ANTIBIOTIC SUSCEPTIBILITY IN ACUTE PYOGENIC MENINGITIS: A CASE STUDY

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Abstract: Background and Aims: Acute pyogenic meningitis (APM) is a severe central nervous system infection with significant morbidity and mortality. While conjugate vaccines have reduced its incidence in children, the burden remains high in adults, particularly in developing countries. This study aimed to identify the bacteriological profile and antibiotic susceptibility patterns of APM in patients from a tertiary care hospital in western Uttar Pradesh, India.

Methods: A hospital-based cross-sectional study was conducted on 50 patients diagnosed with APM at J.N. Medical College, Aligarh, from October 2017 to October 2019. Inclusion criteria included informed consent, patients aged above 14 years, and those presenting with clinical and cerebrospinal fluid (CSF) findings suggestive of APM. CSF was analyzed microbiologically, biochemically, and cytologically. Culture and antibiotic susceptibility testing were performed using the Kirby-Bauer disc diffusion method as per CLSI 2017 guidelines. Statistical analysis was done using SPSS v20, with a p-value <0.05 considered significant.

Results: Among 50 patients, 62% were male, and 67% were aged 20–60 years. The most common pathogen was Streptococcus pneumoniae (70% of culture-positive cases), followed by Staphylococcus aureus (10.8%). All gram-positive organisms were sensitive to vancomycin and linezolid, while gram-negative isolates showed 100% sensitivity to carbapenems. Gram staining had a sensitivity of 70%, and culture positivity was 74%. Resistance to commonly used antibiotics like cotrimoxazole and gentamicin was noted.

Conclusion: APM remains a critical public health challenge in developing regions. Early culture sensitivity testing and empirical treatment based on local susceptibility patterns are vital. Vaccination and continued surveillance are necessary to reduce the disease burden and address antimicrobial resistance.

Keywords: Acute pyogenic meningitis, Streptococcus pneumoniae, Antibiotic resistance, Gram staining, Carbapenems

INTRODUCTION

Meningitis is inflammation of the meninges, caused by infections (*Streptococcus pneumoniae*, *Mycobacterium tuberculosis*, viruses, fungi) or non-infectious factors (trauma, drugs, autoimmune). Pyogenic and tubercular meningitis are most common, with viral causes like enteroviruses and herpes simplex. Fungal meningitis, such as cryptococcal, is seen in immunocompromised patients. Symptoms include fever, headache, neck stiffness, and altered mental status, though not all are always present.

Pyogenic meningitis is a serious CNS infection with significant morbidity and up to 30% mortality in adults, despite decreased incidence in children due to widespread use of conjugate vaccines. Common pathogens include *Streptococcus pneumoniae* (30-50%), *Neisseria meningitidis* (10-35%), *Staphylococci* (5-15%), other *Streptococcus* species, *Haemophilus influenzae* (1-3%), gram-negative bacilli (1-10%), and *Listeria monocytogenes*.[1,3–6] Pathogen prevalence varies with age, geography, and time, requiring periodic reviews.[7,8] While studies are available from developed countries,[9–12] data from developing countries like India remain limited.[2,6,13,14] Early administration of appropriate antibiotics is critical, but antimicrobial resistance complicates treatment.[15] In India, effective disease management is vital to reduce cognitive impairment, morbidity, and mortality. This study aimed to identify the bacteriological profile and antibiotic susceptibility of pyogenic meningitis patients at a tertiary care center in western Uttar Pradesh.

MATERIAL AND METHODS

An observational, cross sectional hospital based study was carried out on 50 patients recruited from the emergency and medicine wards of J.N. Medical College and Hospital (JNMCH), AMU, Aligarh during the period October 2017 to October 2019. The study protocol was approved by Board of Studies of the Faculty of Medicine JNMCH, Aligarh. The inclusion criteria was informed consent taken from each patient or from their attendants if patient in altered sensorium prior to study, patients having pyogenic meningitis with more than 14 years of age, patients with all risk factors such as age, diabetes, smoking, alcoholism.

Criteria for acute pyogenic meningitis included headache not relieved by analgesics, nausea or vomiting not relieved by anti-emetics, fever of acute onset, altered sensorium, neck rigidity, positive Kernig's sign or positive Brudzinski sign etc and CSF examination including positive CSF culture with or without positive CSF gram stain, CSF protein level >45mg/dl, CSF glucose level <40mg/dl, CSF total cell count >10cells/mm3 with predominance of neutrophils.[16]

Specimen and Clinical Isolates for Study

Cerebrospinal fluid (CSF): CSF was collected using standard procedure from intervertebral space L3-4, L4-5. Cytological, biochemical and microbiological analysis was done using 2ml CSF in each case.

