

Clinical Outcomes of Antibiotic Therapy in the Management of Infections Caused by Gram-Positive and Gram-Negative Organisms in a Tertiary Care Hospital

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ABSTRACT

Background: Infections caused by Gram-Positive and Gram-Negative bacteria are still a major cause of morbidity, mortality and prolonged hospital stay. The differences that are present in the cell wall structure play a major role in antibiotic susceptibility and the clinical outcomes, since Gram-negative infections are usually associated with higher rates of multidrug resistance and septic shock. This study evaluates the clinical and laboratory outcomes to antibiotic therapy in such infections at a tertiary care hospital. **Materials and Methods:** This prospective observational study was performed using antibiogram to find susceptibility and resistance for Gram-Positive and Gram-Negative bacteria. Biomarkers such as CRP, procalcitonin and hematological parameters were used to analyse the clinical outcomes of the antibiotics. **Results:** Of the 105 patients enrolled, most were male (67.6%) and nearly half were elderly (45.7%). Gram-negative organisms dominated the culture reports (78%) with *Klebsiella* and *E. coli* being the majority at 40% and 38%. Meropenem (25.4%) and piperacillin+tazobactam (20.9%) were the most commonly prescribed antibiotics. The most resistant drugs were cefuroxime (65.5%), ampicillin (62.1%) and ciprofloxacin (60.3%). A Student's *t*-test was performed, and PCT ($p=0.02$) significantly decreased in Gram-Positive infections, while CRP ($p=0.01$) improved markedly in Gram-Negative infections. Overall survival rates were 88.4% and 89.5% for Gram-positive and Gram-negative infections, respectively. **Conclusion:** This study highlights the challenges of growing resistance to commonly used antibiotics, caused by Gram-Positive and Gram-Negative organisms. It also shows the need for antimicrobial stewardship to improve patient care and outcomes.

Keywords: Antibiotic susceptibility, C-reactive protein (CRP), Gram-negative infections, Gram-positive infections, Procalcitonin (PCT), Resistance.

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INTRODUCTION

Bacterial infections are among the most common reasons for tertiary care admission and carry a significant mortality burden (Ghanshani *et al.*, 2015; Gandra *et al.*, 2019). Gram-positive and Gram-negative organisms account for most clinically significant cases, from lower respiratory tract infections and urosepsis to septic shock (Micek *et al.*, 2010; Alexandraki and Palacio, 2010). The structural difference between the two has real clinical weight: Gram-negative bacteria carry a lipopolysaccharide-rich outer membrane that limits antibiotic penetration and drives a more aggressive inflammatory response than Gram-positive infections typically produce (Havey *et al.*, 2011). *Klebsiella pneumoniae* and *E. coli* dominate Gram-negative bacteremia in most reported

series, and both are linked to higher rates of septic shock and multiorgan failure, largely because endotoxin-mediated SIRS escalates faster and is harder to interrupt (Hussain *et al.*, 2021; Holland *et al.*, 2014). Resistance has narrowed the options. Gram-negative pathogens have progressively acquired ESBL production, carbapenemase activity, and efflux mechanisms that leave most first- and second-line antibiotics ineffective (Cosgrove *et al.*, 2003; Wang *et al.*, 2011). ICMR surveillance consistently documents resistance rates in India above global averages, a pattern attributed to over-the-counter antibiotic availability, variable prescribing practices, and uneven infection control across facilities (Barra *et al.*, 2017; Lodise *et al.*, 2020). In this setting, regimen choice- mono-, dual, or triple therapy has direct consequences for survival and duration of admission (Tartof *et al.*, 2018).

PCT and CRP are now routinely used to guide antibiotic initiation, track response, and inform de-escalation (Herrera *et al.*, 2024; Ahmed *et al.*, 2018). PCT appears more sensitive in Gram-positive infections; CRP correlates more strongly with Gram-negative treatment response, though how consistently this distinction



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holds in real inpatient populations is not well characterised (Konwar *et al.*, 2024). This study tested the hypothesis that outcomes, biomarker trajectories, and antibiotic efficacy differ between the two infection groups, and that combination therapy produces better results than monotherapy where resistance rates are high.

