

Original Research Article

BACTERIOLOGICAL PROFILE AND ANTIBIOTIC SENSITIVITY PATTERN OF ORGANISMS CAUSING MENINGITIS IN A TERTIARY CARE HOSPITAL: A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Acute bacterial meningitis remains a life-threatening central nervous system infection associated with substantial morbidity and mortality worldwide. Rising antimicrobial resistance among the causative organisms is increasingly complicating empirical therapy. This study evaluated the bacteriological profile and antibiotic susceptibility pattern of organisms isolated from cerebrospinal fluid (CSF) of patients with suspected meningitis at a tertiary care teaching hospital.

Materials and Methods: A hospital-based descriptive cross-sectional study was conducted in the Department of Microbiology from June 2024 to December 2024. All CSF samples received from patients with clinically suspected meningitis were processed by direct microscopy, Gram staining and culture on chocolate agar, blood agar and MacConkey agar. Antimicrobial susceptibility testing (AST) of the isolates was performed by the Kirby-Bauer disc diffusion method as per Clinical and Laboratory Standards Institute (CLSI) M100 guidelines. Clinical and laboratory parameters were compared between culture-positive and culture-negative participants using appropriate statistical tests, with $p < 0.05$ considered significant.

Results: Of 630 participants, paediatric patients formed the largest group (45.9%) and males predominated (60.5%). Fever (70.0%) was the commonest presenting symptom, and 69.2% of participants had received antibiotics before CSF collection. CSF culture yielded bacterial growth in only 14 of 630 samples (2.2%). *Acinetobacter* spp. (35.71%) and *Klebsiella pneumoniae* (28.57%) were the leading isolates, and Gram-negative organisms accounted for 78.6% of isolates. Half of the isolates (50.0%) were multidrug-resistant; no methicillin-resistant *Staphylococcus aureus* or carbapenem-resistant isolate was detected. Resistance was highest to penicillin (66.67%) and ceftazidime (62.50%), while complete susceptibility was retained to carbapenems, aminoglycosides, colistin and vancomycin. Culture-positive patients had significantly lower Glasgow Coma Scale scores, higher CSF opening pressure, higher CSF cell counts and protein, lower CSF glucose, and longer hospital stay than culture-negative patients (all $p < 0.05$). Turbid/purulent CSF (OR 25.29), moderate/plenty pus cells (OR 19.14) and neck stiffness (OR 18.22) showed the strongest association with culture positivity, whereas prior antibiotic exposure reduced the odds of a positive culture (OR 0.24).

Conclusion: Although culture positivity in suspected meningitis was low, largely attributable to widespread pre-CSF antibiotic use, the culture-positive subset showed a clear Gram-negative and multidrug-resistant predominance, with *Acinetobacter* spp. and *Klebsiella pneumoniae* as the leading pathogens. Continuous local surveillance of the bacteriological and resistance profile is

essential to guide rational empirical therapy and antimicrobial stewardship in meningitis.

Keywords: Meningitis; Cerebrospinal fluid; Bacteriological profile; Antibiotic susceptibility testing; Multidrug resistance; Acinetobacter; Klebsiella pneumoniae.

INTRODUCTION

Meningitis is inflammation of the meninges surrounding the brain and spinal cord, most commonly caused by viral, bacterial or fungal pathogens. Acute bacterial meningitis (ABM) is a medical emergency that can progress rapidly to mental status change, hearing loss, learning disability and death if diagnosis and treatment are delayed.^[1,2] According to the Global Burden of Disease (GBD) 2016 study, meningitis incident cases increased globally from 2.50 million in 1990 to 2.82 million in 2016, even though overall mortality declined over the same period, with the greatest burden persisting in low- and middle-income countries.^[3,5] In recognition of this continuing burden, the World Health Organization launched the "Defeating Meningitis by 2030" global road map, which sets out visionary goals to eliminate bacterial meningitis epidemics, reduce vaccine-preventable cases and deaths, and improve post-meningitis quality of life.^[4]

CSF culture remains the diagnostic gold standard for bacterial meningitis, and determination of the causative organism's antimicrobial susceptibility is essential to rationalise treatment.^[1,2] Empirical antimicrobial therapy for suspected meningitis is typically initiated on presumptive grounds and should be guided by the antibiotic susceptibility pattern and aetiology of the most frequent local pathogens, since delay in appropriate therapy is independently associated with worse outcome.^[1,2,6] Knowledge of the prevalent aetiological agents and their antibiogram is therefore central to selecting the best empirical regimen, and periodic local surveillance is necessary because the microbial profile and resistance pattern can change over time and differ by region.^[6,7] Classical teaching identifies *Streptococcus pneumoniae*, *Neisseria meningitidis* and *Haemophilus influenzae* as the dominant community-acquired pathogens,^[1,5] but several recent series from tertiary care and neurosurgical settings have documented a shift toward Gram-negative bacilli such as *Acinetobacter* spp., *Klebsiella pneumoniae* and *Escherichia coli*, particularly in patients with neurosurgical intervention, head trauma or other predisposing conditions,^[10-26] frequently accompanied by multidrug resistance that narrows therapeutic options.^[14-17]

