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Prevalence of acute bacterial meningitis among children who present as first complex febrile seizure

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Abstract
Generally, the incidence of FS decreases markedly after 4 years of age (and the condition rarely occurs in children older than 7 years of age. FS occurs more frequently in the Asian population, affecting 3.4%-9.3% of Japanese children and 5%-10% of Indian children, but only 2%-5% of children in the United States and Western Europe. The highest prevalence is 14% in Guam. The study was conducted in the department of pediatric medicine, at a tertiary care center, and the study includes the children between the ages of 6 months to 5 years admitted as first complex febrile seizure in the department of pediatric medicine. Out of the total 125 study subjects, the prevalence of ABM in 6-12 months is 44.4% (n=4), 13-24 months is 33.3% (n=3), 25-36 months is 11.1% (n=1) and 37-48 months is 11.2%. None of the patients in the age group of 49-60 months had ABM.

Keywords: Prevalence, acute bacterial meningitis, first complex febrile seizure

Introduction
Fever is an elevation of body temperature induced by the thermoregulatory center of the hypothalamus in response to certain situations. This sign is believed to be an adaptive mechanism, developed with the purpose of stimulating the immune system and preserving cell membrane integrity in the presence of threats. Although there is broad disagreement in the literature concerning normal body temperature in children, normal axillary temperature is generally considered to range between 36.0 °C in the morning to 37.7 °C in the afternoon. Any values above this range should be regarded as abnormal [1].
The correlation between fever and epileptic seizure is strong and has been well-established for years. When treating the child with fever and epileptic seizure, the clinician may actually be faced with at least four distinct patient subgroups: children with febrile seizures; patients with controlled epilepsy in whom fever triggered new seizures; patients with acute symptomatic seizure, that is, seizure as a manifestation of non-epileptic conditions, such as metabolic changes or acute illness (central nervous system infection or severe water-electrolyte imbalance secondary to diarrhea with dehydration, for instance). Finally, the fourth group comprises patients in whom onset of fever occurred postictal; these cases are extraordinarily difficult to distinguish from actual febrile seizure, particularly in children presenting with low-grade fever and early in the course of the episode [2].
FSs occur in 2% to 5% of children 6 months to 5 years of age. The peak incidence occurs at approximately 18 months of age and is low before 6 months or after 3 years of age.
Generally, the incidence of FS decreases markedly after 4 years of age (and the condition rarely occurs in children older than 7 years of age. FS occurs more frequently in the Asian population, affecting 3.4%-9.3% of Japanese children and 5%-10% of Indian children, but only 2%-5% of children in the United States and Western Europe. The highest prevalence is 14% in Guam.
Males have consistently emerged as having a higher frequency of FS (male to female ratio, 1.1:1 to 2:1). However, some large studies have shown no significant gender difference. There are two seasonal peaks in FS incidence: November-January, corresponding to the peak of viral upper respiratory infection, and June-August, when common viral gastrointestinal illnesses occur. Variation in prevalence is related to differences in case definitions, ascertainment methods, geography, and cultural factors [3].
In a study of children with a first FS, most seizures were simple, and at least one complex feature was noted in approximately 35% of cases, including features of focality (16.1%), multiple seizures (13.8%), prolonged duration (>15 minutes, 9.3%) and recurrent febrile seizure within 24 hours (16.2%); 6.5% showed two complex features, and 0.7% showed

three complex features. Febrile status epilepticus, that is, seizures that last more than 30 minutes, represents only 5% of FS, and represents about 25% of all episodes of childhood status epilepticus with more than two thirds of cases occurring at 2 years of age. Only 21% of children experience seizures either prior to or within 1 hour of the onset of fever; 57% have seizure after 1 to 24 hours of fever, and 22% experience febrile seizure more than 24 hours after the onset of fever [4].

FS is mostly generalized and convulsive in character, but approximately 5% of FS cases have non convulsive features presenting with unconsciousness, staring, eye deviation, atonia, or cyanosis.

