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Frequency of Meningitis Among Infants and Young Children With Clinically Diagnosed First Time Febrile Seizure

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First Time Febrile Seizure, Meningitis, Lumbar puncture, CSF

Abstract:

Background: *Patients with bacterial meningitis (BM) frequently present with febrile seizures (FS) without any signs or symptoms of BM. To perform a lumbar puncture on all FS patients to rule out meningitis is still debatable. The goal of this study was to estimate the frequency of meningitis among first-time febrile seizures (FTFS).*

Methods: *From July 2013 to June 2014, a cross-sectional study was conducted at Sir Salimullah Medical College and Mitford Hospital, Dhaka. CSF and blood reports and detailed histories and examinations were examined in children aged 6 months to 36 months with FTFS (simple or complex).*

Results: *The first complex febrile seizure (FCFS) and the first simple febrile seizure (FSFS) occurred in 58% and 42% of the 73 children included in this study. 11 (15%) cases had meningitis based on CSF and blood reports, where 2 (3%) had confirmed BM, 2 (3%) had probable BM, and 7 (10%) had viral meningitis (PVM). One of two children with confirmed BM had Klebsiella spp. in CSF culture and Streptococcus pneumoniae in CSF gram stain. Others with probable BM had CSF pleocytosis with low sugar and high protein levels. Leukocytosis was found in all four children with BM. Two of the seven children with PVM had isolated pleocytosis, one had low sugar, and four had high protein CSF. Blood cultures were negative in all 11 meningitis cases.*

Conclusion: *Although meningitis is common in FCFS, this study found no cases of BM children with FSFS, though PVM was not uncommon.*

Introduction:

Seizures associated with fever is a leading cause of pediatric hospitalization worldwide.[1–4] Febrile seizures (FS) are the most common type of childhood seizure, affecting between 2% and 5% of children aged 6 months to 5 years in western Europe and the United States of America.[5–8] In Japan, the incidence is as high as 8% and even higher in developing countries.[3,9]

The National Institutes of Health (Bethesda, MD) defined the term "febrile seizure" as "an event in

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infancy or childhood, usually occurring between 3 months to 5 years of ÿþage, associated with fever but without the evidence of intracranial infection or defined cause. Seizures accompanied by fever in children who have suffered a previous nonfebrile seizure are excluded".[10] However, the International League Against Epilepsy (ILAE) considers the minimum age limit to be one month.[11]

Febrile seizures are further classified as simple or complex. Simple febrile seizures lasted for less than 15 minutes and did not recur within 24 hours. Complex febrile seizures are focal, prolonged (e"15 minutes), and/or recurrent within 24 hours.[1,8,12] The majority of FS are benign, and self-limiting occur due to electrical abnormality in the brain triggered by the rapid rise of temperature.[13] However, a substantial number of them are suggestive of underlying pathology.[1,14,15]

FS may be triggered by fevers from viral infections, focal bacterial infections and meningitis.[1,16] A lumbar puncture (LP) is typically recommended prior to antibiotic administration in children who have experienced their first simple febrile seizure (FSFS).[1,17,18] Given that a seizure in the presence of a fever may indicate bacterial meningitis, deciding whether to perform LP may be difficult. The American Academy of Pediatrics (AAP) recommends lumbar puncture in infants aged 6-12 months and considering it in children aged 12-18 months, who manifest first simple febrile seizures.[19,20] The recommendation is based on the fact that meningeal signs may be minimal, subtle, or absent in these age groups.

The association between seizure and bacterial meningitis (BM) is well established.[19,21–23] Seizures are the first manifestation of BM in 16.7% of children and one-third of these patients present without any evident meningeal signs and symptoms.[20,24] Children with meningitis often present with apparent FS in the pediatric emergency department. The reason for missing BM in apparent FS is that signs and symptoms of BM such as lethargy, irritability, decreased feeding, and drowsiness is often lacking particularly in infants and young children. Seizures may be the sole presentation of bacterial meningitis in febrile infants (FSFS).

