Clinical and Laboratory Profile of Acute Bacterial Meningitis in a Tertiary Care Hospital in Mumbai

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Abstract

Introduction: Acute bacterial meningitis (BM) is a major health concern worldwide, even with the best antimicrobials and available vaccines. A high degree of clinical suspicion, prompt diagnosis, and effective treatment is critical. Laboratory investigations form the cornerstone for correct diagnosis.

Objectives: The present study was undertaken to determine the common causative microorganisms of BM and evaluate their antimicrobial susceptibility patterns to establish evidence-based therapeutic strategies.

Materials and Methods: Over 1 year, cerebrospinal fluid (CSF) samples from suspected cases of acute pyogenic meningitis were analyzed for biochemical parameters, cell counts, microscopy, and culture on routine and special media. Growth identification and antibiotic susceptibility were performed using standard guidelines.

Results: A total of 2326 CSF samples were received, with 111 (4.77%) suggestive of acute pyogenic meningitis. The majority were adults (63%), with male predominance (69.37%). Cases from wards (87.39%) exceeded intensive care units (12.61%). Predominant symptoms/signs were fever (77.48%), neck rigidity (54.05%), and altered sensorium (53.15%). CSF protein value >100 mg/dl and sugar <40 mg/dl were seen in 77.48% and 84.68%, respectively. CSF total leukocyte count >100 cells/µl and polymorphonuclear leukocyte >80% were seen in 92.79% and 51.35%, respectively. On culture, growth was seen in 12.61% samples. Gram-negative bacilli predominated (64.29%). The most common organisms isolated were Acinetobacter species (28.57%) and Streptococcus pneumoniae (21.43%). Neisseria meningitidis and Haemophilus influenzae could not be recovered. Gram-positive cocci were 100% susceptible to gentamicin, vancomycin, and linezolid. S. pneumoniae isolates were 100% susceptible to penicillin. Acinetobacter isolates were 100% susceptible to imipenem. Enterobacteriaceae were resistant to amoxicillin-clavulanic acid with 20% susceptibility to cefotaxime and 100% to Imipenem. Paralysis and muscular hypertonia as complications were seen in 2.70% patients. Mortality rate was 5.41% (6/111).

Conclusion: BM continues as a public health menace. A combination of clinical and laboratory parameters helps reach the correct diagnosis. Prevailing antimicrobial susceptibility patterns guide effective management.

Key words: Antimicrobial susceptibility, Bacterial meningitis, Clinical and laboratory profile

INTRODUCTION

Bacterial meningitis (BM) is an acute purulent infection within the subarachnoid space often resulting in decreased consciousness, seizures, raised intracranial pressure, and stroke. The meninges, the subarachnoid space, and the brain parenchyma are all frequently involved in the inflammatory reaction (meningoencephalitis). Meningitis is predominantly aseptic and resolves spontaneously (82-94%), but 6-18% are of bacterial origin. Over 1.2 million cases of BM are estimated to occur worldwide each year. It is the most common and notable infection of the central nervous system, which can progress rapidly and can result in death or permanent debilitation. Not surprisingly, this infection justifiably elicits strong emotional responses and hopefully immediate medical intervention.

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It is much more common in developing countries than developed countries.\textsuperscript{4,5} Many factors predispose to BM including age, male gender, winter season, smoking and exposure to smokers, low socioeconomic status, and stress.\textsuperscript{6} Congenital anomalies or injury to the central nervous system and primary infection elsewhere, especially that adjacent to the meninges are other well-established predisposing factors.\textsuperscript{7}

BM is caused by a number of organisms, the most common being \textit{Streptococcus pneumoniae} (\textit{S. pneumoniae}), \textit{Neisseria meningitidis}, and \textit{Haemophilus influenzae}.\textsuperscript{5,7-9} \textit{H. influenzae} Type b (Hib) used to be a common cause of BM worldwide before the Hib vaccines. Over the last two decades, however, the causative agents of meningitis have changed with the introduction of new highly effective vaccines.\textsuperscript{10} More recently, \textit{S. pneumoniae} and \textit{N. meningitidis} have become the predominant organisms causing meningitis. In countries with high HIV prevalence, \textit{Cryptococcus neoformans} may also be significant.\textsuperscript{9}

