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# The Cross Sectional Study on the Profile of Acute Bacterial Meningitis Prevalence and Risk Factors Among Different Age Group of Children with First Complex Febrile Seizure

Deepak Tiwari[1], Saurabh Bhargava[2]

[1]Associate Professor, Department of Emergency Medicine, National Institute of Medical Science & Research, Jaipur, Rajasthan, India.

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## ABSTRACT

**Background:** Most common seizure in children occurring is fever with seizure, the reason behind it may be because of febrile seizure or a most ominous condition like meningitis. It is a common presentation for which a child may come to the emergency and may occur in up to 10% of children presenting to the emergency. Acute Bacterial Meningitis and febrile seizure association are well established. **Methods:** Demographic, current illness like fever type, duration and grading (>104ºF temperature was considered high grade fever), co-morbid diseases, past history of convulsion, birth and development history, convulsion (type, duration and number of episodes), prior hospitalization, immunization history and family history of febrile seizure was obtained. Laboratory investigation was done. CSF analysis was done after stabilizing the patients within 24 hours of admission. To predict the risk of future seizure and identification of underlying ceberal pathology EEG were done in all patients after 2 weeks of febrile seizures. **Results:** Total 125 patients between ages of 6 months to 5 years were included in this study. The mean age (mean± SD) of patients was 22±13.6 months. Out of the total 125 respondents, 43 (34.4%) belonged to 6- 12 months of age, 38 (30.4%) belonged to 13-24 months, 26 (20.8%) belonged to 25-36 months, 10 (8%) belonged to 37-48 months and 8 (6.4%) were aged 49-60 months. 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. 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%. In this study, the prevalence of ABM was higher in males 8 (88.8%) compared to females 1 (11.1%). Among 9 ABM cases, 4 (44.4%) presented as febrile status epilepticus. This demonstrates a substantial association between febrile status epilepticus and ABM. 8.8% (n=11) had h/o post-ictal drowsiness and 91.2% (n=114) didn't have h/o post-ictal drowsiness. Among 9 ABM patients, 7 (77.7%) had h/o post-ictal drowsiness compared to 4 (3.4%) of patients with no bacterial meningitis. **Conclusion:** We conclude that less than 2 years children have higher prevalence rate of acute bacterial meningitis among different age group of children with first complex febrile seizure. The main clinical risk factors of acute bacterial meningitis among different age group of children with first complex febrile seizure are febrile status epileptic, posticta drowsiness, high fever(>104°F) and abnormal neurological examination.

***Keywords:*** Febrile Seizure, Acute Bacterial Meningitis Prevalence.

## INTRODUCTION

Most common seizure in children occurring is fever with seizure, the reason behind it may be because of febrile seizure or a most ominous condition like meningitis.[1] It is a common presentation for which a child may come to the emergency and may occur in up to 10% of children presenting to the emergency.[2] Mostly Seizures are self-limiting with no long-term sequelae however,[3] about 1- 6% of the patients develop epilepsy later in life, especially those with the history of complex febrile seizures.[4]

**Name & Address of Corresponding Author**
Dr. Saurabh Bhargava
Associate Professor
Department of Emergency Medicine,
National Institute of Medical Science & Research,
Jaipur, Rajasthan, India.
Email: drsaurabbhb@gmail.com

Febrile Seizure are defined as seizures accompanied by fever without evidence of intracranial infection, metabolic disturbance, or a history of previous afebrile seizures.[5] simple and complex are two different type of febrile seizures [Table 1]. The most prevalent is simple febrile which occurs 60-90% of all seizures.[6]

**Table 1: classification of febrile seizures.**

| S.N. | Classification of Febrile Seizures | Characteristics |
|---|---|---|
| 1 | Simple Febrile Seizures | Duration of less than 15 minutes<br>Generalized<br>No previous neurologic problems<br>Occurs once in 24 hours |
| 2 | Complex Febrile seizures | Duration of 15 minutes or more<br>Focal neurologic signs<br>Recurs within 24 hours |

Four times and 31% incidence of febrile seizures increases if history of seizure in family and relatives respectively.

