

The Etiologic Profile of the Pediatric Seizure: An Epidemiological Study from Iran

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ABSTRACT

Background: Seizures are one of the most common neurologic disorders in children. The aim of this study is to determine the main etiologies of seizure in children.

Methods: Children with a complaint of seizure in Loghman Hakim hospital, from June 2014 to January 2016 were evaluated. The final diagnosis of seizure was made by a pediatric neurologist. The age, sex, type of seizure, associated fever, history of head trauma and other variables related to seizure in pediatric group were reviewed from the medical records.

Results: A total of 200 children with a diagnosis of seizures were included in this study. A total of 59% were male patients. The age of the patients ranged from 3 months to 102 months with a mean of 23 months. About one-quarter of the patients had focal seizures while others had generalized seizures. Sixteen patients (8%) had a positive family history of epilepsy. Of total 126 patients (63%) experienced their first lifetime seizure. The body temperature of the patients ranged from 36.1 °C to 39.8 °C with a mean of 38.2 °C. The etiologies of seizures were febrile seizure (82%), vaccine-associated seizures (3%), hypoglycemia (6%), hypocalcemia (2%), hyponatremia (2%), encephalopathy (2%), hyperglycemia (1%), epilepsy (1%) and intracerebral hemorrhage (1%).

Conclusion: While fever is the most common etiology of seizure in children, hypoglycemia should be taken into consideration as the second most common etiology of seizure. Although other etiologies such as hyponatremia and intracerebral hemorrhage are less common, they should be kept in mind due to their life-threatening complications. Hence, the results of this study underscores the importance of history and laboratory findings of the children with seizure.

Keywords: Seizures; Pediatrics; Febrile Seizures

INTRODUCTION

Seizures are the most common neurologic emergency in pediatrics and can be terrifying for patients and families. They occur in approximately 4-10% of children and account for 1% of all emergency department visits ¹. There are a variety of potential causes for

seizures; however, they have a final common pathway which includes abnormal electrical discharges of neurons. The extent of this abnormal discharges and their location in the brain leads to a variety of clinical presentation which range from subtle, nonconvulsive events to dramatic generalized convulsions ². Although some types

of seizure such as simple febrile seizures are benign and self-limited in essence³, others can cause brain damage or death. Furthermore, current controversies on benefits of neuroimaging, electroencephalography and different laboratory panels in the management of children with seizure underscores the importance of investigating etiologic profile of it.

Common etiologies of a first attack of seizure in children include infection/fever, developmental/neurological disorders, traumatic head injury and metabolic disturbances⁴. Febrile seizures are the most common type of childhood seizures, occurring in 2 to 5 percent of children six months to five years of age⁵. In a study by Chen, et al, 68% of patients with first attack of seizure were presented to emergency department with fever and about 62% of them were finally diagnosed as febrile seizure⁶. Although febrile seizure have a good prognosis, coexistence of fever and seizure is also seen in bacterial meningitis which is often associated with poor outcomes⁷.

Due to different potential etiologies, first attack of a non-febrile seizure often pose a great diagnostic challenge. Sever electrolyte imbalance, i.e., hypocalcemia or hyponatremia, and hypoglycemia are reported to be the etiology of seizure in less than 1% of children⁶. Although mild traumatic brain injury in children is associated with a low risk for posttraumatic seizures, the rate of posttraumatic seizure may be as high as 19% in sever cases⁸. Therefore, the necessity of routine arrangement of neuroimaging and examination of glucose, electrolytes and calcium in the patients with first attack of non-febrile seizure is under debate. This uncertainty regarding the initial management of the childrens with seizure underscores the importance of investigation of etiologic profile of pediatric seizures in every region.

MATERIALS AND METHODS

This is a descriptive hospital-based study conducted in the department of Pediatrics, Loghman hospital, during the period from May 2013 to April 2015. All the children below 12 years of age who were hospitalized at emergency department were enrolled in this study. Neonates, patients with previous history of epilepsy, patients who had an underlying disease, such as metabolic disorders, and children with seizures onset after hospitalization were excluded.