In the absence of typical meningeal signs, some studies suggest that an LP should be considered in children who have complex seizures, have previously received antibiotic therapy, are younger than 12 months, or have an incomplete vaccination history.[5,8,12]

There is currently no such guideline for children who present with their first complex febrile seizure, and current treatment plans for this population vary significantly among pediatric emergency providers. Numerous studies conducted in developed countries discovered very few or no cases of meningitis in patients with FSFS. However, studies from developing countries found that BM rates were higher.

The first simple febrile seizure is a benign condition that has an excellent long-term prognosis even in the absence of treatment. On the other hand, meningitis is a medical emergency that can result in increased morbidity and mortality if proper diagnosis and treatment are not initiated promptly. However, data on developing countries such as Bangladesh are scarce. Additionally, our country, particularly in rural areas, has a scarcity of laboratory facilities. Meningitis may be missed in cases where febrile seizure is diagnosed clinically, particularly in infants and young children.

Understanding the prevalence of BM in various subgroups of children with FS can assist clinicians in making appropriate clinical decisions in these difficult situations. This study aimed to determine the prevalence of meningitis in infants and young children with FTFS.

Materials and Methods:

A cross-sectional study was conducted from July 2013 to June 2014 at the Department of Pediatrics, Sir Salimullah Medical College, and Mitford Hospital in Dhaka. Children aged 6 months to 3 years who had their first febrile seizure were included in the study population. Patients with neuro-developmental co-morbidity like cerebral palsy, developmental delay, or mental retardation were excluded, as were those with contraindications to lumbar puncture such as papilloedema, local infections, or low platelet count.

The study was approved by the Ethical Review Committee and Internal Review Committee of Sir Salimullah Medical College. We included

participants who provided written informed consent. At first, 80 children were selected. However, seven of them refused to consent to lumbar puncture, resulting in a total of 73 children in the study.

A detailed history was taken, including age at first febrile seizure, sex, family history of febrile seizure, the time interval between onset of fever and seizure, the duration of seizure, and the number and types of to distinguish between simple and complex febrile seizure. A detailed immunization history was obtained and recorded, emphasizing Hib, Pneumococcal, and Meningococcal vaccinations and prior antibiotic treatment. Patients' neurological status was evaluated for signs of meningeal irritation such as bulged anterior fontanelle (6 to 18 months) and were essentially excluded from the study if positive. The principal investigator examined each patient. If convulsions were present at admission, they were initially controlled with per-rectal Diazepam or intravenous Phenobarbitone. We observed and documented post-ictal drowsiness or neurological deficits. A thorough history and physical examination were conducted to ascertain the underlying cause of the seizure with fever, including possible viral fever, pneumonia, bronchiolitis, pharyngotonsillitis, otitis media, possible urinary tract infection, diarrhea, and sepsis.

Under strict aseptic conditions, LP was performed as soon as possible after admission. RBS was done and noted about a half-hour before LP. The CSF was analyzed using established laboratory procedures. Each patient underwent a blood count and blood culture in addition to the CSF study.

According to provisional diagnosis, relevant investigations were done to determine the cause of fever and children were managed according to hospital protocol.

SPSS (Statistical Package for Social Science) Version 20 for Windows was used to analyze all data. Where appropriate, proportions were compared using the chi-square or Fisher exact test. A p-value of <0.05 was considered significant when comparing baseline patient characteristics.

Results:

A total of 73 children were included in this study. As viral meningitis is difficult to diagnose in our settings compared to bacterial meningitis (BM), all children were diagnosed with BM or no BM. Here, no BM cases also included presumed viral meningitis (PVM).

Table I shows that most of the studied children belonged to 13-18 months of age comprising 34.2%. The mean age of the studied children was 16.75±7.83 months. Among the studied children, 41 (56.2%) were male, and 32 (43.8%) were female. The male-female ratio was 1.2:1. Family history of FS was present in only 16.5% of studied children (5.5% were in siblings and 11% in parents). All 73 studied children received the Hib vaccine as a part of the Penta-valent vaccine through routine EPI. None received Pneumococcal or Meningococcal vaccine.