Microbiological analysis included Gram staining to identify the isolates as Gram positive or Gram negative. **CSF culture** involved inoculation on blood agar (BA), MacConkey agar (MCA), Teepol Lactose agar (TLA), nutrient broth and then incubation overnight at 37°C, and finally carrying biochemical reactions. The cultural characteristics, morphology and biochemical tests (Bailey & Scotts., 2007; Mackie & McCartney., 2007) led to identification of organisms. **Antibiotic susceptibility testing** was carried out using Kirby-Bauer disc diffusion method on Mueller Hinton Agar. Results were interpreted as per Clinical and Laboratory Standards Institute (CLSI 2017) guidelines. Commercially prepared antibiotic discs (Hi- media Laboratories, Mumbai, India) were used and the details of discs for respective microorganism are mentioned in Table 1.

Table 1: Discs used for respective microorganism

	Name of microorganism	Antibiotic disc
1.	Gram positive cocci (CLSI 2007)	Levofloxacin (5µg), Amikacin (30µg), Gentamicin (10µg), Clindamycin (2µg), Vancomycin (30µg), Ampicillin (10µg), Azithromycin (15µg), Ceftriaxone (30µg), Linezolid (30µg), Amoxyclav (30µg), Cefoxitin (30µg), Cotrimoxazole (25µg).
2.	Enterobacteriaceae (CLSI 2007)	Ceftriaxone (30µg), Ceftazidime (30µg), Amoxyclav (30µg),

		Ciprofloxacin (5µg), Chloramphenicol (30µg), Cotrimoxazole (25µg), Cefoperazone-sulbactam (150µg), Levofloxacin (5µg), Amikacin (30µg), Gentamicin (10µg), Piperacillin-tazobactam (110µg), Imipenem (10µg) Meropenem (10µg)
3.	For Pseudomonas species (CLSI 2007)	Ceftriaxone (30µg), Ceftazidime (30µg), Levofloxacin (5µg), Amikacin (30µg), Gentamicin (10µg), Piperacillin- tazobactam (110µg), Ciprofloxacin (5µg), Meropenem (10µg), Imipenem (10µg)

CSF cytological analysis was done by BeneSphera 3-PART HEMATOLOGY ANALYZER H33 and biochemistry performed using BeneSphera Clinical Chemistry Analyzer C61 each using standard techniques respectively.

Statistical analysis: All statistical data were analyzed by using SPSS software version 20. Continuous variables were expressed as mean ± SD, while proportions were expressed as count. Comparison of categorical variables between the groups was done by Chi-square teat while continuous variables were compared using student t test for independent groups. A 'p' value of less than 0.05 was considered significant.

RESULTS

The study analyzed 50 clinically diagnosed acute pyogenic meningitis cases. The majority of patients (67%) were within the age group of 20–60 years, accounting for 34 individuals, while 16 patients (33%) were either below 20 or above 60 years of age. Gender-wise, 31 patients (62%) were male, and 19 patients (38%) were female, resulting in a male-to-female ratio of 1.63:1.

Table 2: Distribution of Patients by Age Group and Gender

Category	Number of Patients	Percentage (%)
Age Group		
20–60 years	34	67%
Others (≤20 or >60)	16	33%
Gender		
Male	31	62%
Female	19	38%