If the family history of febrile seizure is present, this incidence increases to four times and 31% in first-degree relatives. This also shows there is some genetic aetiology behind these seizures, but little is known about it.[7] This also shows there is some genetic aetiology behind these seizures, but little is known about it.[7] No longer treatment is given to simple febrile seizure patients. Lorazepa, diazepam and midazolam used to treat the febrile seizure patient who persist more than 5 minutes along with treatment counselling of parents is another important aspect of management.[8] Bacterial meningitis is defined as the severe infectious diseases of meninges which surrounds the brain and spinal cord and protect the central nervous system (CNS) together with cerebrospinal fluid (CSF). Bacterial meningitis can cause neurologic and systemic complications in both children and adult.[9] Acute Bacterial Meningitis and febrile seizure association are well established.[9-12] The prevalence of acute bacterial meningitis with febrile seizure and fever is 0.6-6.7%.[13] Better and appropriate early management of patients can be done after differentiation between febrile seizure from meningitis.[14,15] Awareness of the prevalence and other complications of bacterial meningitis among various subgroups of children with febrile seizures can helps clinicians to make appropriate clinical decisions in such challenging situations. It is mandatory to look for signs of raised intracranial pressure i.e. bulging fontanel, papilloedema and signs of meningeal irritation to exclude meningitis.8 Febrile seizure may be the sole manifestation of bacterial meningitis in infants; complex features of seizure can increase the risk of bacterial meningitis in others.[15-19]

The early diagnosis and prompt treatment of acute bacterial meningitis are essential and cerebrospinal fluid (CSF) examination helps in this objective.[16,20] Acute bacterial meningitis major presenting sing may be febrile seizures, it remains a major concern, more so in cases of complex febrile seizures. It is essential to exclude underlying meningitis in all children presenting as CFS by lumber puncture (LP). The majority of such cases of meningitis are bacterial in origin, and delay in diagnosis can result in serious neurologic morbidity, and even death. The aim of study reflects prevalence, risk factors and utility of lumber puncher among different age group of children with first complex febrile seizure.

## MATERIALS AND METHODS

The hospital based cross sectional prospective study was conducted in the Department of Emergency Medicine, National Institute of Medical Science & Research, Jaipur, Rajasthan. The study includes the children between the ages of 6 months to 5 years from January 2016 to June 2018. Written informed consent were taken from the parents of patients admitted in pediatric ward who were fulfilling the inclusion criteria after taking approval from ethics committee of institute.

**Inclusion criteria:**

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

**Exclusion criteria:**

The patients who did not meet the criteria for CFS, with prior history of simple/complex febrile seizures, with unprovoked seizures (afebrile seizures), with any neurological abnormalities, with a preceding history of trauma were excluded from the study.

Demographic, current illness like fever type, duration and grading (>104ºF temperature was considered high grade fever), co-morbid diseases, past history of convulsion, birth and development history, convulsion (type, duration and number of episodes), prior hospitalization, immunization history and family history of febrile seizure was obtained. Laboratory investigation were done. CSF analysis were done after stabilizing the patients within 24 hours of admission. To predict the risk of future seizure and identification of underlying ceberal pathology EEG were done in all patients after 2 weeks of febrile seizures. Patients having abnormal examination before lumber puncture and those who shown febrile status epilepticus were examined by CT scan.

## RESULTS

Total 125 patients between ages of 6 months to 5 years were included in this study. The mean age (mean± SD) of patients was 22±13.6 months. Out of the total 125 respondents, 43 (34.4%) belonged to 6-12 months of age, 38 (30.4%) belonged to 13-24 months, 26 (20.8%) belonged to 25-36 months, 10 (8%) belonged to 37-48 months and 8 (6.4%) were aged 49-60 months [Table 2].

**Table 2: Distribution of study participants according to age groups**

| Age | Frequency | Percent |
|---|---|---|
| 6-12 months | 43 | 34.4 |
| 13-24 months | 38 | 30.4 |
| 25-36 months | 26 | 20.8 |
| 37-48 months | 10 | 8.0 |
| 49-60 months | 8 | 6.4 |
| Total | 125 | 100.0 |

The gender distribution of the study subjects indicated the bulk of the patient were males accounting 64% (n=80) and 36% (n=45) were females, indicating male preponderance with a male to female ratio 1.7:1 shown in [Figure 1].