Table I: *Demographic characteristics and history of the participants*

Characteristics	Frequency (n=73)	Percentage (%)
Age (months)	Mean ± SD: 16.73 ± 8.83	
6-12	24	32.9
13-18	25	34.2
19-24	15	20.5
25-36	9	12.3
Sex		
Male	41	56.2
Female	32	43.8
Family history of FS		
None	61	83.5
Siblings	4	5.5
Parents	8	11.0
History of vaccine		
Penta-valent (Hib + DPT + Hepa B)	73	100
Pneumococcal	0	0
Meningococcal	0	0

In addition to the history and clinical examination, the majority of the children studied, 26 (35.62%), were diagnosed as having a possible viral fever based on lymphocytosis on the complete blood count (CBC). Fifteen (20.55%) children were diagnosed with pneumonia due to neutrophilic

leukocytosis on the CBC and patchy opacity on the chest radiograph, while two (2.74%) children were diagnosed with bronchiolitis due to hyperinflation and hypertranslucency on the chest radiograph. Six (8.22%) children were diagnosed with pharyngotonsillitis due to neutrophilic leukocytosis on the CBC and/or a positive throat swab culture; and one (1.37%) child was diagnosed with otitis media due to neutrophilic leukocytosis on the CBC. Six (8.22%) children were diagnosed with a possible urinary tract infection due to five pus cells/HPF in the urine and/or positive urine culture. Three (4.11%) patients were diagnosed with sepsis due to positive blood culture. Laboratory investigations revealed no focal point in eight (10.95%) cases (Fig. 1).

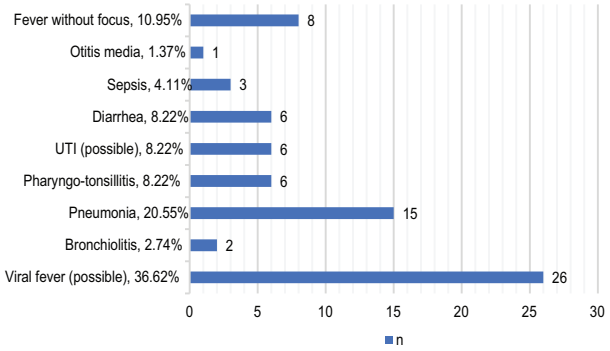

Fig.- 1: *Distribution of studied children by possible clinical cause of fever at presentation.*

As illustrated in Figure 2, FCFS was prevalent in the 73 children studied. FCFS was found in 42 (57.5%) cases, while FSFS was found in 31 (42.5%) cases.

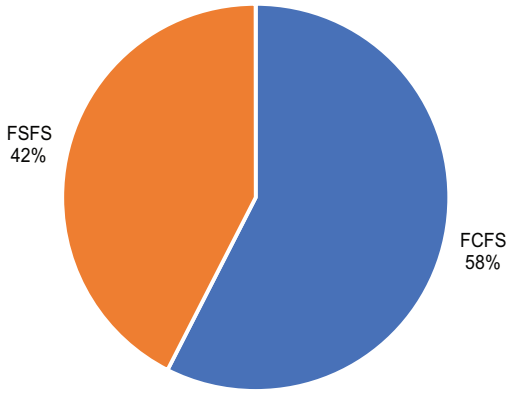

Fig.-2: *Distribution of children with FSFS and FCFS*

According to Table II, the majority of children with FCFS had seizures lasting between 16 and 29 minutes, with 21 (50%) having seizures lasting less than 15 minutes. The remaining 6 (14.3%) cases had a duration greater than 30 minutes. FCFS had an average duration of 31.8±11 minutes. In the majority of studied children with FCFS, 32 (76.2%) had two seizures, while four (9.52%) had a single seizure. The remaining 6 (14.3%) presented with status. The majority of children with FCFS, 39 (92%) had generalized seizures, while the remaining 3 (7.1%) had focal seizures. The majority of children with FCFS, 38 (90.5%), had no post-ictal drowsiness and 4 (9.5%) were drowsy after the convulsion ended.