Information such as age, sex, nature of seizure, fever, history of head trauma, infectious diseases, intoxication and developmental history were obtained from each patient. In each patient following laboratory tests were obtained: serum electrolytes and blood sugar. Seizures

were classified into generalized tonic-clonic (GTC) and partial based on the Commission on Epidemiology and Prognosis, 1993 International League Against Epilepsy⁹. Febrile seizure was defined by the 1993 International League Against Epilepsy as, “an epileptic seizure occurring in childhood after 1 month of age, associated with febrile illness not caused by an infection of the central nervous system, without previous neonatal seizure or previous unprovoked seizure, and not meeting criteria for other acute symptomatic seizure”⁹. The study was approved by the ethics committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Descriptive statistics and testing of hypothesis were used for the analysis. The data was analyzed using SPSS V.16.0 (SPSS Inc; Chicago, IL, USA). The Chi-square test was used to examine the association between different variables. Strength of the relationships were determined using logistic regression analysis. Odds ratios and their 95% confidence intervals (95% CI) were calculated. $P < 0.05$ was considered as statistically significant.

RESULTS

A total of 200 children presented to the emergency department with a first attack of seizure were included in this study. The mean age of participants was 22.63 ± 16.94 months and 41% of them were female. The body temperature of the patients ranged from 37 °C to 39.5.2 °C with a mean of 38.2 °C. In this study, 112 (56%) of the children who presented with a first attack of seizure were between 1-3 years old (Table 1). The prevalence of seizure was significantly higher in females compared to males in 4-6 years old age group. Among the patients enrolled in this study, 148 (74%) presented with generalized seizure and 52 (26%) had focal seizure. No difference was observed between the prevalence of type of seizure between males and females. Family

history of seizure-related disorders was noted in only 16 (8%) patients. A previous history of seizure was mentioned in 74 (37%) patients. Febrile seizure was the most common etiology of seizure in this study (82% of patients). No significant difference was observed in the prevalence of seizure between males and females. Hypoglycemia (6% of the patients) and vaccine-associated seizure (3% of the patients) were the second and third common etiologies of seizure in our list (Table 1).

Table 2 shows distribution of the etiologies of seizure based on the age groups. Except the patients aged 7-12 years old, febrile seizure was the most common etiology of seizure. Hypoglycemia and vaccine-associated etiologies of seizure were more common in the 1-3 years age group.

Table 1. Descriptive statistics of patients with a first attack of seizure disorder.

	Total (n=200)	Male (n=118)	Female (n=82)	P-value
Age (yrs)				
< 1	40 (20%)	25 (21%)	15 (18%)	0.24
1-3	112 (56%)	69 (58%)	43 (53%)	0.75
4-6	44 (22%)	21 (18%)	23 (28%)	0.06
7-12	4 (2%)	3 (3%)	1 (1%)	0.52
Type of seizure				
Generalized	148 (74%)	90 (76%)	58 (71%)	0.12
Focal	52 (26%)	28 (24%)	24 (29%)	0.08
Etiology of seizure				
Febrile seizure	164 (82%)	98 (83%)	66 (80%)	0.82
Hypoglycemia	12 (6%)	6 (5%)	6 (7%)	0.65
Vaccine-associated	6 (3%)	2 (2%)	4 (5%)	0.06
Hypocalcemia	4 (2%)	4 (3%)	0 (0%)	0.09
Hyponatremia	4 (2%)	2 (2%)	2 (3%)	0.16
Encephalopathy	4 (2%)	2 (2%)	2 (3%)	0.07
Hyperglycemia	2 (1%)	0 (0%)	2 (3%)	0.84
Epilepsy	2 (1%)	2 (2%)	0 (0%)	0.34
Intracranial Hemorrhage	2 (1%)	2 (2%)	0 (0%)	0.27
Family history of seizure	16 (8%)	11 (9%)	5 (6%)	0.08
Previous history of seizure	74 (37%)	47 (40%)	27 (33%)	0.21

Table 2. Distribution of the etiology of seizure based on the age groups.

	<1 year N (%)	1-3 years N (%)	4-6 years N (%)	7-12 years N (%)
Febrile seizure	29	95	40	0
Hypoglycemia	2	6	2	2
Vaccine-associated	1	4	1	0
Hypocalcemia	2	2	0	0
Hyponatremia	1	2	0	1
Encephalopathy	2	1	0	1
Hyperglycemia	0	1	1	0
Epilepsy	2	0	0	0
Intracranial Hemorrhage	1	1	0	0
Total	40	112	44	4

DISCUSSION

This was a hospital based cross-sectional study of children admitted with acute episode of seizure in Loghman hospital, Tehran, Iran, during the period from May 2013 to April 2015. The study aimed to determine the main etiologies and potential sex-specific pattern of seizure in children admitted to emergency department. Our results show that except the 7-12 years age group, febrile seizure is the most common etiology of seizure in all age groups. No sex-specific difference was observed between the prevalence of etiology of seizure in males and females.