The primary objective was to evaluate clinical outcomes of antibiotic therapy in adult inpatients with confirmed Gram-positive or Gram-negative infections at a tertiary care hospital in Bengaluru. Secondary objectives included assessing PCT and CRP responses to treatment, comparing mono, dual, and triple regimens directly, mapping organism prevalence and distribution, and recording ADRs and drug interactions. Institution-specific data of this kind is what actually shapes prescribing decisions.

MATERIALS AND METHODS

Study design

A prospective, observational study was conducted over six months in a tertiary care hospital in Bengaluru, Karnataka, India. The study was carried out in the Intensive Care Unit (ICU), High Intensive Care Unit (HICU), and General Medicine departments, using an antibiogram to find susceptibility, resistance and the right antibiotic use for specific species of Gram-positive and Gram-negative bacteria.

Data collection

The patients who met the inclusion criteria were enrolled in the study. The first step was to collect the baseline information such as demographic details like age, sex, date of admission, clinical diagnosis, comorbidities, microbiological data including culture reports and antibiogram results. Following this, therapeutic data such as antibiotic class, dose, route, duration, date of initiation and discontinuation were collected and documented in a well-structured data collection form. Biomarker values like CRP and PCT and hematological parameters were recorded before and after therapy, the treatment chart was reviewed daily, with adverse drug reactions, drug-drug interactions and final clinical outcomes were recorded throughout the hospital stay.

Methods

Adult patients (≥ 18 years) of both sexes with confirmed Gram-positive or Gram-negative bacterial infections were eligible. Comorbidities were not an exclusion criterion. Pregnant or lactating women, patients with malignancy, and those with incomplete records were excluded. Demographic and clinical data were collected. Empirical antibiotic therapy initiated prior to culture confirmation was recorded -drug, dose, route, and duration. Blood, urine, sputum, wound swabs, and ascitic fluid were sent for culture and sensitivity testing. Antibiogram results confirmed the infecting organism and susceptibility

profile, which was correlated with the empirical regimen. Where susceptibility was inadequate, switch or de-escalation therapy and the reason for change were documented. Efficacy was assessed on symptomatic improvement, normalisation of CRP and procalcitonin, haematological trends, and outcome at discharge. Days of therapy and regimen modifications were recorded against infection resolution and final patient outcome.

Statistical analysis

The data was entered and analysed using Microsoft Excel. Descriptive statistical data including mean, standard deviation and percentage were calculated. Statistical analysis was performed using paired *t*-test for the laboratory data of CRP, Procalcitonin, WBC, neutrophils and lymphocytes, the values of those as mentioned earlier were taken from the patients' consisting of the Gram-negative or Gram-positive bacterial infection at the time of admission and at the time of discharge. Chi-square and Fisher's exact tests were used for categorical association. *p*-values < 0.05 were considered statistically significant.

RESULTS

The study included 105 patients, of whom 67.62% were male and 32.38% were female. The age distribution indicated that the study was predominantly conducted on older adults, with 45.7% of patients aged above 65 years, followed by those in the 45-64 age group (27.6%). Patients aged 18-29 years constituted the smallest proportion of the cohort at 3.8%. Among the clinical presentations documented, septic shock accounted for the highest proportion at 61.9%, followed by lower respiratory tract infection at 30.5% and urosepsis at 24.8%. Sepsis and urinary tract infection were recorded in 18.1% and 16.2% of patients respectively. Cellulitis, encephalopathy, and meningitis were less commonly observed, present in 12.4%, 6.7%, and 4.8% of patients respectively (Table 1).