Table II: *Characteristics of seizure of patients with FCFS*

Duration of seizure (minutes)	Initial diagnosis of FCFS	
	Frequency	Percentage (%)
0-15	15	35.7
16-29	21	50
>30	6	14.3
Mean ±SD	31.8 ±11	
Number of seizures		
Single	4	9.52
Two	32	76.2
Status	6	14.28
Nature of seizure		
Generalized	39	92.9
Focal	3	7.1
Post-ictal drowsiness		
No	38	90.5
Yes	4	9.5

Table III shows that out of 73 children, 11 (15.06%) were diagnosed with meningitis either BM (5.4%) or PVM (9.6%). Among 42 children with FCFS 2 (2.7%) were diagnosed as confirmed BM; 2 (2.7%) were as probable BM and 2 (2.7%) were as PVM. Among 31 children with FSFS 5 (6.9%) were diagnosed as PVM.

Table III: Distribution of the studied children with FTFS finally diagnosed as Meningitis

Final Diagnosis			Initial Diagnosis (n, %)		Total
			FSFS	FCFS	(n, %)
			(31, 42.5%)	(42, 57.5%)	
Meningitis	BM	Confirmed BM	0	2, 2.7%	2, 2.7%
(11, 15.06%)	(4, 5.47%)	Probable BM	0	2, 2.7%	2, 2.7%
	Presumed viral meningitis		5, 6.9%	2, 2.7%	7, 9.6%
No Meningitis			26, 35.6%	36, 49.3%	62, 84.9%

Table IV: *Distribution of study participants by final diagnosis*

Initial diagnosis	Final diagnosis	Basis of final diagnosis	n, (%)
FCFS (1 case)	Confirmed BM	Organism found in gram stain of CSF (*Strept. pneumoniae*) plus Neutrophilic leukocytosis	1 (1.4%)
FCFS (1 case)	Confirmed BM	Positive CSF culture (Klebsiella. Spp) plus Neutrophilic leukocytosis	1 (1.4%)
FCFS (2 cases)	Probable BM	CSF pleocytosis with low sugar and high protein plus Neutrophilic leukocytosis	2 (2.7%)
FSFS (1 case) FCFS (1 case)	Presumed Viral Meningitis	Isolated pleocytosis	2 (2.7%)
FSFS (1 case)	Presumed Viral Meningitis	Isolated low sugar content	1 (1.4%)
FSFS (3cases)	Presumed Viral Meningitis	Isolated high protein content	4 (5.5%)
FSFS (26 cases) FCFS (36 cases)	No Meningitis	Normal CSF study	62 (84.9%)

The distribution of study participants by final diagnosis is shown in Table IV. Meningitis was finally diagnosed in 11 children out of 73 cases. Among 11 cases of meningitis, two were confirmed BM; one (1.4%) child had a positive CSF culture, and another (1.4%) had an organism in the CSF gram stain. Two (2.7%) children were diagnosed as having probable BM based on the case definition of CSF pleocytosis with low sugar and high protein content. Seven children were diagnosed with PVM, with four (5.5%) having isolated high protein content, two (2.7%) having isolated pleocytosis, and one (1.4%) having low CSF sugar content. None of the 11 meningitis cases resulted in a positive blood culture. 62 (84.9%) children lacked evidence of meningitis; 26 had FSFS and 36 had FCFS.

Discussion:

The current study discovered that the majority (34.3%) of 73 children with FTFS were between 13 and 18 months. The mean age of the participants was 16.7±7.8 months. Other studies have reported similar findings.[19,25] Male to female ratio was 1.2:1 in this study. It is well known that the male sex predominates in febrile seizures, and the current study is no exception. Kimia AA et al.[19] and Chung B et al.[26] observed comparable findings.

