RESEARCH PAPER

From Infection to Resistance: Clinical Predictors and Outcomes of Antimicrobial-Resistant Infections in Hospitalized Patients

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ABSTRACT

Background: Antimicrobial resistance (AMR) poses a severe threat to patient safety and healthcare systems in developing nations. Identifying clinical determinants and patient outcomes associated with AMR is vital for optimizing antibiotic stewardship in resource-limited settings.

Objective: To evaluate the clinical predictors and patient outcomes associated with antimicrobial-resistant infections among hospitalized patients at a tertiary care hospital in Lahore, Pakistan.

Methods: An analytical cross-sectional study was conducted among 385 hospitalized patients with culture-confirmed bacterial infections. Patient demographics, clinical history, prior antibiotic exposure, and clinical outcomes were documented using a structured collection tool. Microbiological identification and susceptibility testing were performed using standard CLSI protocols. Multivariable logistic regression analysis was utilized to determine independent predictors of resistance, while clinical outcomes were compared between resistant and susceptible cohorts.

Results: The overall prevalence of antimicrobial-resistant infections was 48.3 percent (186 out of 385 patients), with multi-drug resistance predominantly identified in Gram-negative isolates (54.2 percent). Prior antibiotic exposure within 30 days (Adjusted Odds Ratio = 2.85, 95 percent Confidence Interval: 1.65 to 4.92, p-value less than 0.001), invasive mechanical ventilation (Adjusted Odds Ratio = 3.12, 95 percent Confidence Interval: 1.84 to 5.28, p-value less than 0.001), and prolonged pre-infection hospitalization greater than 7 days (Adjusted Odds Ratio = 2.10, 95 percent Confidence Interval: 1.28 to 3.44, p-value equal to 0.003) emerged as strong independent clinical predictors of resistance. Patients with resistant infections demonstrated a significantly prolonged median length of hospital stay (14 vs. 7 days, p-value less than 0.001) and higher ICU admission rates (28.5 percent vs. 11.6 percent, p-value less than 0.001). Furthermore, in-hospital mortality was substantially higher in the resistant group compared to the susceptible group (16.7 percent vs. 6.5 percent, Adjusted Odds Ratio = 2.87, p-value equal to 0.002).

Conclusion: Prior antimicrobial consumption, mechanical ventilation, and extended hospital stays are key clinical drivers of resistance in tertiary hospital settings in Lahore. Antimicrobial-resistant infections significantly escalate hospital stay, ICU utilization, and in-hospital mortality. Urgent implementation of institutional antibiotic stewardship programs and early risk stratification are essential to mitigate this burden.

Keywords: Antimicrobial Resistance, Cross-Sectional Study, Clinical Predictors, Mortality, Tertiary Care Hospital.

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INTRODUCTION

Antimicrobial resistance (AMR) has emerged as one of the most critical global public health threats of the 21st century, severely threatening the efficacy of life-saving medical interventions (1). The rapid emergence and dissemination of multi-drug resistant (MDR) pathogens have compromised conventional empirical antibiotic therapies, leading to prolonged illnesses, increased healthcare expenditures, and elevated mortality rates globally (2). While AMR is a worldwide phenomenon, the burden is disproportionately higher in developing countries, where high infectious disease burdens coincide with suboptimal infection control practices and unregulated antibiotic utilization (3, 4).

In hospitalized patients, particularly those admitted to tertiary care facilities, the risk of acquiring resistant infections is markedly elevated. Invasive diagnostic and therapeutic procedures, such as central venous catheterization, urinary catheterization, and mechanical ventilation, disrupt natural physiological barriers and create pathways for opportunistic, resistant pathogens to colonize and infect vulnerable

hosts (5, 6). Furthermore, healthcare settings serve as reservoirs for resistant strains like extended-spectrum beta-lactamase (ESBL)-producing *Enterobacteriaceae*, methicillin-resistant *Staphylococcus aureus* (MRSA), and carbapenem-resistant *Acinetobacter baumannii* (7, 8). Identifying specific patient-level clinical predictors—such as prior broad-spectrum antibiotic exposure, prolonged initial hospitalization, advanced age, and underlying comorbidities—is paramount for early risk stratification and target-driven intervention (9, 10).

The consequences of antimicrobial resistance extend beyond therapeutic failure; they profoundly impact clinical outcomes and healthcare administration (11). Patients infected with resistant strains consistently demonstrate significantly longer lengths of hospital stay, higher rates of intensive care unit (ICU) admission, and elevated in-hospital mortality compared to those infected with susceptible strains (12, 13). In low- and middle-income countries like Pakistan, tertiary care hospitals face additional challenges including overcrowded wards, limited diagnostic resources, and variable adherence to institutional antibiotic stewardship programs (14, 15). Local epidemiological data from major healthcare centers, such as those in Lahore, are crucial for tailoring local guidelines, yet comprehensive studies evaluating both the independent predictors and real-world clinical outcomes of resistance remain limited.