The most common neurological complication of BM is hearing impairment, especially with \textit{S. pneumoniae}.\textsuperscript{11} Other complications include subdural effusions, subdural empyema, brain abscesses, seizure, disseminated intravascular coagulation, shock, and mortality. Children may develop neuromotor and learning disabilities, speech and behavioral problems.\textsuperscript{12}

Before the introduction of antibiotics in the 1940s, case fatality rates for epidemic and endemic BM exceeded 70%. Since then, antibiotic use has reduced case fatality rates of the same to \textless 25%.\textsuperscript{13} However, both the morbidity and the mortality of untreated and inappropriately treated BM patients remain high.\textsuperscript{7,8} In economically advanced countries, the mortality from BM is \textless 10%, but it may be \textless 30% in developing countries.\textsuperscript{8} Majority of patients with BM survive, but neurological sequelae occur in 10-35% of all survivors (especially newborns and children).\textsuperscript{12}

Microbiology laboratories and the microbiologists play a critical role not only in the early identification of the causative bacteria and their antibiotic susceptibility pattern but also in providing valuable information regarding the common pathogens prevalent in a particular area.\textsuperscript{3,5} Regional information regarding changing trends in etiology of meningitis and antimicrobial susceptibility pattern is essential for correct and timely management of meningitis. Microbiology laboratories are the foundation of public health surveillance for BM\textsuperscript{8} and are guides to the clinicians for starting empiric as well as specific therapies.

Several published studies of acute BM are available from the developed countries,\textsuperscript{10,14-16} but there is paucity of data regarding the same in the developing countries like India.\textsuperscript{13,17-19}

Therefore, the present study was undertaken to determine the common microorganisms responsible for BM in a tertiary care hospital in Mumbai, to evaluate the antimicrobial susceptibility pattern of microorganisms isolated from the cerebrospinal fluid (CSF) samples and to establish evidence-based therapeutic strategies for the treatment of BM.

**MATERIALS AND METHODS**

This was a prospective study carried over 1 year (from June 2012 to May 2013) in a tertiary care hospital in Mumbai, with institutional ethical clearance. 111 consecutive patients admitted with signs and symptoms of acute pyogenic meningitis and of any age and gender were included in this study. Exclusion criteria were patients without any signs and symptoms of acute pyogenic meningitis, HIV seropositive patients and patients not willing to participate in the study.

A written informed consent was taken from the patient (or the relatives/guardians, in case of unconscious patients and children). A detailed clinical history and a thorough physical examination were done and a pro forma filled up, recording all the relevant details.

CSF samples from each patient were collected using sterile, aseptic technique. Around 2 ml of CSF was taken into two sterile test tubes for cell counts, biochemical parameters and bacterial culture studies. CSF from both the sterile culture tubes was centrifuged at 1500 rpm for 15 min. The supernatant from the first tube was used for total cell count, differential count, and sugar and protein estimation. Around 0.5 ml of the deposit from the first tube was utilized for Gram-staining. The deposit from the second tube was divided into two parts. One part was processed by a conventional method on blood agar (BA), chocolate agar (CA), and MacConkey agar (MA). BA and CA were incubated at 37°C in a candle jar at 5% CO\textsubscript{2} atmosphere for 48 h. MA was incubated at 37°C for 18-24 h. The other part was plated on modified CA (MCA) incorporated with isovitalex and vitamin K2 and incubated at 37°C at 5% CO\textsubscript{2} atmosphere for 48 h (Figure 1). The remaining CSF was kept in the incubator at 37°C as a backup for potential reculture.\textsuperscript{20} All isolates grown were identified by colony characteristics and standard biochemical tests.\textsuperscript{21}

