

# A Hospital Based, Cross-Sectional Study to Determine the Prevalence of Meningitis in 6-18 months Old Children with First Episode of Febrile Seizure

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Received: 10-02-2023 / Revised: 13-03-2023 / Accepted: 08-04-2023

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Conflict of interest: Nil

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## Abstract

**Introduction:** In spite of the fact that there are epidemiological differences between India and the United States, the AAP 2010 guiding principles are adhered to perform Lumbar Puncture in the first occurrence of febrile seizures, having incidence of 2-5% in >1month old children and most frequently between 6 months to 5 years old children.

**Aim and Objectives:** To determine the prevalence and risk factors for meningitis for the first incidence of febrile seizures among children between the ages of 6 and 18 months.

**Materials and Methods:** In a tertiary care centre in northeastern India, 200 children between the ages of 6 and 18 months who had been admitted with their first episode of FS underwent this cross-sectional research. The lumbar puncture was carried out, and clinical, blood, CSF variables were analyzed by the SPSS version 21.0.

**Results:** Children aged 6 to 18 months who presented with the initial episode of FS had a meningitis prevalence of 16% (n=32). In 3% (n=6) of patients, bacterial meningitis (BM) was seen. Higher Total Leukocyte Count (TLC) i.e. >16500 cells/mm<sup>3</sup> with positive C - reactive protein (CRP) were the independent predictors of meningitis. Seven patients (3 of *S. pneumoniae*, 2 of MRSA, 1 each of *K. pneumoniae*, and *N. meningitidis*) had positive blood cultures. In 56.2% (n=18) among the meningitis cases, monocytes were the most prevalent kind of cell to be found.

**Conclusion:** Given that meningitis is more common in kids with initial episodes of FS in India as compared to the USA and that India has a much lower immunization rate for the Haemophilus (Hib) & pneumococcal vaccine (PCV) than the USA; India have to develop its own criteria to perform lumbar puncture in instances with initial occurrence of FS. In patients who have elevated TLC (>16500 cells/mm<sup>3</sup>) and positive CRP, meningitis might be anticipated.

**Key words:** Meningitis; CRP; Febrile seizures; Lumbar puncture, TLC.

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## Introduction

Febrile seizures (FS) are the commonest type of convulsions that occur in children. Around 2-5% of kids are affected between the ages of

six months and five years [1,2]. Globally, FS is a significant factor for pediatric hospitalization [3]. Seizures with a high

temperature but no cerebral illness, a history of prior afebrile seizures, or a metabolic imbalance are referred to as febrile seizures [4].

Simple (typical) FS are tonic-clonic, generalized, persist for no longer than 15 minutes, and are not repeated within a 24-hour of time interval. Atypical complex FS are protracted (lasting >15min), focal, and/or reoccur during 24 hrs [4].

Seizures are the initial sign of meningitis in approximately 16.7% of children, and meningeal manifestations may not be visible in 1/3 of those affected [5]. Therefore, in order to rule out underlying meningitis in children reporting with fever and seizures, FS must first be ruled out. [6] The lumbar puncture (LP) technique is invasive. As a result, it should only be done when necessary. Meningitis is prevalent in 18.65 among those in the 6 months-5 years age group in the Indian population with FS. [7]

For those older than one month, *Streptococcus pneumoniae* and *Neisseria meningitidis* are the most typical causes of Bacterial Meningitis (BM).[8] In India, the rates of vaccination against Hib and PCV are unknown, but in the USA, they are 82.4% and 84.1%, respectively. As a result, the prevalence of meningitis in FS cannot be compared between the two countries. [9,10]

According to the most recent AAP 2010 recommendations, LP should be done in the following situations:

- Children with febrile seizure as well as manifestations of meningitis;
- Patients whose medical history or physical examinations suggest meningitis or an intracranial infection;
- Infants aged 6 to 12 months with FS who didn't receive the Hib or PCV vaccine doses or whose immunization status is not known;

- Children with febrile seizure who received prior antibiotics;
- Very sick kids. [11]

There is a need for our own guidelines because India being a developing nation in comparison to the developed nation USA, where immunization rates are greater than that of India. It is therefore improper to compare and apply the recommendations of a developed country where the socioeconomic position, vaccination coverage, epidemiology of meningitis, and rates of prior antibiotic treatment are all significantly different. Children aged 6 to 18 months who had the initial episode of febrile seizures were included in the research to determine the prevalence & risk factors for meningitis.