The height or duration of the fever may be important but there are problems in evaluating the temperature recordings because febrile convulsions usually occur randomly at home. Viral infections commonly cause the fever that is associated with febrile convulsions. Synthesis of immunoglobulin in the CSF of children with febrile convulsions has been demonstrated, suggesting that encephalitis may sometimes occur and not be recognised. There is evidence that human herpes virus-6 (HHV-6) is linked with exanthem subitum, a condition that is frequently complicated by febrile convulsions. More recent work suggests that acute HHV-6 infection is a frequent cause of febrile convulsions in young children that do not have the signs of exanthem subitum. HHV-6B infection has been shown to be commonly associated with febrile status epilepticus, HHV-7 less frequently so. Together they accounted for one third of the cases in a study of febrile status epilepticus, a condition associated with an increased risk of both hippocampal injury and subsequent temporal lobe epilepsy. Bacterial infections may be associated with febrile convulsions-urinary tract infections, shigella and pneumococcal bacteraemia, for instance. Children with bacterial meningitis sometimes have convulsions and it is important to remember this when deciding whether or not to perform a lumbar puncture. It has been shown that there are increased risks of febrile seizures on the day of receipt of DPT vaccine and 8-14 days after MMR vaccine, apparently not associated with long-term adverse consequences. A study in the UK found that 6-11 days after MMR vaccine there was an increased risk of complex febrile convulsions lasting more than 30 minutes. However, a Danish study found that the increased risk of febrile convulsions after MMR vaccination was small and transient. Also the long-term rate of epilepsy was not increased in children who had febrile convulsions following MMR vaccination compared with children who had febrile convulsions of a different Aetiology [5, 6].

Methodology

The study was conducted in the department of pediatric medicine, at a tertiary care center, and the study includes the children between the ages of 6 months to 5 years admitted as first complex febrile seizure in the department of pediatric medicine.

Study design

Cross sectional study. All the pediatric patients fulfilling the inclusion criteria, admitted in the pediatric medicine ward during the study period were enrolled in the study.

Sample size with justification

As per the study conducted by Seltz LB *et al*, the prevalence of acute bacterial meningitis was 4% in children with first complex febrile seizure.

The sample size is calculated using the formula of single proportions.

Sample size, $n = \{Z^2 \times P (1-P)\}/E^2$

Where Z=value from standard normal distribution corresponding to desired confidence level (Z=1.96 for 95% CI)

P is expected true prevalence =5% =0.05

E is desired precision of estimate =0.05

After applying the formula the minimum sample size is calculated to be equal to 62.

Expecting the non-response, the final sample size of 125 was taken for the study.

Inclusion criteria

All patients between the ages of 6 months to 5 years admitted in pediatric medicine department as first complex febrile seizures [prolonged (>15min) and/or focal and/or reoccurs within 24 hr.].

Exclusion criteria

- The patients who did not meet the criteria for CFS
- The patients with prior history of simple/complex febrile seizures
- Those patients who presented with unprovoked seizures (afebrile seizures)
- The patients with any neurological abnormalities
- The patients with a preceding history of trauma

Results

Table 1: Distribution of study subjects according to Etiology

Etiology	Frequency	Percentage
ABM	9	7.2
Acute otitis media	10	8
Age	17	13.6
Dengue fever	7	5.6
LRTI	11	8.8
Malaria	1	.8
Unknown	14	11.2
URTI	43	34.4
UTI	9	7.2
Viral meningitis	4	3.2
Total	125	100.0

Away of the 125 study subject's majority of the subjects 34.4% had URTI followed by 13.6% had AGE, 8.8% had LRTI, 8% had acute otitis media, 7.2% had ABM and UTI.

Table 2: Distribution of study participants

Etiology	Frequency	Percent
ABM	9	7.2
No ABM	116	92.8
Total	125	100.0

Based on CSF sample analysis study subjects were generally classified as patients with ABM and those without ABM for further analysis. Among the survey subjects, ABM was found only in 7.2%.

Table 3: Prevalence of meningitis in different age groups

Age recoded	Etiology			Total			P value
	ABM	%	No ABM	%	Number	%	
6-12 months	4	44.4	39	33.6	43	34.4	
13-24 months	3	33.3	35	30.1	38	30.4	
25-36 months	1	11.1	25	21.5	26	20.8	0.0144
37-48 months	1	11.2	9	7.7	10	8	
49-60 months	0	0	8	6.8	8	6.4	
Total	9	100	116	100	125	100	

Out of the total 125 study subjects, the prevalence of ABM in 6-12 months is 44.4% (n=4), 13-24 months is 33.3% (n=3), 25-36 months is 11.1% (n=1) and 37-48 months is 11.2%. None of the patients in the age group of 49-60 months had ABM.

