

Original Article

High Rates of Carbapenem Resistance Among Respiratory Pathogens in ICU Patients: A Single-Centre Study in Iran

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Abstract

Background: Respiratory tract infections are a leading cause of morbidity among hospitalized patients, with antimicrobial resistance increasingly complicating treatment decisions. This study aimed to determine the distribution and antimicrobial resistance patterns of respiratory pathogens isolated from intensive care unit (ICU) patients at a tertiary care hospital in Tehran, Iran.

Materials and Methods: This retrospective cross-sectional study analyzed sputum samples collected between April 1, 2024 and March 1, 2025, at a tertiary care hospital in Tehran, Iran. Bacterial identification and antimicrobial susceptibility testing were performed using standard microbiological methods according to Clinical and Laboratory Standards Institute (CLSI) guidelines. Data were analyzed using SPSS version 26.

Results: A total of 114 ICU patients were included, with a mean age of 74.5 years. Gram-negative bacteria predominated (85.1%), with the most common pathogens being *Acinetobacter baumannii* (50 isolates, 43.9%), *Klebsiella pneumoniae* (26 isolates, 22.8%), and *Pseudomonas aeruginosa* (16 isolates, 14.0%). *A. baumannii* exhibited 100% resistance to imipenem, meropenem, ceftriaxone, and ciprofloxacin, with 95.7% resistance to amikacin and 97.1% to ceftazidime. *K. pneumoniae* showed 91.7% resistance to imipenem, 100% to ceftriaxone, ciprofloxacin, and aztreonam, and 64.0% resistance to amikacin. *P. aeruginosa* demonstrated 87.5% resistance to imipenem and ciprofloxacin, 83.3% to ceftazidime, and 50.0% to amikacin. Colistin remained active against 97-100% of isolates across all three pathogens.

Conclusion: This study documents high levels of antimicrobial resistance among the predominant respiratory pathogens, particularly *A. baumannii* and *K. pneumoniae*, with carbapenem and cephalosporin resistance exceeding 90% in most cases. These findings highlight the urgent need for robust antimicrobial stewardship programs, enhanced infection control measures, and continuous surveillance to preserve remaining therapeutic options and prevent further spread of resistant organisms in hospital settings.

Keywords: Antimicrobial resistance, *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, multidrug resistance, Iran

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Introduction

Respiratory tract infections are a leading cause of

morbidity and mortality among hospitalized patients, particularly in intensive care units (ICU) where individuals are often immunocompromised and undergo

invasive procedures^{1,2}. The emergence of antimicrobial resistance has become a global public health crisis, severely limiting treatment options³⁻⁶.

Multidrug-resistant organisms, including carbapenem-resistant *Acinetobacter baumannii*, extended-spectrum beta-lactamase-producing *Klebsiella pneumoniae*, and carbapenem-resistant *Pseudomonas aeruginosa* are increasingly reported as causes of healthcare-associated respiratory infections⁷⁻¹². These pathogens exhibit a remarkable capacity to acquire resistance determinants, often leaving clinicians with limited therapeutic options such as colistin, which carries potential toxicity concerns.

Iran has witnessed alarming increases in antimicrobial resistance rates among Gram-negative bacteria, particularly in ICU settings¹³⁻¹⁶. However, resistance patterns vary significantly between institutions, necessitating local surveillance data to guide empirical antibiotic therapy and infection control policies. Understanding local epidemiology is essential for selecting appropriate empirical antibiotics, developing treatment guidelines, and identifying emerging resistance threats.

Therefore, this study aimed to determine the distribution of bacterial pathogens isolated from sputum cultures of hospitalized patients in ICU settings and to characterize their antimicrobial resistance patterns.

Methods

Study Design and Setting: This retrospective cross-sectional study was conducted in ICU at a tertiary care hospital in Tehran, Iran, from April 1, 2024 to March 1, 2025. All sputum samples submitted to the microbiology laboratory for culture and antimicrobial susceptibility testing from ICU patients with suspected respiratory tract infections during this period were included. The study protocol was approved by the institutional ethics committee [IR.SBMU.MSP.REC.1399.80].