A further diagnostic challenge is that a large proportion of patients with suspected meningitis receive antibiotics before CSF is collected, which can substantially reduce the yield of Gram stain and culture without necessarily altering the CSF cytological and biochemical profile within the first few days of illness.^[7-9] This makes the interpretation

of culture-negative results, and the comparison of culture-positive with culture-negative cases on clinical and biochemical grounds, an important part of any bacteriological surveillance study.

Meningitis is a serious infection that, if inadequately treated, can lead to considerable morbidity, including mental illness and hearing loss, and to mortality. A varying spectrum of Gram-positive and Gram-negative organisms causes meningitis, and this variation differs by geography and over time. The present study was therefore proposed to determine the organisms prevalent in our setting; the resulting antibiotic sensitivity pattern is intended to help clinicians institute early, rational empirical treatment and thereby prevent sequelae. The emergence of multidrug-resistant organisms is a serious and escalating problem, and this study also aimed to characterise the resistance pattern of the isolated organisms.

The objective of this study was to evaluate the bacteriological profile, in terms of pathogen frequency, and the antibiotic sensitivity pattern of organisms isolated from the cerebrospinal fluid of patients with suspected meningitis at a tertiary care hospital, and to correlate culture positivity with clinical and CSF biochemical parameters.

Aims and Objectives

1. To determine the common organisms causing meningitis in cerebrospinal fluid samples of patients with clinically suspected meningitis.
2. To determine the antibiotic sensitivity pattern of the organisms isolated.
3. To assess the burden of multidrug resistance among the isolated organisms.
4. To identify clinical, demographic and CSF parameters associated with culture positivity, so as to guide rational empirical antibiotic therapy for meningitis.

MATERIALS AND METHODS

Study design and setting: This was a hospital-based, descriptive, cross-sectional study conducted in the Department of Microbiology of a tertiary care teaching hospital.

Study duration: June 2024 to December 2024.

Sample size: All cerebrospinal fluid samples received in the bacteriology section of the Department of Microbiology from patients with suspected meningitis during the study period were included, yielding a total of 630 samples.

Inclusion criteria

All CSF samples from patients with suspected meningitis admitted to the inpatient departments of the hospital were included.

Exclusion criteria

Unlabelled samples, samples with delayed transportation, contaminated samples and samples from patients with an alternative definitive diagnosis were excluded.

Sample processing: All CSF samples collected from patients with suspected meningitis were transported without delay to the bacteriology section of the Department of Microbiology and processed as per standard operating guidelines. Samples were first subjected to direct microscopy and Gram staining for detection of pus cells, red blood cells and microorganisms. Each sample was then inoculated on chocolate agar, blood agar and MacConkey agar and incubated overnight at 37 °C; culture plates were read the following day, and samples without growth after 48 hours of incubation were reported as sterile/no growth.

Antimicrobial susceptibility testing: Antimicrobial susceptibility testing (AST) of all bacterial isolates was performed by the Kirby-Bauer disc diffusion method as per Clinical and Laboratory Standards Institute (CLSI) M100 guidelines.^[24,25] A standardised 0.5 McFarland inoculum was prepared for each isolate and inoculated on Mueller-Hinton agar by the lawn-culture technique, followed by overnight incubation at 37 °C; zone diameters were read the next day and interpreted as sensitive, intermediate or resistant according to current CLSI breakpoints.^[24] Isolates resistant to at least one agent in three or more antimicrobial categories were classified as multidrug resistant (MDR), consistent with the terminology used in comparable Indian surveillance studies.^[14,15,17]

Statistical analysis: Data were entered and analysed using SPSS statistical software. Categorical variables were expressed as frequencies and percentages and compared using the chi-square test or Fisher's exact test where cell counts were small. Continuous variables were expressed as mean $\pm$ standard

deviation and compared between culture-positive and culture-negative groups using the Mann-Whitney U test in view of the small size and non-normal distribution of the culture-positive subgroup. Odds ratios (OR) with 95% confidence intervals (CI) were calculated for selected clinical and laboratory predictors of culture positivity, using Fisher's exact test for the corresponding p-value. A p-value <0.05 was considered statistically significant.