Table 4: Distribution of sex in study subjects

Sex	Etiology						P value
	ABM	%	No ABM	%	Number	%	
Female	1	11.1	44	37.93	45	36	
Male	8	88.8	72	62.06	80	64	0.106
Total	9	100	116	100	125	100	

Chi square -2.607, df-1 P value-0.106

In this study, the prevalence of ABM was higher in males 8 (88.8%) compared to females 1 (11.1%). But this deviation in the prevalence of ABM between males and females was not found to be statistically important.

Discussion

Acute bacterial meningitis is one, among the 10 major causes of mortality from infectious disease all over the world, mainly in the pediatric population. Despite the availability of potent newer antibiotics, the mortality due to ABM remains significantly high in India and other developing countries ranging from 16-32%. The importance of diagnosing acute bacterial meningitis in young pediatric patients is paramount as the disease progresses quickly and can cause long-term damage in less than a day after symptoms arise so, immediate medical attention is vital to the patient's survival and long-term well-being. Lumbar puncture is gold standard for the diagnosis of ABM and therefore should be considered in patient's presents as first complex febrile seizure. The association between seizures (of any type, either prolonged, focal, or recurrent) and meningitis is well established. The rate of seizure among children with ABM has been reported to be from 12% to 27%. Recently, Nigrovic *et al.* [7] developed and validated a clinical prediction rule for ABM in which the presence of seizure was the only clinical predictor, suggesting its importance. The question is not whether patients with meningitis may present with seizures but, rather, whether there is a risk of bacterial meningitis among patients who present solely as a CFS.

In this study the mean age was found to be 22 months with a minimum age of 6 months and maximum age of 60 months and majority of cases were within six months and two years of age (64.8%). Among the enrolled children 36% were female and 64% were male with a male female ratio of 1.7:1. In our study, the most common feature of complex febrile seizure was focal, compared to other features. Family history of febrile seizure was present in 12.8% of children. 71.2% of babies were vaccinated against H. influenza and none of our study subjects were vaccinated for Streptococcus pneumonia. In a study done by Kimia *et al*. [8]. The median age was 17 months with 44% of study population were females and family history of seizures was present 24% of cases. Fletcher and Sharieff [9] also had a median age of 17.2 months with 51.3% were females in their study.

Regarding the etiology of febrile illness leading to the seizures, URTI (34.4%) was the most common cause followed by AGE(13.6%), LRTI (8.8%) and acute otitis media (8%) which was close to the study conducted by Sangeeta VB *et al*., [10] in which URTI was the most common cause followed by LRTI and AGE. One of the reason for high prevalence of respiratory tract infections as the cause of fever might be attributed to the high dependence of respiratory tract infections on seasonal variation. In a country like India, where extreme seasonal variability is quite frequent, the high incidence of respiratory tract infections cannot be ruled out.

In our study we found that the overall prevalence of acute bacterial meningitis was 7.2% which was comparative with Seltz LB *et al*., [11] who reported a prevalence of 4% in children with first complex febrile seizure who underwent lumbar puncture and Tavasoli A [12] also got a prevalenc of 5.7% in patients aged 1 month to 6 years with complex febrile seizure. On the other hand, Reddy *et al*. [13] found a higher prevalence of meningitis (25.8%) in children with atypical febrile seizure. This high prevalence may be due to small sample size in their study. There are few studies which reported a lower prevalence of acute bacterial meningitis. Kimia *et al*., reported a rate of 0.9% and Fletcher *et al*., reported 0.7% prevalence of ABM among children with complex febrile seizure.

In the present study the prevalence of ABM was higher in the age group 6-24 months (8.6%) and out of 9 patients of acute bacterial meningitis, 7 (77.7%) cases were reported in this age group. Other studies also showed that the prevalence of acute bacterial meningitis is higher in the younger age group. Nahid Khosroshahi [14] showed the prevalence of 4.3% in children aged 6-18 months with 80% of the cases were in this age group and also Sangeeta VB *et al*., [10] reported 4.2% prevalence of bacterial meningitis in the age group 6-24 months and all cases were between of 6-12 months.

Conclusion

Study results suggest higher prevalence of meningitis in children who present as first episode of complex febrile seizure with children less than 2 years constitutes a special group. Lack of meningeal signs doesn't exclude meningitis especially in young infants. Hence we suggest LP should be done in all cases who present as first episode of complex febrile seizure irrespective of presence or absence of meningeal signs.

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