ORIGINAL ARTICLE

# Clinical Profile, Cerebrospinal Fluid Findings, and Outcome of Acute Meningitis in Children: A Recent Audit from a Tertiary Center in India

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## Abstract

**Aim and objective:** Periodic surveillance of causative organisms of acute meningitis in children is helpful. Cerebrospinal fluid (CSF) findings characterize the type of meningitis and guide therapy to improve the outcome. We aimed to analyze clinical features, CSF characteristics, causative organisms, and the outcome of meningitis in children.

**Materials and methods:** Children aged from 1 month to 18 years admitted to a teaching hospital with a provisional diagnosis of meningitis were studied retrospectively. Clinical data, CSF analysis, and complications of meningitis were retrieved from medical records. Meningitis was further classified depending on laboratory findings into acute bacterial meningitis (ABM), probable bacterial meningitis (APBM), and aseptic meningitis (ASM).

**Results:** Among 50 children with meningitis, 9 (18%) had ABM, 34 (68%) had APBM, and 7 (14%) had ASM. The causative bacteria included *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Escherichia coli*, *Enterobacter cloacae*, *Streptococcus viridians*, *Brucella,* and *Salmonella typhimurium*. Important clinical features included fever (96%), seizures (50%), headache (44%), vomiting (70%), altered sensorium (56%), neck stiffness (56%), cranial nerve palsy (16%), and focal neurological deficits (10%). The median CSF WBC levels in ABM, APBM, and ASM groups were 310, 125, and 140 cells/mm$^3$, respectively. The mean CSF glucose and protein levels in the same groups, respectively, were 29.5 ± 23.1, 51.2 ± 23.8, and 51.7 ± 8.7 mg/dL; and 441.5 ± 546.9, 99.1 ± 79.1, and 100.1 ± 82.6 mg/dL. Complications among 43 bacterial meningitis included hydrocephalus (8, 18.6%), hearing loss (4, 9.3%), visual impairment (3, 6.9%), brain abscess (3, 6.9%), subdural effusion (1, 2.3%), and infarct (1, 2.3%).

**Conclusion:** The present study has explored the causative bacteria in acute meningitis in children. Furthermore, the study explored the characteristics of CSF and identified the important complications.

**Keywords:** Bacteria, Cerebrospinal fluid, Children, Infants, Meningitis.

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## Introduction

Acute meningitis in children causes significant morbidity.[1] Infectious agents of meningitis include bacteria, viruses, fungus, and other microorganisms. Viral meningitis is more common and bacterial meningitis is more severe. About 5–20% of meningitis is caused by bacteria.[2,3]

The spectrum of disease-causing organisms may change over a period of time. The availability of new β-lactam antibiotics, immunization against *Haemophilus influenzae*, pneumococci, meningococci, advanced intensive care, and supportive management in developed countries has reduced the prevalence of bacterial meningitis and improved the prognosis. Poor immunization coverage, delay in seeking medical attention, malnutrition, delay in diagnosis, and initiating appropriate antibiotic therapy in bacterial meningitis prevail as the major causes of childhood morbidity and mortality in developing countries.[4]

Early diagnosis and initiating appropriate antibiotics in bacterial meningitis reduces morbidity and improves the outcome. Cerebrospinal fluid (CSF) examination for cell type and cell count, biochemistry, bacterial antigen testing, Gram stain, culture, and PCR for viral DNA used alone or in various combinations will further characterize the possible etiology whether it is bacterial meningitis or viral meningitis.[5–7] In this context, we aimed to analyze the clinical features, CSF characteristics, causative organisms, and outcomes of various types of acute meningitis in children.

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**Conflict of interest:** None

## Materials and Methods

All children from 1 month to 18 years admitted in the Department of Paediatrics, in a tertiary care teaching hospital with the provisional diagnosis of meningitis during the period between September 2016 and September 2018 were studied retrospectively.

Children with associated comorbidities like malignancy, bleeding disorder, ventriculoperitoneal shunt *in situ* or infections like human immunodeficiency virus infection/neurocysticercosis, those on immunosuppressive therapy, recurrent or chronic meningitis, and in whom lumbar puncture was contraindicated were excluded.