### Aims and Objectives

To determine the prevalence and risk factors for meningitis for the first incidence of febrile seizures among children between the ages of 6 and 18 months.

### Materials and Methods

A tertiary care institution in northeastern India's pediatric wards was the site of this hospital-based cross-sectional investigation. Patients were enrolled in the research with the parents' or guardians' consent in writing after getting approval from the institutional ethics committee.

**Sample size calculation:** According to a research conducted at the Ali Asghar Hospital located at Iran (N=681), the sample size of present study was determined. 4.5% of prevalence rate of meningitis were recorded.[12] As a result, sample of 200 participants were needed to reach the 5% level of significance, 3% margin of error and adding 10% for any losses for children reporting with their first FS.

Equation used:  $n = \frac{z^2 \alpha / 2}{pq/d^2}$ , where, p: observed prevalence, q=1-p, d: margin of

error,  $Z_{\alpha/2}$ : ordinate of standard normal distribution at  $\alpha$  % level of significance

#### **Inclusion/exclusion criteria:**

- The research comprised 267 children (aged 6 to 18 months) who were hospitalized to the hospital with their first episode of FS.
- Six parents or guardians declined to take part in the research. (n=6)
- Children with a history of prior non-FS or known congenital neurological abnormalities (n=20)
- Children with an underlying condition known to cause seizures (n = 18)
- Children with a history of head trauma (n=3) Children exhibiting characteristics indicative of elevated intracranial tension (anterior fontanelle bulging, papilloedema) (n=20) were excluded from the study.
- Thus, finally 200 patients were included in the study.

#### **Procedure**

Participants were divided into two groups, one aged 6-12 months and the other aged 12-18 months. Every case was thoroughly examined. After receiving consent in writing, all participants underwent lumbar puncture. We collected cerebrospinal fluid (CSF) in three separate sterile vials and sent one for cell counting, one to biochemistry for protein and sugar analysis, and one for culture. CBC, serum electrolyte (sodium, potassium, and calcium) levels, CRP, blood culture and sensitivity, and fundus inspection if anterior fontanelle was closed were all performed after 8 mL of blood was drawn via venepuncture while using all appropriate aseptic precautions. Meningitis in children experiencing their first episode of FS was investigated to ascertain its prevalence and to identify potential risk factors.

A temperature of more than 100.4°F in the axilla was considered to be fever.

Simple (typical) FS has been defined as occurring just once in 24 hours for no longer as 15 minutes [13]. Seizures lasting more than 15 minutes or recurring within 24 hours were deemed to be complex FS (atypical) [13].

In meningitis, CSF pleocytosis (more than 5 cells per mL of CSF), CSF protein more than 45 mg/dL, along with CSF sugar less than 50 mg/dL were all considered diagnostic criteria [8].

The WBC count of the traumatized LP was determined after making the following adjustments:

Corrected CSF WBC count = {CSF WBC count – (CSF red blood cell count/500)}.

Bacterial meningitis (BM) was diagnosed by either the presence of a pathogen in a cerebrospinal fluid (CSF) culture or by any of the aforementioned criteria in conjunction with the spread of a pathogen in a blood culture. CSF pleocytosis with mononuclear cell dominancy and no pathogen in CSF or blood culture is consistent with a diagnosis of aseptic meningitis if the patient has not been pretreated with antibiotics for at least a week.