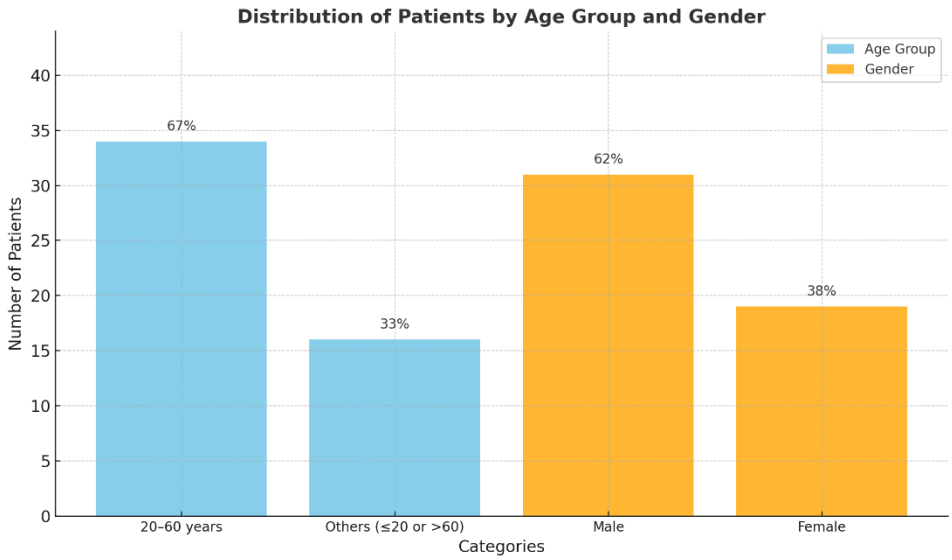

Figure 1: Distribution of Patients by Age group and Gender

Various symptoms with which patients presented were fever (96%), nausea and vomiting (44%), altered sensorium (42%), headache (40%), neck rigidity (16%) and seizures (10%). Demonstration of correlation between the findings of culture and smear positivity in patients of acute pyogenic meningitis is shown by table given below. Demonstration of organism by gram stain in CSF was present in 35 (70%) of patients while culture positivity in CSF samples was present in 37 (74%) patients. Most common organism isolated from culture positive cases was *Streptococcus pneumonia,* it was present in 26 (70%) of culture positive cases followed by *Staphylococcus aureus,* present in 4 (10.8%) cases. Gram negative organisms were less commonly isolated and included *Escherichia coli* (8.1%), *Klebsiella spp* (5.4%), *Proteus spp* (2.7%) and *Pseudomonas spp* (2.7%).

Table 3: Symptoms, Findings, and Organisms in Acute Pyogenic Meningitis

Category	Number of Cases	Percentage (%)
Symptoms		
Fever	48	96
Nausea and Vomiting	22	44
Altered Sensorium	21	42
Headache	20	40
Neck Rigidity	8	16
Seizures	5	10
Findings		
Gram Stain Positivity (CSF)	35	70
Culture Positivity (CSF)	37	74
Organisms in Culture-Positive Cases		
Streptococcus pneumoniae	26	70
Staphylococcus aureus	4	10.8
Escherichia coli	3	8.1
Klebsiella spp	2	5.4
Proteus spp	1	2.7
Pseudomonas spp	1	2.7

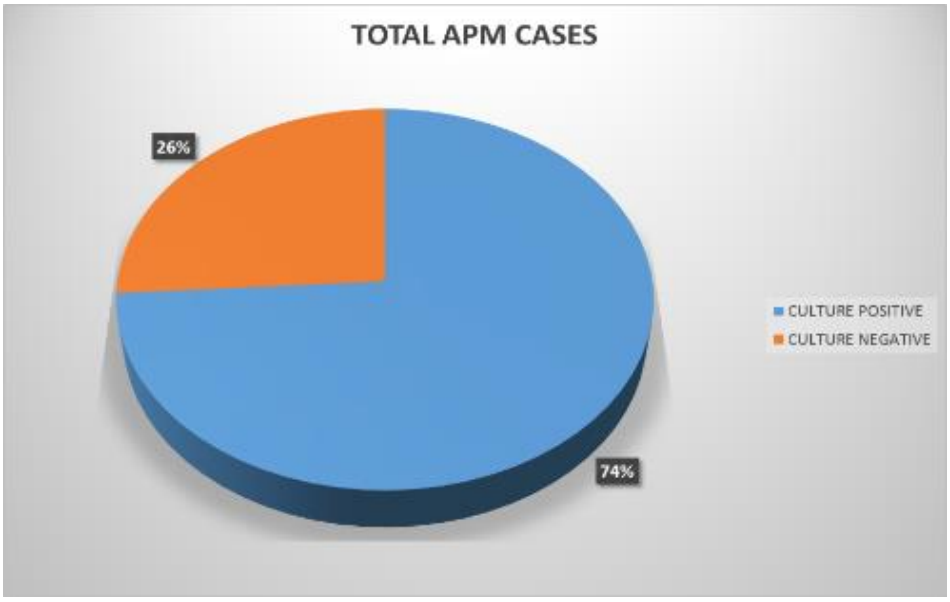

Figure 2: Culture positive patients of APM

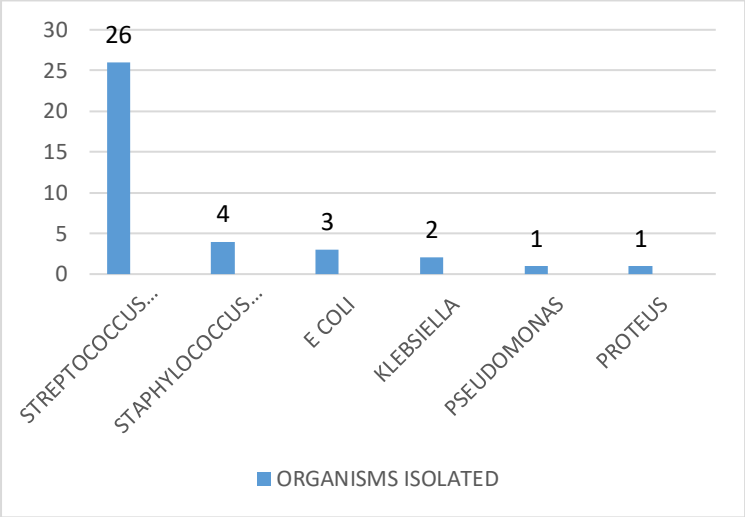

Figure 3: Organisms Isolated in culture positive CSF samples

The correlation between smear and culture findings in acute pyogenic meningitis (APM) showed that Gram stain positivity was observed in 70% of cases, with 31 cases (62%) being culture-positive and 4 cases (8%) culture-negative. Among Gram stain-negative cases, 6 (12%) were culture-positive, and 9 (18%) were culture-negative. Overall, culture positivity was noted in 74% of cases, emphasizing the reliability of culture methods in diagnosing APM.

