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Clinical and Laboratory Presentations of Children with First Time Febrile Seizure: Findings from a Tertiary Level Hospital in Bangladesh

Abu Shoyeb Md. Mahamuduzzaman[1*], Md. Anisur Rahman[2], Md. Shafiq Ullah[3], Md. Fazlul Kader Khan[4], Sadia Tabassum[5], Umme Qulsum Sonia[6], Rawshon Saleha[7]

[1]Assistant Professor, Department of Paediatrics, Shaheed Suhrawardy Medical College, Dhaka, Bangladesh
[2]Assistant Professor, Department of Paediatrics, Sir Salimullah Medical College, Dhaka, Bangladesh
[3]Assistant Professor, Department of Paediatrics, Bangabandhu Sheikh Mujib Medical College, Faridpur, Bangladesh
[4]Assistant Professor, Department of Paediatrics, Shaheed Suhrawardy Medical College, Dhaka, Bangladesh
[5]Registrar, Department of Paediatric Neurology and Development, Shaheed Suhrawardy Medical College, Dhaka, Bangladesh
[6]Assistant Registrar, Department of Paediatrics, Shaheed Suhrawardy Medical College, Dhaka, Bangladesh
[7]Deputy Chief Medical Officer and Center Incharge, NHN, Keranigonj, Dhaka, Bangladesh

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***Corresponding author:** Dr. Abu Shoyeb Md. Mahamuduzzaman
Assistant Professor, Department of Paediatrics, Shaheed Suhrawardy Medical College, Dhaka, Bangladesh

Abstract **Original Research Article**

Background: Seizures associated with fever are a leading cause of pediatric hospitalization. The purpose of this study was to explore the clinical characteristics and laboratory findings of children with first time febrile seizure in local settings, which are limited in Bangladesh. ***Methods:*** From July 2013 to June 2014, this Cross-sectional, Observational study was conducted at Sir Salimullah Medical College and Mitford Hospital in Dhaka. The study included all admitted children aged 6 months to 60 months who had their first febrile seizure. A thorough history, clinical examination, and laboratory investigations were performed and analyzed. ***Results:*** Among the 87 study population, mean age of presentation was 25.62 ± 12.64 months, male were predominant (56%) and 17% had family history of FS. Majority of them presented with respiratory illness-like symptoms(23%). 54% of them experienced two seizures, and 75% of the seizures were generalised. 23% of them revealed chest X-ray features consistent with lung infection, 31% had neutrophilic leukocytosis, and 8% had positive blood culture growth. Streptococcus pneumoniae in Gram stain of 2% CSF and Klebsiella in 2% of the CSF culture cases were identified. Pneumonia was the underlying cause in 20% of case; viral syndrome in17% of cases, meningitis in 13% of cases, and in 15% of cases, the underlying cause could not be identified. ***Conclusion:*** The majority of febrile seizures in our study participants were caused by various respiratory illnesses and meningitis. White blood cell counts, blood culture and cerebrospinal fluid analyses can aid in determining the underlying cause and facilitating appropriate and timely management.

Keywords: Febrile Seizure, Demography, Clinical features, Laboratory features.

INTRODUCTION

According to the National Institutes of Health, febrile seizure is defined as "an event in infancy or childhood, usually occurring between 3 months to 5 years of age, associated with fever but without the evidence of intracranial infection or defined cause. Seizures accompanied by fever in children who have suffered a previous non-febrile seizure are excluded" [1]. However, there is dispute on the minimum age; for example, the International League Against Epilepsy (ILAE) suggests that the minimum age to be one month [2]. Febrile seizures are classified as simple and complex. Simple febrile seizures are generalized tonic-clonic, last less than 15 minutes and do not recur within 24 hours; complex febrile seizures are focal, last ≥15 minutes, and/or recur within 24 hours [3-5]. While the majority of febrile seizures are benign and self-limiting, they can occasionally be provoked by underlying pathology such as upper respiratory infection, gastroenteritis, urinary tract infection (UTI) or more serious conditions such as septicemia or meningitis [3, 6, 7].