Therefore, this study was designed to evaluate the clinical predictors and patient outcomes associated with antimicrobial-resistant infections among hospitalized patients in a tertiary care hospital in Lahore, Pakistan. By identifying the primary drivers of resistance and measuring their impact on clinical trajectory, this research aims to provide actionable evidence to strengthen institutional antibiotic stewardship protocols and optimize patient management strategies.

MATERIALS AND METHODS

Study Design and Setting

This study was conducted as a hospital-based analytical cross-sectional study at a major tertiary care hospital in Lahore, Pakistan. The study evaluated hospitalized patients across multiple clinical departments, including General Medicine, General Surgery, Intensive Care Units (ICU), and High Dependency Units (HDU).

Study Population

The study population comprised adult patients admitted to the inpatient wards and ICUs who developed microbiologically confirmed bacterial infections during their hospital stay.

Eligibility Criteria

- **Inclusion Criteria:**
- Inpatients aged 18 years or older of both genders.
- Patients with a confirmed bacterial infection validated by positive culture and antimicrobial susceptibility testing (AST) results.
- Patients with a minimum hospital stay of 48 hours prior to specimen collection.
- Patients or their legal guardians who provided informed written consent.
- **Exclusion Criteria:**
- Patients with viral, fungal, or mycobacterial (e.g., *Tuberculosis*) infections only.
- Contaminated specimens or isolates identified as normal flora/colonizers rather than true pathogens.
- Outpatients or patients transferred from other facilities with incomplete medical records.
- Readmitted patients who were previously enrolled in this study to prevent duplicate sampling.

Sample Size Determination

The required sample size was calculated using Cochrane's formula for cross-sectional studies in finite/large populations:

$n = (Z^2 * p * (1 - p)) / d^2$

Where:

- **n** = Calculated sample size
- **Z** = Standard normal deviation corresponding to a 95 percent confidence level (1.96)
- **p** = Anticipated proportion/prevalence of antimicrobial resistance (0.50 or 50 percent, selected to yield the maximum variance and conservative sample size estimate)
- **d** = Absolute precision / margin of error allowable (0.05 or 5 percent)

Calculation:

$n = ((1.96)^2 * 0.50 * 0.50) / (0.05)^2 = 384.16$

To ensure statistical power and account for potential missing data or incomplete records, the calculated value of 384.16 was rounded up to a target sample size of **385 patients**.

Sampling Technique

A non-probability consecutive sampling method was employed. All eligible patients admitted to the respective inpatient units and ICUs who met the inclusion criteria were continuously enrolled until the required sample size of 385 was attained.

Data Collection and Measurements

Data were collected using a pre-tested, structured questionnaire and medical record review form. The variables recorded included:

1. **Demographic Profile:** Age, gender, and ward/unit type.
2. **Clinical Predictors (Exposures):** Underlying comorbidities (e.g., diabetes mellitus, chronic kidney disease, hypertension), history of prior antibiotic consumption within the preceding 30 days, length of hospital stay prior to infection

onset, and use of invasive medical devices (e.g., mechanical ventilation, central venous catheters, urinary catheters).

3. **Microbiological Data:** Specimen type (blood, urine, sputum, wound swab, tracheal aspirates), isolated bacterial species, and resistance profiles.
4. **Clinical Outcomes:** Total length of hospital stay (LOS), requirement for ICU transfer, and in-hospital mortality status (discharged vs. deceased).

Microbiological Procedures and Resistance Identification

Clinical specimens were collected under aseptic conditions and processed at the institution's diagnostic microbiology laboratory. Bacterial identification was performed using standard microbiological methods (Gram staining, colony morphology, and biochemical testing). Antimicrobial susceptibility testing was executed using the Kirby-Bauer disk diffusion method or automated systems (e.g., VITEK-2), and interpretive zone diameters were reported in accordance with the Clinical and Laboratory Standards Institute (CLSI) guidelines. Strains demonstrating resistance to at least one agent in three or more antimicrobial categories were classified as multi-drug resistant (MDR).

Statistical Analysis

Data entry and statistical computations were conducted using IBM SPSS Statistics (Version 26.0). Categorical variables were presented as frequencies and percentages. Continuous variables were assessed for normality and expressed as mean with standard deviation or median with interquartile range (IQR). Bivariable analysis using Chi-square test or Mann-Whitney U test was performed, followed by multivariable binary logistic regression to identify independent clinical predictors of resistance while controlling for potential confounders. Adjusted Odds Ratios (aOR) with 95 percent Confidence Intervals (CI) were reported, with p-value less than 0.05 considered statistically significant.