Antimicrobial susceptibility test was performed for each of the isolates by Kirby-Bauer Disc Diffusion Method (KBDDM). The media used were \textit{Haemophilus} test medium (HTM) for \textit{H. influenzae} and Mueller-Hinton agar (MHA)
with 5% sheep blood for *S. pneumoniae* and *N. meningitidis*. For other bacteria, MHA was used for antimicrobial susceptibility testing by KBDDM. Appropriate control strains were used. The agar plates were incubated at 35°C for 18 h, and antimicrobial susceptibility pattern was interpreted as per the Clinical and Laboratory Standards Institute guidelines, 2012.²²

The data from each patient were compiled on the Microsoft Excel sheet by OpenEpi software version 2.3. The quantitative data were expressed as mean ± standard deviation (SD).

**RESULTS**

A total of 2326 CSF samples were received in the laboratory, of which, 111 were cases of acute pyogenic meningitis, indicating a prevalence of 4.77% in this tertiary care hospital. The majority of cases were seen among adults (63.06%), with an adult to child ratio of 1.71:1. Males (69.37%) were affected more than females with male to female ratio of 2.26:1. Among the pediatric patients, maximum number of cases were in the age group of 0-2 years (58.5%). Among the adults, maximum number of cases were in the age group of 16-40 years (67.1%). Almost 87.39% (97/111) of the cases were from wards and only 14 cases (12.61%) were from intensive care units (ICUs). Among ICUs, maximum cases were from pediatric intensive care unit (42.9%), and among wards, maximum cases were from adult medicine wards (62.89%), followed by pediatric medicine wards (26.80%). Cases from ICU areas were more in children, i.e., 11 (9.91%), in comparison to adults, i.e., 3 (2.7%), whereas in wards, the majority of the cases were from adults, i.e., 67 (60.36%). Maximum cases presented with fever, i.e., 86 (77.48%), followed by neck rigidity in 60 (54.05%), altered sensorium in 59 (53.15%), headache in 46 (41.4%), and vomiting in 40 (36.04%) cases. The different combinations of the presenting symptoms and signs were analyzed. Maximum patients presented with fever and altered sensorium (9.01%), followed by fever, headache, and neck rigidity (7.21%). Combination of 2 or 3 signs/symptoms were seen in 36 (32.43%) cases.

Of the predisposing factors, post-operative status was the most common (4.5%), followed by trauma (3.6%). In the majority of the cases (89.2%), predisposing factor could not be identified.
Mean ± SD of CSF protein was 309.16 ± 400.10 mg/dl. Maximum cases (34.24%) had CSF protein values between 101 and 200 mg/dl. CSF protein value >100 mg/dl was seen in 77.48% cases.

Mean ± SD of CSF sugar was 28.17 ± 16.52 mg/dl. Maximum cases (72.07%) had CSF sugar values between 11 and 40 mg/dl. CSF sugar value < 40 mg/dl was seen in 84.68% cases.

Mean ± SD of CSF total leukocyte count (TLC) was 1057.72 ± 1871.86 cells/µl. Maximum cases (49.55%) had CSF TLC between 101 and 500 cells/µl. CSF TLC >100 cells/µl was seen in 92.79% cases.

Mean ± SD of CSF polymorphonuclear (PMN) leukocytes was 74.41 ± 20.10%. Maximum cases (51.35%) had CSF PMN leukocytes between 81% and 100%. CSF PMN leukocytes >40% was seen in 90.1% cases.

In 87.4% CSF samples, pus cells could be seen on microscopy after Gram-stain. 10.8% CSF samples showed Gram-stained microorganisms. Gram-negative organisms predominated (66.67%) and the rest were Gram-positive organisms (33.33%). In 89.2% CSF samples, no organisms were detected on Gram-stain.

