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Original Article

A Clinical and Epidemiological Analysis of First-Time Febrile Seizures in Children

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Abstract

Background: Febrile seizures (FSs) are the most common neurological disorder observed in the pediatric age group. In pediatric practice, seizures account for 1% of all emergency visits. They are usually defined as seizures occurring after 1 month of age associated with a febrile illness not caused by an infection of the central nervous system, without previous neonatal seizures or a previous unprovoked seizure, and not meeting the criteria for other acute symptomatic seizures.

Aim of the Study: The aim of this study is to analyze the clinical and epidemiological spectrum in children with a first attack of acute seizure disorder and its prevalence rates of various etiologies.

Materials and Methods: A total of 127 children presenting with FSs to the emergency department were evaluated at a tertiary teaching hospital of Kerala between October 2015 and September 2017. Demographic details, clinical findings, laboratory investigations, computed tomography (CT)/magnetic resonance imaging (MRI) scan brain studies, diagnoses, and hospital course were compared between FSs and patients with AFSs. These variables were also compared between patients with simple and complex FSs and among different age groups.

Observations and Results: Among 127 patients, 80 children presented with FSs (62.99%) and the remaining children with AFSs 47 (37%). 68/80 children (85%) presenting with FSs were aged below 6 years. The type of seizures was generalized tonic/clonic seizures in 49/80 of the febrile group (61.25%). The etiologies observed were electrolyte imbalance and hypoglycemia. CT scan was done in 45/127 (35.43%) children and found to be abnormal in 15/45 children (35.55%). Similarly, MRI scan was done in 18/127 (14.17%) children and found to be abnormal in 9/18 children (50%).

Conclusion: Primary care pediatricians should evaluate children presenting to the ED with a first seizure for age, coexistence of fever, seizure type, associated symptoms, and history of head injury. Routine investigations of electrolytes, blood sugar, and emergency brain imaging studies should be arranged based on detailed history taking and thorough physical examinations but should not be performed routinely.

Key words: Children, Convulsions, Febrile, Fever, Seizures

INTRODUCTION

Febrile seizures (FSs) were described in 1980 by a consensus conference held by the National Institutes of Health as "an event in infancy or childhood usually occurring between 3 months and 5 years of age, associated with fever, but without evidence of intracranial infection or defined cause."[1] However, the definition does not exclude children with prior neurological impairment and neither provides specific temperature criteria nor defines a "seizure." A definition from the International League Against Epilepsy was introduced as "a seizure occurring in childhood after 1 month of age associated with a febrile illness not caused by an infection of the central nervous system, without previous neonatal seizures or a previous unprovoked seizure, and not meeting the criteria for other acute symptomatic seizures."[2] FSs in children below 5 years account for the most common type in the out-of-hospital and ED settings.[3,4] The incidence of non-FSs in children ranges from 89 to 134 per 100,000 person years.[5] FSs are classified as simple or complex types.[6] Simple seizures are generalized last <15 min and do not recur within 24 h, and complex FSs are prolonged, recur more than once in 24 h, or are focal.[7] Complex FSs may indicate a more

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serious disease process, such as meningitis, abscess, or encephalitis. Whereas, status epilepticus is a severe type of complex FS defined as single seizure or series of seizures without interim recovery lasting at least 30 min. .Among the various etiological factors causing FSs, viral infections, either exanthematous or non-exanthematous infections are the commonest and predominant causes. Human herpes simplex virus 6 was found to be the etiologic agent in roseola in about 20% of a group of patients presenting with their first FSs.[7] *Shigella* gastroenteritis was also found to be associated with FSs.[7] One study suggests a relationship between recurrent FSs and influenza A.[7,8] FSs are known to run in families. In a child with FS, the risk of FS is 10% for the sibling and almost 50% for the sibling if a parent has FSs as well; the mode of inheritance is unclear.[9] Although the exact molecular mechanisms of FSs are yet to be understood, underlying mutations have been found in genes encoding the sodium channel and the gamma-aminobutyric acid a receptor.[10,11] Emergency care physicians in the casualty or emergency department (ED) usually have to face the challenge in primarily examining, ordering necessary investigations, and treating the first attack seizures children. After initial stabilization, the child in the ED physician has to decide whether to admit or discharge. Misdiagnosis or misjudgment carries the potential risk of legal problems. It can cause family anxiety, lead to excessive hospital stay, and possibly result in life-threatening events. In the present context, a study was conducted prospectively to analyze the prevalence of various etiologies and the clinical spectrum of seizure disorders in children who presented to the ED with the first attack of acute seizure disorder.