Clearance was obtained from the Institutional Ethics Committee before the commencement of the study (IEC-800/2019). Following data were collected from the medical records—detailed history, demographic data, primary diagnosis, treatment, and outcome. Cerebrospinal fluid analysis data included cell type, cell count, glucose level, protein level, chloride, adenosine deaminase (ADA), lactate, Gram stain, culture and sensitivity, CSF antigen testing, CSF CBNAAT, viral studies for HSV and JE virus. Other investigations such as magnetic resonance imaging (MRI) of the brain, computed tomography (CT) brain, blood culture reports if carried out were obtained from the records.

Clinically suspected cases of meningitis were further classified depending on laboratory findings. Cerebrospinal fluid with WBC >10 cells/mm$^3$ and CSF culture and/or antigen test positive were considered as acute bacterial meningitis (ABM). Cerebrospinal fluid with WBC >10 cells/mm$^3$ and CSF culture sterile but protein >45 mg/dL, glucose <40 mg/dL or CSF to blood glucose ratio <0.6 was considered as probable bacterial meningitis (APBM). Cerebrospinal fluid with WBC >10 cells/mm$^3$ and CSF culture sterile, protein >45 mg/dL, normal glucose, was considered as aseptic meningitis (ASM).

### Statistical Analysis

Data obtained were analyzed using SPSS version 20 software. Descriptive statistics were used for different variables. Data analyzed was expressed as percentages, mean ± SD or median (IQR).

## Results

There were 62 cases with a provisional diagnosis of meningitis during the study period. After excluding 12 cases, 50 cases were further analyzed. Among 50 cases, 9 (18%) children had culture-proven bacterial meningitis, 34 (68%) children had APBM, and 7 (14%) children had ASM (Flowchart 1).

In the present study, the mean age of the study children was 7.3 ± 5.5 years. There were 20 female and 30 male children (Table 1). Overall male:female ratio is 1.5:1.

Among the study, children's fever was present in 96% of cases (Table 2). Seizures, headache, vomiting, and altered sensorium were present in 50, 44, 70, and 56% of the study children, respectively. None of the cases had a rash at presentation. On physical examination, neck stiffness and other meningeal signs were observed in 56% and 26% of cases, respectively. Bulging anterior fontanelle and cranial nerve palsy was observed in 16% of cases each. Focal neurological deficit was observed in 10% of cases. Features of raised intracranial pressure (ICP) at admission were observed in 12% of cases.

Out of 43 children with ABM, 8 (18.6%) children had cranial nerve palsy. Facial nerve palsy and abducens nerve palsy were observed in 6 (13.9%) and 4 (9.3%) children, respectively. Hypoglossal nerve palsy and oculomotor nerve palsy were observed in one case each.

In the present study, mean CSF WBC levels observed in bacterial meningitis, APBM, and ASM groups are 955 ± 1547, 434 ± 879, and 315 ± 366 cells/mm$^3$, respectively (Table 3).

Mean CSF neutrophil (%) observed in bacterial meningitis and APBM groups are 55 ± 39 and 28 ± 30 cells/mm$^3$, respectively.

Mean CSF glucose levels observed in bacterial meningitis, APBM, and ASM groups are 29.5 ± 23.1, 51.2 ± 23.8, and 51.7 ± 8.7 mg/dL, respectively.

Mean CSF protein levels observed in bacterial meningitis, APBM, and ASM groups are 441.5 ± 546.9, 99.1 ± 79.1, and 100.1 ± 82.6 mg/dL, respectively.

In the present study, out of 43 cases of ABM, 9 (20.9%) had positive CSF culture growth and 6 (13.9%) had positive blood culture growth. The bacterial profile is given in Table 4. Out of the

