

# Neurosurgical Meningitis: Clinico-Microbiological Profile and Treatment Outcome from a Tertiary Care Center in India

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## Abstract

**Background** Meningitis following neurosurgical procedure is a well-recognized and potentially fatal complication. The Indian literature on microbiological epidemiology is scarce. The aim of our study was to know clinical, microbiological profile and treatment outcomes of patients with neurosurgical meningitis at our center.

**Methods** This was a retrospective observational cohort study of 25 culture-proven neurosurgical meningitis cases performed at the Apollo Speciality Hospital, Chennai, India, between January 2009 and May 2012.

**Results** In our study, nine patients had skull fracture and cerebrospinal fluid leak, nearly 50% of the patients underwent craniotomy, and five patients had endoscopic surgery while 64% of the patients required shunt placement or drains. Only nine patients (36%) had definite clinical signs of meningitis and mean duration of onset of symptoms from surgery was 11.12 days. A total of 18 patients (72%) had gram-negative bacterial meningitis and majority (83.3%) was due to carbapenem-resistant organisms. Predominant isolate was *Pseudomonas aeruginosa* (44.4%), and the second most common isolate was *Acinetobacter baumannii* (33.3%). Among cases of gram-negative bacterial meningitis, patients who had carbapenem-resistant isolates were given combination antimicrobials (carbapenem/cefepime tazobactam with colistin/gentamicin) as per susceptibility via intravenous and intrathecal through the drain (extraventricular or lumbar). Only five patients (27.7%) had a complete cure.

**Conclusion** Gram-negative organisms, mainly *Pseudomonas* and *Acinetobacter*, are predominant pathogen in neurosurgical meningitis in our center. While treating multidrug-resistant gram-negative meningitis, device removal and a combination of antimicrobial agents via both intravenous and intraventricular routes are crucial to achieve cure.

## Keywords

- ▶ neurosurgical meningitis
- ▶ multidrug-resistant gram-negative meningitis
- ▶ carbapenem-resistant meningitis

## Introduction

Meningitis following neurosurgical procedure is a well-recognized and potentially fatal complication.<sup>1,2</sup> Knowledge of risk factors and local microbiological epidemiology is crucial for the successful treatment of these patients.<sup>3</sup> Increasing prevalence of multidrug-resistant organisms in health care settings makes it an

even more difficult to treat entity. The Indian literature is scarce; however, a study from National Institute of Mental Health and Neurosciences (NIMHANS) showed gram-negative pathogens as a major causative agents.<sup>4</sup> The aim of our study was to know clinical, microbiological profile and treatment outcomes of patients with neurosurgical meningitis at our center.

## Methods

This was a retrospective observational cohort study performed at the Apollo Speciality Hospital, which is an oncology and neurosurgical center in Chennai, India, between January 2009 and May 2012.

A total of 588 cerebrospinal fluid (CSF) cultures were done during the same period, out of which 25 were culture positive (►Table 1). The Universal Hospital Identification Numbers of the culture-positive cases were tracked from the microbiology laboratory and then records were retrieved from the medical records department and were analyzed.

Patient characteristics such as age, demographics, sex, presence of comorbidities, Glasgow Coma Scale (GCS), presence of CSF rhinorrhea, fracture of skull base, prophylactic antibiotics, receipt of steroids, type of surgery, intraoperative antibiotics, presence of a device, clinical signs of meningitis, CSF picture with microbiological details, and treatment outcome were recorded (►Table 2).

Centers for Disease Control and Prevention's criteria were used to define nosocomial meningitis.<sup>5</sup> Definitive meningitis was defined if the patients had the following: (1) new onset mental status change, (2) CSF cell count > 1,000 cells with polymorph predominance, (3) CSF to serum glucose ratio < 0.4, and (4) positive CSF culture for organism. Probable meningitis was diagnosed if the patients had the following: (1) new onset mental status change, (2) CSF cell count between 500 and 1,000 cells with mixed or polymorphic, (3) CSF to serum glucose ratio < 0.5, and (4) positive CSF culture for organism.

Complete cure was defined by full clinical recovery and resolution of CSF pleocytosis with negative CSF culture at the end of treatment.