Table 4: Correlation of smear and culture findings in APM

All APM Cases	Culture Positive	Culture Negative	Total
Gram Stain Positive	31	4	35 (70%)
Gram Stain Negative	6	9	15 (30%)
Total	37 (74%)	13 (26%)	50 (100%)

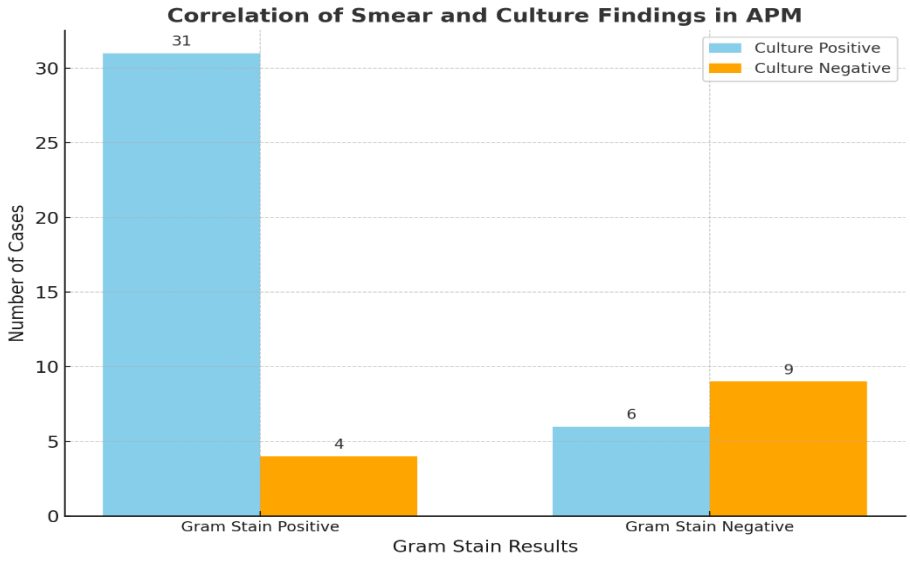

Figure 4: Correlation of Smear and Culture Findings in APM

Isolates of *S. pneumonia, S. aureus, E. coli, Klebsiella spp, Proteus spp* and *Pseudomonas spp* underwent antibiotic susceptibility testing. All the isolates of *S. pneumoniae* were sensitive to vancomycin, linezolid and ceftriaxone with variable sensitivity towards other antibiotics as depicted in figure 4. Isolates of *S. aureus* were susceptible to vancomycin with increased resistance to cotrimoxazole, gentamicin, azithromycin and variable sensitivity pattern to other drugs. Susceptibility to vancomycin and linezolid was very high among all the isolated gram positive organisms, with 100% sensitivity to vancomycin.

Table 5: Antibiotic Susceptibility Pattern of Isolated Organisms in Acute Pyogenic Meningitis

Organism	Antibiotic	Sensitivity (%)
Streptococcus pneumoniae	Linezolid	100%
	Vancomycin	100%
	Ceftriaxone	100%
	Levofloxacin	100%
	Ampicilin	65%
	Gentamicin	50%
	Azithromycin	46%
Staphylococcus aureus	Amoxicillin	100%
	Azithromycin	25% (Low)
	Amikacin	75% (Moderate)
	Cefoxitin	75% (Moderate)
	Clindamycin	75% (Moderate)
	Ceftriaxone	75% (Moderate)
	Cotrimoxazole	25% (Low)
	Levofloxacin (LCIN)	75% (Moderate)
	Vancomycin	100% (High)
	Gentamicin	25% (Low)
Gram-Positive Organisms	Vancomycin	100%
	Linezolid	100%