Ethical considerations: The study was conducted after approval from the Institutional Ethics Committee. As this was a laboratory-based observational study using samples and data collected as part of routine clinical care and individual informed consent/waiver of consent was obtained, per local IEC decision.

RESULTS

A total of 630 participants evaluated for suspected meningitis were included in the study. Paediatric patients constituted the largest age group (45.9%), followed by adults (33.7%) and geriatric patients (20.5%). Males predominated overall (60.5%). Half of the participants were initially managed under the Department of Medicine (50.5%), while 31.3% were managed under Paediatrics and 18.3% under Neurology. Most participants required ICU admission (68.4%), whereas 31.6% were managed in the general ward. Fever was the most frequent presenting symptom (70.0%), followed by headache (53.8%), vomiting (48.3%), neck stiffness (31.9%), altered sensorium (27.8%) and seizures (12.7%); shock at presentation was uncommon (3.3%). A substantial proportion of participants (69.2%) had received antibiotics before CSF collection, with ceftriaxone being the most frequently recorded empirical antibiotic [Table 1].

Table 1: Demographic, clinical and admission characteristics of study participants (N = 630)

Variable	Category	Frequency (n)	Percentage (%)
Age group	Paediatric	289	45.9
	Adult	212	33.7
	Geriatric	129	20.5
Sex	Male	381	60.5
	Female	249	39.5
Initial department	Medicine	318	50.5
	Paediatrics	197	31.3
	Neurology	115	18.3
Admission location	ICU	431	68.4
	Ward	199	31.6
Presenting symptom	Fever	441	70.0
	Headache	339	53.8
	Vomiting	304	48.3
	Neck stiffness	201	31.9
	Altered sensorium	175	27.8
	Seizures	80	12.7
	Shock at presentation	21	3.3
Antibiotics before CSF collection	Yes	436	69.2
Predisposing factor	Immunocompromised status	70	11.1
	Otitis/sinusitis/mastoiditis	58	9.2
	Head trauma	53	8.4
	Recent neurosurgery	35	5.6

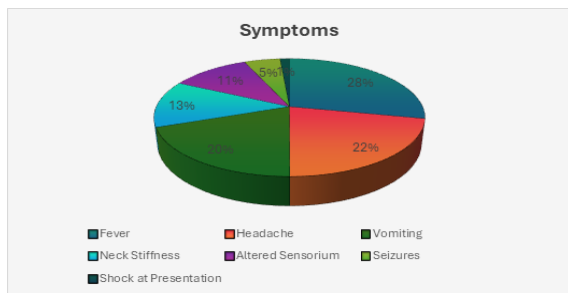


Figure 1: Distribution of Symptoms among the subjects

Empirical antibiotics administered before CSF collection included ceftriaxone alone (18.3%), ceftriaxone with vancomycin (12.7%), meropenem (11.4%), piperacillin-tazobactam (10.0%), cefotaxime with ampicillin (8.6%) and amoxicillin-clavulanate (8.3%). Comorbidities included diabetes mellitus (7.3%), malignancy (4.4%), chronic kidney disease (2.5%), steroid use (1.6%) and HIV infection (1.3%).

CSF was predominantly clear on gross appearance (73.2%), while turbid and purulent appearances were observed in 11.6% and 2.5% of samples, respectively; bloody and xanthochromic CSF

accounted for 8.7% and 4.0%. Gram staining was positive in only 10 of 630 samples (1.6%), and culture demonstrated bacterial growth in 14 patients (2.2%), indicating a low overall culture positivity rate. Pus cells on smear were absent in 45.5% of samples, few in 30.3%, moderate in 19.8% and plenty in 5.4%. Regarding outcome, 88.3% of participants recovered, 4.1% developed neurological sequelae (hearing loss 1.4%, seizure disorder 1.1%, motor deficit 0.6%, cognitive deficit 0.3%), 2.9% were referred, 2.7% died and 2.1% left against medical advice [Table 2].

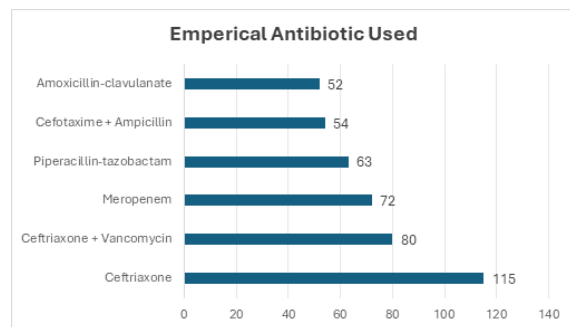


Figure 2: Empirical antibiotics used among the subjects

Table 2: CSF findings, culture result and clinical outcome (N = 630)