Growth was seen in 14 samples (12.61%) and contamination was noted in 4 (3.61%) samples (three with micrococci and one with diphtheroids). No growth was seen in 83.78% samples. Gram-negative bacilli were grown in 64.29% and Gram-positive cocci in 35.71% cases. The most common organism isolated was *Acinetobacter* species (28.57%), followed by *S. pneumoniae* (21.43%) (Table 1).

All the three *S. pneumoniae* isolates were susceptible to penicillin, gentamicin, trimethoprim-sulfamethoxazole (TMP-SMX), cefuroxime, vancomycin, and linezolid. One methicillin-resistant *S. aureus* (MRSA) was sensitive to gentamicin, vancomycin, and linezolid. One methicillin-sensitive *S. aureus* (MSSA) was sensitive to gentamicin and TMP-SMX.

All *Acinetobacter* isolates were susceptible to imipenem. Piperacillin-tazobactam (PIT) and netilmicin susceptibility was seen in 75% isolates of *Acinetobacter*. None of the isolates was susceptible to cefotaxime (Table 2). All *Enterobacteriaceae* were susceptible to imipenem. Susceptibility to ciprofloxacin, PIT, and netilmicin was 60% each. Amikacin (AK), cefotaxime, and piperacillin susceptibility was only 20% each. None of the isolates was susceptible to amoxicillin-clavulanic acid. No carbapenem resistance was detected (Table 2).

Among complications, paralysis and muscular hypertonia each were seen in 2.70% patients. No complications were seen in 94.6% cases.

Overall, mortality rate was 5.41% (6/111). Out of six cases, one was culture positive for *Acinetobacter* species and in five cases cultures were negative.

### DISCUSSION

This study was aimed at understanding the clinical and laboratory profile of BM. Although the disease continues to be a major public health concern, there is no single parameter that can define the illness and the outcome. The isolation of the causative organism and confirmation by culture continues to be the gold standard for diagnosis.

The disease prevalence in this hospital was 4.77% (111/2326), with 63% of the affected being adults. Studies

| Table 1: Organisms isolated from CSF in cases of acute pyogenic meningitis |
|-----------------------------|-----------------|-----------------|
| **Organism**                | **n (%)**       |                 |
| *S. pneumoniae*             | 3 (21.43)       |                 |
| *N. meningitidis*           | 0 (0)           |                 |
| *H. influenza*              | 0 (0)           |                 |
| *Acinetobacter species*     | 4 (28.57)       |                 |
| *Klebsiella pneumoniae*     | 1 (7.14)        |                 |
| *Escherichia coli*          | 1 (7.14)        |                 |
| *Enterobacter aerogenes*    | 2 (14.30)       |                 |
| *Salmonella typhi*          | 1 (7.14)        |                 |
| *MRSA*                      | 1 (7.14)        |                 |
| *MSSA*                      | 1 (7.14)        |                 |
| **Total**                   | 14 (100)        |                 |


| Table 2: Antimicrobial susceptibility pattern of Gram-negative bacilli isolated from CSF |
|--------------------------------------|-----------------|-----------------|
| **Antibiotic**                       | **Acinetobacter species** | **Enterobacteriaceae** |
|                                      | *(n=4) (%)*      | *(n=5) (%)*      |
| AK                                   | 2 (50)           | 1 (20)           |
| CIP                                  | 1 (25)           | 3 (60)           |
| CTX                                  | 0 (00)           | 1 (20)           |
| PI                                   | 2 (50)           | 1 (20)           |
| AMC                                  | 1 (25)           | 0 (00)           |
| IPM                                  | 4 (100)          | 5 (100)          |
| CPM                                  | 1 (25)           | 1 (20)           |
| NET                                  | 3 (75)           | 3 (60)           |
| PIT                                  | 3 (75)           | 3 (60)           |
| CIS                                  | 2 (50)           | 1 (20)           |
| CAS                                  | 2 (50)           | 1 (20)           |

from South India\textsuperscript{19} and Niger\textsuperscript{8} have reported 86.8\% and 70\% adult population, respectively, among their patients. Males predominated (69.37\%) in this study. Almost all studies have shown male preponderance.\textsuperscript{5,19,23}