Although the link between seizures and bacterial meningitis (BM) is widely established, it is not always straight forward to establish [8-11]. The American Academy of Pediatrics (AAP) recommends lumbar puncture for CSF study in infants 6-12 months

of age and considers it in children 12-18 months of age who have their first simple febrile seizures [8, 12]. It is based on the fact that these individuals frequently lack signs of meningitis such as bulged anterior frontanelle, neck rigidity, Kernig sign or Brudzinski sign.

Febrile seizure is the most prevalent type of childhood seizure and is one of the major reasons of hospitalization in children globally [3, 13-15]. The incidence varies by country, with between 2% and 5% of children in western Europe and the United States of America being affected by febrile seizures [4, 16-19]. However, the incidence is significantly higher in developing countries [14, 20]. The data for frequency of febrile seizure available from developed countries are difficult to apply to our settings because of differences in immunization schedule, their antibiotic policy and limited laboratory facilities.

Although it is a leading cause of childhood hospitalization and the incidence and pattern frequently vary by country, we have very limited data on the demographic profile, clinical characteristics, and laboratory analysis in Bangladesh.

Given the widespread prevalence of febrile seizures in children, it is critical to understand the demographic, clinical, and laboratory characteristics of the local population in order to develop more precise management recommendations. Additionally, it will assist healthcare providers in recognizing more complex instances with more significant underlying diseases.

The purpose of this study was to describe the clinical and laboratory characteristics of children with first time febrile seizures in order to supplement existing data on febrile seizures in Bangladesh.

MATERIALS AND METHODS

This cross-sectional, observatinal study was conducted from from July 2013 to June 2014 at the Department of Pediatrics, Sir Salimullah Medical College, and Mitford Hospital, Dhaka.

During this timeframe, we enrolled 87 children aged between 6 to 60 months who were admitted with their first febrile seizure and whose parents consented to participate in the study.

On arrival, children with active convulsions received emergency care with per-rectal Diazepam or intravenous Phenobarbitone. Standard treatment guidelines were followed for all children. To classify the type of seizure, a complete history was taken, including the patient's age, sex, immunization history, family history of febrile seizures, the time interval between the onset of fever and the seizure, the duration of the seizure, and the number. Symptoms on admission along with fever were noted. The investigators conducted a thorough physical examination of all patients to identify probable underlying causes of fever.

Children with definite signs of meningeal irritation (bulged anterior frontanelle, neck rigidity, Kernig sign or Brudzinski sign), unconscious, papilloedema, known case of cerabral palsy, epilepsy were excluded from the study.

Maintaining strict aseptic conditions, from all children blood was collected for complete blood count (CBC) and blood culture, lumber puncture was done for CSF study. Children with abnormal lung findings on auscultation were sent for chest X-ray; with pain during micturation urine was collected for urinalysis; with sore throat swab were collected for culture.

All investigation findings were recorded in a pre-structured data collection form. Based on the clinical and laboratory findings, final diagnoses were made as per operational definition by standard treatment guidelines.

SPSS version 23.0 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) was used to analyze the data. Quantitative data were presented as mean ± standard deviation and categorical data were presented as number and frequency.

The study received approval from the Sir Salimullah Medical College Hospital's Ethical Review Committee and Internal Review Committee.

RESULTS

A total of 87 children were included in this study. The demographic characteristics of the study participants are summarized in Table-I. The mean age of the participants was 25.62 ± 12.64 months, and the majority (31%) of individuals was between the ages of 13 and 24 months. Males made up the majority (56.3%) of study participants, and only 17.2% of affected children had a family history of febrile seizure. We found no child who had received either a pneumococcal or a meningococcal immunization but all of the children were immunized against Hib, DPT and Hepatitis B.

Table-I: Demographic characteristics of the patients

Characteristics	Number (n=87)	Percentage (%)
Age (months)		
6-12	21	24.1
13-24	27	31.0
25-36	17	19.5
37-48	12	13.8
49-60	10	11.5
Mean ± SD Range	25.62 ± 12.64 6-60	
Sex		
Male	49	56.3
Female	38	43.7
Male: Female ratio	1.2: 1	
Family history of FS		
None	72	82.8
Siblings	6	6.9
Parents	9	10.3
History of vaccination		
Penta-valent (Hib+DPT+ Hepa B)	87	100.0
Pneumococcal	0	0.0
Meningococcal	0	0.0

At the time of admission, the mean temperature of the patients was 38.62 ± 0.79°C. 56.3% of children had their first complex febrile seizure (FCFS), and the majority (54%) had two seizures, while 13.8% had status. The mean duration of the seizure was 4.45 ± 2.23 minutes, the majority (74.7%) were generalized, and only a few (10.3%) experienced post-ictal drowsiness following the seizure (Table II).