Variable	Category	Frequency (n)	Percentage (%)
CSF appearance	Clear	461	73.2
	Turbid	73	11.6
	Bloody	55	8.7
	Xanthochromic	25	4.0
	Purulent	16	2.5
Gram stain	Negative	620	98.4
	Positive	10	1.6
Pus cells on smear	None	280	45.5
	Few	191	30.3
	Moderate	125	19.8
	Plenty	34	5.4
Culture result	No growth	616	97.8
	Growth	14	2.2
Outcome	Recovered	556	88.3
	Neurological sequelae	26	4.1
	Referred	18	2.9
	Death	17	2.7
	LAMA	13	2.1

Among the 14 culture-positive samples, *Acinetobacter* spp. was the commonest isolate, accounting for 5 cases (35.71%), followed by *Klebsiella pneumoniae* in 4 (28.57%), *Escherichia coli* and *Staphylococcus aureus* in 2 each (14.29%), and *Streptococcus pneumoniae* in 1 (7.14%) [Table 3]. Gram-negative organisms therefore constituted 11 of 14 isolates (78.6%), demonstrating a clear Gram-negative predominance consistent with

reports from other Indian tertiary care and neurosurgical settings.^[10,15,17] Seven isolates (50.0%) were classified as multidrug resistant. Both *S. aureus* isolates were methicillin-susceptible (MSSA); no methicillin-resistant *S. aureus* (MRSA) or carbapenem-resistant isolate was identified, and 2 of 8 applicable Gram-negative isolates (25.0%) were extended-spectrum beta-lactamase (ESBL) producers [Table 3].

Table 3: Distribution of bacterial isolates and resistance markers among culture-positive samples (n = 14)

Organism	n	% of culture-positive	% of all CSF samples	Gram category	MDR (n)
<i>Acinetobacter</i> spp.	5	35.71	0.79	Gram-negative	4
<i>Klebsiella pneumoniae</i>	4	28.57	0.63	Gram-negative	1
<i>Escherichia coli</i>	2	14.29	0.32	Gram-negative	2
<i>Staphylococcus aureus</i>	2	14.29	0.32	Gram-positive	0
<i>Streptococcus pneumoniae</i>	1	7.14	0.16	Gram-positive	0
Total	14	100	2.22	-	7

Antimicrobial susceptibility testing demonstrated variable resistance patterns across the 14 isolates [Table 4]. Resistance was highest to penicillin (66.67%) and ceftazidime (62.50%), while cefotaxime and ceftriaxone each showed 64.29% sensitivity and 35.71% resistance. Ciprofloxacin and trimethoprim-sulfamethoxazole showed similar resistance (35.71%), and erythromycin and oxacillin/cefoxitin showed resistance of 33.33%. Complete susceptibility (100%) was observed among

the tested isolates to ampicillin-sulbactam, cefepime, piperacillin-tazobactam, amikacin, tobramycin, levofloxacin, clindamycin, vancomycin, linezolid, imipenem, meropenem, aztreonam, colistin, chloramphenicol and rifampicin. These figures should be interpreted cautiously, as they are derived from only 14 culture-positive isolates and the number tested varied by antimicrobial agent, in keeping with CLSI recommendations on minimum isolate numbers for reporting cumulative susceptibility.^[24,25]

Table 4: Antimicrobial susceptibility profile of culture-positive isolates (n = 14)

Antibiotic	Tested (n)	Sensitive (%)	Intermediate (%)	Resistant (%)
Ampicillin	8	50.00	0.00	50.00
Amoxicillin-clavulanate	8	75.00	0.00	25.00
Ampicillin-sulbactam	8	100.00	0.00	0.00
Penicillin	6	16.67	16.67	66.67
Oxacillin/Cefoxitin	6	66.67	0.00	33.33
Cefotaxime	14	64.29	0.00	35.71
Ceftriaxone	14	64.29	0.00	35.71
Ceftazidime	8	37.50	0.00	62.50
Cefepime	8	100.00	0.00	0.00
Piperacillin-tazobactam	8	100.00	0.00	0.00
Amikacin	8	100.00	0.00	0.00
Tobramycin	8	100.00	0.00	0.00
Ciprofloxacin	14	64.29	0.00	35.71
Levofloxacin	14	100.00	0.00	0.00
Trimethoprim-sulfamethoxazole	14	64.29	0.00	35.71
Erythromycin	6	66.67	0.00	33.33
Clindamycin	6	100.00	0.00	0.00
Vancomycin	6	100.00	0.00	0.00
Linezolid	6	100.00	0.00	0.00
Imipenem	8	100.00	0.00	0.00
Meropenem	8	100.00	0.00	0.00
Aztreonam	8	100.00	0.00	0.00
Colistin	4	100.00	0.00	0.00
Chloramphenicol	14	100.00	0.00	0.00
Rifampicin	6	100.00	0.00	0.00