Data Collection: Patient demographic and clinical data were retrospectively collected from laboratory records and hospital information systems. Collected variables included patient age, gender, hospital ward, admission and discharge dates, length of hospitalization, specimen collection date, and underlying medical conditions. Each isolate was

assigned a unique laboratory identification number to avoid duplication, and in cases where multiple samples were collected from the same patient, only the first isolate was included in the analysis.

Microbiological Procedures: Sputum samples were collected from patients with suspected respiratory infections and processed following standard microbiological protocols. Samples were cultured on blood agar, chocolate agar, and MacConkey agar, then incubated at 37°C for 24-48 hours. Bacterial isolates were identified using standard biochemical tests, including catalase, coagulase, oxidase, indole, urease, citrate utilization, and sugar fermentation tests, as well as automated systems according to routine laboratory procedures.

Antimicrobial Susceptibility Testing: Susceptibility testing was performed using the Kirby-Bauer disk diffusion method on Mueller-Hinton agar following Clinical and Laboratory Standards Institute (CLSI) guidelines¹⁷. A panel of antibiotics was tested, including aminoglycosides (amikacin, gentamicin), penicillins (ampicillin, penicillin G, piperacillin), beta-lactam combinations (piperacillin/tazobactam, co-amoxiclav), cephalosporins (cefazolin, cefoxitin, cefotaxime, ceftazidime, ceftizoxime, ceftriaxone), carbapenems (imipenem, meropenem), fluoroquinolones (ciprofloxacin, nalidixic acid), folate pathway inhibitors (co-trimoxazole), tetracyclines (doxycycline, tetracycline), polymyxins (colistin), macrolides (azithromycin, erythromycin), lincosamides (clindamycin), chloramphenicol, nitrofurantoin, fosfomycin, aztreonam, and glycopeptides/oxazolidinones (vancomycin, linezolid). Results were interpreted according to CLSI breakpoints (CLSI M100, 34th edition, 2024). Quality control was performed using the following reference strains: *Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC 25923, and *P. aeruginosa* ATCC 27853.

Data Analysis: Data were analyzed using SPSS version 26. Descriptive statistics, including frequencies, percentages, mean, and range were calculated. Resistance rates were calculated for each antibiotic-organism combination as the number of resistant isolates divided by the total number tested, expressed as a percentage.

Results

suspected respiratory tract infections were included, with a mean age of 74.5 years.

A total of 114 patients admitted to the ICU with

Bacterial Spectrum: Gram-negative bacteria

Table 1. Antimicrobial Resistance Profile of Major Bacterial Isolates.

Antibiotic	<i>A. baumannii</i> , n/N (n=50)	<i>K. pneumoniae</i> , n/N (n=26)	<i>P. aeruginosa</i> , n/N (n=16)
Amikacin	44/46 (95.7%)	16/25 (64.0%)	7/14 (50.0%)
Ampicillin	1/1 (100%)	10/10 (100%)	1/1 (100%)
Aztreonam	0/1 (0%)	13/13 (100%)	7/7 (100%)
Cefotaxime	5/5 (100%)	5/5 (100%)	0/1 (0%)
Ceftazidime	34/35 (97.1%)	13/13 (100%)	5/6 (83.3%)
Ceftriaxone	42/42 (100%)	24/24 (100%)	5/6 (83.3%)
Chloramphenicol	0/0 (0%)	0/0 (0%)	0/0 (0%)
Ciprofloxacin	50/50 (100%)	25/25 (100%)	14/16 (87.5%)
Clindamycin	1/1 (100%)	0/0 (0%)	0/0 (0%)
Colistin	1/33 (3.0%)	0/23 (0%)	0/15 (0%)
Co-Amoxiclav	4/4 (100%)	20/20 (100%)	1/1 (100%)
Co-Trimoxazole	34/36 (94.4%)	18/19 (94.7%)	0/2 (0%)
Doxycycline	6/41 (14.6%)	9/25 (36.0%)	0/1 (0%)
Erythromycin	1/1 (100%)	0/0 (0%)	0/0 (0%)
Gentamicin	12/34 (35.3%)	9/10 (90.0%)	3/5 (60.0%)
Imipenem	49/49 (100%)	22/24 (91.7%)	14/16 (87.5%)
Linezolid	0/0 (0%)	0/0 (0%)	0/0 (0%)
Penicillin G	1/1 (100%)	0/0 (0%)	0/0 (0%)
Piperacillin	21/22 (95.5%)	7/7 (100%)	7/13 (53.8%)
Piperacillin/Tazobactam	2/2 (100%)	7/7 (100%)	1/2 (50.0%)
Tetracycline	12/13 (92.3%)	3/4 (75.0%)	0/0 (0%)
Vancomycin	0/0 (0%)	0/0 (0%)	0/0 (0%)