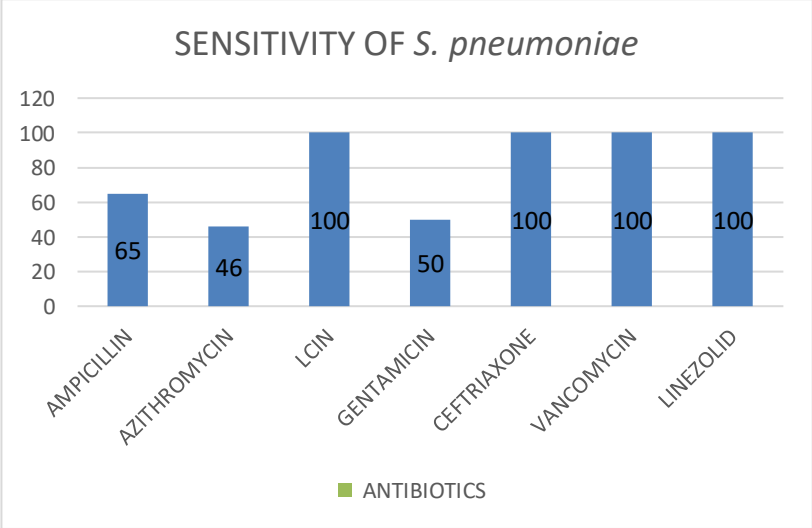

Figure 4: Antibiotics sensitivity pattern of S. pneumoniae

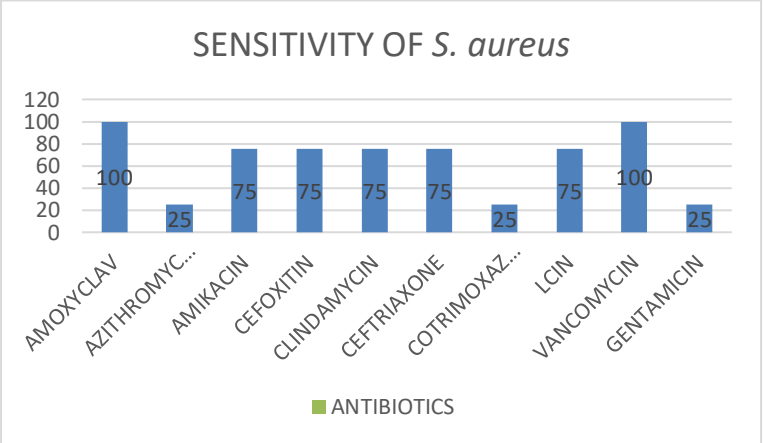

Figure 5: Antibiotics sensitivity pattern of S. aureus

Among gram negative isolates, *E. coli* showed lowest sensitivity towards amikacin (33.3%), gentamicin (33.3%), ciprofloxacin (33.3%), ceftriaxone (33.3%), cotrimoxazole (33.3%), levofloxacin (33.3%), ceftazidime (33.3%) while none of the isolate was sensitive to chloramphenicol. However sensitivity was high for amoxycillin+clavulanic acid, cefoperazone-sulbactum and piperacillin+tazobactum (66.6%) each. 100% sensitivity was shown for imipenem and meropenem.

Table 6: Antibiotic Sensitivity Table for Escherichia coli

Antibiotic	**Sensitivity (%)**
Imipenem	100%
Meropenem	100%
Amoxicillin + Clavulanic Acid	66.6%
Cefoperazone-Sulbactam	66.6%
Piperacillin + Tazobactam	66.6%
Amikacin	33.3%
Gentamicin	33.3%
Ciprofloxacin	33.3%
Ceftriaxone	33.3%
Cotrimoxazole	33.3%
Levofloxacin	33.3%
Ceftazidime	33.3%
Chloramphenicol	0%

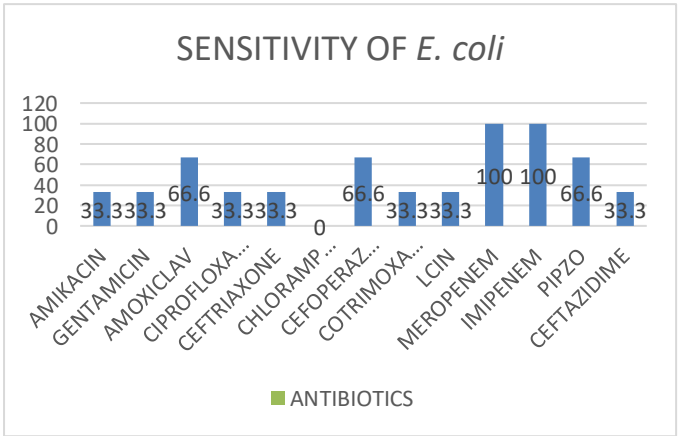

Figure 6: Antibiotics sensitivity pattern of E. coli

Two *Klebsiella spp* were isolated and both showed resistance to gentamycin and cotrimoxazole and variable sensitivities to other drugs. Both species were sensitive to imepenem and meropenem. However, these results needs to be interpreted carefully in view of low culture yield of these gram negative organisms.