Comparison of culture-positive and culture-negative participants showed no statistically significant difference in mean age (38.61 ± 27.92 vs 31.36 ± 26.45 years; $p = 0.320$) or in several other parameters [Table 5]. However, culture-positive patients had significantly lower Glasgow Coma Scale (GCS) scores (11.71 vs 13.20 ; $p = 0.023$), shorter pre-CSF antibiotic exposure (6.41 vs 18.31 hours; $p = 0.010$), higher CSF opening pressure (28.15 vs 17.66

cmH₂O; $p < 0.001$), markedly higher CSF total cell counts (649.29 vs 55.83 cells/mm³; $p < 0.001$), greater neutrophil predominance (85.29% vs 42.75% ; $p < 0.001$), higher CSF protein (190.22 vs 77.23 mg/dL; $p < 0.001$), lower CSF glucose (25.61 vs 53.91 mg/dL; $p < 0.001$) and a lower CSF-to-blood glucose ratio (0.25 vs 0.58 ; $p < 0.001$). Culture-positive patients also had a longer length of hospital stay (11.86 vs 9.10 days; $p = 0.015$).

Table 5: Comparison of quantitative clinical and laboratory parameters between culture-positive and culture-negative participants

Variable	Total (Mean $\pm$ SD)	Culture-positive (Mean $\pm$ SD)	Culture-negative (Mean $\pm$ SD)	p-value
Age (years)	31.52 ± 26.49	38.61 ± 27.92	31.36 ± 26.45	0.320
Duration of symptoms (days)	4.00 ± 2.62	4.64 ± 4.27	3.98 ± 2.57	0.986
GCS score	13.17 ± 1.61	11.71 ± 2.58	13.20 ± 1.57	0.023*
Antibiotic duration before CSF (hours)	18.04 ± 19.80	6.41 ± 10.81	18.31 ± 19.88	0.010*
CSF volume received (mL)	2.92 ± 1.10	2.93 ± 0.85	2.92 ± 1.11	0.909
Opening pressure (cmH ₂ O)	18.00 ± 5.60	28.15 ± 5.86	17.66 ± 5.27	<0.001*
Total cell count (cells/mm ³)	69.02 ± 177.74	649.29 ± 715.19	55.83 ± 116.87	<0.001*
Neutrophils (%)	43.70 ± 23.25	85.29 ± 11.85	42.75 ± 22.57	<0.001*
Lymphocytes (%)	56.30 ± 23.25	14.71 ± 11.85	57.25 ± 22.57	<0.001*
RBC count (cells/mm ³)	18.43 ± 30.03	28.93 ± 22.21	18.19 ± 30.16	0.005*
Protein (mg/dL)	79.74 ± 46.57	190.22 ± 58.92	77.23 ± 43.13	<0.001*
CSF glucose (mg/dL)	53.29 ± 16.76	25.61 ± 11.22	53.91 ± 16.34	<0.001*
Paired blood glucose (mg/dL)	98.62 ± 24.40	108.16 ± 21.05	98.40 ± 24.44	0.078
CSF : blood glucose ratio	0.57 ± 0.23	0.25 ± 0.13	0.58 ± 0.23	<0.001*
Length of hospital stay (days)	9.16 ± 5.51	11.86 ± 4.42	9.10 ± 5.52	0.015*

*Statistically significant, $p < 0.05$ (Mann-Whitney U test).

Categorical analysis demonstrated significant associations of culture positivity with CSF appearance, Gram-stain positivity and increased pus cells (all $p < 0.001$), as well as with outcome ($p = 0.014$) [Table 6]. Notably, purulent CSF was seen in

50.0% of culture-positive but only 1.5% of culture-negative samples, and Gram-stain positivity was present in 71.4% of culture-positive samples versus none of the culture-negative samples, confirming the internal consistency of the microbiological findings.

Table 6: Comparison of categorical CSF and outcome variables between culture-positive and culture-negative participants

Variable	Category	Culture-positive n (%)	Culture-negative n (%)	p-value
CSF appearance	Bloody	2 (14.3)	53 (8.6)	<0.001*
	Clear	1 (7.1)	460 (74.7)	
	Purulent	7 (50.0)	9 (1.5)	
	Turbid	4 (28.6)	69 (11.2)	
	Xanthochromic	0 (0.0)	25 (4.1)	
Gram stain	Negative	4 (28.6)	616 (100.0)	<0.001*
	Positive	10 (71.4)	0 (0.0)	
Pus cells on smear	Few	2 (14.3)	189 (30.7)	<0.001*
	Moderate	4 (28.6)	121 (19.6)	
	None	0 (0.0)	280 (45.5)	
	Plenty	8 (57.1)	26 (4.2)	
Outcome	Death	0 (0.0)	17 (2.8)	0.014*
	LAMA	0 (0.0)	13 (2.1)	
	Neurological sequelae	3 (21.4)	23 (3.7)	
	Recovered	10 (71.4)	546 (88.6)	
	Referred	1 (7.1)	17 (2.8)	

*Statistically significant, $p < 0.05$ (chi-square/Fisher's exact test).

