

# Antimicrobial Sensitivity and Resistance Trends in Bacterial Respiratory Isolates from Adults with Lower Respiratory Tract Infections

Sadia Talib, Syeda Hira Abid, Umber Adnan, Chahat Hussain, Shomaila Malik, Fatima Sana

## ABSTRACT

**Objective:** To characterize the bacteriological profile and antimicrobial resistance patterns of respiratory isolates from adults with LRTIs at a tertiary care hospital in Karachi, Pakistan.

**Methods:** A retrospective observational study was conducted at Combined Military Hospital (CMH) Malir, Karachi, from October 2024 to March 2025. Of 112 symptomatic hospitalized adults evaluated, 67 provided adequate respiratory specimens. Of these, 24 (36%) were Tuberculosis (TB) positive and were excluded from bacterial culture analysis. The remaining 43 (64%) underwent bacterial culture. Isolates were identified using standard biochemical methods. Antimicrobial susceptibility testing followed CLSI guidelines (M100, 36th edition; M07, 12th edition), with broth microdilution exclusively for colistin. SPSS version 25 was used for statistical analysis.

**Results:** Gram-negative bacteria accounted for 88% of isolates. *Acinetobacter baumannii* (35%), *Klebsiella pneumoniae* (21%), and *Pseudomonas aeruginosa* (14%) predominated. All Gram-positive isolates were methicillin-resistant *Staphylococcus aureus* (MRSA, 11%), susceptible to linezolid and vancomycin. *A. baumannii* showed 80% carbapenem resistance; *K. pneumoniae* showed 77% resistance to fluoroquinolones and co-trimoxazole, while 67% *P. aeruginosa* isolates were carbapenem-resistant. Prior antibiotic use (49%), smoking (46%), and COPD (19%) were common risk factors.

**Conclusion:** High resistance among respiratory Gram-negative pathogens underscores the need for antimicrobial stewardship, culture-guided prescribing, and continuous local surveillance.

**Keywords:** *Acinetobacter baumannii*; Antimicrobial resistance; Antimicrobial stewardship; Colistin resistance; Lower respiratory tract infections; Methicillin-resistant *Staphylococcus aureus*; Pakistan

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## INTRODUCTION

Lower respiratory tract infections (LRTIs) continue to be a leading cause of infectious disease-related illness and death worldwide, despite progress in antimicrobial treatments and vaccination efforts. According to the Global Burden of Disease (GBD) Study 2023, LRTIs caused around 2.18 million deaths in 2021: with South and Southeast Asia and sub-Saharan Africa among the most affected regions.<sup>1</sup> These infections also continue to contribute substantially to disability-adjusted life years (DALYs), highlighting their sustained public health importance. The continued burden of LRTIs reflects their substantial contribution to both mortality and overall disease burden. This burden is particularly relevant in healthcare settings, where patients may require antimicrobial treatment for suspected or confirmed bacterial infections. Consequently, timely identification of bacterial pathogens and selection of appropriate antimicrobial therapy remain important aspects of LRTI management. The increasing prevalence of antimicrobial resistance (AMR) has further complicated the management of respiratory infections. Estimates indicate that resistant bacterial infections directly caused more than 1.5 million deaths in 2019, with respiratory pathogens

accounting for a substantial proportion of this burden.<sup>2</sup> The emergence of resistance reduces the effectiveness of commonly used antimicrobial agents and can make the selection of appropriate treatment increasingly difficult, particularly when therapy needs to be initiated before definitive microbiological and susceptibility results are available. The continuing increase in AMR therefore represents an important challenge in the management of bacterial respiratory infections, where delays or limitations in effective antimicrobial therapy may further complicate clinical care. Forecasts suggest that the global impact of AMR will continue to rise over the coming decades, with approximately 39 million deaths projected between 2025 and 2050 if such trends persist. Lower respiratory infections are expected to remain among the most significant contributors to AMR-associated mortality.<sup>3</sup> These projections emphasize the continuing need for surveillance of AMR and for reliable susceptibility data to support appropriate antimicrobial selection. Reflecting this concern, the World Health Organization (WHO) revised its Bacterial Priority Pathogens List in 2024, designating carbapenem-resistant *Klebsiella pneumoniae* and *Acinetobacter baumannii* as critical-priority organisms requiring urgent attention because of their rapid dissemination, high mortality, and limited therapeutic options.<sup>4</sup> The inclusion of these organisms in the critical-priority category highlights the particular concern surrounding carbapenem resistance among Gram-negative-pathogens. Their presence in respiratory infections can substantially limit available treatment options and further complicate empirical antimicrobial therapy. Consequently, monitoring the occurrence of these organisms and their antimicrobial susceptibility patterns is particularly important in healthcare settings where resistant pathogens are encountered.