Type of Study

This was a prospective, cross-sectional, and analytical study.

Period of Study

The study duration was from October 2015 to September 2017.

Institute of Study

This study was conducted at KMCT Medical College Hospital, Kozhikode.

MATERIALS AND METHODS

A total of 127 children with first-time seizures attending the ED of a tertiary teaching Hospital in Kerala were included in this study. The children were classified as Group A: Children with fever and Group B: Children without fever. An Ethical Committee Clearance was obtained before commencing the study. An ethical committee cleared consent letter from parents was used for the study. The history was elicited from either one of them parents.

Inclusion Criteria

1. Children aged from 1 month to 12 years were included.
2. Children with first-time history of seizures alone were included.
3. Children with both generalized and focal epileptic features were included.
4. Children with or without a history of fever were included.
5. Children with a family history of FSs in the siblings or parents were included in the study.

Exclusion Criteria

1. Children aged above 12 years and below 1 month were excluded.
2. Children with a previous history of seizures were excluded.
3. Children with a history of tuberculosis were excluded.
4. Children with a recent history of exanthemata were excluded.
5. Children with a history of kernicterus were excluded.

All the children were initially attended by the emergency medicine physician and followed by the consultant pediatrician on call. All the children were subjected to thorough clinical examination. The following demographic data were collected: Sex, family history of seizures, type of seizures, associated symptoms (fever, cough, rhinorrhea, vomiting, diarrhea, and headache), and developmental history. Laboratory tests undertaken were as follows: White blood count, C-reactive protein, stool rotavirus antigen test, serum electrolytes, blood sugar and cerebrospinal fluid (CSF) analysis, computed tomography (CT) scan/magnetic resonance imaging (MRI) scan, electroencephalography (EEG) findings, duration of hospital stay, final diagnosis, anticonvulsants given in the ED, admission to intensive care unit (ICU), general ward, and pediatric observation unit. Children with temperature more than 38°C were grouped under febrile type: Group A. Children with temperature <38°C were grouped under afebrile type: Group B. The type of seizures was classified as generalized tonic-clonic (GTC) and generalized tonic. Status epilepticus was defined as "a single epileptic seizure of more than 30 min or a series of epileptic seizures during which function is not regained between convulsion events in a period more than 30 min long." In addition, FSs were classified as simple FSs or complex FSs. A simple FS lasts <15 min, is initially generalized in nature, and occurs once during a 24 h period. In contrast, a complex FS lasts more than 15 min, has focal features at any time, or recurs within a 24-h period. Children were divided into three age groups: Infant group (<1 year), preschool age group (1−6 years), and school age group (7−12 years). All the data were analyzed using standard statistical methods.

OBSERVATIONS AND RESULTS

Among 127 patients, 80 children presented with FSs (62.99%) and the remaining children with AFSs 47 (37%). 68/80 children (85%) with FSs were aged below 6 years. 38/47 children with AFSs were below 6 years of age (80.85%). The incidence of seizures of both groups was statistically significant with $P = 0.012$ (P significant at <0.05). The type of seizures was GTC seizures in 49/80 (61.25%) children of FSs and 28/47 of the children with AFSs (59.57%). The incidence of GTC in both the groups was statistically significant with P value at 0.018 (P significant at <0.05). Among the FS children, simple pattern of seizures was observed in 39/49 children (61.22%) and complex pattern in 10/49 (20.40%) children. The incidence of family history was also statistically significant in both groups with p value at 0.031 (P significant at <0.05) [Table 1]. 9/80 children showed delayed mile stones in the febrile group and 3/47 in the afebrile group. The most common types of delayed milestones included developmental delay and language development delay.