Among children, 58.5\% of the cases were in the age group of 0-2 years and 80.5\% cases were below 5 years of age, together contributing to 30\% of all cases of meningitis. Studies from Niger\textsuperscript{8} and India\textsuperscript{22} have reported 42.2\% and 66.67\% cases, respectively, in children below 5 years of age. A major risk factor for meningitis is the lack of immunity to specific pathogens associated with young age. Incidence of meningococcal disease increases in infants <1 year old, and this may be attributable to immuno-suppression and lectin complement pathways and lack of acquired serum antibodies.\textsuperscript{25}

Among 111 cases of acute pyogenic meningitis, fever was the most common symptom (77.5\%), followed by neck rigidity (54\%), altered sensorium (53\%), and headache (41.4\%). Thomas et al.\textsuperscript{26} have also reported fever, neck rigidity, and headache in 71\%, 48\%, and 92\% cases, respectively. van de Beek et al.\textsuperscript{15} have reported neck rigidity in 83\%, headache in 87\%, and altered sensorium in 69\% of their cases, which are much higher as compared to this study. Convulsions were seen to the extent of 9.9\% in this study. Thomas et al.\textsuperscript{26} and van de Beek et al.\textsuperscript{15} have reported figures of 9\% and 15\%, respectively, in their studies. However, Mwaniki et al.\textsuperscript{22} have reported convulsion in 38.7\% cases. Kernig's/Brudzinski's sign was seen in 10\% cases in this study as compared to 5\% reported by Thomas et al.\textsuperscript{26} The classic triad of acute pyogenic meningitis includes fever, neck stiffness, and altered sensorium.\textsuperscript{15} In this study, classic triad was present in 1.8\% of the cases. At least two of the four signs (classic triad + headache) were present in 21.6\% of the cases. Any one of the four signs and symptoms was present in 10.8\% of the cases. All four were present in 5.4\% of the cases. van de Beek et al.\textsuperscript{15} have reported 44\% of cases characterized by classic triad, 95\% presenting with at least two of the four signs/symptoms and 4\% with any one of the four.

In this study, maximum patients presented with fever and altered sensorium (9\%), followed by fever, headache, and neck rigidity (7.2\%). Combinations of 2 and 3 signs/symptoms were maximum (32.4\% each). Thomas et al.\textsuperscript{26} have reported a combination of fever, headache, vomiting, photophobia, and neck rigidity as maximum. Post-operative status was the commonest predisposing factor (4.5\%), followed by trauma in 3.6\% cases.

CSF examination of a normal adult shows TLC <5 cells/µl (in case of newborns, TLC is <20 cells/µl) with no PMN leukocytes. Normally, CSF glucose and protein value in a healthy person is ≥45 mg/dl and <40 mg/dl, respectively.\textsuperscript{1}

Different authors have reported CSF TLC >79 cells/µl in their cases.\textsuperscript{15,16,19,26} The present study had TLC >100 cells/µl in 92.79\% cases and CSF TLC between 101 and 500 cells/µl in 49.55\% cases. TLC as high as >1000 cells/µl was seen in 25.22\% cases and a low TLC <100 cells/µl was seen in 7\%. Although high TLC is a marker of acute BM, Lussiana et al.\textsuperscript{28} Mani et al.\textsuperscript{19} have reported even <10 cells/µl in some cases. In this study, mean ± SD of TLC was 1057.72 ± 1871.86 cells/µl. Thomas et al.\textsuperscript{26} have reported TLC Mean ± SD of 359 ± 1543 cells/µl. A predominance of lymphocytes also occurs in some cases, as is also seen in this study in 11 cases, where PMN leukocytes were <40\%. A marker of BM is the presence of >80-85\% of PMN leukocytes in CSF,\textsuperscript{8,29} and this study reported PMN leukocytes >80\% in 51.35\% cases. The Mean ± SD of CSF PMN leukocyte % was 74.41 ± 20.10\% in this study.

