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Article

Antimicrobial Resistance Trends in Healthcare-Associated Infections in Lahore: A Tertiary Care Perspective

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ABSTRACT

Background: Antimicrobial resistance (AMR) is a critical global health concern, particularly in healthcare-associated infections (HCAIs) where multidrug-resistant (MDR) pathogens compromise treatment efficacy and increase mortality. Tertiary care hospitals in low-resource settings like Lahore face growing threats due to poor antimicrobial stewardship, limited surveillance, and the emergence of resistance to last-line antibiotics. **Objective**: This study aimed to assess the prevalence, resistance profiles, and molecular mechanisms of AMR in HCAI pathogens in tertiary care hospitals in Lahore, focusing on high-risk Gram-negative organisms and their clinical impact in ICU settings. **Methods**: A retrospective observational study was conducted via systematic review of 53 peer-reviewed articles and regional surveillance reports published between 2014 and 2023. Inclusion criteria included studies from Lahore reporting resistance profiles of nosocomial pathogens; community-acquired infections and non-English sources were excluded. Data were extracted on pathogen distribution, resistance rates, and associated risk factors. Ethical compliance with the Declaration of Helsinki was ensured through exclusive use of anonymized, published data. Descriptive statistics were computed using SPSS v27. **Results**: E. coli (24%), Acinetobacter spp. (23%), and P. aeruginosa (19%) were the most prevalent pathogens. Carbapenem resistance reached 98% in Acinetobacter and 89% in Pseudomonas, while colistin retained 93–100% activity. Extended hospital stays and prior antibiotic exposure were associated with 85.5% of MDR cases. Only 38.1% of hospitals adhered to stewardship guidelines. **Conclusion**: MDR pathogens in Lahore's tertiary care hospitals present a significant challenge to patient safety and treatment efficacy. Strengthening antimicrobial stewardship, infection control, and molecular surveillance is urgently needed to curb the clinical impact of AMR.

Keywords: Antimicrobial Resistance, Healthcare-Associated Infections, Multidrug-Resistant Organisms, Intensive Care Units, Carbapenem Resistance, Polymyxin Resistance, Infection Control.

INTRODUCTION

Antimicrobial resistance (AMR) has emerged as one of the most pressing global health threats of the 21st century, fundamentally challenging the efficacy of modern medicine. It occurs when microorganisms, particularly bacteria, evolve mechanisms to withstand previously effective antimicrobial treatments, rendering common infections increasingly difficult to treat (1). The World Health Organization has identified AMR among the top ten global health concerns, highlighting its rapidly escalating impact on morbidity, mortality, and healthcare costs (2). This crisis is exacerbated by the widespread misuse and overuse of antibiotics in both human and veterinary medicine, poor adherence to prescribing guidelines, and limited public awareness, all of which contribute to the selective pressure driving resistance (3). In developing countries such as Pakistan, the situation is particularly acute due to fragile healthcare infrastructure, inadequate infection control, and weak regulatory oversight (4).

Healthcare-associated infections (HCAIs), defined as infections acquired during medical or surgical treatment and not present at the time of hospital admission, are among the most significant contributors to AMR's clinical burden (5). These infections are especially prevalent in intensive care units (ICUs), where patients are often immunocompromised and subjected to invasive procedures that increase susceptibility to opportunistic and drug-resistant pathogens (6). Global estimates suggest that the incidence of HCAIs in ICU settings may exceed 40% in high-income countries, with significantly higher rates in low- and middle-income countries (LMICs), including Pakistan (7). The prevalence of multidrug-resistant organisms (MDROs) and extensively drug-

resistant organisms (XDROs) in such settings has resulted in limited therapeutic options, prolonged hospitalization, elevated treatment costs, and increased mortality rates (8).

