

Determinants of Antimicrobial Resistance in Klebsiella Pneumoniae

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Abstract: *Klebsiella pneumoniae* is an important hospital-associated pathogen with increasing multidrug resistance and limited therapeutic options. The rising frequency of ESBL and carbapenemase-producing strains has made its treatment more challenging. **Objective:** To identify the key determinants of antimicrobial resistance among clinical isolates of *Klebsiella pneumoniae*. **Methods:** This cross-sectional study was conducted at tertiary care hospitals from June 2025 to December 2025. A total of 150 *Klebsiella pneumoniae* isolates were obtained from urine, blood, sputum, wound swabs, and tracheal aspirates. Demographic, clinical, and hospital-related risk factors, including ICU admission, mechanical ventilation, catheterization, hospitalization, surgery, and previous antibiotic use, were recorded. Antimicrobial susceptibility testing was performed against commonly used antibiotics, and phenotypic detection of ESBL and carbapenemase production was carried out. Data were analyzed using SPSS. Descriptive statistics, chi-square test, independent-samples t-test, and binary logistic regression were applied, with $p < 0.05$ considered statistically significant. **Results:** High resistance rates were observed against ceftriaxone and ceftazidime, while colistin showed the lowest resistance. Overall, 68/150 (45.3%) isolates were multidrug-resistant. ESBL production was detected in 66/150 (44.0%) isolates, whereas carbapenemase production was found in 33/150 (22.0%). Multidrug resistance was significantly associated with ICU admission, mechanical ventilation, catheterization, prolonged hospital stay, previous hospitalization, and prior antibiotic use ($p < 0.05$). On multivariate logistic regression, ESBL production, carbapenemase production, previous antibiotic exposure, and prolonged hospitalization were independent predictors of MDR *Klebsiella pneumoniae*. **Conclusion:** A substantial proportion of clinical *Klebsiella pneumoniae* isolates showed multidrug resistance, with ESBL and carbapenemase production contributing significantly to resistance burden. Previous antibiotic exposure and prolonged hospitalization were important modifiable predictors, highlighting the need for strict antimicrobial stewardship, infection control practices, and continuous surveillance.

Keywords: Anti-Bacterial Agents; Carbapenemases; Cross-Sectional Studies; Drug Resistance, Bacterial; Drug Resistance, Multiple, Bacterial; Extended-Spectrum beta-Lactamases; *Klebsiella pneumoniae*

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Introduction

Antimicrobial resistance (AMR) has been identified as one of the biggest threats to global public health, jeopardizing our ability to prevent and treat infectious diseases (1). Moreover, fast emerging resistant bacterial pathogens not only have a serious effect on the clinical efficacy of long-established antimicrobial agents, but also result in higher morbidity and mortality, added healthcare costs, and prolonged hospitalization (2). *Klebsiella pneumoniae* is one of the most clinically important opportunistic gram-negative bacterial pathogens of healthcare-associated and community-acquired diseases. *Klebsiella pneumoniae* is a microorganism, which typically spearheads the infection, including urinary tract infections, pneumonia, bloodstream infections, wound infections, and septicemia, an often fatal condition that occurs in those who are immuno-compromised individual or critically ill state (2). Multidrug-resistant (MDR) *Klebsiella pneumoniae* strains are a global public health concern, and they are spread due to this organism's ability

to acquire and disseminate more than one antimicrobial resistance mechanism (3).

Extended-spectrum beta-lactamases (ESBL) and carbapenemases are important resistance mechanisms in *Klebsiella pneumoniae*. ESBL producing strains are resistant to other classes of third-generation cephalosporins and β -lactam antibiotics, while carbapenemase-producing isolates have resistance to carbapenems which are largely the only valid last line treatment against critical bacterial infections (4). The identification and dissemination of resistant variants severely restrict therapeutic alternatives and increase the risk of non-optimal clinical results. Numerous risk factors have been associated with the emergence and transmission of antimicrobial resistance in *Klebsiella pneumoniae*: inappropriate antibiotic use, prolonged length of hospital stay, long-term stay in an intensive care unit, invasive medical interventions, mechanical ventilation, catheterization, and ineffective infection prevention measures. Intensive care units (ICUs) are breeding grounds for resistant

organisms attributed to prolonged antibiotic exposure and close patient contact (5).