The specimen distribution was also evaluated; blood cultures were the most frequently submitted sample, constituting 47.0% of all specimens collected, followed by urine at 28.5% and sputum at 14.2%. Wound swabs accounted for 7.1% of samples, while ascitic fluid was the least commonly submitted specimen at 2.8%. Among Gram-positive isolates, blood (14%) and wound swabs (5%) were the predominant specimen sources, whereas Gram-negative organisms were most frequently recovered from blood (13%), urine (10%), and sputum (10%). No Gram-positive organisms were isolated from ascitic fluid. A total of 61 organisms were identified across all specimen types (Table 2).

The antibiotic prescribing pattern of the study population was also evaluated. Among 105 patients, a total of 160 antibiotic prescriptions were recorded. Meropenem was the most frequently prescribed antibiotic, accounting for 25.4% of prescriptions ($n=45$), followed by piperacillin-tazobactam at 20.9% ($n=37$). Azithromycin was prescribed in 10.2% of cases ($n=18$), while

colistin and ceftriaxone were administered in 9.6% ($n=17$) and 7.3% ($n=13$) of patients, respectively. Metronidazole accounted for 6.8% ($n=12$) of prescriptions, followed by teicoplanin at 3.4% ($n=6$). Vancomycin, imipenem/cilastatin, and doxycycline were the least frequently prescribed agents, each constituting 2.3% ($n=4$) of the total prescriptions. This pattern indicates a preference for broad-spectrum antibiotics, particularly meropenem and piperacillin-tazobactam, across both Gram-positive and Gram-negative infections (Table 3).

The biomarker and hematological parameters of the study population were subjected to a paired t -test to compare values before and after antibiotic therapy. In Gram-positive infections, procalcitonin showed a statistically significant decline from a mean of 18.34 (± 29.8) before therapy to 3.69 (± 8.07) after therapy ($p=0.02$). C-reactive protein, white blood cell count, neutrophil percentage, and lymphocyte percentage showed post-therapy changes but were not statistically significant ($p=0.3, 0.3, 0.2$, and 0.1 , respectively). In Gram-negative infections, CRP recorded a statistically significant reduction from a mean of 159.1 (± 116.6) to 79.7 (± 78.3) ($p=0.01$), while procalcitonin declined from 15.21 (± 31.3) to 8.48 (± 16.54), though this was not statistically significant ($p=0.2$). The remaining haematological parameters showed modest post-therapy changes without statistical significance (Table 4).

The association between infecting pathogen and patient survival was also assessed. Among Gram-positive infections ($n=26$), 88.4% of patients survived. Coagulase-negative *Staphylococcus* recorded the highest case volume ($n=16$) with a survival rate of 93.7%, while Beta-haemolytic *Streptococcus* and Vancomycin-resistant *Enterococcus* sp. both achieved 100% survival. The lowest survival among Gram-positive organisms was observed in *Staphylococcus aureus*, where only 1 of 2 patients (50%) survived. Among Gram-negative infections ($n=38$), the overall survival rate was 89.47%. Complete survival was noted in *Escherichia coli*, *Pseudomonas aeruginosa*, *Aeromonas* sp., and *Citrobacter koseri*. Higher mortality was associated with *Klebsiella* sp. at 21.4% and *Acinetobacter* sp. at 25% (Table 5).

The efficacy of different antibiotic regimens was compared among the 105 patients, of whom 90 recovered and 15 did not survive. Triple therapy demonstrated the most favourable outcome, with all 15 patients recovering and zero mortality recorded. Dual therapy was administered to 48 patients, with 42 achieving recovery and 6 deaths recorded. Monotherapy was used in 39 patients, of whom 32 recovered and 7 did not survive. Quadruple therapy, used in only 3 patients, was associated with the poorest outcomes, with 2 deaths and only 1 recovery. Statistical analysis revealed a highly significant association between antibiotic regimen type and clinical outcome ($p<0.001$), indicating that triple combination therapy was the most effective regimen in this study population (Table 6).

The association between length of hospital stay and patient outcomes was evaluated. A statistically significant association was found between duration of hospitalisation and mortality ($p<0.0001$). The highest mortality rate of 32.1% was observed in patients hospitalised for 15-28 days, whereas patients with shorter stays of 1-7 days and 8-14 days recorded lower mortality rates of 6.25% and 5.71% respectively. All patients in the 29-42-day group survived, while a 50% mortality rate was observed in those hospitalised for more than 42 days, reflecting the clinical complexity associated with prolonged hospital stays (Table 7).