In univariate odds-ratio analysis, the strongest associations with culture positivity were turbid/purulent CSF appearance (OR 25.29, 95% CI 6.90-92.66; $p < 0.001$), moderate/plenty pus cells (OR 19.14, 95% CI 4.24-86.52; $p < 0.001$), neck stiffness (OR 18.22, 95% CI 2.31-143.42; $p < 0.001$), shock at presentation (OR 9.06, 95% CI 2.33-35.30; $p = 0.01$) and a history of otitis/sinusitis/mastoiditis (OR 4.16, 95% CI 1.26-13.72; $p = 0.03$). Prior antibiotic

administration was associated with significantly lower odds of culture positivity (OR 0.24, 95% CI 0.08-0.72; $p = 0.01$), consistent with the known reduction in culture yield after antibiotic pre-treatment.^[7-9] After accounting for admission location, ICU admission itself was not significantly associated with culture positivity (OR 0.45, 95% CI 0.16-1.31; $p = 0.15$) [Table 7].

Table 7: Predictors of culture positivity: univariate odds ratio analysis

Predictor	OR	95% CI (low)	95% CI (high)	p-value
ICU admission	0.45	0.16	1.31	0.15
Fever	5.71	0.74	43.97	0.08
Vomiting	2.74	0.85	8.82	0.10
Altered sensorium	1.98	0.68	5.80	0.23
Seizures	1.91	0.52	7.00	0.40
Shock at presentation	9.06	2.33	35.30	0.01*
Antibiotics before CSF	0.24	0.08	0.72	0.01*
Recent neurosurgery	2.94	0.63	13.70	0.18
Head trauma	1.85	0.40	8.48	0.33
Otitis/sinusitis/mastoiditis	4.16	1.26	13.72	0.03*
Immunocompromised status	2.23	0.61	8.21	0.20
Neck stiffness	18.22	2.31	143.42	<0.001*
Turbid/purulent CSF	25.29	6.90	92.66	<0.001*
Pus cells moderate/plenty	19.14	4.24	86.52	<0.001*
Healthcare- vs community-associated	0.90	0.25	3.28	1.00
Any comorbidity vs none	0.80	0.18	3.64	1.00
Adverse outcome vs recovered	3.12	0.95	10.21	0.07
Death vs non-death	1.18	0.07	20.61	1.00

*Statistically significant, $p < 0.05$ (Fisher's exact test).

Overall, culture-positive cases formed a small but clinically distinct subgroup, characterised by more pronounced inflammatory and biochemical CSF abnormalities, a predominance of multidrug-resistant Gram-negative organisms, and a lower likelihood of prior antibiotic exposure than culture-negative cases.

DISCUSSION

This cross-sectional analysis of 630 CSF samples from patients with suspected meningitis at a tertiary care hospital demonstrates a predominantly

paediatric and male patient population, a very low overall culture positivity rate of 2.2%, a marked Gram-negative and multidrug-resistant organism profile among the isolates recovered, and strong biochemical and cytological correlates of true culture positivity. These findings both echo and extend observations from recent Indian and international series.^[5,6,10,11,12,13]

Demographic and clinical profile: The predominance of paediatric patients (45.9%) and males (60.5%) in this cohort is consistent with several recent Indian

studies of pyogenic and acute bacterial meningitis, which similarly report a higher burden in children and a male preponderance.^[10-13] Fever, headache, vomiting and neck stiffness were the leading presenting features in our series, mirroring the clinical picture reported in contemporary paediatric meningitis audits from India, in which fever was near-universal and neck stiffness and altered sensorium were frequent findings.^[11-13] The high proportion of ICU admission (68.4%) in our cohort reflects both the severity of suspected CNS infection at presentation and the referral pattern of a tertiary care centre, similar to patterns described in low- and middle-income country settings where bacterial meningitis continues to carry a disproportionate burden of severe presentations.^[5]