Table 7: Antibiotic Sensitivity for Klebsiella spp

Antibiotic	Sensitivity (%)
Imipenem	100%
Meropenem	100%
Gentamicin	0% (Resistant)
Cotrimoxazole	0% (Resistant)
Other Antibiotics	Variable

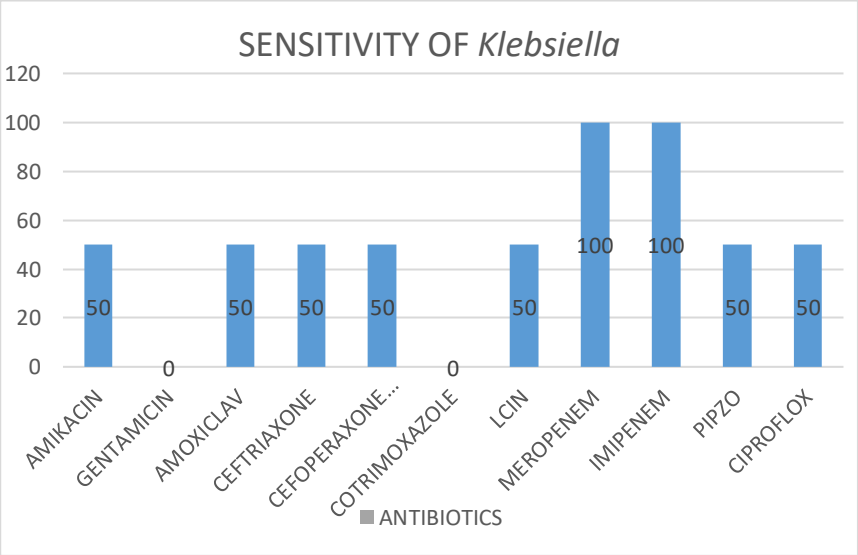

Figure 7: Antibiotics sensitivity pattern of Klebsiella

Only one *Pseudomonas spp* was isolated showing resistance to ceftazidime, ceftriaxone, levofloxacin and ciprofloxacin. It was sensitive to piperacillin+tazobactum, meropenem and imipenem. One *Proteus spp* was isolated showing sensitivity to imepenem, meropenem, piperacillin+tazobactum and amoxicillin+clavulanate while resistance to other tested drugs as depicted in the figure below. All gram negative organisms showed maximum sensitivity to carbapenems.

Table 8: Antibiotic Sensitivity Table for Pseudomonas spp and Proteus spp

Organism	Antibiotic	Sensitivity (%)
Pseudomonas spp	Amikacin	100%
	Ceftazidime	0% (Resistant)
	Gentamicin	0% (Resistant)
	Levofloxacin (LCIN)	0% (Resistant)
	Meropenem	100%
	Piperacillin + Tazobactam	100%
	Imipenem	100%
	Ceftriaxone	0% (Resistant)
	Ciprofloxacin	0% (Resistant)
Proteus spp	Amikacin	0% (Resistant)
	Gentamicin	0% (Resistant)
	Amoxicillin + Clavulanate	100%

	Ceftriaxone	0% (Resistant)
	Chloramphenicol	0% (Resistant)
	Cotrimoxazole	0% (Resistant)
	Levofloxacin (LCIN)	0% (Resistant)
	Meropenem	100%
	Imipenem	100%
	Piperacillin + Tazobactam	100%
	Ceftazidime	0% (Resistant)
	Ciprofloxacin	0% (Resistant)