A particularly concerning dimension of HCAIs is the dominance of ESKAPE pathogens—Enterococcus faecium, Staphylococcus aureus, Klebsiella spp., Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter spp.—which are recognized for their virulence, persistence in hospital environments, and resistance to multiple antimicrobial classes (9). These pathogens have been identified as key drivers of nosocomial infections in Pakistani hospitals and have shown resistance to even last-resort antibiotics such as carbapenems and polymyxins (10). Mechanisms such as beta-lactamase production, efflux pumps, target site modification, and plasmid-mediated gene transfer are increasingly implicated in the survival and spread of these bacteria in healthcare settings (11). Moreover, regional data from Lahore indicate a disturbingly high prevalence of Gram-negative bacterial infections in tertiary care ICUs, particularly involving Escherichia coli, Klebsiella pneumoniae, Acinetobacter spp., and Pseudomonas aeruginosa, all of which exhibit resistance to critical antimicrobial agents (12). The mcr-1 gene-mediated resistance to colistin and extensive production of extended-spectrum beta-lactamases (ESBLs) have been documented, raising alarm over therapeutic limitations (13).

Despite recognition of the issue, surveillance data in Pakistan remain fragmented and inconsistent, especially across provinces such as Baluchistan, leading to an incomplete understanding of resistance dynamics (14). Additionally, poor adherence to antimicrobial stewardship programs—reported in fewer than 40% of Lahore's hospitals—and indiscriminate empirical use of third-generation cephalosporins have further compounded the problem (15). Ethical concerns also arise from insufficient infection control measures, unstandardized prescribing practices, and a lack of transparency regarding antibiotic use policies in many healthcare facilities. These institutional gaps not only facilitate the propagation of resistance but also threaten the broader public health ecosystem, as resistant organisms may spread into communities through patients discharged from hospitals or improper disposal of medical waste (16).

The One Health approach—emphasizing the interconnectedness of human, animal, and environmental health—has gained global recognition as a framework for addressing AMR comprehensively. However, its implementation in Pakistan remains limited, often constrained by systemic inefficiencies and a lack of cross-sector collaboration (17). There is an urgent need for multidisciplinary interventions that strengthen local antimicrobial surveillance, standardize infection control protocols, and promote judicious antibiotic prescribing based on susceptibility data. Existing literature underscores the severity of AMR among hospital-acquired infections in Lahore, yet a consolidated regional analysis focusing on tertiary care facilities, especially ICUs, remains lacking (18). This knowledge gap hinders the development of evidence-based policies and intervention strategies tailored to the Pakistani healthcare context.

This study aims to address this critical gap by reviewing the trends and mechanisms of antimicrobial resistance in healthcare-associated infections within tertiary care hospitals of Lahore. Specifically, it seeks to analyze resistance profiles of major pathogens, examine risk factors linked to the emergence of multidrug resistance, and evaluate the role of stewardship and surveillance practices. By synthesizing available evidence, this research contributes to the national and international discourse on AMR and supports the formulation of targeted interventions suited to high-risk hospital environments in resource-constrained settings (19).

MATERIALS AND METHODS

The present study employed a retrospective observational design, aiming to analyze antimicrobial resistance (AMR) patterns in healthcare-associated infections (HCAIs) within tertiary care hospitals in Lahore, Pakistan. The analysis focused on previously published literature, hospital surveillance reports, and antimicrobial susceptibility data collected from peer-reviewed regional studies conducted between 2014 and 2023. Because this was a secondary data-based review, no individual patient recruitment was conducted, and thus informed consent was not applicable. The included studies were selected based on the following criteria: peer-reviewed articles published in English, with data specific to tertiary care hospitals in Lahore and including antimicrobial susceptibility profiles of nosocomial pathogens. Studies were excluded if they lacked pathogen-specific resistance data, were focused on community-acquired infections, or did not originate from Lahore-based hospital settings.

Data collection involved a systematic review of antimicrobial susceptibility testing (AST) results reported in the included studies. The primary outcomes assessed were prevalence rates of multidrug-resistant organisms (MDROs) among common HAI pathogens and their resistance profiles against major antibiotic classes, including carbapenems, cephalosporins, fluoroquinolones, aminoglycosides, and polymyxins. Secondary outcomes included the identification of key resistance mechanisms, such as extended-spectrum beta-lactamase (ESBL) production, carbapenemase expression, efflux pump activation, and plasmid-mediated resistance genes like mcr-1 and bla_NDM. Data were extracted on pathogen distribution (e.g., Escherichia coli, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and MRSA), rates of resistance to specific antibiotics, and associated clinical and epidemiological factors such as ICU stay duration, device use, and empirical antibiotic therapy. The studies reviewed used standardized AST methods, including disk diffusion and minimum inhibitory concentration (MIC) testing, interpreted according to Clinical and Laboratory Standards Institute (CLSI) guidelines, although methodology may have varied slightly across hospitals.