Low culture positivity and the effect of prior antibiotic use: The culture positivity rate of only 2.2% observed in this study is markedly lower than the rates reported in several other Indian series, which have ranged from approximately 7% to over 70% depending on patient selection and prior antibiotic exposure.^[10-12] A key explanation is the very high proportion of participants (69.2%) who had already received antibiotics, most often ceftriaxone, before CSF collection. Antibiotic pre-treatment is well documented to reduce the sensitivity of CSF Gram stain and culture substantially while having comparatively little early effect on CSF cell count, protein or glucose.^[7-9] Rogers et al., in a large cohort of healthcare-associated ventriculitis and meningitis, similarly found that antibiotic administration before CSF sampling significantly reduced the sensitivity of Gram stain and culture,^[9] and this is corroborated by our own finding that the median duration of pre-CSF antibiotic exposure was significantly shorter in culture-positive than culture-negative patients (6.41 vs 18.31 hours; $p = 0.010$) and that prior antibiotic administration halved the odds of a positive culture (OR 0.24, 95% CI 0.08-0.72). This underscores the importance of obtaining CSF for culture before, or as close as possible to, the first dose of antibiotics whenever clinically feasible, and of not relying on a negative culture alone to exclude bacterial meningitis in a pre-treated patient.^[1,2,9]

Bacteriological profile: a Gram-negative and multidrug-resistant predominance: Among the 14 culture-positive isolates in our study, *Acinetobacter* spp. (35.71%) and *Klebsiella pneumoniae* (28.57%) were the leading organisms, together with *Escherichia coli* and *Staphylococcus aureus* (14.29% each) and *Streptococcus pneumoniae* (7.14%); Gram-negative bacilli accounted for 78.6% of isolates. This contrasts with the classical epidemiology of community-acquired bacterial meningitis, in which *Streptococcus pneumoniae* and *Neisseria meningitidis* are traditionally the dominant pathogens,^[1,5] but is concordant with a growing body of literature describing a shift toward Gram-negative bacilli, particularly *Acinetobacter* spp. and *Klebsiella pneumoniae*, in tertiary care and neurosurgical settings, often related to nosocomial acquisition,

invasive procedures or prior antibiotic pressure.^[10,14,15,16,17,20] Similar organism shifts toward *Acinetobacter* and *Klebsiella* species have been documented in Indian neonatal sepsis and ICU surveillance studies, several of which also report an increasing prevalence of multidrug-resistant Gram-negative bacilli in hospitalised patients.^[14-19] Case reports of spontaneous *Escherichia coli* meningitis in immunocompetent adults further illustrate that Gram-negative bacillary meningitis, though classically associated with neurosurgery or trauma, can occasionally occur without an obvious predisposing focus and carries a comparatively higher mortality than pneumococcal or meningococcal disease.^[22,23]

Half of our culture-positive isolates (50.0%) were multidrug resistant, a proportion broadly comparable to contemporary Indian antimicrobial resistance surveillance in ICU and neonatal settings, where MDR rates among Gram-negative bacilli of 45-75% have been reported.^[14-18] Reassuringly, both *S. aureus* isolates in our series were methicillin-susceptible and no carbapenem-resistant isolate was detected, in contrast to some ICU-based Indian series reporting substantial carbapenem resistance among *Acinetobacter* and *Klebsiella* isolates,^[15,17] this may reflect the smaller sample of CNS-restricted isolates in our study compared with the larger, more heterogeneous specimen types (blood, endotracheal aspirate, wound swabs) included in ICU-wide surveillance.

Antibiotic susceptibility pattern: Resistance in our isolates was highest to penicillin and ceftazidime, while complete in vitro susceptibility was preserved to carbapenems (imipenem, meropenem), aminoglycosides (amikacin, tobramycin), fluoroquinolones (levofloxacin), colistin, vancomycin, linezolid and chloramphenicol. This pattern is consistent with current CLSI-based susceptibility reporting recommendations,^[24,25] and supports the continued empirical utility of a carbapenem, or a combination of a third-generation cephalosporin with an aminoglycoside, while awaiting final culture and sensitivity results, in line with international treatment guidance for bacterial meningitis.^[1,2,6] For the subset of isolates demonstrating multidrug resistance, particularly *Acinetobacter* spp. and *Klebsiella pneumoniae*, colistin retained complete in vitro activity in our series. Since systemically administered colistin achieves poor cerebrospinal fluid penetration, several case reports and small series have described successful use of adjunctive intrathecal or intraventricular colistin, alone or combined with intravenous meropenem or tigecycline, for CNS infection caused by MDR *Acinetobacter baumannii* or *Klebsiella pneumoniae* unresponsive to systemic therapy alone,^[20,21] an option that should be considered in consultation with infectious disease and neurosurgical teams when MDR Gram-negative meningitis fails to respond to intravenous therapy.