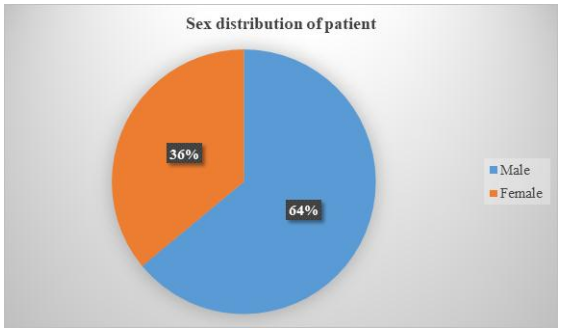


**Figure 1: Pie diagram showing the gender distribution**

Among the study subjects, 12.8 %( n=16) had family history of febrile seizure, compared to 87.2% (n=109) who had no family history.

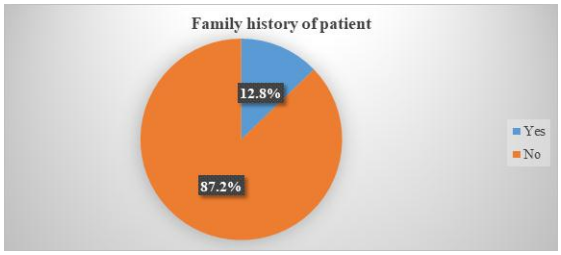


**Figure 2: Pie diagram showing the percentage distribution of family history**

In our study, the most common presentation of complex febrile seizure was focal.

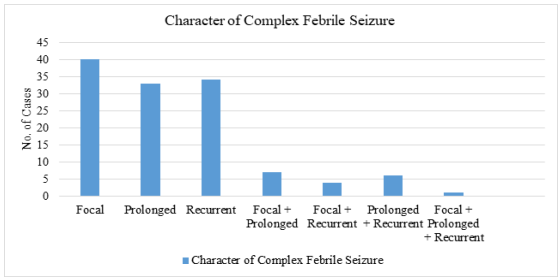


**Figure 3: Bar Diagram showing percentage distribution according to character of complex febrile seizure.**

Among the total 125 study participants, 71.2% were immunized against Hemophilus influenzae type b and none of them were immunized against streptococcus pneumonia. Away of the 125 study subjects' 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 shown in [Table 3].

**Table 3: 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 | 0.8 |
| Unknown | 14 | 11.2 |
| URTI | 43 | 34.4 |
| UTI | 9 | 7.2 |
| Viral Meningitis | 4 | 3.2 |
| Total | 125 | 100 |

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. 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. 14.4% (n=18) suffered high grade fever while 85.5% (n=107) didn't suffer high grade fever. Whole cases of ABM were having high grade fever. This association of high grade fever with ABM was significant. 4%(n=5) presented with febrile status epilepticus while 96%(n=120) were normal. Among 9 ABM cases, 4 (44.4%) presented as febrile status epilepticus. This demonstrates a substantial association between febrile status epilepticus and ABM. 8.8% (n=11) had h/o post-ictal drowsiness and 91.2% (n=114) didn't have h/o post-ictal drowsiness. Among 9 ABM patients, 7 (77.7%) had h/o post-ictal drowsiness compared to 4 (3.4%) of patients with no bacterial meningitis. This association between post-ictal drowsiness and ABM was significant in our study. Among 9 ABM cases, 2(22.2%) had abnormal neurological examination at the time of admission and none of the patients without acute bacterial meningitis had abnormal neurological examination. This association between abnormal neurological examination and ABM was found to be statistically significant.