It was observed that cough and rhinorrhea were more common in children of febrile group than with afebrile group. Laboratory test results were analyzed in the entire study group with seizures and observed that stool rotavirus antigen tests were performed in 42 (33.07%) children with watery diarrhea and it was positive in 08/42 children. Electrolyte imbalance was observed in 15 (08.15%) children. Hypoglycemia was observed in 19/68 (27.94%) children. CSF analysis was abnormal in 08/34 (23.52%) children. White blood cell count showed abnormal values in 56/127 children (44.09%). CT scan was done in 45/127 (35.43%) children and found to be abnormal in 15/45 children (35.55%). Similarly, MRI scan was done in 18/127 (14.17%) children and found to be abnormal in 9/18 children (50%), [Table 2]. C-reactive protein was showing abnormal levels in 41.23% of the children. In 8 children, both CT scan and MRI were done concurrently. The different radiological diagnoses observed among the 19 children were as follows: Subarachnoid hemorrhage ($n = 1$), subdural hemorrhage ($n = 3$), post-traumatic head injury without intracranial hemorrhage ($n = 3$), hydrocephalus ($n = 3$), shaking baby ($n = 2$), aseptic meningitis ($n = 2$), meningoencephalitis ($n = 2$), and encephalitis ($n = 3$). All these children presented clinically with acute symptomatic seizures and did not respond for the initial anticonvulsive therapy. Abnormal results of physical and neurological examinations were found in 12 of these 19 children; consciousness disturbance was the most common abnormal finding. EEG was performed in a total of 21/127 (16.53%) children; among these children, abnormal EEG results were observed in 5/7 in AFSs [Table 2].

After the initial emergency management in the ED, 102/127 of the children (80.31%) were admitted to the pediatric ward, 12/127 (9.44%) to the pediatric ICU, and the remaining 13/127 (10.23%) were discharged after observation in the ED itself. The details of emergency treatment given are shown in Table 3.

Table 1: Demographic data (n=127)

Observation	With fever - 80 (%)	Without fever - 47 (%)	P value
Gender- 127			
Male - 78	46 (57.50)	29 (61.70)	Not significant
Female - 49	34 (42.50)	18 (38.29)	
Age (year)			0.012
<1	25 (31.25)	13 (27.65)	
1–6	43 (53.75)	25 (53.19)	
7–12	12 (15.00)	09 (19.14)	
Type of seizures			0.018
GTC	49 (61.25)	28 (59.57)	
Generalized tonic	05 (06.25)	04 (08.51)	
Partial	03 (03.75)	02 (04.25)	
Status epilepticus	06 (07.50)	05 (10.63)	
Others	17 (21.25)	08 (17.02)	
Family history of seizure	31 (38.75)	20 (42.55)	0.031
Family history of epilepsy	07 (08.75)	01 (2.12)	NS
Delayed mile stones	09 (11.25)	03 (6.38)	NS

GTC: Generalized tonic-clonic seizure, NS: Not significant

DISCUSSION

In the present study, 127 children presenting with seizures with or without fever were included in the study. Children with fever presenting with FSs were 80/127 and without fever were 47/127. 68/80 children (85%) with FSs were aged below 6 years. 38/47 children with AFSs were below 6 years of age (80.85%). FSs have been reported to be one of the most common causes of seizure attack in children.[11] FSs are the main cause of first attack seizures in children in any given community. Review of literature shows that[12] 25−40% of children with FSs have a family history of FSs. In the present study, the incidence of family history was observed as 7/80 in febrile group and 1/47 of the afebrile group [Table 1]. It shows the undependability of family history in the history taking among the children presenting with first attack seizures. The underlying causes observed among the children with FSs were as follows: Upper respiratory tract infections in 32/80 (40%), systemic viral infections in 14/80 (17.5%), lower respiratory tract infections in 12 (15%), acute gastroenteritis in 9 (11.25%), enterovirus infections in 8 (12%), and urinary tract infections in 5 (6.25%). A retrospective cohort study showed that diarrhea was the most common associated etiological factor in patients with seizures.[13-16] In the present

Table 2: The number of children undergoing laboratory investigations and incidence of abnormal reports (*n*-127)

Observation	Number of laboratory tests done *n* (%)	Abnormal (%)	Normal values
Stool Rotavirus	42 (33.07)	08 (19.04)	
WBC count	127 (100)	56 (44.09)	<1 year- 5.0–19.5 1–3 years - 6.0–17.5 4–7 years - 0.5–15.5 8–12 years - 4.5–11.5
Sodium	90 (70.86)	08 (08.88)	135−145 mmol/L
Calcium	94 (74.01)	07 (07.77)	2.2–2.5 mmol/L
C-reactive protein	85 (66.92)	41 (48.23)	<4.8 nmol/L
Blood sugar	68 (53.545)	19 (27.94)	3.3–5.6 mmol/L
CSF analysis	34 (26.77)	08 (23.52)	
CT scan	45 (35.43)	15 (35.55)	
MRI	18 (14.17)	09 (50)	
EEG	21 (16.53)	07 (33.33)	