This literature-based review did not involve new data collection from human subjects. However, all original studies included in the analysis were reviewed to confirm their adherence to ethical standards. The synthesis of findings was conducted in compliance with the Declaration of Helsinki, and the confidentiality of data was ensured by relying exclusively on aggregated and anonymized published results.

Statistical analysis was performed using IBM SPSS Statistics version 27. Descriptive statistics, such as means and percentages,

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were used to summarize pathogen prevalence and antibiotic resistance patterns. Comparative assessments were made between the resistance rates reported across different hospitals and years to identify trends and variations. Where possible, cross-study consistency was assessed to validate findings. Due to the nature of the review, no patient-level data or missing data imputation was required. Confounding variables such as hospital-specific infection control protocols and differences in stewardship implementation were noted qualitatively and considered when interpreting resistance trends (36).

RESULTS

A total of 82.2% of healthcare-associated infection (HAI) isolates reported in tertiary care hospitals in Lahore were Gram-negative bacteria, while Gram-positive organisms constituted a smaller fraction of infections. Among Gram-negative pathogens, Escherichia coli (24%), Acinetobacter spp. (23%), Pseudomonas aeruginosa (19%), and Klebsiella pneumoniae (13%) were the most prevalent. Methicillin-resistant Staphylococcus aureus (MRSA) accounted for 11% of Gram-positive isolates. High resistance levels were observed across all major pathogens to first-line antibiotics, particularly among Gram-negative organisms, which demonstrated extensive drug resistance patterns.

Table 1. Resistance Profiles and Mechanisms of Major HAI Pathogens in Lahore

Pathogen	Resistance Profile	Key Resistance Mechanisms
Acinetobacter baumannii	98% carbapenem resistance; 94–98% cephalosporin resistance	MBL, ESBL production
Pseudomonas aeruginosa	89% carbapenem resistance; 92.9% ciprofloxacin resistance	Efflux pumps, β-lactamase genes
Escherichia coli	100% resistance to ceftazidime and ampicillin	ESBL, mcr-1 gene (colistin resistance)
MRSA	100% resistance to β-lactams; emerging vancomycin resistance	mecA gene, altered PBPs

Resistance to carbapenems was highest in Acinetobacter baumannii (98%) and P. aeruginosa (89%). Resistance in E. coli and Klebsiella pneumoniae remained relatively lower, with 68–72% susceptibility to carbapenems. Colistin retained high efficacy across Gram-negative isolates, with 100% susceptibility in Acinetobacter and 86–93% in Klebsiella and Pseudomonas, although plasmid-mediated mcr-1 gene presence in E. coli remains a significant emerging threat.

Table 2. Prevalence and Antibiotic Susceptibility of Major Pathogens in HAIs

Pathogen	Prevalence (%)	High-Resistance Antibiotics	Susceptibility to Last-Line Agents
Escherichia coli	24	Ceftazidime (100%), Ampicillin (100%)	Meropenem (71%), Imipenem (63%)
Acinetobacter spp.	23	Cephalosporins (94–98%), Carbapenems (98%)	Colistin (100%)
Pseudomonas aeruginosa	19	Ciprofloxacin (92.9%), Carbapenems (89%)	Colistin (93%), Amikacin (52%)
Klebsiella pneumoniae	13	Ampicillin (0%), Co-trimoxazole (0%)	Imipenem (60%), Colistin (86%)
MRSA	11	Penicillin (1.1%), Ceftazidime (0%)	Vancomycin (100%), Linezolid (98%)

Extended-spectrum β-lactamase (ESBL) production was a predominant resistance mechanism in E. coli, particularly among urinary tract infections (70.8% prevalence in UTI cases). Carbapenem resistance in Acinetobacter spp. and P. aeruginosa was primarily driven by efflux mechanisms and β-lactamase gene overexpression. Carbapenems displayed variable efficacy across Gram-negative pathogens. While susceptibility remained moderate in Klebsiella pneumoniae (60%) and E. coli (71%), it was markedly reduced in Acinetobacter (21%) and Pseudomonas (52%). Aminoglycosides offered slightly better efficacy, with E. coli showing 78% susceptibility and Klebsiella 50%, though Acinetobacter (31%) and Pseudomonas (52%) exhibited considerable resistance. All tested isolates were resistant to third-generation cephalosporins.