Majority of the patients in this study were male (59%) which is consistent to study done by Al Sulaiman AA et al where they had 153 males out of 263 children¹⁰. It is

notable that most of the patients were between 1-3 years old (56%) and 4-6 years old (22%) and <1 year old (20%), respectively. These results corroborate to the findings of previous studies which show a low prevalence of seizure in children aged >6 years old^{11,12}. This result is related to the high prevalence of patients with febrile seizure in these age groups. Febrile seizures have been reported as one of the most common cause of seizure attack in children¹³. Our results show that febrile seizure (82%) was the main etiology of seizure in patients admitted to emergency department. Upper respiratory tract infection and systemic viral infections are reported to be the main underlying diagnoses in febrile seizure⁶. Interestingly, a study in Nepal showed that the most common cause of seizure in their patients was seizure disorder (33.4%) which was followed by febrile seizures (30.7%)¹¹. This shows that the etiology of seizure differs in different populations and in different places.

Hypoglycemia was the second most common etiology of seizure in our study. Idiopathic ketotic hypoglycemia is the most common etiology of hypoglycemia beyond infancy in non-diabetic children^{14,15}. Other Potential etiologies of hypoglycemia presenting in infancy and the toddler years include glycogen storage disorders and other inborn errors of metabolism, hypopituitarism, ingestions, and sepsis¹⁶. Although in a study by Chen et al in Taiwan⁶, hypoglycemia was an infrequent cause of seizure, our results recommend measuring blood sugar level in every child with seizure, routinely. Vaccination

was another common etiology of seizure in our population. Administration of the diphtheria and tetanus toxoids and whole-cell pertussis (DTP) vaccine and measles, mumps and rubella (MMR) vaccine has been associated with adverse neurologic events, including seizures¹⁷. In this study, we considered seizures in children with a history of vaccination during 14 days before, even when they were febrile, as vaccination seizure. No afebrile child was detected with a vaccination seizure. Hence, it seems that vaccination causes seizure by inducing fever. Barlow et al, reported significantly elevated risks of febrile seizures on the day of receipt of DTP vaccine and 8 to 14 days after the receipt of MMR vaccine. Neither vaccination was associated with an increased risk of nonfebrile seizures in their study¹⁷. However, vaccination-related seizure may be onset of epilepsy¹⁸. Hence, These results have significant added value in counseling of parents of children with vaccination-related first seizures, and they might help to support public faith in vaccination programs.

No sex-specific difference was observed between the prevalence of etiologies of seizure. Moreover, prevalence of type of seizure was not different between males and females. However, in adults, Clinical and experimental evidence supports the role of sex and influence of sex hormones on seizures and epilepsy as well as alterations of the endocrine system and levels of sex hormones by epileptiform activity¹⁹.

In this study, generalized seizure was the most common type of seizure which accounted 74%. Study by Adhikari¹¹ and others^{6,20} revealed that majority of seizures as generalized one. In contrast, the majority of seizures in the study by Kaaranen T et al were focal in nature²¹. This may be because most of the patients had febrile seizure which predominantly presents with generalized feature³.

Only 8% of the patients had a family history of seizure which most of them (15/16) had the family history of a febrile seizure (data not shown). This suggests that a negative family history of seizure can not be helpful in ruling out seizure or diagnosing its etiology. Consistently, a previous study reported that family history of seizure-related disorders was noted in only 8.2% of children presented to pediatric emergency with new-onset seizures⁶.

As one of the first, the study present a clinico-etiological profile of etiologies of Iranian children with seizure. However, our results should be interpreted in the light of certain limitations. First, the cross-sectional design of this study precludes making definitive diagnosis of the etiology of seizure in the patients. Indeed, we suggest

other researchers to follow their patients to investigate further repetitions of seizure in them and epileptiform activities. Second, we have not used imaging techniques in this study. Using these techniques in further studies helps to better elucidate the etiologies of seizure in each patient. In conclusion, age, fever coexistence, seizure type, associated symptoms, physical and neurological examinations, and history of head injury may provide important information for primary emergency physicians when evaluating children with a first attack of seizures. Routine measurement of serum blood sugar level seems to be very helpful to differentiate the etiologies of seizure in our population.

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