Lower respiratory tract infections encompass several clinical syndromes, including community-acquired pneumonia (CAP), ventilator-associated pneumonia (VAP), hospital-acquired pneumonia (HAP) and acute exacerbations of chronic obstructive pulmonary disease (AECOPD). Although the microbial spectrum varies according to the clinical setting, resistant Gram-negative bacteria have become increasingly predominant among hospitalized and critically ill patients. The organisms responsible for infection may differ according to the nature of the underlying illness and the healthcare setting in which infection develops. This variation is particularly relevant in hospitalized patients, where healthcare exposure and the severity of illness may be accompanied by a greater likelihood of infection with resistant bacterial pathogens.

Members of the ESKAPE group, particularly *A. baumannii*, *K. pneumoniae*, and *Pseudomonas aeruginosa*, are frequently isolated from severe respiratory infections and are associated with poor clinical outcomes. These organisms are of particular concern because of their prominent role among multidrug-

resistant Gram-negative-pathogens and the consequent challenges they pose for antimicrobial treatment. Data from a tertiary care intensive care unit in Peshawar highlighted that *K. pneumoniae* (21.7%), *A. baumannii* (20.7%), and *P. aeruginosa* (17.4%) were the most frequently recovered multidrug-resistant organisms among critically ill patients.<sup>5</sup> The predominance of these organisms in a Pakistani tertiary care setting provides relevant local context for evaluating the bacterial profile and antimicrobial resistance patterns of respiratory isolates in other tertiary care institutions. Treatment of these infections has become increasingly challenging because of the widespread emergence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) organisms. The efficacy of carbapenems, which were formerly considered an important treatment option for serious Gram-negative infections, has been significantly diminished by resistance mediated by carbapenemase enzymes, including New Delhi metallo- $\beta$ -lactamase (NDM), *Klebsiella pneumoniae* carbapenemase (KPC), and OXA-48.<sup>6</sup> The emergence of these resistance mechanisms is of particular concern because it further narrows the range of effective antimicrobial options available for infections caused by MDR Gram-negative organisms. In addition, the emergence of plasmid-mediated colistin resistance through the *mcr-1* gene threatens the effectiveness of one of the few remaining treatment options for carbapenem-resistant pathogens. Colistin has been used as an important therapeutic option against infections caused by highly resistant Gram-negative organisms, making the emergence of resistance to this agent particularly concerning. The presence of transferable resistance mechanisms may further compromise treatment options in patients infected with organisms that are already resistant to multiple antimicrobial classes. In Pakistani clinical isolates, the existence of this resistance mechanism raises additional concerns regarding future therapeutic choices.<sup>7</sup> These findings emphasize the importance of continued susceptibility surveillance, particularly for organisms in which resistance to commonly used and last-resort antimicrobial agents may coexist.

Methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the important Gram-positive bacteria associated with healthcare-related pneumonia. Compared with methicillin-susceptible strains, MRSA infections are associated with prolonged hospitalization, greater mortality and higher healthcare costs.<sup>8</sup> The presence of MRSA among respiratory pathogens therefore represents an additional consideration in the management of hospitalized patients with LRTIs. Although glycopeptides and oxazolidinones generally remain active against MRSA, resistance to fluoroquinolones is widespread, limiting the reliability of empirical fluoroquinolone-based therapy in suspected MRSA respiratory infections. Consequently, identification of MRSA and knowledge of its local susceptibility profile remain important when selecting antimicrobial therapy for patients

with suspected healthcare-associated respiratory infections. The likelihood of isolating MDR pathogens is influenced by several patient-related and healthcare-associated factors. Previous exposure to antibiotics, prolonged hospitalization, mechanical ventilation, chronic respiratory disease, and greater illness severity have consistently been identified as independent predictors of MDR bacterial infection in patients with LRTIs.<sup>9</sup> These factors may influence both the likelihood of acquiring resistant organisms and the complexity of subsequent antimicrobial treatment. Previous antibiotic exposure is particularly relevant in patients presenting with respiratory infections, as prior treatment may influence the organisms recovered and their susceptibility profiles. Similarly, prolonged hospitalization and mechanical ventilation represent important healthcare-associated circumstances in which resistant pathogens may be encountered. In Pakistan, additional environmental exposures, including tobacco smoking and biomass fuel combustion, further impair respiratory defense mechanisms and may increase susceptibility to recurrent and difficult-to-treat respiratory infections.