The antibiotic susceptibility pattern of the study population was also analysed. Amikacin demonstrated the highest susceptibility at 38.3%, followed by linezolid and co-trimoxazole at 36.0% each. Teicoplanin and meropenem both recorded susceptibility rates of 33.3%, while vancomycin was effective in 28.3% of isolates. Moderate susceptibility was observed for imipenem (25.0%), chloramphenicol (23.3%), cefepime (21.7%), and cefoperazone-sulbactam (21.7%). Ciprofloxacin and gentamicin each recorded 20.0% susceptibility, while tetracycline and tigecycline registered 18.3% each. Piperacillin-tazobactam and levofloxacin showed susceptibility in 16.7% of cases. Clindamycin, ertapenem, and ceftriaxone recorded the lowest susceptibility rates at 13.3% each, with cefuroxime demonstrating the least activity at 10.0% (Figure 1).

The antibiotic resistance pattern of the study population was further evaluated. The highest resistance was observed with cefuroxime (65.5%), ampicillin (62.1%), and ciprofloxacin (60.3%). Moderate resistance was noted for co-trimoxazole (46.6%), cefazolin

Table 1: Demographic and Clinical Profile of the Study Population.

Demographics	Number of patients ($n=105$)
Gender	N (%)
Males	71(67.62)
Females	34(32.38)
Age (years)	N (%)
18-29	4(3.8)
30-44	24(22.8)
45-64	29(27.6)
>65	48(45.7)
Comorbidities	N (%)
Septic shock	65(61.9)
LRTI	32(30.5)
Urosepsis	26(24.8)
Sepsis	19(18.1)
UTI	17(16.2)
Cellulitis	13(12.4)
Encephalopathy	7(6.7)
Meningitis	5(4.8)

(43.1%), and ceftriaxone (36.2%), while levofloxacin (34.5%) and piperacillin-tazobactam (29.3%) also showed considerable resistance. Gentamicin and cefoxitin each recorded resistance in 27.6% of cases, while imipenem, amoxicillin-clavulanate, cefepime, and meropenem ranged between 24.1% and 25.9%. Lesser resistance was observed with erythromycin (22.4%), clindamycin (20.7%), cefoperazone-sulbactam (19.0%), ertapenem (19.0%), and tetracycline (17.2%) (Figure 2).

DISCUSSION

This study provides important real-world insights into antibiotic therapy outcomes in a high-acuity tertiary care setting in India. The male predominance (67.6%) and high proportion of elderly patients (73.3% aged ≥ 45 years) are consistent with data from similar settings. Ghanshani *et al.* (2015) documented a comparable male predominance and age distribution in ICU infection studies in India, attributing these patterns to higher comorbid burden and greater occupational exposures in men. Gandra *et al.* (2019) further identified advanced age as a key risk factor for mortality from multidrug-resistant infections.

Septic shock was the most frequent diagnosis (61.9%), underscoring the critical severity of infections in this setting. The prominence of LRTI (30.5%) and urosepsis (24.8%) reflects global patterns of severe hospital-acquired infections and aligns

with existing literature on common infection portals in critically ill patients.

The dominance of Gram-negative organisms (78%), particularly *Klebsiella* species and *E. coli*, is consistent with the Indian AMR scenario documented by Gandra *et al.* (2019). The high resistance rates to cefuroxime (65.5%), ampicillin (62.1%), and ciprofloxacin (60.3%) reflect widespread misuse of antibiotics and support the need for local antibiogram-guided empirical therapy. Even meropenem showed 24.1% resistance, indicating emerging carbapenem resistance in this tertiary care setting.