If a diagnosis of BM was made out of an abundance of caution in patients with CSF pleocytosis & a history of premedication by antibiotics, then the patient was treated for BM.

Immunoturbidimetry was used to measure the CRP, and a positive result was defined as greater than 6 mg/L. The management of the FS followed unit protocol.

#### **Statistical Analysis**

The statistical software for SPSS version 21.0 was used for the statistical testing. For non-normally distributed data, continuous variables were shown as mean±SD or median (IQR). Frequencies (N) and percentages (%) were the two ways categorical variables were expressed. The Student's t-test was used to

compare normally distributed continuous data variables among the groups. Nominal categorical data were compared between the groups using the relevant chi-squared test or fisher's exact test. The Mann-Whitney U test was used to compare continuous variables with non-normal distribution.

In children reporting with their first FS, logistic regression was applied to identify the determinants of meningitis. A p-value of  $\leq 0.05$  was used to denote a significant significance in all performed tests.

## Results

**Table 1** displays the distribution, comparability, and association of cases between the meningitis and non-meningitis groups.

**Table 2** compares the meningitis group with the non-meningitis group and displays the distribution of cases by age, clinical, and blood data.

Seven patients (3 of *S. pneumoniae*, 2 of MRSA, 1 each of *K. pneumoniae*, and *N. meningitidis*) had positive blood cultures.

Blood culture results that were positive in 6 out of 7 (81.2%) individuals had meningitis, while the remaining case had MRSA sepsis.

The 200 patients' average CSF protein concentration was  $55.1 \pm 70.57$  mg/dL. Three instances of *S. pneumoniae*, one each of *K. pneumoniae*, *N. meningitidis*, and MRSA, and six (3%) of the patients showed positive CSF cultures. *S. pneumoniae* was the most frequently isolated organism in the CSF culture and was found in 9.3% of all the cases of meningitis. The other three species were found in 3.1% of the meningitis cases. It was observed that 18.8% of the cases of meningitis exhibited CSF cultures to be positive. The study's average TLC was  $9947.3 \pm 4315.1$  cells/mm<sup>3</sup>. The mean TLC for meningitis cases was  $16715.63 \pm 4171.48$  cells/mm<sup>3</sup> and  $8659.2 \pm 2916.85$  cells/mm<sup>3</sup> for non-meningitis cases, respectively. In patients with the first occurrence of FS between 6–18 months of age, a strong association with high TLC ( $>16500/\text{mm}^3$ ) and meningitis was discovered, thus rendering it a potential predictor of meningitis ( $p < 0.001$ ).

**Table 1: Distribution, comparability, and association of cases between the meningitis and non-meningitis groups**

Variables		Meningitis Absent (n) (%)	Meningitis Present (n) (%)	p-value
Age (months)	6-12	98 (58.3)	14 (43.7)	0.128 (NS)
	12-18	70 (41.7)	18 (56.3)	
Gender	Male	122 (72.6)	13 (40.6)	<0.001 (S)
	Female	46 (27.4)	19 (59.4)	
Febrile Seizure type	Typical	75 (44.6)	04 (12.5)	0.001 (S)
	Atypical	93 (55.4)	28 (87.5)	
C-reactive protein	Positive	03 (1.8)	14 (43.8)	<0.001 (S)
	Negative	165 (98.2)	18 (56.2)	
Blood culture	Positive	01 (0.6)	06 (18.8)	<0.001 (S)
	Negative	167 (99.4)	26 (81.2)	
Prior antibiotic history	Yes	02 (1.1)	02 (6.25)	0.121 (NS)
	No	166 (98.9)	30 (93.75)	
CSF cell type	PMNL	03 (1.8)	01 (3.1)	
	Monocytes	05 (3.0)	18 (56.2)	