In this study, CSF sugar <40 mg/dl was seen in 84.68\% cases. Studies by Wu et al.\textsuperscript{26} and Lussiana et al.\textsuperscript{28} have reported the same in 30\% and 74\%, respectively. In this study, mean ± SD of CSF sugar was 28.17 ± 16.52 mg/dl which is similar to the mean ± SD 31.15 ± 22.37 mg/dl reported by Lussiana et al.\textsuperscript{28}

CSF protein >100 mg/dl was seen in 77.48\% cases in this study. Other studies have reported >85\% cases with high CSF protein value.\textsuperscript{26,28} However, Wu et al.\textsuperscript{26} have reported only 53.7\% cases with CSF protein >100 mg/dl. Mean ± SD of CSF protein in this study was 309.16 ± 400.10 mg/dl. van de Beek et al.\textsuperscript{15} have reported high protein Mean ± SD of 490 ± 450 mg/dl.

Pus cells were seen on Gram-stain from the centrifuged deposit of CSF (1500 revolutions per minute for 15 min) in 87.4\% cases. However, organisms were seen only in 12 samples (10.8\%) on Gram-stain. Gram-positive cocci were seen in four cases, Gram-negative cocci in two cases and Gram-negative bacilli in six. In 89.2\% CSF samples, no organisms were detected on Gram-stain. A reltively high yield of organisms on Gram stain can be obtained using Cytospin as seen in studies by Mani et al\textsuperscript{19} (65.7\% with cytospin at 800 revolutions per minute for 10 minutes) and Shanholtzer et al.\textsuperscript{10} (75\% with cytospin at 2000 revolutions per minute for 10 minutes). Low positivity in this study can be attributed to not using cytospin to concentrate the smear for Gram-stain. Wu et al.\textsuperscript{16} have reported a predominance of Gram-positive organisms (69.4\%) on Gram-stain, whereas the present study had predominance of Gram-negative organisms (66.67\%).

Among 111 CSF samples, organisms could be recovered on culture in only 14 (12.6\%) cases. No growth was seen in 83.8\% of the samples. Wu et al.\textsuperscript{16} have shown culture positivity of 22.2\%. Several studies have reported a low
CSF culture positivity, ranging from 3.3% to 45.5%. In this study, contamination was seen in four samples (three micrococci and one diphtheroids), which may be due to improper aseptic precautions while performing lumbar puncture.

*S. pneumoniae* was isolated from 21.43% of culture positive samples. Overall culture positivity of *S. pneumoniae* in various studies varies from as low as 2.4% from Bengaluru to as high as 77% from Ghana.

This study failed to recover *N. meningitidis* and *H. influenzae* even though selective media such as MCA and HTM were used for these fastidious organisms (Table 1). Isolation of *N. meningitidis* in CSF is very low in India, 1% from Bengaluru and varying from 1% to 25% in western countries. A study from Niger had high isolation rate (63%) of *N. meningitidis* from CSF.

The *H. influenzae* Type b (Hib) study working group has reported a high culture positivity of *H. influenzae* (34.62%). In all other studies, *H. influenzae* positivity rate varied from 0.9% to 12.6%. The incidence of *H. influenzae* disease has remained low for the past several decades in India and vaccination of Hib, though not included in national immunization program, is recommended by the Indian Academy of Pediatrics and World Health Organization (WHO), for all children below 6 years of age with 3 doses at 6, 10, and 14 weeks.

Campagne et al. have reported that 80% cases of BM were caused by the three bacteria *S. pneumoniae*, *N. meningitidis*, and *H. influenzae*. However, in this study, Gram-negative bacilli predominated (64.29%). Mwaniki et al. have reported 24.5% Gram-negative bacilli from culture positive cases of CSF. Other studies have reported lesser isolation of Gram-negative bacilli in the range of 2.4-8.3%.