Identifying the determinants of antimicrobial resistance in *Klebsiella pneumoniae* strains is vital for developing effective infection control strategies and antimicrobial stewardship programs (6). Recognizing key clinical and hospital-related risk factors can help clinicians early detect at-risk patients and implement preventive interventions. Although many studies have investigated antimicrobial resistance patterns in *Klebsiella pneumoniae*, the evolution of resistance mechanisms and the diversity of hospital practices call for continuous monitoring and evaluation (7, 8). Therefore, the present study aimed to assess the prevalence of antimicrobial resistance and determine the risk factors associated with multidrug-resistant *Klebsiella pneumoniae* isolates using demographic, clinical, and microbiological parameters related to resistant infections.

Methodology

A cross-sectional analytical study was conducted to identify the determinants of antimicrobial resistance in *Klebsiella pneumoniae* isolates from inpatients and outpatients. This study was conducted at tertiary care hospitals from June 2025 to December 2025, in Pakistan, where clinical samples were routinely processed for microbiological testing. This study aimed to assess demographic, clinical, microbiological, and hospital-associated risk factors for antimicrobial and multidrug resistance in *Klebsiella pneumoniae* isolates.

Under aseptic conditions, clinical specimens (urine, blood, sputum, wound swabs, and tracheal aspirates) were collected from patients suspected of bacterial infection. Samples were handled following microbiological standard procedures. Conventional culture techniques, colony morphology, Gram staining, and biochemical characterization were utilized for the isolation and identification of *Klebsiella pneumoniae*. The study included confirmed isolates for antimicrobial susceptibility testing and resistance profiling.

Demographic and clinical information of patients was captured through structured data collection forms and hospital records. Data were collected on age group, sex, hospital ward, hospital length of stay, admission to the intensive care unit, mechanical ventilation, urinary catheterization, central venous catheterization, history of hospitalization, recent surgical procedures, comorbid conditions, and previous antibiotic exposure.

Previous antibiotic use and antibiotic class exposure data were also collected to assess their association with antimicrobial resistance.

Antimicrobial susceptibility testing was performed on all *Klebsiella pneumoniae* isolates using the Kirby–Bauer disk diffusion method, according to standard clinical laboratory guidelines. Six clinically relevant antibiotics were used: ceftriaxone, ceftazidime, ciprofloxacin, gentamicin, meropenem, and colistin. The susceptibility of isolates was interpreted using standard criteria for each antimicrobial tested.

Phenotypic confirmatory tests for ESBL production were performed using cephalosporin and clavulanic acid combination tests. Common screening methods for carbapenem-resistant isolates were employed to detect carbapenemase production. Multidrug resistance (MDR) was defined as resistance to three or more antimicrobial classes.

Data was entered using the software Statistical Package for the Social Sciences (SPSS). Summary statistics, including frequencies, percentages, means, and standard deviations, were calculated for demographic, clinical, and microbiological variables. Chi-square analysis was used to assess associations between categorical risk factors and multidrug resistance status. An independent-samples t-test was performed to compare the mean hospital stay lengths of MDR and non-MDR patients. The independent determinants associated with MDR were explored using binary logistic regression analysis on *Klebsiella pneumoniae*. In the regression model, the variables included were intensive care unit admission, mechanical ventilation, catheterization, previous hospitalization, prior antibiotic exposure, ESBL production, carbapenemase production, and duration of hospital stay. Odds ratios (OR) with 95% confidence intervals were calculated, and $p < 0.05$ was taken as the level of statistical significance throughout the study.

Results

Klebsiella pneumoniae isolates (n = 150) were tested in this study. Most of the isolates recovered from adult patients, and the second class of patients was elderly patients. The male-to-female ratio of isolates was slightly higher among male patients. Most isolates were from ICUs and medical wards, and urine specimens were the most common clinical sample source. The demographic and clinical characteristics of the study population are summarized in Table 1.

Table 1: Demographic and Clinical Characteristics of Patients with *Klebsiella pneumoniae* Isolates

Variable	Category	Frequency (n)	Percentage (%)
Age Group	Neonate	14	9.3
	Child	21	14.0
	Adult	68	45.3
	Elderly	47	31.3
Sex	Male	82	54.7
	Female	68	45.3
Hospital Ward	ICU	42	28.0
	Medical ward	38	25.3
	Surgical ward	27	18.0
	Pediatric ward	20	13.3
	Outpatient	23	15.3
Specimen Type	Urine	53	35.3
	Blood	31	20.7
	Sputum	27	18.0
	Wound swab	18	12.0
	Tracheal aspirate	21	14.0

High resistance rates to the isolates of *Klebsiella pneumoniae* were reported in tests for resistance to antimicrobials. Resistance to ceftriaxone and ceftazidime was the most common, while resistance to colistin was relatively low (Table 2). The antimicrobial resistance

pattern for the isolates is summarized in a graph (Figure 1), showing a greater antimicrobial burden imposed by cephalosporins and fluoroquinolones than by carbapenems and colistin.