NT: Not tested. n/N for *A. baumannii* against amikacin means that out of 46 isolates tested, 44 were resistant, giving a resistance rate of 95.7%.

Table 2. Class-Level Resistance Summary for Major Gram-Negative Pathogens.

Antibiotic Class	Representative Drug	<i>A. baumannii</i>	<i>K. pneumoniae</i>	<i>P. aeruginosa</i>
Carbapenems	Imipenem	100%	91.7%	87.5%
Cephalosporins (3rd gen)	Ceftazidime	97.1%	100%	83.3%
Fluoroquinolones	Ciprofloxacin	100%	100%	87.5%
Aminoglycosides	Amikacin	95.7%	64.0%	50.0%
Polymyxins	Colistin	3.0%	0%	0%
Tetracyclines	Doxycycline	14.6%	36.0%	0%*

*For *P. aeruginosa*, doxycycline testing was limited (only 1 isolate tested).

predominated, accounting for 97 isolates (85.1%), while Gram-positive organisms comprised 17 isolates (14.9%). The three most common pathogens were *A. baumannii* with 50 isolates (43.9%), *K. pneumoniae* with 26 isolates (22.8%), and *P. aeruginosa* with 16 isolates (14.0%), together accounting for 92 isolates (80.7%) of all positive cultures. The remaining 22 isolates (19.3%) included *Staphylococcus aureus*, *Escherichia coli*, *Enterococcus faecalis*, *Enterobacter aerogenes*, *Proteus mirabilis*, *Stenotrophomonas maltophilia*, Coagulase-negative Staphylococci, and *Staphylococcus pneumoniae*. Due to the low number of these remaining isolates, antimicrobial resistance data are reported only for the three main pathogens.

Antimicrobial Resistance Patterns: Table 1 presents the resistance profile for the three most clinically relevant organisms, showing the number of resistant isolates over the total number tested with percentage resistance in parentheses.

A. baumannii (n=50) exhibited near-complete resistance to most antibiotics, with 100% resistance to imipenem, ceftriaxone, and ciprofloxacin, and over 94% resistance to ceftazidime, amikacin, and co-trimoxazole, while colistin remained highly active with only 3.0% resistance and doxycycline showed

85.4% susceptibility.

K. pneumoniae (n=26) demonstrated similarly extensive resistance with 100% to ceftazidime, ceftriaxone, ciprofloxacin, and aztreonam, 91.7% to imipenem, and over 94% to co-trimoxazole, while colistin retained 100% susceptibility and doxycycline showed 64.0% susceptibility.

P. aeruginosa (n=16) showed 87.5% resistance to imipenem and ciprofloxacin, 83.3% to ceftazidime, and 50.0% to amikacin, with colistin maintaining 100% susceptibility.

Table 2 summarizes resistance rates for key antibiotic classes against the three major Gram-negative pathogens. Carbapenem resistance was alarmingly high across all three organisms, while third-generation cephalosporin and fluoroquinolone resistance were similarly extensive, each exceeding 83% in all pathogens. Aminoglycoside resistance varied considerably, highest in *A. baumannii* and lowest in *P. aeruginosa*. Notably, colistin was the only consistently active agent with 0-3% resistance across all pathogens, and doxycycline demonstrated moderate activity against *A. baumannii* and *K. pneumoniae*.