The reliance on meropenem (25.4%) and piperacillin-tazobactam (20.9%) as the most prescribed agents reflects clinical necessity driven by local resistance profiles and is consistent with patterns described in other Indian tertiary hospitals. Amikacin demonstrated the highest susceptibility rate (38.3%), aligning with Hussain *et al.* (2021), who also reported amikacin as a key agent against Gram-negative respiratory isolates.

The superior outcomes of triple antibiotic therapy (100% recovery, zero mortality, $p < 0.001$) corroborate findings from Micek *et al.* (2010), who demonstrated that combination therapy significantly reduced mortality in Gram-negative sepsis. The poor outcomes associated with quadruple therapy likely reflect the severity of underlying disease rather than a direct drug effect, as patients requiring four agents typically have advanced multidrug-resistant infections.

Table 2: Organism distribution by specimen type.

Specimen	Gram-positive organisms N (%)	Gram-negative organisms N (%)	Total N (%)
Blood	56 (14)	36 (13)	27
Urine	20 (5)	27 (10)	15
Sputum	4 (1)	27 (10)	11
Wound swab	20 (5)	5.5 (2)	7
Ascitic fluid	0	2.7 (1)	1
Total	25	36	61

Table 3: Antibiotics prescribed /Prescribing pattern.

Drug	Gram-positive	Gram-negative	Total N (%)
Meropenem	21	24	45
Piperacillin + tazobactam	18	19	37
Azithromycin	10	8	18
Colistin	7	10	17
Ceftriaxone	8	5	13
Metronidazole	4	8	12
Teicoplanin	4	2	6
Vancomycin	2	2	4
Imipenem/cilastatin	3	1	4
Doxycycline	2	2	4

Table 4: Paired t-test Analysis of Biomarkers and Hematological Parameters.

Parameters	Before therapy		After therapy		p value
Gram positive	Mean	Standard deviation	Mean	Standard deviation	
Procalcitonin	18.34	29.8	3.69	8.07	0.02
C reactive protein	77.7	60.7	47.7	48.4	0.3
White Blood Cells	13.98	6.11	12.5	5.61	0.3
Neutrophils	76.34	11.7	72.46	13.4	0.2
Lymphocytes	13.3	8.88	17.24	11.16	0.1
Gram Negative					
Procalcitonin	15.21	31.3	8.48	16.54	0.2
C reactive protein	159.1	116.6	79.7	78.3	0.01
White Blood Cells	11.7	6.4	10.8	4.2	0.4
Neutrophils	80.3	10.53	76.54	12.87	0.1
Lymphocytes	12.3	7.45	13.3	7.5	0.5