**Table 4: Distribution, prevalence and association of various factors like age, sex, high fever, epilepticus, post ictal drowsiness, anemia, EEG, hyponatremia, CRP, CSF and acute bacterial meningitis.**

| | Etiology | | | | Total | | P-Value |
|---|---|---|---|---|---|---|---|
| | ABM | % | NO ABM | % | Number | % | |
| **Prevalence of meningitis in different age groups** | | | | | | | |
| 6-12 months | 4 | 44.4 | 39 | 33.6 | 43 | 34.4 | 0.0144 |
| 13-24 months | 3 | 33.3 | 35 | 30.1 | 38 | 30.4 | |
| 25-36 months | 1 | 11.1 | 25 | 21.5 | 26 | 20.8 | |
| 37-48 months | 1 | 11.1 | 9 | 7.7 | 10 | 8 | |
| 49-60 months | 0 | 0 | 8 | 6.8 | 8 | 6.4 | |
| **Distribution of sex in study subjects** | | | | | | | |
| Female | 1 | 11.1 | 44 | 37.93 | 45 | 37.93 | 0.106 |
| Male | 8 | 88.8 | 72 | 62.06 | 80 | 64.0 | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Distribution of High grade fever** | | | | | | | |
| Yes | 9 | 100 | 9 | 7.7 | 18 | 14.4 | 0.0000001 |
| No | 0 | 0 | 107 | 92.3 | 107 | 85.6 | |
| **Association between febrile status epilepticus and acute bacterial meningitis** | | | | | | | |
| Yes | 4 | 44.4 | 1 | 0.9 | 5 | 4 | 0.0001 |
| No | 5 | 55.5 | 115 | 99.1 | 120 | 96 | |
| **Association between post ictal drowsiness and acute bacterial meningitis** | | | | | | | |
| Yes | 7 | 77.7 | 4 | 3.4 | 11 | 8.8 | 0.0001 |
| No | 2 | 22.2 | 112 | 96.6 | 114 | 91.2 | |
| **Association between abnormal neurologic examination and acute bacterial meningitis** | | | | | | | |
| Abnormal | 2 | 22.2 | 0 | 0 | 2 | 1.6 | 0.0046 |
| Normal | 7 | 77.7 | 116 | 100 | 123 | 98.4 | |
| **Association of Anemia with ABM** | | | | | | | |
| Anemia | 7 | 77.7 | 42 | 36.2 | 49 | 39.2 | 0.00001 |
| No Anemia | 2 | 22.2 | 74 | 63.8 | 76 | 60.8 | |
| **Association between increased Total leucocyte count and acute bacterial meningitis** | | | | | | | |
| Increased | 8 | 88.8 | 18 | 15.6 | 26 | 20.8 | 0.0000001 |
| Normal | 1 | 11.1 | 98 | 84.4 | 99 | 79.2 | |
| **Association between positive CRP and ABM** | | | | | | | |
| Positive | 9 | 100 | 22 | 19 | 31 | 24.8 | 0.0000001 |
| Negative | 0 | 0 | 94 | 81 | 94 | 75.2 | |
| **Association between hyponatremia and ABM** | | | | | | | |
| Yes | 7 | 77.7 | 18 | 15.5 | 25 | 20 | 0.0000001 |
| No | 2 | 22.2 | 98 | 84.4 | 100 | 80 | |
| **Association between CSF culture and ABM** | | | | | | | |
| Positive | 3 | 33.3 | 0 | 0 | 3 | 2.45 | 0.0000001 |
| Negative | 6 | 66.6 | 116 | 100 | 122 | 97.6 | |
| **Distribution of EEG abnormalities among study population** | | | | | | | |
| Abnormal | 8 | 88.8 | 28 | 24.1 | 36 | 28.8 | 0.0000001 |
| Normal | 1 | 11.1 | 88 | 75.9 | 89 | 71.2 | |