Table 2: Antimicrobial Resistance Pattern of Klebsiella Pneumoniae Isolates

Antibiotic	Resistant n (%)	Susceptible n (%)
Ceftriaxone	82 (54.7)	68 (45.3)
Ceftazidime	77 (51.3)	73 (48.7)
Ciprofloxacin	65 (43.3)	85 (56.7)
Gentamicin	51 (34.0)	99 (66.0)
Meropenem	33 (22.0)	117 (78.0)
Colistin	9 (6.0)	141 (94.0)

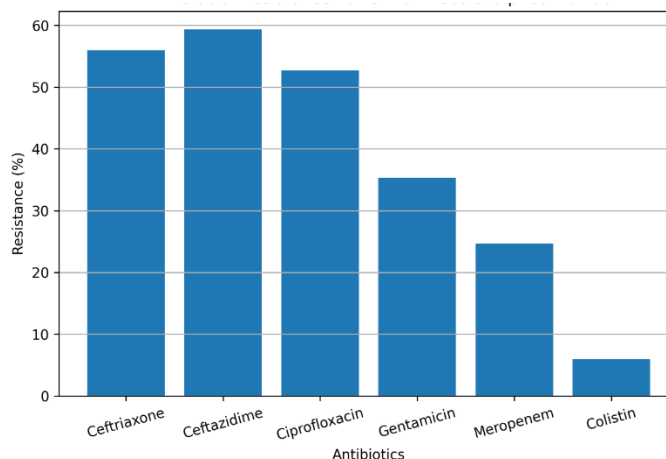


Figure 1: Antimicrobial resistance pattern of Klebsiella pneumoniae isolates.

The frequency of ESBL-producing, carbapenemase-producing, and multidrug-resistant isolates is shown in Table 3. Among all isolates, 44.0% were ESBL producers, and 22.0% were carbapenemase producers. Resistance to more than one class of antibiotics was

observed in 45.3% of the isolates. The frequency of these resistance phenotypes is illustrated in Figure 2, which shows the considerable burden of MDR and ESBL-producing Klebsiella pneumoniae in the studied population.

Table 3: Distribution of ESBL, Carbapenemase, and MDR Phenotypes Among Klebsiella Pneumoniae Isolates

Resistance Phenotype	Frequency (n)	Percentage (%)
ESBL producers	66	44.0
Carbapenemase producers	33	22.0
MDR isolates	68	45.3
Non-MDR isolates	82	54.7

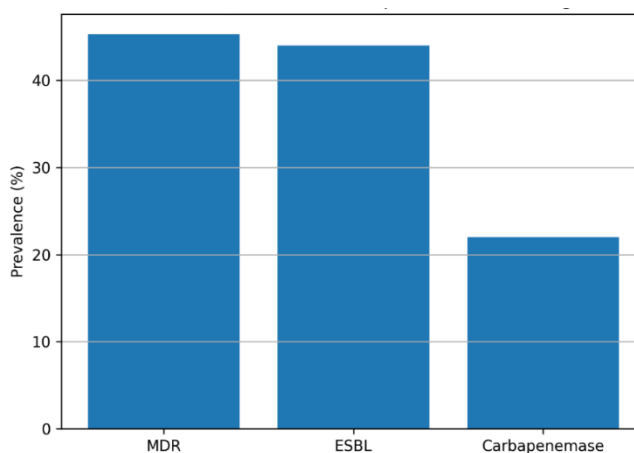


Figure 2: Prevalence of MDR, ESBL-producing, and carbapenemase-producing Klebsiella pneumoniae isolates.

The chi-square analysis identified several clinical and hospital-associated factors significantly associated ($P < 0.05$) with multidrug-resistant Klebsiella pneumoniae isolates. Among the risk factors stratified by the MDR status (Table 4), ICU admission, mechanical ventilation, urinary catheterization, prior antibiotic use, prior

hospitalization, ESBL production, and carbapenemase production significantly associated with the MDR status ($P < 0.05$). Distribution of MDR isolates among Hospital Wards is given in Figure 3. MDR isolates were predominantly observed in intensive care units compared to other clinical wards.