It should be emphasised that these percentages are derived from a small number of isolates ($n = 14$, with fewer tested against some agents), and, as recommended in CLSI guidance, cumulative susceptibility figures based on fewer than 30 isolates should be interpreted with caution and supplemented by a longer period of surveillance before being used to finalise institutional antibiograms.^[24,25]

Clinical and biochemical correlates of culture positivity: Culture-positive patients in our cohort had significantly lower GCS scores, higher CSF opening pressure, more pronounced CSF pleocytosis with neutrophilic predominance, higher CSF protein, lower CSF glucose and CSF:blood glucose ratio, and a longer hospital stay than culture-negative patients, and turbid/purulent CSF, abundant pus cells and neck stiffness were the strongest independent correlates of a positive culture. These findings are consistent with the classical CSF profile of bacterial meningitis described in international guidelines and reviews, in which marked pleocytosis, hypoglycorrhachia and elevated protein reliably distinguish bacterial from non-bacterial or culture-negative presentations even when culture itself is negative because of prior antibiotic exposure.^[1,2,6] The association between lower GCS and culture positivity, together with the higher opening pressure observed in culture-positive patients, is in keeping with reports that a depressed level of consciousness and raised intracranial pressure are markers of more severe, and often bacteriologically confirmed, CNS infection.^[1,6] Shock at presentation and a history of otitis/sinusitis/mastoiditis, both of which showed a significant positive association with culture positivity in our odds-ratio analysis, are recognised predisposing and severity markers for bacterial meningitis and its complications.^[1,6]

Outcome: The overall recovery rate in our cohort (88.3%) is comparable to outcomes reported in recent paediatric and adult Indian meningitis series, while the proportion with neurological sequelae (4.1%) and mortality (2.7%) falls within the range described in low- and middle-income country cohorts, where mortality and long-term neurological morbidity after bacterial meningitis remain higher than in high-income settings despite modern intensive care.^[5,11-13] The significant association between culture positivity and adverse outcome ($p = 0.014$) in our data reinforces the clinical importance of achieving microbiological confirmation, wherever possible, to guide targeted rather than purely empirical therapy. **Implications for antimicrobial stewardship:** Taken together, our findings support three practical implications. First, clinicians should make every effort to obtain CSF for Gram stain and culture before, or as early as possible after, the first dose of antibiotics, given the substantial reduction in culture yield associated with pre-treatment observed both here and in prior studies.^[7-9] Second, given the observed Gram-negative and multidrug-resistant predominance in our setting, empirical regimens that rely solely on a third-generation cephalosporin may

be inadequate for healthcare-associated or post-neurosurgical meningitis, and local antibiograms should inform empirical choices, consistent with international recommendations for healthcare-associated ventriculitis and meningitis.^[8] Third, sustained local surveillance, feeding into the broader goals of the WHO Defeating Meningitis by 2030 road map,^[4] is essential to detect emerging resistance early and to preserve the efficacy of last-line agents such as carbapenems and colistin.

Limitations: This study has several limitations. First, the very small number of culture-positive isolates ($n = 14$) limits the statistical power and generalisability of the antibiotic susceptibility figures, and cumulative antibiogram data derived from fewer than 30 isolates per agent should be interpreted cautiously, as recommended by CLSI.^[24,25] Second, the high rate of prior antibiotic exposure (69.2%) almost certainly underestimates the true bacteriological burden of meningitis in this population, since culture-negative results in pre-treated patients cannot reliably exclude bacterial aetiology.^[7-9] Third, this being a single-centre, cross-sectional study conducted over a six-month period, seasonal variation in pathogen distribution could not be assessed, and the findings may not be generalisable to other geographic or healthcare settings. Fourth, molecular or antigen-based diagnostic methods, which can improve detection in culture-negative or antibiotic-pretreated CSF, were not used in this study and would be a valuable addition in future surveillance. Finally, as a descriptive cross-sectional study, causal inferences cannot be drawn from the reported associations, which should be interpreted as correlative.

CONCLUSION

In this tertiary care cohort of patients with suspected meningitis, CSF culture positivity was low overall (2.2%), largely attributable to the high prevalence of antibiotic administration before CSF collection. Among culture-confirmed cases, however, *Acinetobacter* spp. and *Klebsiella pneumoniae* were the leading pathogens, Gram-negative organisms clearly predominated, and half of the isolates were multidrug resistant, while susceptibility to carbapenems, aminoglycosides, colistin and vancomycin remained largely preserved. Turbid or purulent CSF, abundant pus cells, neck stiffness and a lower GCS reliably distinguished culture-positive from culture-negative cases. These findings support prompt CSF sampling before antibiotic initiation wherever feasible, judicious empirical use of carbapenem-based or combination regimens pending susceptibility results in settings with a similar resistance profile, and continued periodic local bacteriological surveillance to guide rational antimicrobial stewardship and align with the broader global goal of defeating meningitis by 2030 [4].

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