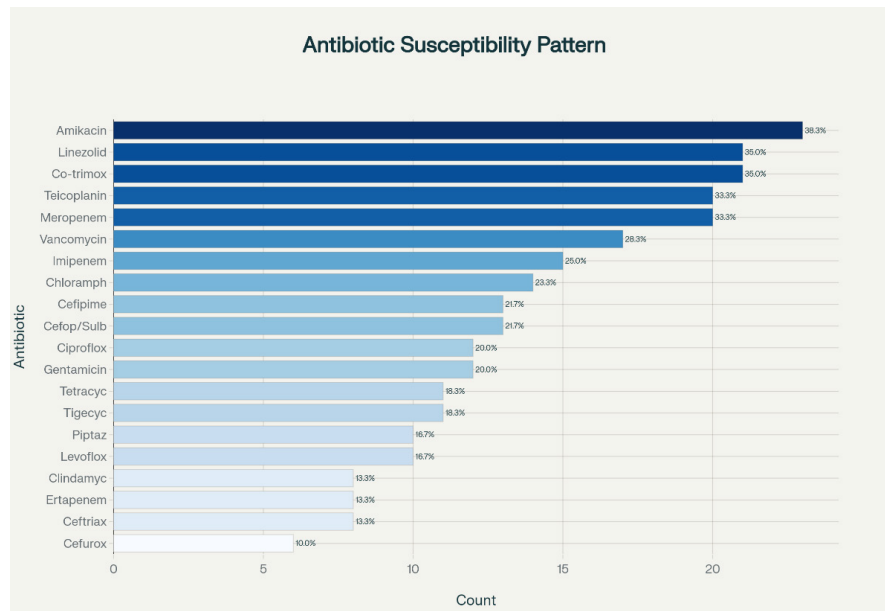
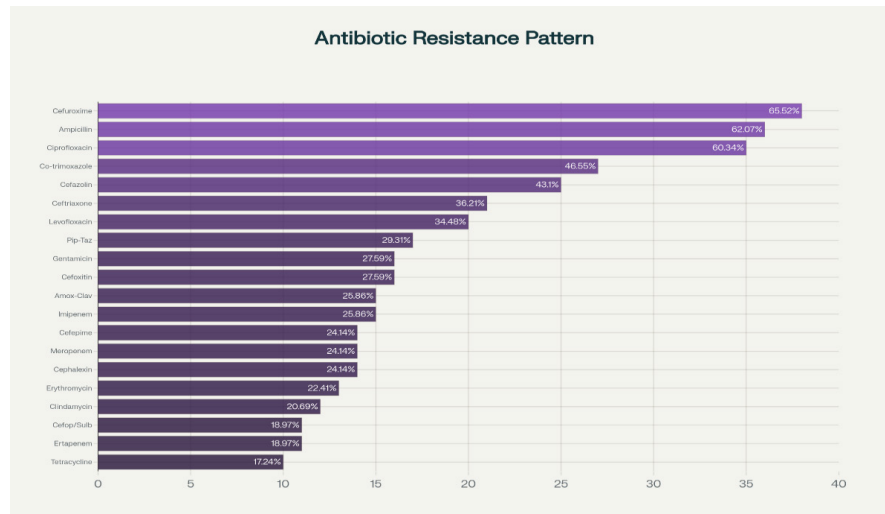
**Figure 1: Susceptibility Pattern of The Antibiotics.****Figure 2: Resistance Pattern of The Antibiotics.**

Table 5: Association Between Infecting Pathogen and Patient Survival Status.

		Survivors (%)	Non-survivors (%)
Gram-positive	N=26	N=23 (88.4)	N=3 (11.5)
Coagulase-negative <i>Staphylococcus</i>	16	15 (93.7)	1 (6.25)
<i>Enterococcus</i> sp.	5	4 (80)	1 (20)
<i>Staphylococcus aureus</i>	2	1 (50)	1 (50)
Beta-hemolytic streptococcus	2	2 (100)	0 (0)
Vancomycin-resistant <i>Enterococcus</i> sp.	1	1 (100)	0 (0)
Gram-negative	N=38	N=34 (89.47)	N=4 (10.5)
<i>Klebsiella</i> sp.	14	11 (78.5)	3 (21.4)
<i>Escherichia coli</i>	14	14 (100)	0 (0)
<i>Pseudomonas aeruginosa</i>	4	4 (100)	0 (0)
<i>Acinetobacter</i> sp.	4	3 (75)	1 (25)
<i>Aeromonas</i> sp.	1	1 (100)	0 (0)
<i>Citrobacter koseri</i>	1	1 (100)	0 (0)

Table 6: Efficacy Analysis by Antibiotic Therapy Regimen: Monotherapy, Dual and Multiple Therapy.

	n=105	Death (n=15)	Recovery (n=90)
Mono therapy	39	7	32
Dual therapy	48	6	42
Triple therapy	15	0	15
Quadruple therapy	3	2	1
Mean		3.75	22.5
Std. deviation		2.86	15.7
p value		<0.001	

Table 7: Patient Outcomes Stratified by Length of Hospital Stay.