The challenge is compounded by healthcare system limitations within Pakistan. Easy access to antibiotics without prescription, inconsistent implementation of antimicrobial stewardship programs (ASPs), and inadequate microbiology laboratory capacity continue to encourage inappropriate antimicrobial use. These challenges can contribute to inappropriate empirical prescribing and make it more difficult to ensure that antimicrobial treatment is aligned with the resistance pattern of locally circulating organisms. Recent surveillance from Karachi identified *K. pneumoniae* and *S. aureus* as predominant respiratory pathogens among mortality cases, yet institution-specific susceptibility data remain limited, particularly for military tertiary care hospitals.<sup>10</sup> Since empirical antimicrobial therapy relies heavily on local resistance patterns, periodic surveillance is essential for optimizing treatment recommendations and supporting stewardship initiatives. Institution-specific data are particularly useful because they provide clinicians with information on the organisms encountered in their own patient population and their corresponding susceptibility profiles. The objective of the current study was to characterize the bacterial profile and antibiotic susceptibility patterns of respiratory isolates obtained from adult patients with lower respiratory tract infections at Combined Military Hospital (CMH) Malir, Karachi. The study aimed to identify the predominant bacterial pathogens and determine their antimicrobial resistance patterns including resistance to commonly used and critically important antimicrobial agents. The findings were intended to provide institution-specific susceptibility data that may assist clinicians in selecting appropriate empirical antimicrobial therapy and support antibiotic stewardship and infection control initiatives within the hospital.

## METHODOLOGY

This retrospective observational study was carried out from October 2024 to March 2025 at the Combined Military Hospital (CMH) Malir, a tertiary care hospital in Karachi, Pakistan. The Institutional Review Board granted ethical permission (IRB approval File# 161/2025Trg/ERC CMH). Patient confidentiality was maintained in compliance with the Declaration of Helsinki. Convenience sampling was used because the study was retrospective in nature and had a limited study duration. All eligible adult patients admitted to the inpatient respiratory and general medicine wards of CMH Malir during the study window were systematically screened for inclusion. Adult patients ( $\geq 18$  years) admitted with clinical and radiological features of LRTI, including fever, productive cough, and chest radiographic evidence of pulmonary consolidation were included. Respiratory specimens included expectorated sputum (37%), bronchoalveolar lavage (BAL) (31%), Nasobronchial lavage (19%), and endobronchial washings (12%). Exclusion criteria were confirmed pulmonary tuberculosis, inadequate or salivary specimens (Murray–Washington criteria:  $<25$  polymorphonuclear leukocytes or  $>10$  squamous epithelial cells per low-power field), and patients with incomplete clinical data. All specimens underwent Gram staining for adequacy assessment and direct smear microscopy for acid-fast bacilli (AFB) prior to culture. All included samples were inoculated on blood, chocolate, and MacConkey agar and incubated aerobically at  $35 \pm 2^\circ\text{C}$  for 24–48 hours. BAL specimens were also cultured semi-quantitatively according to standard guidelines. A pure culture from sputum was considered clinically significant. Isolated organisms were identified using standard biochemical tests, including oxidase, catalase, triple sugar iron (TSI), citrate utilization, urease, indole production, and motility tests. Gram-positive cocci were further characterized using coagulase and DNase tests. The cefoxitin disk diffusion test was used to confirm MRSA according to the Clinical and Laboratory Standards Institute (CLSI) standards.

Antimicrobial susceptibility testing (AST) was carried out in strict compliance with published guidelines from the CLSI.<sup>12</sup> Mueller-Hinton agar (MHA) was used for disk diffusion. Zone diameters were interpreted against CLSI-defined breakpoints. Colistin minimum inhibitory concentration (MIC) was determined exclusively by the broth microdilution (BMD) method using cation-adjusted Mueller-Hinton broth (CAMHB), consistent with CLSI M07 recommendations and the CLSI-endorsed position that disk diffusion is unreliable for colistin. A standardized inoculum of  $5 \times 10^5$  CFU/mL was prepared. Plates were incubated for 16–20 hours at  $35 \pm 2^\circ\text{C}$ . Susceptibility breakpoints were defined as follows: MIC  $>2$  mg/L, resistant; MIC  $=2$  mg/L, susceptible (CLSI M100, 36th edition). Quality control was performed using *Escherichia coli* ATCC 25922 in accordance with CLSI standards.

Ampicillin (AMP), amoxicillin–clavulanic acid (AMC), cefepime, ceftazidime (CAZ), ciprofloxacin (CIP), co-trimoxazole (COT), ceftriaxone (CRO), imipenem (IMP), levofloxacin (LEV), meropenem (MEM), piperacillin–tazobactam (TZP), gentamicin (GEN), amikacin (AK), doxycycline (DOX), colistin (COL), and linezolid (LNZ). Vancomycin (VAN) and cloxacillin (CLO) were tested for all bacterial isolates as per CLSI guidelines. Descriptive statistics were used throughout. Frequencies and percentages were calculated for all categorical variables. Statistical analysis was performed using SPSS version 25.