	Mainly PMNL	0	08 (25)	
	Mainly monocytes	0	05 (15.7)	
	None	160 (95.2)	0	

NS- Not Significant, S- Significant, PMNL: Polymorphonuclear leucocytes

**Table 2: Comparison of the meningitis group with the non-meningitis group and the distribution of cases by age, clinical, and blood data**

Variables	Meningitis Absent (Mean±SD)	Meningitis Present (Mean±SD)	p-value
Age (months)	12.89±4.37	12.73±4.35	0.129 (NS)
Hemoglobin (gm %)	12.07±1.78	11.38±1.87	0.581 (NS)
Total Leukocyte Count (cells/mm <sup>3</sup> )	8658.2±2916.85	16715.63±4171.48	<0.001 (S)
Platelet count (cells/mm <sup>3</sup> )	304636.8±114677.48	255937.51±160810.83	0.133 (NS)
Mean corpuscular volume (fL)	77.22±8.75	73.21±6.62	0.007 (S)
Post-ictal state duration (min)	8.35±7.56	14.54±11.97	0.003 (S)
Fever duration (days)	2.64±1.17	3.17±1.66	0.095 (NS)
Dextrose (mg/dL)	94.93±24.56	96.57±21.64	0.447 (NS)
Serum Calcium (mg/dL)	9.56±7.62	9.06±1.02	0.373 (NS)
Serum sodium (MEq/L)	139.37±5.93	140.01±6.27	0.593 (NS)
Serum potassium (MEq/L)	4.43±0.68	4.39±0.72	0.769 (NS)
CSF cytology(cells/mm <sup>3</sup> )	0.22±0.97	74.18±119.92	0.457 (NS)
CSF protein (mg/dL)	47.74±61.14	93.76±99.97	0.004 (S)
CSF sugar (mg/dL)	62.71±17.88	58.83±25.46	0.664 (NS)
Seizure duration (min)	6.33±5.75	12.63±8.84	<0.001 (S)

NS- Not Significant, S- Significant

## Discussion

One of the most prevalent forms of childhood seizures, the FS affects 1-5% of children between the ages of six months and five years. This study was conducted to determine the incidence of meningitis among children aged 6 to 18 months who presented with the initial episode of FS and to determine if the AAP recommendations for LP in kids with FS were also appropriate in the Indian context. The current study also sought to identify the risk factors for meningitis in kids between the ages of 6 and 18 months who presented with the initial episode of FS. A handful of investigations [7, 14] have been conducted to determine the determinants of meningitis among kids with initial episodes of FS, despite several additional researches being conducted all over the world to

determine the incidence of meningitis among these children.

In the current study, meningitis prevalence was estimated to be 16% and BM prevalence to be 3%, respectively. CRP positivity and high TLC were distinct risk variables for meningitis among kids presenting with their initial episode of FS between the ages of 6 and 18 months. In Iran, a retrospective investigation by Tavasoli A *et al.* in the age range of just over a month to six years revealed a prevalence of 4.5%, that was lower than that of the present study. 22 of the kids had their LP done [12].

An evidence-based review by Horn J. and Medwid K. from the USA examined the Cochrane, Medline, and Embase library

databases for cases in the 6–18 month age range with uncomplicated FS and performed LP on those patients. In contrast to this study, it was shown that 2.5% of patients had CSF pleocytosis, and meningitis was seen in 0% of cases [2].

Another retrospective research conducted in the USA by Kimia A *et al.* on 340 children with atypical FS aged from six months up six years revealed 2.7% of CSF pleocytosis and 0.9% of ABM. In contrast to this study, it also demonstrated that meningitis prevalence in kids with their first occurrence of FS is significantly lower in the United States [1].

Meningitis was found in only 5% of patients, according to a retrospective research conducted by Casasoprana A *et al.* to determine whether AAP recommendations for LP in the first occurrence of FS are valid in France. In 63 of a total of 157 cases, LP was performed. There were three viral meningitis cases, 3 of BM (*S. pneumoniae*) cases, and two cases of non-herpetic viral encephalitis. In the research, there were 1.9% cases of acute bacterial meningitis (ABM) [14].