Out of total 125 subjects, 39.2 % (n=49) of them had anaemia and 60.8% (n=76) had normal Haemoglobin level.7 (77.7%) cases of ABM had anaemia compared to 36.2% without acute bacterial meningitis had anaemia. This association between anemia and ABM was significant. Among 9 meningitis patients, 88.8% (n=8) had increased Total leucocyte count while 11.1 % (n=1) had normal Total leucocyte count. This difference between increased total leucocyte count and ABM was found to be statistically significant. 14.4% (n=18) had hyponatremia while 85.6% (n=107) had normal serum sodium level. Hyponatremia was found in 7 (77.7%) cases of ABM compared to 15.5% without bacterial meningitis. The association between Hyponatremia and ABM was statistically significant. Among 125 subjects, CSF cell culture was positive in 2.45% and negative in 97.6%. Out of 9 ABM cases, CSF culture was positive in 33.3% (n=3) and negative in 66.6%. This difference between CSF culture and ABM was found to be statistically significant. Out of total 125 cases, 28.8% (n=36) had Abnormal EEG findings while 71.2% (n=89) had normal EEG findings. Among 9 ABM cases, EEG was abnormal in 88.8% (n=8) and was normal in 11.1% (n=1). This difference between EEG abnormality and ABM was found to be statistically significant.

## DISCUSSION

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. In a study done by Kimia et al,[21] the median 92 age was 17 months with 44% of study population were females and family history of seizures was present 24% of cases. Fletcher and Sharieff,[22] 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,[23] 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.[24,25]

In our study we found that the overall prevalence of acute bacterial meningitis was 7.2% which was comparative with Seltz LB et al,[19] who reported a prevalence of 4% in children with first complex febrile seizure who underwent lumbar puncture and Tavasoli A also got a prevalenc of 5.7% in patients aged 1 month to 6 years with complex febrile seizure.[26] On the other hand, Reddy et al,[27] found a higher prevalence of meningitis (25.8%) in

children with atypical febrile seizure. There are few studies which reported a lower prevalence of acute bacterial meningitis. Kimia et al,[21] reported a rate of 0.9% and Fletcher et al,[22] 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,[28] 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,[23] reported 4.2 % prevalence of bacterial meningitis in the age group 6-24 months and all cases were between of 6-12 months. We didn't find any significant correlation between gender and bacterial meningitis although majority of cases of ABM were males in our study. In our study, 13 subjects (10.4%) had CSF pleocytosis (WBC>5).

CSF examination revealed patients who presented as febrile status epilepticus had increased risk of having bacterial meningitis. Similar case series were reported by RFM Chin,[29] out of 49 children with convulsive status epilepticus with fever 4 (17%) children aged 3 months, 9.5 months, 18 months, 26 months were confirmed to have ABM and was concluded that the risk of ABM in a convulsive status epilepticus with fever is much higher than that of short febrile seizures. In a case control study done in India, it was seen that the iron deficiency anemia is the most important risk factor for febrile convulsion.[30]

In present study, we found that 39.2% of patients of complex febrile seizures were having haemoglobin level 104°F, increased WBC count above the age wise reference range, positive CRP are the predicting factors for bacterial meningitis in our study. A study conducted in Iran also concluded that postictal drowsiness, neurological deficit, body temperature ≥ 38.5°C, WBC count > 15000/cumm and Hb < 10.5g/dl were clinical and laboratory factors predictive of meningitis in cases with first attack of seizure and fever.[28] In our study 28.8% of children who are presented as complex febrile seizure had abnormal EEG findings and among 9 cases of ABM, 8 (88.8%) had abnormal EEG findings due to structural and functional alterations of the brain resulting from the meningitic process that may induce seizures include vasculitis and infarction, fever, electrolyte imbalances and metabolic changes. Yucel et al reported EEG abnormalities in 71 (44.4%) of 159 children with complex febrile seizures analysed retrospectively over 7 years.[31] Neuroimaging was done in 6 patients who presented with febrile status epilepticus and having abnormal neurological examination, only one patient had diffuse leptomeningeal enhancement in the contrast enhanced CT scan of brain.

## CONCLUSION

We conclude that less than 2 years children have higher prevalence rate of acute bacterial meningitis among different age group of children with first complex febrile seizure. The main clinical risk factors of acute bacterial meningitis among different age group of children with first complex febrile seizure are febrile status epileptic, postictal drowsiness, high fever(>104°F) and abnormal neurological examination. Meningeal sings cannot excluded in acute bacterial meningitis especially in young adults. In all cases of acute bacterial meningitis among different age group of children with first complex febrile seizure, Lumber puncture should be done either presence or absence of meningeal sign.

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