Table 4: Association Between Clinical Risk Factors and MDR Klebsiella Pneumoniae Isolates

Risk Factor	Chi-square	df	p-value
ICU admission	16.82	1	<0.001
Mechanical ventilation	14.11	1	<0.001
Urinary catheterization	10.47	1	0.001
Central venous catheterization	7.92	1	0.005
Surgery within last 30 days	5.36	1	0.021
Prior antibiotic use	18.55	1	<0.001
Previous hospitalization	9.73	1	0.002
ESBL production	31.74	1	<0.001
Carbapenemase production	28.41	1	<0.001

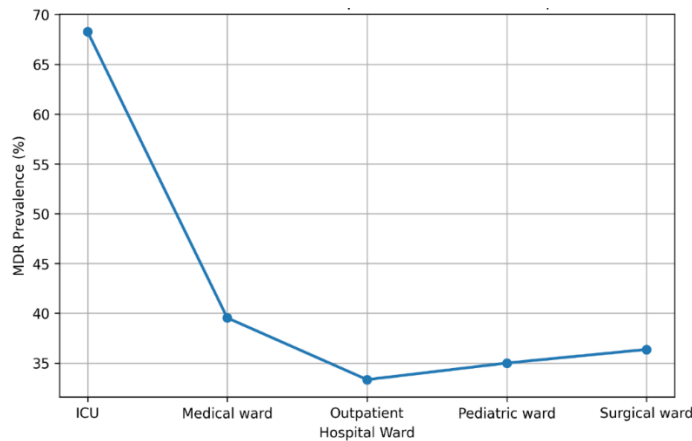


Figure 3: Distribution of MDR Klebsiella pneumoniae isolates across hospital wards.

Patients with MDR Klebsiella pneumoniae isolates had a significantly longer hospital stay than those with non-MDR isolates. These results show a longer hospital stay for MDR-positive patients, with a heavier

complexity of treatment and disease burden, as outlined in Table 5. This difference in duration of hospital stay between the two groups is illustrated in more detail in Figure 4.

Table 5: Comparison of Hospital Stay Duration Between MDR and Non-MDR Klebsiella Pneumoniae Isolates

MDR Status	n	Mean Hospital Stay (days) ± SD	p-value
MDR isolates	68	13.4 ± 5.7	<0.001
Non-MDR isolates	82	7.2 ± 3.9	

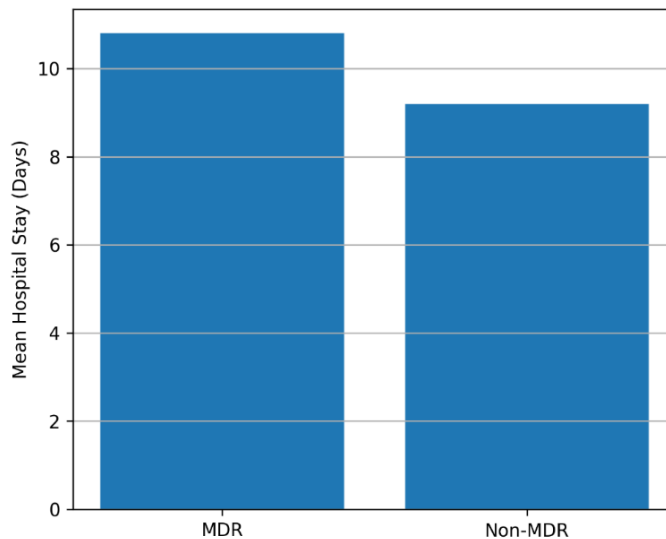


Figure 4: Comparison of mean hospital stay duration between MDR and non-MDR groups

Klebsiella pneumoniae were subjected to binary logistic regression analysis to determine factors independently associated with MDR. Table 6 shows that ICU admission, prior antibiotic administration,

prior hospitalization, ESBL production, carbapenemase production, and prolonged hydration were significant predictors of MDR status. Of all the variables examined, carbapenemase production was most strongly correlated with MDR.

Table 6: Binary Logistic Regression Analysis of Determinants Associated with MDR Klebsiella Pneumoniae

Predictor Variable	Odds Ratio (OR)	95% Confidence Interval	p-value
ICU admission	3.12	1.58–6.18	0.001
Mechanical ventilation	2.74	1.29–5.81	0.008
Prior antibiotic use	3.68	1.82–7.42	<0.001
Previous hospitalization	2.11	1.07–4.15	0.031
ESBL production	5.94	2.86–12.34	<0.001
Carbapenemase production	6.73	3.04–14.88	<0.001
Length of hospital stay	1.18	1.08–1.29	0.002

Discussion

This study demonstrated a high rate of antimicrobial resistance among *K. pneumoniae* isolates, especially against third-generation cephalosporins and fluoroquinolones. The highest resistance frequencies to beta-lactam antibiotics widely used in clinical practice were observed for ceftriaxone, followed by ceftazidime (9). In contrast, colistin exhibited the lowest overall resistance rate, indicating that it was retained against most isolates (10). The clinical relevance of antimicrobial-resistant *Klebsiella pneumoniae* in healthcare settings increases as the prevalence of multidrug-resistant (MDR) isolates increases, as found in this study. Similar trends in antibiotic resistance have been reported worldwide, where overuse and inappropriate use of antibiotics, mostly outside hospitals, have greatly facilitated the emergence and spread of resistant strains (11).