The identification and antibiotic susceptibility pattern of isolates were performed using microbroth dilution on VITEK 2 (bioMérieux, France) as per the Clinical and Laboratory Standards Institute guidelines. The minimum inhibitory concentration (MIC) for antibiotics, such as cefoperazone-sulbactam and cefepime/tazobactam, are not elucidated in the current Clinical and Laboratory Standards Institute guidelines; hence, the breakpoint of cefoperazone and cefepime was applied for cefoperazone/sulbactam and cefepime/tazobactam, respectively. Antibiotic discs for these drugs were obtained from HiMedia Laboratory India. Colistin and vancomycin MICs were performed using the Etest strip (bioMérieux, France).

## Results

During the study period, a total of 25 cases were diagnosed and treated for definitive or probable neurosurgical meningitis at our center. The median age of patients was 38 years with 18 (72%) being male patients. Twelve patients (48%) were admitted with traumatic head injury while rest had tumors and congenital anomalies. Only six patients had comorbid condition, that is, diabetes in four patients, coronary artery disease and hypertension in two patients, and one patient was human immunodeficiency virus positive.

All patients underwent neurosurgical intervention. Nine patients had skull fracture and CSF leak. Nearly 50% of the patients underwent craniotomy, while 16 patients (64%) required shunt placement or drain in situ. (Seven patients had a shunt; out of which, one was ventriculosubgaleal, one was thecoperitoneal, and five were ventriculoperitoneal shunts.) Drains which were either lumbar or external ventricular drainage (EVD) were present in nine patients. Endoscopic surgeries were performed in five patients, out of which four were elective procedures and one was an emergency procedure. Four out of the five procedures were CSF leak repair and one was an excision of the tumor. A total of 14 surgeries (56%) were emergent in nature. Two patients were operated at the other facility and were shifted for further care to our center and were later diagnosed to have meningitis at our hospital. The median time of hospitalization was 37 days with a mean of 11.36 days of intensive care unit stay. All these patients received perioperative antibiotics for a mean duration of 3.24 days which mainly included third-generation cephalosporin and aminoglycosides. Only nine patients (36%) had classical clinical signs of meningitis, and mean duration of onset of symptoms from surgery was 11.12 days. CSF analysis was performed with a mean of 3 days after the symptom onset.

Out of 25 cases, 16 (64%) cases met the definitive diagnostic criteria while remaining 9 cases were diagnosed as probable meningitis.

Overall, 18 patients (72%) had gram-negative bacterial meningitis and 15 out of these (83.3%) were due to carbapenem-resistant organisms. Predominant isolate was *Pseudomonas aeruginosa* (44.4%), the second most common was *Acinetobacter baumannii* (33.3%), and *Enterobacteriaceae* was isolated in 16.6% of these cases. Gram-positive organisms were isolated in seven cases (28%) and among them *Staphylococcus epidermidis* and *Staphylococcus aureus* were in five cases, both were methicillin susceptible while *Streptococcus pneumoniae* and *Enterococci* were found in one patient each.

Among the cases of gram-positive meningitis, patients who had *S. epidermidis* and *S. aureus* (methicillin-sensitive *S. epidermidis* and methicillin-sensitive *S. aureus*) were successfully treated with first-generation cephalosporin intravenously for 2 weeks. Methicillin-sensitive *S. aureus* meningitis patient required shunt removal which was done a few days after the diagnosis of meningitis. Enterococcal meningitis patient was given vancomycin intravenously but died on the 10th day.

Among cases of gram-negative bacterial meningitis (►Table 3), patients who had carbapenem-resistant isolates were given 3 weeks of combination therapy (meropenem or cefepime-tazobactam as per susceptibility plus colistin) intravenously along with 5 to 7 days of intrathecal colistin or gentamicin as per susceptibility through drain (extraventricular or lumbar). Nine patients received intrathecal or intraventricular antibiotics. The drugs that were used for therapy via this route were colistin, polymyxin B, amikacin, and vancomycin. If the patient had organisms that were carbapenem resistant particularly *Pseudomonas* and *Acinetobacter*, this route was