Three common causes of neonatal meningitis are Group B *Streptococcus*, *Listeria monocytogenes*, and *Escherichia coli*. However, we did not encounter any case of Group B *Streptococcus* or *L. monocytogenes*, but one *E. coli* was isolated from a CSF sample of an adult male. A study from Atlanta, in 1997, has reported both the above organisms, and a recent study from the same country, in 2013, has also reported *Listeria* in 0.2% cases. From Chennai, a case of *L. monocytogenes* has been reported from a CSF of 17-year-old girl. In the present study, one *Salmonella typhi* was isolated from CSF of a 4-month-old female child in this study. *Salmonella* species and *Flavobacterium meningosepticum* meningitis have been reported earlier in cases of acute meningitis from Bengaluru.

The most common organisms of nosocomial meningitis are Coagulase-negative *Staphylococcus*, *Acinetobacter* species, and *S. aureus*. This study isolated four *Acinetobacter* species of which three were male children and one, a young adult male. The latter was a post-operative case of neurosurgery. Of these, one child expired (25% mortality due to *Acinetobacter*). *Acinetobacter* species are becoming increasingly important as nosocomial pathogens and *Acinetobacter* meningitis typically occur the following neurosurgery, with mortality exceeding 15%.

Low yield of bacteria on culture may be due to prior antibiotic use as most patients take antibiotics from private practitioners or over the counter as community antibiotic use is very prevalent in India. Other reasons are delay in the transport of sample to the laboratory, nonavailability of selective/special media for the fastidious pathogens, presence of autolytic enzymes in CSF, and a lack of 24-h facility for processing of CSF samples. This hospital, however, has 24-h emergency services and also selective media were used for culture.

All three *S. pneumoniae* isolates were susceptible to penicillin, cefuroxime, gentamicin, linezolid, and vancomycin. In a study from Bengaluru, all *S. pneumoniae* isolates were sensitive to penicillin and vancomycin. Although high-level resistance (24%) to TMP-SMX was reported in invasive pneumococcal infections from South India, in this study, all *S. pneumoniae* isolates were susceptible to TMP-SMX. Jain et al. from Delhi have reported high TMP-SMX resistance and low penicillin resistance in pneumococcal isolates.

Two *S. aureus* isolated: One MSSA and another one MRSA were 100% susceptible to gentamicin. The MRSA was also susceptible to vancomycin and linezolid. No vancomycin-intermediate *S. aureus* and vancomycin-resistant *S. aureus* (VRSA) were detected. In the present study, no *Enterococcus* species was isolated. A study from Aligarh has reported increase in the prevalence of MRSA causing meningitis from 44.4% in 2005 to 69.4% in 2008-2009 and increase in high-level aminoglycoside resistance among *Enterococcus faecalis* isolates from 52.9% in 2005 to 60% in 2008-2009. However, no VRSA or vancomycin-resistant *Enterococcus* was encountered in that study.

An outbreak due to *N. meningitidis* serogroup A in Delhi, in 2007, have reported decreased susceptibility of these isolates to ciprofloxacin (only 14.3%). Furthermore, resistance to ampicillin and chloramphenicol is common among *H. influenzae* isolates and seems to be increasing. However, in this study, *N. meningitidis* and *H. influenzae* could not be recovered from CSF culture, and thus, antibiotic susceptibility cannot be commented upon.
Currently in India, the third generation cephalosporin is the drug of choice for management of invasive pneumococcal and *H. influenzae* diseases.\(^7\) In addition, vancomycin should be added in invasive pneumococcal infection. Alternative therapy for *S. pneumoniae* is meropenem/fluoroquinolone. Alternative therapy for *N. meningitidis* and *H. influenzae* are chloramphenicol/fluoroquinolone. In addition, penicillin G/ampicillin can also be given in meningococcal meningitis.\(^33\)