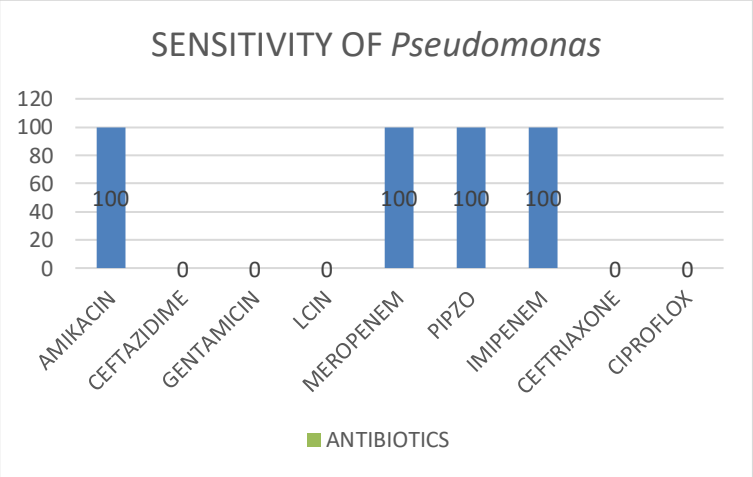

Figure 8: Antibiotics sensitivity pattern of Pseudomonas

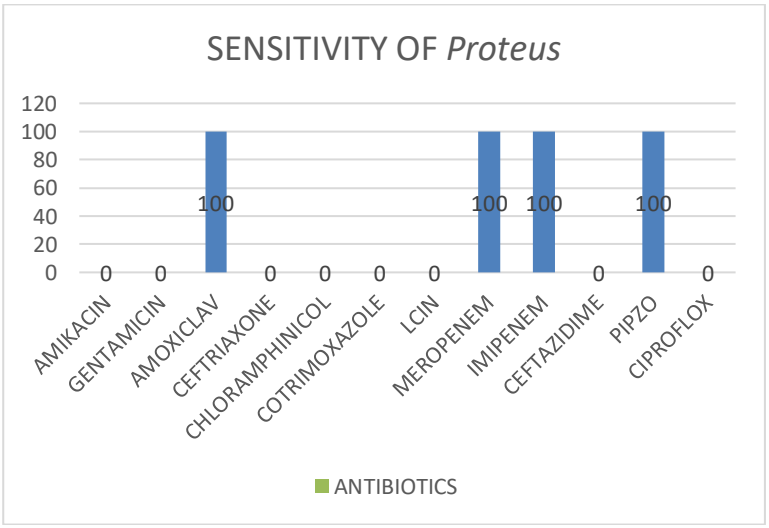

Figure 9: Antibiotics sensitivity pattern of Proteus

DISCUSSION

Acute bacterial meningitis occurs globally, often in developing countries, with high morbidity and mortality. WHO estimates 1.2 million cases annually, with 135,000 deaths.[18] Mortality rates include 20,000 deaths in Africa, 18,000 in America, 15,000 in Europe, 73,000 in Southeast Asia, 25,000 in the Eastern Mediterranean, and 20,000 in the Western Pacific.[19] In India, 8,367 cases were reported in 2005, with 485 deaths, predominantly in Andhra Pradesh (3,734 cases; 36 deaths), Uttar Pradesh (659 cases; 124 deaths), and West Bengal (702 cases; 64 deaths).[20] Early diagnosis and treatment are critical to reducing mortality and neurological sequelae.

CSF Gram staining is an effective and rapid diagnostic tool for acute pyogenic meningitis, with sensitivity ranging from 60-90% and specificity >97%.[1,6,21,22] In this study, males were affected 1.63 times more than females, consistent with previous studies.[2,6,8,23,24] Clinical symptoms observed were fever (96%), nausea/vomiting (44%), altered sensorium (42%), headache (40%), neck rigidity (16%), and seizures (10%), similar to findings in other studies.[6,26,27,28]

Table 9: Comparison of clinical features in different studies on APM

DETAILS	1	2	3	4	5	6	7	8
AUTHOR	**Shrestha RG et al**	**Modi S et al**	**Khan F et al**	**Farag HFM et al**	**Yadhav KML et al**	**Basri R et al**	**Singh AK et al**	**Our Study**
YEAR	2015	2013	2011	2005	2014	2015	2015	2017
PLACE	Nepal	Patna, India	Aligarh, India	Alexindria, Egypt	Bangalore, India	Malaysia	Gorakhpur, India	Aligarh, India
JOURNAL	BMC Paediatrics	JCDR	Neurology Asia	IJMM	JCDR	Nagoya J. Med. Sci.	IJRMS	
APM PATIENTS NUMBER	18	164	403	202	24	125	343	50
CLINICAL FEATURES %								
FEVER	78	96.5	96.5	92.1	NA	73.6	96.5	96
HEADACHE	NA	99	33	55.7	NA	24.8	39.8	40
NAUSEA VOMITING	NA	90	NA	75.2	NA	48	42.8	44
NECK RIGIDITY	63	89.2	51	NA	NA	15.2	13.7	16
ALTERED SENSORIUMNA	NA	16.3	62	NA	NA	NA	43.2	42

Normal CSF examination in an adult shows total cell count <5/µl with no PMN leukocytosis. Normally CSF protein and glucose in healty person is ≥45µg/dl and <40µg/dl respectively.[29] CSF TLC as reported by different authors in their cases is >79 cells/µl in APM.[2,11,12,30] Although TLC is high in acute pyogenic meningitis [30] some studies have reported <10cells/µl as well. [2] Mean ± SD of CSF TLC was 350 ± 302.73 in this study. Mean ±SD of CSF TLC was 359 ± 1543 cells/µl in other study. [31] Mean ± SD of CSF sugar in this study observed was 31 ± 4.4 mg/dl and mean ± SD was 31.15 ± 22.37 mg/dl in other study.[30] Mean ± SD of CSF protein in this study was 89.48 ± 8.7 mg/dl. Increased level of CSF protein and decreased level of CSF sugar as observed in this study was also observed by other workers. [2,8,15,32,33]