Ethical Considerations

Ethical approval for this protocol was formally granted by the Institutional Review Board (IRB) / Institutional Ethics Committee of the hospital. Confidentiality and anonymity of patient data were rigorously maintained using unique patient identification codes.

RESULTS

Demographic and Clinical Characteristics

A total of 385 hospitalized patients with culture-confirmed bacterial infections were evaluated. The mean age of the patient population was 47.8 ± 14.3 years, with 55.1 percent (n = 212) being male. The majority of participants were admitted to General Medical Wards (38.7 percent), followed by Surgical Wards (33.5 percent) and Intensive Care Units (27.8 percent). Comorbid conditions were present in 61.3 percent of patients, with diabetes mellitus (34.8 percent) and chronic kidney disease (18.2 percent) being the most prevalent. Overall, 48.3 percent (n = 186) of the cohort were diagnosed with antimicrobial-resistant (AMR) infections, while 51.7 percent (n = 199) had susceptible bacterial infections.

Microbiological Profile and Resistance Distribution

Gram-negative pathogens accounted for 64.7 percent (n = 249) of total isolates, dominated by *Klebsiella pneumoniae* (28.3 percent), *Escherichia coli* (22.1 percent), and *Pseudomonas aeruginosa* (14.3 percent). Gram-positive organisms comprised 35.3 percent (n = 136), primarily represented by *Staphylococcus aureus* (20.5 percent). Among Gram-negative isolates, multi-drug resistance (MDR) was documented in 54.2 percent of cases, with notable rates of extended-spectrum beta-lactamase (ESBL) production (41.3 percent) and carbapenem resistance (19.7 percent). Methicillin resistance (MRSA) was confirmed in 43.0 percent of *S. aureus* strains. The primary clinical specimen sources yielding resistant organisms were respiratory secretions/tracheal aspirates (31.2 percent), urinary specimens (27.4 percent), bloodstream infections (22.6 percent), and wound swabs (18.8 percent).

Multivariable Analysis of Clinical Predictors

Bivariable analysis demonstrated significant associations between AMR and age greater than 60 years, prior antibiotic exposure, length of pre-infection hospitalization, mechanical ventilation, and central venous catheterization (p-value less than 0.05).

To isolate independent clinical drivers of resistance, variables showing significance (p-value less than 0.10) were entered into a multivariable binary logistic regression model **(Table 1).**

Table 1: Multivariable Logistic Regression Analysis of Clinical Predictors for Antimicrobial Resistance (N = 385)

Clinical Predictor Variable	Susceptible Group (n = 199)	Resistant Group (n = 186)	Adjusted Odds Ratio (aOR)	95 percent Confidence Interval	p-value
Prior Antibiotic Exposure (< 30 days)	58 (29.1 percent)	104 (55.9 percent)	**2.85**	1.65 to 4.92	**< 0.001**
Invasive Mechanical Ventilation	23 (11.6 percent)	62 (33.3 percent)	**3.12**	1.84 to 5.28	**< 0.001**
Pre-infection Hospital Stay (> 7 days)	41 (20.6 percent)	71 (38.2 percent)	**2.10**	1.28 to 3.44	**0.003**
Central Venous Catheterization	31 (15.6 percent)	54 (29.0 percent)	**1.74**	1.02 to 2.97	**0.041**
Presence of Diabetes Mellitus	62 (31.2 percent)	72 (38.7 percent)	**1.21**	0.78 to 1.88	0.395

Note: Statistical significance established at p-value less than 0.05.

Prior exposure to antimicrobials within the preceding 30 days tripled the likelihood of developing a resistant infection (aOR = 2.85, 95 percent CI: 1.65 to 4.92, p-value less than 0.001). Similarly, mechanical ventilation (aOR = 3.12, 95 percent CI: 1.84 to 5.28, p-value less than 0.001) and an initial hospital stay exceeding 7 days prior to infection onset (aOR = 2.10, 95 percent CI: 1.28 to 3.44, p-value equal to 0.003) remained strong, independent predictors of resistance.

Assessment of Clinical Outcomes

Comparative evaluation revealed significantly worse clinical outcomes among patients infected with antimicrobial-resistant strains compared to those with susceptible strains across all measured parameters (Table 2).

Table 2: Comparison of Clinical Outcomes Between Resistant and Susceptible Infection Cohorts

Clinical Outcome	Susceptible Cohort (n = 199)	Resistant Cohort (n = 186)	Test Statistic	p-value
Median Hospital Stay (Days, IQR)	7 (5 to 11)	14 (9 to 22)	Z = -6.84	**< 0.001**
ICU Admission Rate (n, percent)	23 (11.6 percent)	53 (28.5 percent)	Chi-square = 17.21	**< 0.001**
In-Hospital Mortality Rate (n, percent)	13 (6.5 percent)	31 (16.7 percent)	Chi-square = 9.87	**0.002**

Patients with resistant infections experienced a doubled median hospital stay (14 days vs. 7 days, p-value less than 0.001). The need for ICU admission was significantly elevated in the resistant group (28.5 percent vs. 11.6 percent, p-value less than 0.001). Crucially, overall in-hospital mortality was more than two-fold higher among patients with resistant pathogens (16.7 percent, n = 31) compared to those with susceptible strains (6.5 percent, n = 13; aOR = 2.87, 95 percent CI: 1.42 to 5.81, p-value equal to 0.002), underscoring the severe clinical burden imposed by AMR in tertiary care environments.