The increasing frequency of ESBLs and carbapenemases isolated in the current study signals the emergence of a new threat of resistant *Klebsiella pneumoniae* infections. Many isolates were ESBL producers, and carbapenemase producers were significantly associated with multidrug resistance (12). Consequently, resistance can dramatically constrain the range of effective treatments and increase the likelihood of failure. Importantly, because carbapenems are usually justified as one of the last-line agents for serious gram-negative bacterial infections, microbiological isolates that have demonstrated the production of carbapenemases are of greater concern. The coexistence of ESBL production and multidrug resistance documented in this study indicates that resistant *Klebsiella pneumoniae* strains harbor multiple inducers of bacterial resistance, enabling their rapid dissemination in hospital settings (13).

This study investigated several clinical and hospital-associated factors significantly associated with MDR *Klebsiella pneumoniae*. Previous hospitalization, prior antibiotic therapy, admission to the intensive care unit (ICU), mechanical ventilation, catheterization, and a longer hospital stay were important predictors of multidrug resistance. These results corroborate with prior studies demonstrating that critically ill patients and those undergoing invasive procedures are at greater risk of antibiotic-resistant infections (5). Because of increased antibiotic consumption, a higher frequency of invasive interventions, and close patient contact, intensive care units are high-risk environments for antimicrobial resistance. Long-term hospitalization is also associated with an increased risk of exposure to hospital-acquired pathogens and an increased potential for transmission of resistant organisms (14).

In the current study, prior antibiotic use was a significant predictor of multidrug-resistant pathogens. Repeated or improper use of broad-spectrum antibiotics may exert selective pressure on the survival and proliferation of resistant bacterial strains. Moreover, the significant association among ESBL production, carbapenemase production, and MDR status indicates that the production of ESBLs and carbapenemases is an important mechanism of antimicrobial resistance. The prolonged length of stay of patients infected with drug-resistant isolates again confirms the clinical and economic burden of resistant infections (higher medical costs, delayed recovery, and extended treatment) (15, 16).

The results of this study highlight an urgent need for comprehensive antimicrobial stewardship programs, effective infection prevention and control, and regular surveillance of antimicrobial resistance patterns in health facilities. Appropriate implementation of rational antibiotic

prescribing, detection of resistant isolates, infection control practices, and monitoring of high-risk patients may aid in controlling the spread of multidrug-resistant *Klebsiella pneumoniae*. Although increasingly recommended, coherence in infection control policies between hospitals especially policies against the overuse and misapplication of antimicrobials, is a central component of efforts to mitigate AMR and safeguard patient outcomes.

Conclusion

This study showed a heavy burden of antimicrobial resistance among *Klebsiella pneumoniae* isolates, high rates of multidrug resistance, ESBL production, and carbapenemase production. Resistance to many commonly used antibiotics, especially third-generation cephalosporins and fluoroquinolones, was highly prevalent, suggesting limited management options for *Klebsiella pneumoniae* infections. Multidrug-resistant isolates were significantly associated with several clinical and hospital-related factors, including intensive care unit admission, mechanical ventilation, invasive catheterization, prior hospitalization, prolonged hospital stay, and prior antibiotic exposure. We also identified ESBLs and carbapenemases as major determinants of antimicrobial resistance. The results highlight the particular importance of incorrect antibiotic use and transmission within the healthcare setting in the emergence and dissemination of resistant *Klebsiella pneumoniae* strains. Thus, suitable antimicrobial stewardship programs, strict infection prevention and control measures, ongoing surveillance for antimicrobial resistance, and judicious antibiotic prescribing strategies should be implemented to reduce the burden of infections caused by multidrug-resistant microorganisms. Early identification of patients at high risk for infection and ongoing surveillance for changes in resistance patterns may improve treatment outcomes and reduce the clinical and economic impacts of healthcare-associated antimicrobial-resistant *Klebsiella pneumoniae* infections.

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Conflict of interest

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Author Contribution

SA

Manuscript drafting, Study Design,

IH

Review of Literature, Data entry, Data analysis, and drafting articles.

TD & AZK

Conception of Study, Development of Research Methodology Design,

MT & AS

Study Design, manuscript review, critical input.

AR & MMS

Manuscript drafting, Study Design,

AF & HMUF

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

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