Table-II: Clinical characteristics of study participants

Characteristics (Fever and seizure)	Number (n=87)	Percentage (%)
Mean temperature on admissiom (º C)	38.62 ± 0.79	
Types of seizure		
First simple febrile seizure (FSFS)	38	43.7
First complex febrile seizure (FCFS)	49	56.3
Number of seizure		
Single	28	32.2
Two	47	54.0
Status	12	13.8
Mean duration of seizure (minutes)	4.45 ± 2.23	
Nature of seizure		
Generalized	65	74.7
Focal	22	25.3
Post- ictal drowsiness		
No	78	89.7
Yes	9	10.3

Additionally, 26.4% had a runny nose; 22.9% had a cough; 9.1% had purulent exudates on tonsil; 8% had loose watery stool with vomiting; 6.9% had history of painful urination; 5.7% had had history of poor feeding with lethargy, 2.2% had pus or discharge from ear and 14.9 % experienced only fever withour localizing sign (Table III).

Table-III: Clinical characteristics of the study participants

Clinical characteristics (Associated symptoms other than fever and seizure)	(n=87)	Percentage (%)
Runny nose	23	26.4
Cough	20	22.9
Respiratory distress (fast breathing, chest indrawing)	8	9.1
Crepitation on auscultation	17	19.5
Rhonchi on auscultation	3	3.4
Sore throat	10	11.5
Purulent exudates & enlarged tonsil	8	9.1
Ear pain	2	2.2
Pus or discharge from ear	2	2.2
Passage of loose stool with vomiting	7	8.0
Painful urination	6	6.9
Supra-pubic tenderness	3	3.4
Poor feeding with lethargy	5	5.7
Only fever without localizing symptom or sign	13	14.9

Table-IV shows the investigation findings of the study participants. On complete blood count report, 31.0% had neutrophilic leukocytosis, 32.1% had lymphocytic leukocytosis and 36.7% were within normal range. The mean WBC count was 14242 ± 8275 per mm3. Among them, 8.0% had positive growth for *Strept. Pneumonia, Klebsiella. Proteus, Pseudomonas, Enterococcus.Spp* in the blood culture. On chest X-ray, 19.5% had patchy opacity in the lung and 3.4% had hyperinflation and hypertranslucent lung field. On urine routine examination, 6.8% had ≥ 5 pus cells/HPF and 4.5% had growth on urine cuture.

Table-IV: Laboratory and radiology findings of the study participants

Investigations	(n=87)	Percentage (%)
Normal total leukocyte count	32	36.7
Neutrophillia	27	31.0
Lymphocytosis	28	32.1
TLC Mean ± SD (per cmm)	14242 ± 8275	
Growth on Blood CS *(Klebsiella. Spp)*	7	8.0
Growth on Throat CS	5	5.7
CXR: Patchy opacity in lung field	17	19.5
CXR: Hyperinflation and hypertranslucent lung field	3	3.4
Urine R/E Pus cell ≥ 5/hpf	6	6.8
Growth on Urine CS	4	4.5

Table-V summarizes the findings from the CSF study. Lumber puncture was performed on 87 study participants for CSF analysis. The majority (93.1%) of children had clean CSF. Color was hazy in only 6.9% of the children. 6.9% of children were found to have CSF pleocytosis. In 5.7% of instances, the CSF sugar level was low, whereas in 9.1% of cases, the CSF protein level was high. Gram positive diplococci (*Streptococcus pneumoniae*) were found by gram stain of CSF in 2.3% of the children, and *Klebsiella Spp*. growth was found in another 2.3% of the children. In all cases of pleocytosis, the predominant cell in CSF was lymphocyte.