**Flowchart 1:** Study flowchart

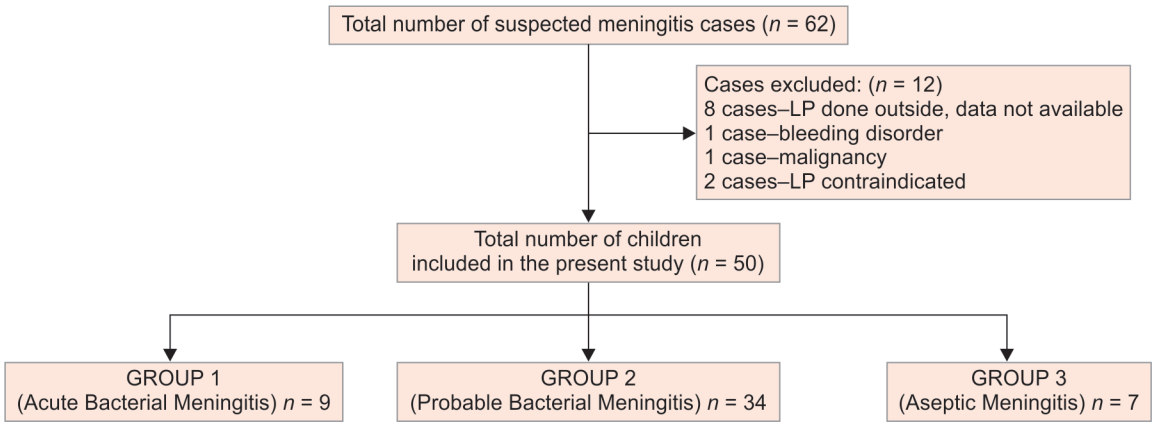


**Table 1:** Demographic characteristics (*n* = 50)

| *Demographic characteristic* | | *Overall n (%)* | *Acute bacterial meningitis (9) n (%)* | *Probable bacterial meningitis (34) n (%)* | *Aseptic meningitis (7) n (%)* |
|---|---|---|---|---|---|
| Age | Below 1 year | 10 (20.0) | 5 (55.6) | 5 (14.7) | 0 |
| | 1–5 years | 10 (20.0) | 0 | 7 (20.6) | 3 (42.9) |
| | 6–10 years | 15 (30.0) | 3 (33.3) | 10 (29.4) | 2 (28.6) |
| | Above 10 years | 15 (30.0) | 1 (11.1) | 12 (35.3) | 2 (28.6) |
| Sex | F | 20 (40.0) | 3 (33.3) | 14 (41.2) | 3 (42.9) |
| | M | 30 (60.0) | 6 (66.7) | 20 (58.8) | 4 (57.1) |

**Table 2:** Clinical features at admission ($n = 50$)

| *Clinical features* | | *Overall n (%)* | *Acute bacterial meningitis (9) n (%)* | *Probable bacterial meningitis (34) n (%)* | *Aseptic meningitis (7) n (%)* |
|---|---|---|---|---|---|
| Fever | | 48 (96) | 9 (100) | 32 (94.1) | 7 (100) |
| Fever duration (days) | 1–5 | 30 (62.5) | 7 (77.8) | 18 (56.3) | 5 (71.4) |
| | 6–10 | 10 (20.8) | 1 (11.1) | 7 (21.9) | 2 (28.6) |
| | >10 | 8 (16.7) | 1 (11.1) | 7 (21.9) | 0 |
| Seizures | | 25 (50) | 6 (66.7) | 17 (50) | 1 (14.3) |
| Headache | | 22 (44) | 4 (44.4) | 16 (47.1) | 2 (28.6) |
| Vomiting | | 35 (70) | 5 (55.6) | 25 (73.5) | 5 (71.4) |
| Altered sensorium | | 28 (56) | 4 (44.4) | 20 (58.8) | 4 (57.1) |
| Neck stiffness | | 28 (56) | 5 (55.6) | 19 (55.9) | 4 (57.1) |
| Other meningeal signs | | 13 (26) | 2 (22.2) | 9 (26.5) | 2 (28.6) |
| Cranial nerve palsy | | 8 (16) | 0 | 8 (23.5) | 0 |
| Focal neurological deficit | | 5 (10) | 1 (11.1) | 4 (11.7) | 0 |

**Table 3:** Comparison of CSF findings among three groups ($n = 50$)

| *CSF parameter* | | *Bacterial meningitis* | *Probable bacterial meningitis* | *Aseptic meningitis* |
|---|---|---|---|---|
| CSF WBC (cells/mm$^3$) | Median | 310 | 125 | 140 |
| | IQR | 100–1,275 | 76–282 | 50–500 |
| CSF glucose (mg/dL) | Median | 26 | 47.5 | 62 |
| | IQR | 5.5–46.5 | 33.5–61 | 49–63 |
| CSF protein (mg/dL) | Median | 252 | 77.5 | 83 |
| | IQR | 166.5–445.5 | 49.5–133.5 | 39–127 |
| CSF chloride (mmol/L) | Median | 115 | 117 | 120 |
| | IQR | 110–120 | 110.75–121.25 | 116–127 |
| CSF neutrophil % | Median | 60 | 13.5 | 3 |
| | IQR | 15–94 | 5–43 | 0–22 |