Out of *Acinetobacter* species isolated from CSF in this study, 50% were susceptible to AK and piperacillin and only 25% to ciprofloxacin and amoxicillin-clavulanic acid. They were 75% susceptible to piperacillin-tazobactam and netilmicin and 100% susceptible to imipenem. Cefotaxime susceptibility was 0% (Table 2). *Acinetobacter* species are frequently resistant to cephalosporins such as cefepime or ceftazidime, and in carbapenem-resistant isolates, this resistance goes up to 95%. Therefore, these cephalosporins are less useful as empirical agents in patients from neurosurgical units, where *Acinetobacter* meningitis is common.\(^36\) Although AK susceptibility in this study was 50%, poor penetration of aminoglycoside through the blood brain barrier does not suggest intravenous administration in the treatment of meningitis. Therefore, aminoglycoside has to be administered by intraventricular route.\(^36\)

In this study, among the first line antibiotics, susceptibility of *Enterobacteriaceae* was 60% to ciprofloxacin and 20% each to AK, cefotaxime, and piperacillin. Susceptibility to amoxicillin-clavulanic acid was 0%. However, all *Enterobacteriaceae* were 100% susceptible to imipenem, followed by 60% to piperacillin-tazobactam and netilmicin (Table 2). Therefore, no carbapenem resistance was detected. A recent study from Aligarh,\(^13\) in 2011, has reported aminoglycoside susceptibility to be as high as 75%, followed by 69% to cefotaxime in. Fluoroquinolone susceptibility of 62.5% and imipenem susceptibility of 100% is almost similar to the present study (60% and 100%, respectively).\(^36\) Mani et al.\(^39\) have reported 73.7% susceptibility to AK, 47.4% to cefotaxime, and 52.6% to ciprofloxacin.

No complications were seen in the majority of the cases (95%) in this study. The common complications seen in cases of acute pyogenic meningitis are cranial nerve palsy, hemiparesis/quadruparesis, stroke, cerebral/cerebellar herniation, and thrombosis of dural venous sinuses.\(^25\) In this study, overall complications seen were paralysis and muscular hypertonia in 2.7% patients each. van de Beek et al.\(^35\) have reported cranial nerve palsy in 19% of their cases, paralysis in 5%, and aphasia in 2%. However, none of the patients developed cranial nerve palsy or aphasia in this study.

In this study, 6 out of 111 cases of acute pyogenic meningitis expired with an overall mortality rate of 5.41%. Various studies have reported mortality rate in acute pyogenic meningitis cases ranging from 10% to 31.3%.\(^5,13,15-17,26,31\) Antibiotic usage has definitely reduced the case fatality rate of acute pyogenic meningitis to 25% or less, with a few exceptions.\(^13\) Mortality due to *S. pneumoniae* in children <5 years of age has been reported to be as high as 73% by the WHO.\(^1\) Kanungo et al.\(^24\) from Pondicherry have reported mortality of 20% in meningitis due to *S. pneumoniae*. In this study, mortality due to *S. pneumoniae* meningitis was seen in 25% (2/8 cases). Small scale studies from India have documented case fatality rate for meningitis due to *H. influenzae* Type b to be 11%.\(^15\) In this study, *H. influenzae* could not be isolated by culture and thus cannot be commented upon. A 65-year-old male patient admitted with high-grade fever, vomiting, altered sensorium, and a known case of chronic obstructive pulmonary disease and who was culture negative, died due to raised intracranial tension due to tuberculous meningitis.

**CONCLUSION**

BM continues to be a public health menace. Although the prevalence of the various causative agents varies with age and the geographical area, *S. pneumoniae, H. influenzae* Type b, and *N. meningitidis* are reported by many researchers to be the main pathogens of acute pyogenic meningitis.

A combination of clinical and laboratory parameters need to be taken into consideration to arrive at the right diagnosis. Emergence of resistant bacterial strains to conventional antibiotics warrants the need to consider the prevailing antimicrobial susceptibility patterns for the effective management of the disease. This also helps in formulating the local treatment guidelines and acts as a proactive public health surveillance system.

**REFERENCES**