Table-V: CSF analysis of the patients with febrile seizure

CSF profile	(n=87)	(%)
Color		
Crystal	81	93.1
Hazy	6	6.9
Pleocytosis	6	6.9
Low sugar level	5	5.7
Raised protein level	8	9.1
Gram stain of CSF		
Organism found Gram positive diplococci *(Strept. pneumoniae)*	2	2.3
CSF culture		
Growth *(Klebsiella. Spp)*	2	2.3

Based on the clinical and laboratory findings, 19.5% of the children were diagnosed with pneumonia, 17.2% with viral syndrome, 12.6% with meningitis, 9.1% with pharyngo-tonsilitis, 8% with gastroenteritis, 6.8% urinary tract infection (UTI), 5.7% sepsis, 3.4% bronchiolitis and 2.3% otitis media. Discharge diagnoses are shown on Table- VI and Figure-1.

Table-VI: Shows the discharge diagnoses of the study participants with first time febrile seizure

Discharge diagnoses	(n=87)	(%)
Pneumonia	17	19.5
Viral syndrome	15	17.2
Unclassified	13	14.9
Meningitis	11	12.6
Pharyngo-tonsillitis	8	9.1
Gastroenteritis	7	8
UTI	6	6.8
Sepsis	5	5.7
Bronchiolitis	3	3.4
Otitis media	2	2.3

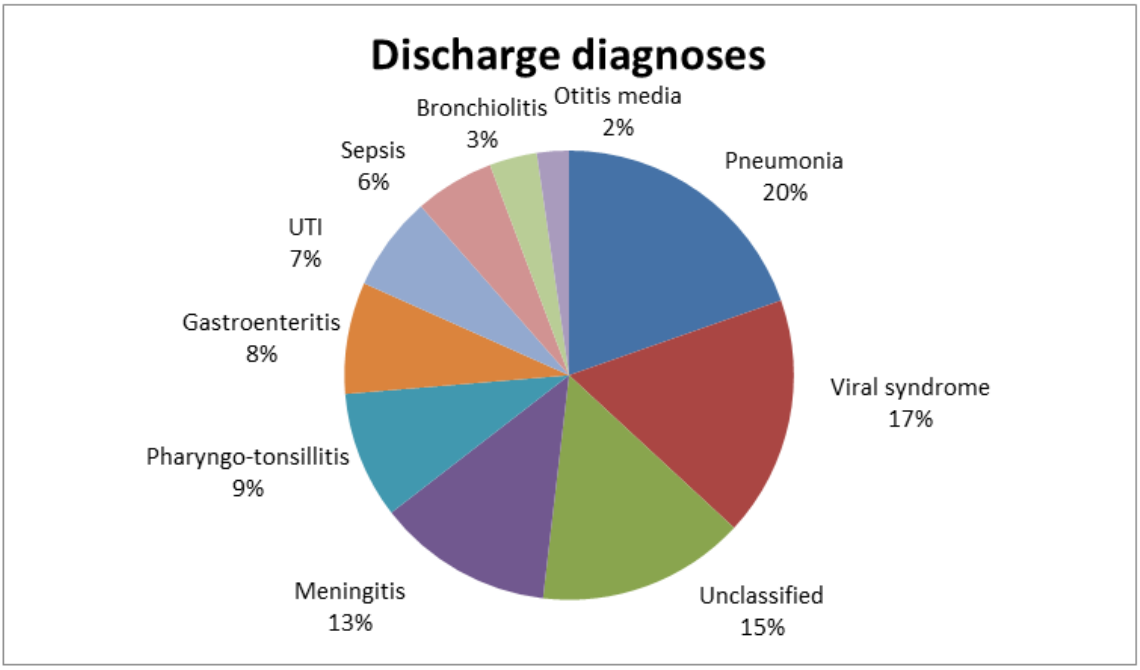

Figure-1: Pie chart shows the discharge diagnosis of the study participants with first time febrile seizure

DISCUSSION

During the one year study period, we have included 87 children with febrile seizures in our study. We have found that the mean age of the children was 25.62 ± 12.64 months. In similar studies done by Aliabad *et al*., Yousefichaijan *et al*., Kantamalee *et al*., and others have also observed comparable ages [19, 21-26]. Males are more susceptible to febrile seizures than females, as demonstrated by several studies conducted by Kantamalee *et al*., Fallah *et al*., Trainor *et al*., and others [19, 22, 25-27]. However, in comparison to prior research, which showed a male proportion of 62% or more, our study found a male proportion of 56 percent, which was considerably higher than female but lower than findings from other studies. Regarding family history, 17% of study participants reported having a positive family history of febrile seizure. Other studies have also reported a familial history of febrile seizure in up to 35% of cases [19, 22-24].