In this study, the most common underlying cause of fever at presentation was possible viral fever, accounting for 35.62% of cases. Following that are pneumonia, diarrhoea, urinary tract infection & pharyngotonsillitis, sepsis, bronchiolitis, and otitis media. Initially, fever without focus occurred in 10.95% of cases. Trainer et al. found that the most common illness associated with FS in children in the United States of America was otitis media (34%), followed by respiratory tract infection, viral syndrome, urinary tract infection, and gastroenteritis. In 34% of cases, the source of the

fever could not be identified.[25] Additionally, Chung B et al. demonstrated in their study that RTI was the most common cause of fever in FS patients.[26] The variation in infection patterns could be explained by the fact that the strain of organism varies between developing and developed countries.[19]

The current research reveals that 42 (57.5%) of 73 consecutive children with FTFS were initially diagnosed with FCFS and 31 (42.5%) with FSFS. Teach and Gail et al. published their experience with 243 febrile children with FTFS, of whom 89% had simple febrile seizures and 11% had complex febrile seizures.[27] This difference from the current study may be due to a lower hospitalization rate for FSFS cases, as seizures typically stop at home and do not recur during the same episode.

Meningitis data from developed countries are often difficult to apply in resource-poor countries such as Bangladesh due to differences in immunization schedules (e.g., pneumococcal and meningococcal vaccines are not routinely used in EPI) and antibiotic regulations. Additionally, our country, particularly in rural areas, has a scarcity of laboratory facilities. This study discovered that while all 73 children studied had received Hib vaccine, none had received Pneumococcal or Meningococcal vaccines. With the introduction of the conjugate Hib vaccine, this organism is now a very rare cause of disease in the United Kingdom. In 2000, H. influenzae type b disease was reported at an incidence rate of 1.8 per 10,000. The reported vaccination rate for the American population was greater than 90%, including the Hib vaccine.[28] Since the introduction of a seven-valent Pneumococcal conjugate vaccine in 2000, the incidence of BM has decreased significantly, lowering the risk of meningitis in young children experiencing simple febrile seizures.[19]

In the current study, 11 (15.06%) of 73 children were diagnosed with meningitis based on their CSF profile and blood reports. Among them, two (2.7%) had been diagnosed with BM; two (2.7%) had been diagnosed with probable BM; and seven (9.6%) had been diagnosed with presumed viral meningitis (PVM). All four children with BM were initially diagnosed as having FCFS, and five of the seven children with PVM were diagnosed as having FSFS and two as having FCFS. Three of the four cases of BM occurred in children aged 6-12 months, while the fourth occurred in a child aged 13-18 months.

Meningitis is a relatively common infection in infants and young children, and is clinically diagnosed as the first complex febrile seizure (FCFS). Although no cases of bacterial meningitis (BM) were found in infants and young children with their first simple febrile seizure (FSFS), presumed viral meningitis (PVM) is not uncommon.

Limitations:

Children diagnosed with FS who arrived after 7 PM were kept overnight due to the lack of a laboratory facility. As a result, those children received empirical antibiotics, which may have obscured the CSF findings.

Due to the difficulty of diagnosing viral meningitis in our settings compared to bacterial meningitis (BM), all children were classified as having BM or not having BM. No BM cases included presumed viral meningitis in this study (PVM). We did not perform virus isolation, PCR, latex agglutination, or CRP of CSF because these tests are not available in our settings.

Parents of otherwise healthy febrile children were reluctant to have their children undergo LP.

Our sample size is relatively small. Additional research can be conducted by enrolling a large number of children at multiple tertiary hospitals.

Conclusion:

BM is frequently observed in infants and young children experiencing their first complex febrile seizure (FCFS). Children with FCFS who are 6 to 18 months old are more likely to have recurrent seizures and post-ictal drowsiness. Presumed viral meningitis (PVM) is a common occurrence in infants and young children who have their first simple febrile seizure (FSFS).

It is necessary to attempt to classify febrile seizures as simple or complex. LP is indicated for recurrent seizures and post-ictal drowsiness in infants and young children with FTFS.

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