected with one plus in 5 patients 10% and two pluses in one patient 2%, anyhow both of

these values were slightly different between groups making the results insignificant statistically, But the total number of patients who had ketonuria in both convulsive and non-convulsive groups was 16 patients distributed to 10 (62.5%) in the non-convulsive group and 6 patients 37.5% in the convulsive group which show significant finding Table (3) below.

**Table (3):** Comparison of serum glucose and ketonuria between groups of the study

Characteristics	Conclusive No. (%)	Non convulsive No. (%)	Total No. (%)
Serum glucose <sup>a</sup>			
Normal	49(98%)	46(92%)	95(95%)
Hypoglycaemia	1(2%)	4(8%)	5(5%)
Ketonuria <sup>b</sup>			
+	5(10%)	8(16%)	13(13%)
++	1(2%)	2(4%)	3(3%)
Negative	44(88%)	40(80%)	84(84%)

<sup>a</sup> p value (0.169), <sup>b</sup> p value (0.275)

## Discussion

According to the results of this study, febrile convulsions occur insignificantly more in children less than 18 months of age this result may indicate that most infections that cause fever especially respiratory causes occurred in children less than 18 months. This is compatible with the study done by Berg et al [4], but it was not agreed with as Sugai study which showed the peak incidence occurs at approximately 18 months of age and is low before 6 months or after 3 years of age [14]. Also it was not agreed with study done by Shinnar, Glauser who showed febrile seizures had a peak incidence at 18 months of age and are most common between 6 months and 5 years [15]. This finding may be due to difference in a number of patients among studies and may be due to social

differences or may be due to difference in the most common type of infection which causes febrile convulsion in these studies. Regarding gender, this study showed that males and females are equally affected, which is almost in agreement with Habib et al. in Pakistan who found that the male sex had a 1.3 times greater risk of febrile seizure [16]. Stafstrom (2002) showed males had consistently emerged as having a higher frequency of febrile seizure (male to female ratio, 1.1:1 to 2:1) [17], This finding also may be due to the difference in a number of patients that were taken among these studies, and statistically insignificant differences.

About growth parameters in this study most of the children had normal weight and only 16% were underweight. Most of the patients

(92%) had normal height, There is no evidence that showed a relation between height and febrile convulsion which indicated that the metabolic and brain malformations may affect the growth. We found upper respiratory tract infection (URI) is commonly associated with febrile seizures 74%, URI was the most important cause of fever in other studies [18-22], This finding may be due to low socioeconomic state which leads to overcrowding and poor hygiene that make respiratory causes more common and may be due to easy transmission of respiratory diseases and comparable with other studies such as Khodapanahande in his survey in Tehran found that nonspecific viral diseases are the main cause of a febrile seizure, with a frequency of 82% [23] and Mahyar et al. in 2010 and Kolahi et al. in 2009 encountered respiratory tract infection as the most prevalent cause of febrile seizure [24,25]. Millichap JJ.,(2008) showed that febrile seizures due to infection were predominantly upper respiratory tract infection in which the cause was unknown or bacterial in the first half of the twentieth century [26]. In Japan a study of febrile seizure showed two peaks of incidence, November to January and June to August, which correspond to peaks of viral upper respiratory infections and gastrointestinal infections, respectively [27]. Regarding criteria of febrile convulsions, this study showed that most of the febrile convulsions had a duration equal or less than 15 minute, This finding may be due to a normal brain structure of febrile convulsive patients which similar to Berg, and Shinnar who showed that 87% of children, the duration of the febrile seizure is less than 10 minutes; while seizures last more than 15

minutes in only 9% of children[28]. About one-third of our patients had recurrent fit within 24 hours, which is comparable with that of Berg and Shinnar. [28]. This study showed that most convulsions were generalized tonic-clonic type like that of the Sugai. study [14]. Many studies showed that febrile seizures are predominantly brief, generalized tonic-clonic seizures, and 4-16% have focal features [28-30]. About hypoglycemia it occurred in only 5%, but 95% of all cases have no hypoglycemia and most of them reported in non – convulsive group 8% and this agreed with Valerio et al. [31]. Ketonuria doesn't reflect real serum KB, ketonuria occurs usually with hypoglycemia which is more in non – convulsive group, this may be a natural response to hypoglycemia to provide energy to the brain and prevent seizures. Of importance both hypoglycemia and ketonuria were less in the febrile convulsive group. This may be due to accidentally discovered or it may reflect that ketonuria was protective in non-convulsive group because febrile convulsion may cause psychological trauma to the parents in our society. So, we can benefit from ketogenic diet in order to further decrease.

## Conclusions

In conclusion, febrile convulsions affect equally males and females and the major cause of fever was respiratory infections. There is no significant relationship between ketonuria and occurrence of febrile convulsions.

## Recommendations

The incidence of febrile convulsions. We recommend a wide-scale study using serum

level of ketone bodies to solidify the results of this study about the relationship between ketogenic diet and febrile convulsions hope to decrease the incidence of febrile convulsions.

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**Ethical clearance:** This study was approved by medical ethics committee of college of medicine ,university of Diyala.

**Conflict of interest:** The authors declare that there is no no conflict of interest .

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