Although *S. pneumoniae*, *N. meningitidis*, and *H. influenzae* are common pathogens in acute pyogenic meningitis (APM), their frequencies vary globally. In the USA, APM is more common in adults due to immunization and increased nosocomial meningitis, with *S. pneumoniae* and *N. meningitidis* as predominant pathogens. In newborns and the elderly, *L. monocytogenes* is significant. [9] In Southeast Asia, meningitis caused by *N. meningitidis*, *H. influenzae*, and *Listeria* is less frequent compared to Western countries, while gram-negative pathogens like *E. coli*, Klebsiella, and *Pseudomonas* are rising in elderly patients with comorbidities.

In this study, gram-positive organisms (81.1%) were more common than gram-negative (18.9%), consistent with a previous study showing 66.18% gram-positive and 28.86% gram-negative organisms.[19] *S. pneumoniae* was the most common pathogen, isolated in 70.3% of culture-positive samples, similar to rates reported in other studies.[3,6,9,34] Culture positivity for *S. pneumoniae* varies globally, from 2.4% in Bengaluru[14] to 77% in Ghana.[35] A common inhabitant of the human nasopharynx, *S. pneumoniae* affects 5-10% of healthy adults and 20-40% of children. It invades via sinusitis, otitis media, or bacteremia, causing meningitis. Risk factors for pneumococcal meningitis include diabetes, alcoholism, malnutrition, chronic liver disease, asplenism, multiple myeloma, hypogammaglobulinemia, glucocorticoid therapy, and chronic renal disease.

S. aureus was isolated in 10.8% of culture-positive cases, similar to 13.6% in another study. [28] Risk factors include trauma, diabetes, neurosurgery, and CSF shunts. Gram-negative organisms accounted for 18.9% of cases in this study, compared to 24.5% in another study.[36] Other studies report lower rates (2.4–8.3%).[2,12,35] No cases of *N. meningitidis* or *H. influenzae* were detected, likely due to the small sample size. *N. meningitidis* isolation in India is low (~1%) but ranges from 1–25% in Western countries. [9,12,35] No *Listeria* was found, consistent with other studies,[26] though it should be suspected in immunocompromised and elderly patients due to resistance to third-generation cephalosporins.

CSF Gram staining diagnosed 70% of cases in this study, similar to 64.3% in another study.[26] Factors affecting Gram stain yield include bacterial load, smear techniques, prior antibiotics, and observer expertise. Despite its limitations, Gram staining remains critical in resource-limited settings. In this study, 62% of cases were both smear- and culture-positive, comparable to 58.7% in another study.[26] Six cases (12%) were culture-positive but smear-negative. Latex agglutination testing (LAT) could have detected additional cases but was not performed, a study limitation. Reduced culture positivity may be due to prior antibiotics, poor sample handling, and fastidious pathogens.[2,27,38,39]

In this study, all Gram positive cocci were sensitive to vancomycin and linezolid which is similar to other Indian studies [2,40], but cotrimoxazole and ampicillin showed less sensitivity.[6] All Gram negative isolates were sensitive to imipenem and meropenem. Among gran negative isolates, high level of resistance was seen with chloramphenicol and ceftriaxone and least with piperacillin tazobactum. These findings were similar to the findings in other study.[19] Overall sensitivity pattern of isolates as observed in this study was also observed in other Indian studies. [2,8 27,31,41]

The reason for development of resistance to many drugs can be due to rampant indiscriminate use of antibiotics. This can be due to the general tendency of Indian people to consult quacks or private practitioners who give antibiotics in an improper way without following proper prescription norms. It is of prime importance for clinicians to possess data on susceptibility pattern of gram positive and gram negative organisms rather than individual organisms. Use of antibiotics have brought down the fatality rate of acute pyogenic meningitis to 25% or even lesser with few exceptions. [6] Final diagnosis of acute bacterial meningitis is based on clinical findings, CSF cytology, biochemical, smear and culture findings and a single parameter cannot be used to decide course of management in the patient. However, use of empirical therapy is necessary considering the high mortality rate of the disease. Antibiotics use should be judicious and based on current sensitivity patterns of organisms in an area.

CONCLUSIONS

Early culture sensitivity testing is essential in acute pyogenic meningitis (APM) due to variable causative organisms. This study found *Streptococcus pneumoniae* as the most common pathogen, with gram-positive isolates sensitive to linezolid and vancomycin and gram-negative isolates to carbapenems. Rapid diagnostic tools like Gram staining and pneumococcal antigen testing remain crucial in resource-limited settings. Vaccination against *S. pneumoniae* can reduce meningitis burden, and continued surveillance is vital to address antimicrobial resistance and improve treatment outcomes.

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