Tinsa F *et al.* conducted a research in Tunisia on 106 newborns to determine the risk factors for meningitis in infants experiencing their first episode of FS; they discovered that the prevalence of meningitis was 10%. Compared to the study's findings, this is lower, but it's higher than research done in industrialized countries. Also found the following risk factors: age 7 months, seizure duration >5 minutes, convulsions recurrence on the identical day, high CRP (>20 mg/L), low sodium (<125 mmol/L), and neurological disorders.[15]

A second retrospective study by Kanik A *et al.* in Turkey found no CSF abnormalities and no incidences of BM in 135 out of 564 children aged 6 to 24 months old who presented with their first episode of FS. Ten patients (1.7%) had CSF pleocytosis, seven

of them had complicated FS and three had simple FS. The low incidence of CSF pleocytosis may be due to the definition of CSF pleocytosis being >10 cells/mm<sup>3</sup>, that is higher than the cut off used in this investigation. [16]

Similar to this study, a retrospective investigation conducted in by Reddy DS *et al.* involving 105 kids aged 6-60 months who presented with their first occurrence of FS found that 18.6% of them had BM. Only 43 instances total had the LP performed, and eight of those cases had BM. All of these individuals showed CSF pleocytosis but no growth in culture [7].

ABM was found in 12 instances (7.6%) among 157 children aged 6 months-5years in a cross-sectional research conducted by Siddiqui HB *et al.*, of which 7 cases (58.3%) had a positive culture. The outcomes were less impressive than those in this trial, most likely as a result of the differing diagnostic standards used in the ABM study. For the age range of 6 to 12 months, *Streptococcus pneumoniae* was detected in 2 (1.3%) cultures, *Haemophilus influenzae* in 1 (0.6%), and there was no growth in 2 (1.3%) CSF samples. In the 13 to 18 month age range, two (1.3%) cultures tested positively for *Streptococcus pneumoniae*, one (0.1%) for *Haemophilus influenzae*, and one (0.6%) sample had no growth [17].

According to a research conducted in Nepal by Shrestha SK, meningitis was present in 14.5% of 110 patients ranging in age between 5 months - 6 years. Six of them (21.4%) were in the 6 to 12 month age range (n=28), in contrast to 12.5% (n=14) in present study; 6 out of the 31 cases in the 12 to 18 month age range (19.3%) in comparison to 20.4% (n=18) in this study; and only four (7.54%) from the 51 cases in the more than 18 month age range had meningitis [18].

After analyzing all of the aforementioned research from throughout the globe, it was

shown that developing nations like India have a substantially higher rate of meningitis following the initial incidence of FS than affluent nations. According to AAP recommendations, performing lumbar puncture in kids >12 months only if specific criteria are satisfied will be incorrect because there is no appreciable difference in meningitis prevalence among age bracket of 6-12 months & 12-18 months. In comparison to the United States, India has a substantially lower vaccination rate for the two most frequent BM-causing pathogens, *Streptococcus pneumoniae* and *Haemophilus influenzae*. In light of the foregoing, authors recommend Indian recommendations for LP in kids with their first episode of FS. The study's strengths were its greater sample size, cross-sectional design, and evaluation of meningitis predictors.

### Limitations of the study

Limitations included a specific single geographic location, a sample that was solely drawn from hospital only, and memory/recall bias with regard to the duration of the seizure.

### Conclusion

Meningitis was common (16%) in kids between 6-18 months who presented with a initial instance of febrile seizure in the present research. Meningitis can also be anticipated in those who have substantially raised TLC (>16500 cells/mm<sup>3</sup>) as well as elevated CRP, according to this study. Antibiotic use within last 7 days might have influenced our findings by turning the CSF values negative, however this was only in the 2% of all patients. The authors advocate larger prospective studies to corroborate these findings.

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