**Table 1** Microbiological profile of CSF culture isolates

Culture isolates (n = 25)	Methicillin		Ampicillin		Glyco-peptides		Gentamicin		Cipro		Piptaz		Cefo-sulb		Cefepime-tazo		Carbapenem		Colistin		
	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	
<i>Staphylococcus epidermidis</i> (n = 3)	3				3				2												
<i>Staphylococcus aureus</i> (n = 2)	2				2				2												
<i>Enterococcus faecalis</i> (n = 1)			1		1			1													
<i>Escherichia coli</i> (n = 2)								2				2	1	1	1	1	2				2
<i>Klebsiella pneumoniae</i> (n=1)								1				1		1							1
<i>Acinetobacter baumannii</i> (n = 5)								1	4			5	3	2	2	3					5
<i>Acinetobacter wolffi</i> (n = 1)								1					1		1						1
<i>Pseudomonas aeruginosa</i> (n = 8)								1							8	4	4				8
<i>Aeromonas sobria</i> (n = 1)								-													1
<i>Streptococcus pneumoniae</i> (n = 1)	-		1		1					1											

Abbreviations: Cefo-sulb, cefoperazone-sulbactam; Cefepime-tazo, cefepime tazobactam; R, resistant; S, sensitive.

**Table 2** Demographics and clinical characteristics

Characteristics	Value
Age (median), y	38
Sex (n)	
Male	18
Female	7
Primary diagnoses (n)	
Traumatic head injury	12
Tumor	9
Congenital anomaly	4
Comorbidity (n)	
Diabetes mellitus	4
HIV	1
Days of hospitalization (median)	37
ICU days (mean)	11.36
Apache score (mean)	16.92
Clinical parameters (no. of patients)	
Fever (> 101°F)	13
Altered sensorium (new onset)	5
Stiff neck	5
CSF leak	7
Skull fracture	9
Antibiotic prophylaxis in days (mean)	3.24
Surgical procedure	
Endoscopic repair	5
Craniotomy	12
Laminectomy	1
Shunt placement	11
Nature of surgery	
Emergency	14
Elective	9
Surgery at other facility	2
Drain in situ for > 7 d (lumbar/EVD)	16 cases
Postoperative days at onset of symptoms (mean)	11.12
Days from symptom onset to CSF analysis (average no. of days from symptom to CSF analysis)	3 d
CSF analysis	
Definite meningitis	16
Probable meningitis	9
Same culture isolates from non-CSF site Three patients had bacteremia with the same organisms. Three patients who grew the organism in the CSF had colonization of the respiratory tract. Patients grew the same organism from the wound swab.	10 patients

Abbreviations: CSF, cerebrospinal fluid; EVD, external ventricular drainage.

chosen as intravenous colistin does not penetrate well into the CSF. Colistin does not penetrate the CSF well. Hence, carbapenems (although showed in vitro resistance on the isolates) were added to intravenous colistin for synergy. Out of these, 14 patients (77.7%) required device removal. Removal of the device was suggested in all the cases if meningitis was due to an extensively drug-resistant organism or *S. aureus*, as these can form biofilms. However, if the patient improved on therapy with microbiological clearance of CSF, the device was retained at the discretion of the surgical team. Five patients (27.7%) were cured completely and two patients died, while others had residual neurological deficit and partial resolution. Some patients were said to have partial resolution because these patients had microbiological cure and resolution of clinical symptoms; however, they did not have adequate improvement in GCS, and we were not sure how much of this was contributed by the meningitis. A single patient with *Aeromonas sobria* was treated with 2 weeks of intravenous meropenem and recovered fully.

## Discussion

Meningitis is a well-known and fatal complication following head trauma and neurosurgical procedures. In our study, we found gram-negative organisms (72%) as a major pathogen causing neurosurgical meningitis similar to a study in NIMHANS by Srinivas et al. Previous studies have also showed this finding as emerging pathogens in nosocomial meningitis.<sup>6</sup> Prior use of third-generation cephalosporins was identified as common feature of patients with gram-negative meningitis in one study.<sup>7</sup> Even in western studies though *S. aureus* is an important pathogen in postsurgical meningitis, gram-negative meningitis is emerging as major syndrome due to increased colonization in hospitalized patients.<sup>8</sup>