DISCUSSION

The findings of this analytical cross-sectional study provide critical insights into the clinical determinants and adverse outcomes associated with antimicrobial resistance (AMR) in a major tertiary care hospital in Lahore. With an observed AMR prevalence of 48.3 percent among hospitalized patients, our results reflect the ongoing public health crisis driven by resistant pathogens in low- and middle-income countries (LMICs) (16). The predominant burden was observed among Gram-negative isolates, particularly *Klebsiella pneumoniae* and *Escherichia coli*, exhibiting high rates of multi-drug resistance (MDR) and extended-spectrum beta-lactamase (ESBL) production. This finding aligns with national surveillance data from Pakistan and global reports emphasizing the alarming rise of resistant Gram-negative bacteria in hospital settings (2, 17).

In our multivariable regression model, prior exposure to broad-spectrum antibiotics within 30 days before infection onset emerged as a principal independent predictor of resistance (aOR = 2.85, p-value less than 0.001). Antimicrobial pressure alters host microflora, eradicating susceptible commensal bacteria and facilitating the selective survival and proliferation of resistant strains (9). In tertiary healthcare facilities across Pakistan, self-medication, empirical over-prescribing of broad-spectrum antibiotics, and incomplete therapeutic courses remain widespread, directly compounding this biological selection pressure (14, 18).

Invasive mechanical ventilation was another strong independent driver of resistant infections (aOR = 3.12, p-value less than 0.001). Mechanical ventilators bypass upper airway mucosal defenses and facilitate the formation of bacterial biofilms on endotracheal tubes, providing a protected niche for opportunistic hospital-acquired pathogens such as *Pseudomonas aeruginosa* and carbapenem-resistant *Acinetobacter baumannii* (5, 19). Additionally, prolonged initial hospitalization prior to infection onset (greater than 7 days) significantly elevated the risk of AMR (aOR = 2.10, p-value equal to 0.003). Extended stays heighten patient exposure to the contaminated clinical environment, healthcare personnel vectoring, and invasive device utilization, all of which accelerate nosocomial transmission (7, 20).

The clinical outcomes evaluated in this study demonstrate the severe human and institutional costs imposed by AMR. Patients infected with resistant strains suffered from a significantly extended median hospital stay (14 days vs. 7 days, p-value less than 0.001) and a higher frequency of ICU transfers (28.5 percent vs. 11.6 percent, p-value less than 0.001). Treatment delays caused by ineffective initial empirical regimens often lead to clinical deterioration, requiring intensive hemodynamic and respiratory support (3). Most critically, in-hospital mortality was more than two-fold higher among patients with

resistant infections compared to those with susceptible infections (16.7 percent vs. 6.5 percent, p-value equal to 0.002). This elevated mortality highlights the limited availability of effective reserve antibiotics (e.g., colistin, ceftazidime-avibactam) in resource-constrained public hospitals, frequently leaving clinicians with narrow or toxic therapeutic alternatives (12, 21).

Limitations

Several limitations should be considered when interpreting these findings. First, as a single-center cross-sectional study conducted at a tertiary care center in Lahore, the results may reflect specific local prescribing habits and hospital ecology, limiting direct generalizability to primary or secondary healthcare facilities. Second, while multivariable analysis controlled for major confounders, unmeasured variables such as molecular resistance mechanisms (e.g., specific gene expression like *bla*NDM) were not evaluated due to laboratory resource constraints.

CONCLUSION

Antimicrobial resistance represents a major clinical challenge in tertiary care hospitals in Lahore, affecting nearly half of all patients with culture-confirmed bacterial infections. Prior antibiotic exposure, invasive mechanical ventilation, and extended pre-infection hospital stays are the primary independent predictors driving resistant infections. Consequently, AMR significantly worsens patient trajectory, resulting in doubled hospital stays, increased ICU admissions, and substantially higher in-hospital mortality.

To mitigate this growing threat, tertiary healthcare institutions must urgently establish robust, multidisciplinary Antimicrobial Stewardship Programs (ASPs) to regulate empirical prescribing. Concurrently, strict infection prevention and control (IPC) protocols—particularly surrounding mechanical ventilation and device management—must be enforced alongside rapid diagnostic testing to minimize treatment delays and curb the spread of resistant pathogens.

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