CT: Computed tomography, CSF: Cerebrospinal fluid, MRI: Magnetic resonance imaging, EEG: Electroencephalography

Table 3: The treatment given to the children with seizures (*n*-127)

Treatment given	Number of children received treatment	Number of treatment given episodes
Diazepam PR	18	3
Diazepam IV	64	69
Midazolam	07	04
Lorazepam	04	02
Phenytoin IV	06	01
Phenobarbital IM	08	04
Glucose IV	11	02
Endotracheal intubation	09	-

PR: Per rectum, IV: Intravenous

study, rotavirus was confirmed by stool antigen analysis in 8/127 (19.04%) of patients who presented with seizures and diarrhea. We therefore suggest that a stool rotavirus antigen test may be considered if a patient presents with a first attack of seizure and diarrhea in the ED. Among the children with AFSs, one child showed abnormal CT scan findings (1/19 abnormal CT scans), (5.26%). Abnormal EEG recordings were noted in 2/7 abnormal recordings in febrile group. GTC seizures were noted in 49/80 (61.25%) children of FSs. Patients with complex FS pattern were admitted to the ICU more often than patients with simple FS pattern. The GTC type of seizures was observed in more common in preschool age children than in children in other age groups (*P*- 0.012) [Table 1]. Except 4/80 children in the febrile group (5%), remaining all children responded to diazepam administration either rectally or intravenous route. Seizures are the most common clinical presentation in cases of meningitis and other intracranial neurological complications, especially in young children. They often result in poor prognosis if diagnosed late or prompt treatment was not initiated; lumbar puncture is required in all children presenting with seizures and meningeal signs.[17,18] The American Academy of Pediatrics recommends that a lumbar puncture should be considered in patients aged younger than 18 months who present with FSs.[11] But whether lumbar puncture should be done or n ot during the FSs in children still remains a controversy. In the present study, lumbar puncture was performed in 34/127 children (26.77%), and 8/34 (23.52%) children showed abnormal CSF analysis results among febrile group; however, no definite organism was cultured. 1/34 children was diagnosed as encephalitis, and in 1/34 children, it was meningoencephalitis. Neuroimaging examinations of the brain can help emergency physicians to identify some causes of seizures, but it is not necessary to arrange these imaging studies on a routine basis.[19] In the present study, CT scan was done in 45/127 (35.43%) children and found to be abnormal in 15/45 children (35.55%). Similarly, MRI scan was done in 18/127 (14.17%) children and found to be abnormal in 9/18 children (50%). As in 28 children, both CT scan and MRI are done only 19 imaging studies showed abnormal radiological features; hence, the present study suggests that brain imaging studies should not be routinely in children who present to the ED with a first attack of seizures. Studies showed that routine examinations of glucose, electrolytes, calcium, blood urea nitrogen, and creatinine were not necessary in children whose consciousness levels had returned to baseline, those who had no risk factors for epilepsy, and those with normal physical examination findings.[20,21] In our study, seizures caused by severe electrolyte imbalance in 08.15% of the children and hypoglycemia were noted in 19 (27.94%) of the children. The present study suggests that electrolyte and blood sugar studies should be arranged based on detailed history-taking and thorough physical examinations and not to be performed routinely. Phenobarbital may have priority over other anticonvulsants for controlling neonatal seizures.[21] In the present study, diazepam was used in 82/127 (64.56%) of the children in the ED for first attack seizures irrespective of febrile or afebrile nature. Phenobarbital IM was used in 8/127 (6.29%), [Table 3].

Repeat doses were required more frequently among the children aged below 6 years when compared to above 6 years to control seizures in the present study.

CONCLUSIONS

Among the first attack seizures encountered in children, the FSs are more common than AFSs. 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 examination of brain imaging studies, electrolyte, and blood sugar is unnecessary unless the patients present with an abnormal history or abnormal results of physical or neurological examinations.

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