The mean temperature of the patients at the time of admission in our study was 38.62 ± 0.79°C. Which was similar to the findings by Yousefichaijan *et al*., Kantamalee *et al*., and other [21, 22, 25, 27]. Over 56% of children in our research had their first complex febrile seizure (FCFS). Winkler *et al*., likewise found out that majority of their study participants had complex febrile seizures [23], while Hussain et al. reported that the majority (78 percent) of their study participants had simple febrile seizures in a 2015 study conducted in Pakistan [24]. This difference with present study might be due to less hospital admission of FSFS cases as seizure stops in most cases at home and do not recur in

the same episode. The majority (54%) of patients in our study had two seizures, whereas 13.8% had status, which required emergency therapy upon admission. The mean duration of the seizure in our study was 4.45 ± 2.23 minutes, which was comparable to the Trainor et al. study [25].

In our study, 22.9% of participants reported having an associated cough, 26.4% reported having a runny nose, and 9.1% reported experiencing respiratory distress. All of these findings suggests that the majority of patients presented with symptoms consistent with various types of respiratory infection and viral syndrome.

On chest X-ray, 19.5% had patchy opacity in the lung and 3.4% had hyperinflation and a hypertranslucent lung area, which are characteristic of pneumonia and bronchioitis, respectively. Teran *et al*., have also discovered abnormalities in X-rays in 21% of the cases in a 2012 research [26].

On complete blood count report, 32% had lymphocytic leukocytosis which was almost similar to the study by Hussain *et al*., [24], but in another study by Teran *et al*., and Yousefichaijan *et al*., found neutrophilic leukocytes [21, 26]. In our study, the mean WBC count was 14242 ± 8275 per mm3 which was higher than the study done by Guneş *et al*., where they have found a mean WBC of 12088.3 ± 5535.8 per mm3 [28] *Strept. Pneumonia, Klebsiella. Proteus, Pseudomonas, Enterococcus.Spp* grew in 8% of the blood cultures in our study participants, which is concerning. On urine routine examination, approximately 6.8% had plenty of pus cells indicative of urinary tract infections.

In CSF study, we noticed that the sugar level was low in 5.7% of patients and the protein level was raised in 9.1% of cases. Additionally, we identified Gram positive diplococci (*Streptococcus pneumoniae*) from CSF in 2.3% of the children and *Klebsiella Spp*. from culture in another 2.3% of the children.

Based on the clinical and laboratory findings, we have found that 19.5% of the children were diagnosed with pneumonia, 17.2% with viral syndrome, 12.6% with meningitis, 9.1% with pharyngo-tonsilitis, 8% with gastroenteritis, 6.8% urinary tract infection (UTI), 5.7% sepsis, 3.4% bronchiolitis and 2.3% otitis media. Other studies have also reported that respiratory tract infections were the most prevalent, accounting for up to 81 percent of cases [22, 24, 28] and viral syndrome in 6 percent of cases [25]. The difference of pattern of infection might be due to the fact that strain of organism varies between developing and developed countries [8].

However, it is alarming that 12.6% of children in our study had meningitis, which is a serious infection requiring immediate management to prevent morbidity and mortality.

LIMITATIONS

Since the study facility's laboratory facilities were unavailable after 7 PM, a few of the children hospitalized after that time period received empirical antibiotics prior to CSF and blood sample collection, which could have masked the culture data. Additionally, there were no laboratory facilities for the identification of viral meningitis. Extensive research with larger samples and multiple study sites is recommended.

CONCLUSION

First time seizures associated with fever is one of the common reasons for hospitalization in children. While our study findings suggest that symptoms of respiratory illness are the most frequently reported associated complaint, a significant percentage of admitted febrile children may present with seizure for first time due to meningitis, necessitating quick identification and management.

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