Length of Stay (days)	No. of patients n=105	Mortality n=15 (%)	Recovery n=90 (%)
1-7	32	2 (6.25)	30 (93.7)
8-14	35	2 (5.71)	33 (94.2)
15-28	28	9 (32.1)	19 (67.8)
29-42	6	0 (0)	6 (100)
>42	4	2 (50)	2 (50)
Mean		3	18
Std. deviation		3.09	12.4
p value		<0.0001	

The differential biomarker responses are clinically significant: PCT was more responsive in Gram-positive infections, consistent with the known role of PCT as a marker of bacterial toxin-mediated systemic inflammation, while CRP was more markedly reduced in Gram-negative infections, aligning with findings by Alexandraki and Palacio (2010) on distinct inflammatory pathway activation in Gram-negative bacteraemia. These findings support a targeted biomarker monitoring strategy based on pathogen type.

The low ADR rate (2.9%) and manageable DDI profile (18.1%) suggest that the antibiotic regimens were relatively safe. All ADRs were cutaneous beta-lactam hypersensitivity reactions, consistent with known safety profiles. The significant association of prolonged hospital stay (>42 days) with 50% mortality emphasises the complexity of managing persistent infections and hospital-acquired complications in a tertiary care environment.

LIMITATIONS

Short six-month study duration could not capture seasonal variations or long-term antimicrobial resistance trends. Multiple Gram-positive and negative bacteria were present at a time in a single patient. Study was restricted to adult patients (≥ 18 years) excluding pediatric population with potentially different infection patterns. Incomplete medical records and missing critical data limited comprehensive analysis in some patient files. Not all bacterial cultures yielded positive results, limiting pathogen specific analysis scope. The study was carried out in a single centre rather than multiple centres.

CONCLUSION

This prospective observational study demonstrates that clinical outcomes of antibiotic therapy in bacterial infections are significantly influenced by pathogen type, antimicrobial resistance patterns, and treatment regimen selection. Gram-negative organisms, particularly *Klebsiella* species and *E. coli*, predominated with high rates of multidrug resistance, necessitating broad-spectrum and combination therapy strategies. Triple antibiotic therapy emerged as the most effective approach for severe infections. Pathogen-specific biomarker monitoring -procalcitonin for Gram-positive and CRP for Gram-negative infections -supports targeted therapeutic management. The findings strongly advocate for locally tailored antimicrobial stewardship programs, early pathogen identification, and evidence-based empirical therapy to optimise patient outcomes while combating antimicrobial resistance in Indian tertiary care settings.

ABBREVIATIONS

A. baumannii: *Acinetobacter baumannii*; **ADR:** Adverse Drug Reaction; **CRP:** C-Reactive Protein; **DDI:** Drug-Drug Interaction; **E. coli:** *Escherichia coli*; **HICU:** High Intensive Care Unit; **ICU:** Intensive Care Unit; **K. pneumoniae:** *Klebsiella pneumoniae*; **LOS:** Length of Stay; **LRTI:** Lower Respiratory Tract Infection; **MDR:** Multi-Drug Resistant; **MRSA:** Methicillin-Resistant *Staphylococcus aureus*; **NKDA:** No Known Drug Allergies; **P. aeruginosa:** *Pseudomonas aeruginosa*; **PCT:** Procalcitonin; **UTI:** Urinary Tract Infection; **WHO:** World Health Organization.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

SUMMARY

This six-month prospective observational study at a tertiary care hospital in Bengaluru, India, enrolled 105 adult patients with Gram-positive and Gram-negative bacterial infections to evaluate clinical outcomes of antibiotic therapy. Key findings include: (1) male predominance (67.6%) and high elderly burden (45.7% aged

>65 years); (2) Gram-negative organisms dominated (78%), with *Klebsiella* species and *E. coli* as the most prevalent pathogens; (3) meropenem and piperacillin-tazobactam were the most commonly prescribed agents; (4) high resistance was observed to cefuroxime, ampicillin, and ciprofloxacin; (5) triple antibiotic therapy achieved the best outcomes (100% recovery, $p < 0.001$); (6) procalcitonin was a better biomarker for Gram-positive infections, while CRP was more responsive in Gram-negative infections; and (7) adverse drug reactions occurred in only 2.9% of patients, all limited to beta-lactam antibiotics. These findings reinforce the need for robust antimicrobial stewardship, local antibiograms, and early pathogen identification in high-resistance tertiary care settings.

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