In our study, 9 patients had skull fracture and CSF leak, 16 patients had prolonged (> 7 days) duration of extraventricular drain or lumbar drain, and 5 had sinus approach surgical procedure, making these possible risk factors for developing neurosurgical meningitis. EVD provides a potential portal of entry for microorganisms and associated with a risk of infection of 4 to 11% for ventriculostomies and 4.2% for lumbar drains.<sup>9</sup> As observed in our study, these factors have been reported as established risk factor for nosocomial meningitis in literature.<sup>10</sup> The mean time to develop meningitis postneurosurgery was 11.12 days in our study. Three out of 25 patients were readmitted with clinical symptoms which is in concordance with the observation in literature.<sup>11</sup> As reported in previous studies, the typical symptoms and signs were noted only in 36% of the patients in our study, suggesting that high index of clinical suspicion in the light of risk factors is crucial for early diagnosis.<sup>12</sup>

In our study, predominant gram-negative isolates were *P. aeruginosa* and *A. baumannii* (77.7%), and all were resistant to carbapenems but susceptible to colistin. Patients with these bacteria were treated with combination of antimicrobial agents administered via both intravenous

**Table 3** Treatment and outcome of various organisms

Causative organism	Treatment		Outcome		
	Intravenous	Intrathecal	Device removal	Complete resolution	Died
Methicillin-sensitive <i>Staphylococcus epidermidis</i>	Cefoperazone–sulbactam–2 d, then cefazolin–12 d	No	–	Yes	
Methicillin-sensitive <i>Staphylococcus aureus</i>	Vancomycin–2 d, then cloxacillin–12 d	No	Shunt removal performed	Yes	
<i>E. faecalis</i>	Vancomycin–10 d	No	–	–	Yes
<i>Streptococcus pneumoniae</i>	Ceftriaxone–14 d		–	Yes	
Carbapenem-resistant gram-negative bacteria (carbapenem-resistant <i>Enterobacteriaceae</i> , <i>Pseudomonas</i> , <i>Acinetobacter baumannii</i> )	Meropenem/cefepime, tazobactam + colistin for 3 wk	Gentamicin/colistin for variable period. (range 5–7 d).	14 cases (77.7%) required device removal with incomplete cure <sup>a</sup>	5 cases (27.7%)	2 patients
Extended spectrum beta-lactamase-producing <i>Enterobacteriaceae</i>	Meropenem–3 wk	Gentamicin/amikacin if susceptible for 5–7 d	–	Yes	
<i>Aeromonas sobria</i>	Meropenem–2 wk		–	Yes	

<sup>a</sup>Incomplete cure: Patients who did not meet the criteria for complete cure or had persistent neurodeficit.

and intrathecal routes. Only 27.7% of these patients achieved complete clinical cure; two patients (11.11%) died; and others developed visible morbidity, organ failures, and partial resolution despite therapy. These findings were different from published literature of very high mortality in such patients.<sup>13–15</sup> Possible explanation to the better outcome in our patients could be the aggressive intraventricular and intrathecal therapy with device removal as needed. This could also be due to a bias in the calculation of mortality data, as we did not include those patients who had partial response initially and later on developed next episode of central nervous system (CNS) or non-CNS infection and remain morbid or expired later on. A study from NIMHANS by Srinivas et al also showed a low mortality similar to our study.

In our study, gram-positive bacterial meningitis represented nearly a quarter of cases with 85% clinical cure achieved with intravenous therapy alone. The limitation of our study was its retrospective design and unavailability of attributable mortality to various risk factors.

## Conclusion

Early recognition and adequate treatment of neurosurgical meningitis, especially caused by multidrug-resistant gram-negative bacteria, is a serious challenge to the treating clinician.

CSF leak, skull fracture, prolonged placement of drains, and sinus approach in surgery are important risk factors in developing neurosurgical meningitis.

Gram-negative organisms, mainly *Pseudomonas* and *Acinetobacter*, are predominant pathogen in neurosurgical meningitis in our center.

Carbapenem resistance in both these pathogens is very high and poses significant therapeutic problems in cure. While treating patients with multidrug-resistant gram-negative meningitis, device removal, combination of antimicrobial agents, and administration via both intravenous and intraventricular routes are crucial to achieve cure.

## Conflict of Interest

None.

## Notes

We did not get any support in the form of grants, equipment, drugs, or all of these. This article has not been presented anywhere else. All the authors have contributed in data collection, analysis, and article writing this article. This article has been read and approved by all the authors and represent honest work.

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