IQR, interquartile range

**Table 4:** Distribution of organisms isolated from CSF ($n = 9$)

| *Organism* | *n* |
|---|---|
| *Streptococcus pneumoniae* | 3 |
| *Staphylococcus aureus* | 1 |
| *Escherichia coli* | 1 |
| *Enterobacter cloacae* | 1 |
| *Streptococcus viridians* | 1 |
| *Brucella* | 1 |
| *Salmonella typhimurium* | 1 |

**Table 5:** Immediate complications of acute bacterial meningitis ($n = 43$)

| *Complication* | *n (%)* |
|---|---|
| Hydrocephalus | 8 (18.6) |
| Subdural effusion | 1 (2.3) |
| Infarct/thrombosis | 1 (2.3) |
| Brain abscess | 3 (6.9) |
| Hearing loss | 4 (9.3) |
| Vision impairment | 3 (6.9) |

seven cases of ASM, four (57%) had positive virology (one each of enterovirus, JEV, West Nile virus, and mumps). None had positivity for pneumococcal antigen test, CSF acid-fast bacilli detection, or positive CSF CBNAAT test.

Of 50 children with meningitis, 48 were discharged from the hospital, 2 were discharged against medical advice, and no case fatality was observed.

Out of the 43 cases of ABM, 16 (37%) cases had immediate complications. Hydrocephalus was observed in 8 (18.6%) children (Table 5). Hearing loss, visual impairment, brain abscess, subdural effusion, and infarct were observed in 9.3, 6.9, 6.9, 2.3, and 2.3%, respectively.

The presence of bulging anterior fontanelle, cranial nerve palsy, and focal neurological deficit at presentation predicted persistent neurological complications at discharge ($p = 0.04$).

Among the ABM with positive CSF culture, 4 (44.4%) cases had complications at discharge. Among the APBM, 13 (38.2%) cases had complications at discharge. None of the ASM cases had complications at discharge.

*Brucella* meningitis was observed in an 11-year-old boy who presented with recurrent episodes of fever and headache in the frontotemporal region for 1 month, vomiting for 10 days, and weight loss of 2 kg in 1 month. On examination, he had neck stiffness, increased tone, and brisk deep tendon reflexes. Cerebrospinal fluid analysis showed cells 100 cells/mm$^3$, glucose 26 mg/dL, protein 133 mg/dL, and lactate 38 mg/dL. Cerebrospinal fluid culture grew *Brucella*. CECT brain showed leptomeningeal enhancement in bilateral temporoparietal lobes.

*Salmonella* meningitis was observed in a 1-month-old female child who presented with fever, lethargy, and poor feeding for 2 days. The child was born at 34 weeks of gestation with a

birth weight of 1,500 g. On examination, the child had lethargy, seizures, and hepatomegaly. CRP was 348.8 mg/L, procalcitonin 48 µg/L. Cerebrospinal fluid analysis showed cells 4,800 cells/mm$^3$ (neutrophils 98%), glucose 1 mg/dL and protein 333 mg/dL, culture grew *Salmonella typhimurium*. CECT brain showed leptomeningeal enhancement in bilateral frontoparietal regions. She was treated with ceftriaxone, amikacin, and levetiracetam.

Neuroimaging findings in the present study included leptomeningeal enhancement, ventriculitis (7), hydrocephalus (8), tuberculoma with communicating hydrocephalus (1), cerebral abscess (3), subdural empyema, subdural effusion (1), thrombosis, and infarct (1).

## Discussion

In the present study, the current trend of microorganisms causing bacterial meningitis, the characteristics of CSF in three different types of meningitis, and the immediate outcome were presented.

Infants constituted 20% and the children above 6 years constituted 60%. Male children predominated in the study population. In a study by Garg et al. conducted in children from 1 month to 5 years age group in Shimla, India in 2013, 57 cases were diagnosed as ABM, cases in the age group of 3–12 months constituted 59.6%. They reported male to female ratio of 2:1.[5]

Karanika et al. studied children with meningitis from 1 month to 14 years age group in South Africa and reported the mean age of patients as 2.6 years.[6] Male predominance with a male:female ratio of 1.3:1 was reported by them.