Table 3. Comparative Efficacy of Antibiotic Classes Against Gram-Negative Pathogens

Antibiotic Class	E. coli	Acinetobacter	P. aeruginosa	Klebsiella
Carbapenems	71%	21%	52%	60%
Aminoglycosides	78%	31%	52%	50%
Polymyxins (e.g., colistin)	100%	100%	93%	86%
3rd-gen Cephalosporins	0%	0%	0%	0%

Among clinical risk factors, prolonged hospitalization (≥5 days) and invasive medical devices (e.g., urinary catheters, ventilators) were significantly associated with multidrug-resistant infections, contributing to 85.5% of MDR cases. Prior exposure to antibiotics was documented in 71.5% of these cases, highlighting poor stewardship compliance. Furthermore, third-generation cephalosporins were used empirically in 38.5% of isolates, despite over 90% resistance among Gram-negative strains, raising concern for inappropriate empirical therapy. Surgical prophylaxis accounted for 33% of total antibiotic use, often exceeding recommended durations and potentially contributing to selective resistance pressures.

Surveillance data analysis revealed geographical imbalances, with Punjab and Sindh contributing 35.48% and 40.86% of national antimicrobial resistance (AMR) reporting, respectively. Baluchistan remained significantly underrepresented in national

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AMR data. Additionally, only 38.1% of tertiary care hospitals in Lahore were found to comply with antimicrobial stewardship guidelines, suggesting variable adherence and underreporting, which may distort local resistance trends.

Collectively, these results highlight the critical role of Gram-negative pathogens in driving resistance in healthcare settings and emphasize the need for improved stewardship practices and surveillance infrastructure. The consistently high resistance to β-lactams and cephalosporins across all studied pathogens and the emerging resistance to polymyxins underscore the urgency of deploying evidence-based interventions in Lahore's tertiary healthcare institutions.

DISCUSSION

The findings of this study underscore a growing crisis of antimicrobial resistance (AMR) in healthcare-associated infections (HAIs) within tertiary care hospitals in Lahore, with Gram-negative pathogens exhibiting particularly alarming resistance profiles. These results are consistent with global and regional trends, where multidrug-resistant (MDR) organisms have become entrenched in high-risk clinical environments such as intensive care units (ICUs)(1). The predominance of pathogens like Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, and Acinetobacter baumannii in HAI isolates, combined with their resistance to frontline therapies including third-generation cephalosporins and carbapenems, reaffirms the critical nature of AMR in nosocomial settings. Such findings parallel earlier studies conducted across South Asia, where Acinetobacter and Klebsiella spp. have emerged as key drivers of XDR infections, posing therapeutic challenges due to limited treatment options (10, 24).

Resistance mechanisms observed in this review, such as extended-spectrum β-lactamase (ESBL) and carbapenemase production, overexpression of efflux pumps, and plasmid-mediated genes like mcr-1, have been widely documented in recent literature as major contributors to the resistance phenotype in Gram-negative bacteria (11, 43). The widespread resistance to β-lactams and fluoroquinolones, and emerging resistance to last-resort agents such as polymyxins, indicate both intrinsic adaptability and extensive horizontal gene transfer among pathogens in hospital environments. The identification of colistin resistance, particularly in E. coli, through plasmid-mediated mcr genes raises serious clinical concerns, given colistin's role as a salvage therapy for XDR infections (52). These molecular findings corroborate previous surveillance efforts in Pakistan and align with WHO warnings about the escalating threat posed by mobile resistance determinants (9, 54).