Discussion

The most important finding was the high level of

antimicrobial resistance among respiratory pathogens, particularly Gram-negative bacteria. *A. baumannii* was most frequently isolated, with considerable resistance to carbapenems, cephalosporins, and fluoroquinolones. *K. pneumoniae* and *P. aeruginosa* also demonstrated substantial resistance to these agents. Colistin retained activity against most isolates, though rare resistance was observed.

Our findings align with recent regional data showing similarly alarming resistance patterns. In a 2025 study from Tehran's ICUs by Ghamari et al., *Acinetobacter baumannii* exhibited >90% resistance to imipenem, meropenem, and ciprofloxacin, with colistin susceptibility preserved in 61.3% of isolates—comparable to our 97% colistin susceptibility, though our lower colistin resistance (3.0% vs. 38.7%) may reflect institutional differences in colistin use and infection control practices¹⁸. A 2025 study from Riyadh, Saudi Arabia, reported that 94% of *A. baumannii* isolates were carbapenem-resistant and 94% ciprofloxacin-resistant, with only 5% colistin resistance, closely mirroring our findings¹⁹.

Several factors may have contributed to the high resistance rates observed in this study, although our retrospective design could not directly measure them. Prior antibiotic exposure, particularly empirical use of broad-spectrum agents such as carbapenems and cephalosporins, might have exerted selective pressure favoring resistant strains. Prolonged mechanical ventilation, common in ICU settings, could also play a role by facilitating biofilm formation and repeated airway instrumentation. The advanced mean age of our patients (74.5 years) may be another contributing factor, as elderly individuals often have multiple comorbidities and repeated healthcare exposures.

Additionally, cross-transmission due to limited isolation capacity or inconsistent infection control practices might have amplified resistance spread. Without active surveillance for carbapenemase-producing organisms, colonized patients may have served as unrecognized reservoirs. Future prospective studies would be needed to clarify the relative contribution of each potential driver.

The clinical implications of these observations merit consideration. The limited susceptibility of these common Gram-negative pathogens to multiple antibiotic classes suggests that therapeutic options

may be restricted in many cases, potentially necessitating the use of agents such as colistin with associated toxicity concerns. The high level of carbapenem resistance observed among *A. baumannii* and *K. pneumoniae* isolates is particularly concerning as these antibiotics are often considered last-line agents for serious hospital-acquired infections. While colistin susceptibility was preserved in most isolates, recent reports indicate increasing colistin resistance globally, underscoring the urgent need for new therapeutic approaches, including combination therapy regimens to enhance efficacy and prevent further resistance emergence²⁰⁻²⁵. Reliance on a single agent with potential nephrotoxicity is far from ideal. These observations underscore the importance of local surveillance data in informing empirical antibiotic selection and the necessity for ongoing review of hospital antibiotic policies.

This study has several limitations that should be taken into account when interpreting the findings. First, the study did not specify clinical or microbiological criteria (e.g., fever, leukocytosis, radiographic infiltrates, Gram stain quality, or quantitative culture thresholds) to distinguish true respiratory infection from colonization, which may have led to the inclusion of colonized patients and potential overestimation of resistance rates among true pathogens. The retrospective design relied on existing laboratory records, and clinical outcome data were not available. Molecular characterization of resistance mechanisms was not performed. Data were collected from a single center, which may not reflect patterns in other institutions, and minimum inhibitory concentration determinations were not available for all isolates.

In conclusion, this study documents concerning levels of antimicrobial resistance among respiratory pathogens in a Tehran hospital, particularly among *A. baumannii*, *K. pneumoniae*, and *P. aeruginosa* isolates, where carbapenem and cephalosporin resistance was frequently observed. The preservation of colistin susceptibility in most isolates is notable, though ongoing monitoring for emerging resistance to this last-line agent is essential.

Conclusion

These findings underscore the critical need for robust antimicrobial stewardship programs, strict infection

control measures to prevent cross-transmission, and continuous surveillance of resistance patterns at both institutional and regional levels. Future research incorporating molecular characterization of resistance mechanisms and clinical outcome data would provide valuable insights to guide evidence-based treatment strategies and infection prevention efforts.

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None.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

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