The clinical features of meningitis in children of the present study agree with the reports in the literature. A systematic review of 10 studies, comparing the clinical features of bacterial meningitis by Curtis et al. reported that fever, neck stiffness, other meningeal signs, bulging anterior fontanel, and seizures independently raised the likelihood of meningitis in children.[7] Indian studies reported wide variation in proportions of symptoms and positive meningeal signs in 26 to 62% of bacterial meningitis.[4,5,8,9]

Fitzwater et al. found that the CSF findings of patients with bacterial meningitis when compared with ASM demonstrated statistically higher WBC counts and protein levels and lower glucose levels ($p < 0.01$ for all). About 71% of cases of bacterial meningitis had >100 WBC/mm$^3$, 40% had glucose levels <40 mg/dL, and 58% had protein level >100 mg/dL, compared with 33, 21, and 23% of respective variables in patients with ASM.[1] In the present study, the median CSF WBC observed in bacterial meningitis, APBM, and ASM groups were 310, 125, and 140 cells/mm$^3$, respectively.

The bacterial profile of acute meningitis in children across the globe varies widely.[10–14] The pattern of bacteria isolated in this study is similar to other documented studies in India and across other parts of Asia in young children.[4,8,15–18] The common organism is *Streptococcus pneumoniae*. On the contrary, Garg et al. in their series consisting of 57 cases diagnosed as ABM reported that 26 (45.6%) cases were caused by group B streptococci followed by 12 (21%) cases by *S. pneumoniae* and 6 (10.5%) cases by *H. influenzae*.[5] Less common pathogens were *Staphylococcus aureus, N. meningitides*, and *Escherichia coli*. In nine (15.7%) cases, pathogens were not isolated. African studies reported more number of *N. meningitidis* among bacterial meningitis in children.[19,20]

The outcome of acute meningitis depends on many factors. The influencing factors include age at the time of diagnosis, level of consciousness at the time of admission, prolonged or complicated seizures, progression of the disease before antibiotic therapy, etiologic agent, delayed sterilization of the CSF, etc.[9,14,20–25] In a study by Türel et al., 38 (13.4%) of 283 children with meningitis developed neurological complications.[20] Subdural effusion and hydrocephalus were observed in 27 and 17 patients, respectively. After discharge, 38 (26%) had at least one sequelae out of 146 patients assessed for sequelae. The most common sequelae were speech or language problems (14.5%). Sensorineural hearing loss was detected in 11 (7.6%) patients. Children <2 years of age developed neurological sequelae more commonly than older children. Focal neurological findings at the time of admission proved to be the most reliable predictor of permanent sequelae of bacterial meningitis. The present study identified hydrocephalus, hearing and vision impairment, and cerebral abscess as important complications of bacterial meningitis. Cases of ASM did not have complications.

The limitations of the study include the small sample size and its retrospective design. Although attempts were made to search for all clinical data and complications, it is possible that if there was a lapse in documentation, such parameters would not have picked up. However, the CSF data were checked from the electronic lab reports, and hence missing data are not a reality. Another limitation of the study is that the outcome assessment was carried out only until discharge. The follow-up was not included and hence long-term sequelae of bacterial meningitis could not be assessed.

## Conclusion

In the present study, we analyzed clinical features, CSF findings, and the outcome of 50 cases of acute meningitis in children. Among them, 9 (18%) children had culture-proven bacterial meningitis, 34 (68%) children had APBM, and 7 (14%) children had ASM. The study has given an insight into the current bacterial agents for meningitis in children along with characteristics of CSF in different types of meningitis in the given geographical area. The study has identified hydrocephalus, hearing loss, visual impairment, brain abscess, subdural effusion, and cerebral infarct as important complications of acute meningitis.

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## Authors' Contributions

Dr Ramesh Bhat Y and Dr Anusha Raj conceptualized the study, involved in the treatment of cases, data collection, analysis, and manuscript writing. Dr Shrikiran Aroor and Dr Pushpa Kini were involved in the treatment of cases and provided expert inputs.

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