Clinically, the implications are profound. High rates of resistance to empirical treatments—particularly third-generation cephalosporins and carbapenems—may lead to increased reliance on combination therapies or more toxic alternatives, potentially elevating the risk of adverse drug events, lengthened hospital stays, and elevated mortality rates. The strong association of MDR infections with prolonged hospitalization and invasive medical devices observed in this review supports earlier observations from Latin America and Southeast Asia, which have identified similar risk patterns in ICU patients (25, 36). Empirical overuse of antibiotics, notably cephalosporins, despite high resistance prevalence, reflects poor adherence to stewardship protocols and highlights the need for evidence-based prescribing guided by antimicrobial susceptibility testing.

Comparatively, this study advances the field by offering a consolidated regional perspective specific to Lahore, addressing a critical gap in local surveillance data. While several national reports have described AMR trends in Pakistan, few have focused exclusively on tertiary care hospitals or disaggregated data at the city level, thereby overlooking important epidemiological nuances (36, 44). The finding that only 38.1% of Lahore's hospitals comply with antimicrobial guidelines is both alarming and indicative of systemic barriers to effective stewardship. This observation aligns with earlier studies emphasizing limited regulatory enforcement and uneven implementation of infection control protocols in public and private sector hospitals across Pakistan (38, 41).

The results also highlight a critical imbalance in national AMR reporting, with Punjab and Sindh dominating the data landscape while provinces like Baluchistan remain underrepresented. This regional disparity hampers national planning and obscures the true geographic spread of resistance. Although this review is strengthened by its comprehensive synthesis of peer-reviewed data spanning nearly a decade, it also faces limitations. As a literature-based review, it is inherently dependent on the methodological rigor and reporting transparency of the included studies. Heterogeneity in antimicrobial susceptibility testing methods, lack of standardized definitions across hospitals, and inconsistent reporting formats limit the ability to conduct meta-analytic assessments or draw robust statistical inferences.

Furthermore, the exclusion of non-English literature and unpublished surveillance data may result in selection bias, and the findings cannot be generalized beyond the tertiary care context without caution. Another limitation is the lack of patient-level data, which precludes analysis of clinical outcomes such as treatment failure, duration of hospitalization, and mortality associated with MDR infections. Nonetheless, the study provides essential insight into local resistance dynamics and can serve as a foundation for targeted interventions.

Future research should prioritize real-time surveillance systems, the molecular characterization of resistance genes using whole-genome sequencing, and the evaluation of stewardship interventions through prospective cohort studies. Strengthening laboratory capacity, improving infection control infrastructure, and integrating antimicrobial stewardship into clinical decision-making are urgently needed steps. Collaborative initiatives between policymakers, clinicians, microbiologists, and public health professionals will be crucial to curb the trajectory of AMR in Pakistan. By addressing the multifaceted drivers of resistance and enhancing the granularity of local data, health systems can better align clinical practices with the emerging realities of antibiotic resistance. This study contributes to that objective by delineating the patterns, drivers, and implications of AMR in Lahore's tertiary care hospitals, thus laying the groundwork for sustainable policy and clinical reform.

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CONCLUSION

This review highlights the alarming rise of antimicrobial resistance (AMR) in healthcare-associated infections (HCAIs) within tertiary care hospitals in Lahore, with Gram-negative pathogens such as Escherichia coli, Acinetobacter baumannii, and Pseudomonas aeruginosa exhibiting extensive resistance to critical antibiotic classes including carbapenems and third-generation cephalosporins. The dominance of ESKAPE pathogens and the emergence of plasmid-mediated resistance mechanisms, particularly to last-resort agents like colistin, underscore a critical threat to patient safety, especially in intensive care settings. These findings emphasize the urgent need for strengthened antimicrobial stewardship programs, standardized infection control protocols, and improved local surveillance to mitigate the spread of multidrug-resistant organisms. Clinically, the persistence of such resistance patterns compromises therapeutic efficacy and escalates healthcare burdens, while from a research perspective, the data call for molecular-level studies to track resistance gene dissemination and evaluate targeted interventions. This study reinforces the necessity of coordinated action at institutional and policy levels to address the escalating AMR crisis in tertiary care healthcare settings.

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