## RESULTS

Of the 112 symptomatic hospitalized patients evaluated, 67 (60%) provided adequate respiratory specimens for microbiological processing, while 45 (40%) provided specimens that were either salivary or otherwise inadequate and were therefore excluded. Prior antibiotic use was documented in 55 (49%) patients. Among the recorded comorbidities, chronic obstructive pulmonary disease (COPD) was the most common, present in 21 (19%) patients, followed by diabetes mellitus in 18 (16%). Interstitial lung disease (ILD) and chronic kidney disease (CKD) were each documented in 9 (8%) patients. The distribution of patient history and comorbidities is presented in Table 1. Of these 67 adequate specimens, 24 (36%) were TB-positive and were excluded from subsequent bacterial culture analysis. The remaining 43 specimens (64%) underwent bacterial culture, and bacterial growth was recovered from all 43, yielding 43 bacterial isolates for antimicrobial susceptibility testing. Demographically, 45 males (67%) and 22 females (33%) were included, with the 61–80-year age group predominating (45%). Current smoking was documented in 46% of patients, while 23% were ex-smokers. Clinical diagnoses included chronic LRTI (36%), acute LRTI in COPD (31%), VAP (19%), and HAP (13%), as presented in Table 2. Gram-negative organisms accounted for 88% of isolates. *Acinetobacter baumannii* was the most prevalent pathogen (n=15, 35%), followed by *Klebsiella pneumoniae* (n=9, 21%), *Pseudomonas aeruginosa* (n=6, 14%), *Burkholderia* spp. (n=5, 11%), and *Escherichia coli* (n=3, 8%). All five Gram-positive isolates (11%) were confirmed as MRSA. *Acinetobacter baumannii* demonstrated high resistance: with 93% of isolates resistant to ceftazidime (CAZ), ceftriaxone (CRO) and piperacillin-tazobactam (TZP), 80% to the carbapenems imipenem (IMP) and meropenem (MEM) and to ciprofloxacin, 73% to levofloxacin and gentamicin, and 66% to amikacin and co-trimoxazole. Colistin retained near-universal activity, with 94% susceptibility; however, one isolate was confirmed colistin-resistant by broth microdilution. Doxycycline, one of the few oral treatment options available for less serious infections, retained partial activity, with 67% susceptibility.

*Klebsiella pneumoniae* showed 77% resistance to amoxicillin–clavulanate, ciprofloxacin, co-trimoxazole, and

levofloxacin, suggestive of extended-spectrum  $\beta$ -lactamase (ESBL) production, and 66% resistance to ceftazidime, ceftriaxone, and piperacillin–tazobactam. Carbapenem resistance reached 55%; one isolate was colistin-resistant. Amikacin retained the highest activity among the aminoglycosides, with 67% susceptibility, compared with

Table 1: Patient History, Sample Details and Comorbidities (n=112)

| Variable                                   | N (%)             |
|--------------------------------------------|-------------------|
| <b>Patient History &amp; Comorbidities</b> | <b>Total: 112</b> |
| History of prior antibiotic use            | 55 (49%)          |
| COPD                                       | 21 (19%)          |
| Diabetes mellitus                          | 18 (16%)          |
| Interstitial lung disease (ILD)            | 9 (8%)            |
| Chronic kidney disease (CKD)               | 9 (8%)            |
| <b>Sample Adequacy</b>                     | <b>Total: 112</b> |
| Adequate specimens (processed for culture) | 67 (60%)          |
| Inadequate/salivary specimens (excluded)   | 45 (40%)          |
| <b>Specimen Type (n=67)</b>                |                   |
| Expectorated sputum                        | 25 (37%)          |
| Bronchoalveolar lavage (BAL)               | 21 (31%)          |
| Naso-bronchial lavage (NBL)                | 13 (19%)          |
| Endobronchial washings                     | 8 (12%)           |
| <b>Tb Status (n=67)</b>                    |                   |
| TB-positive (excluded)                     | 24 (36%)          |
| TB-negative (processed)                    | 43 (64%)          |

COPD=Chronic Obstructive Pulmonary Disease;  
ILD=Interstitial Lung Disease; CKD=Chronic Kidney Disease

Table 2: Demographic and Clinical Characteristics (n=67)

| Variable                              | N (%)    |
|---------------------------------------|----------|
| <b>Age (years)</b>                    |          |
| 20–40                                 | 15 (22%) |
| 41–60                                 | 22 (33%) |
| 61–80                                 | 30 (45%) |
| <b>Gender</b>                         |          |
| Male                                  | 45 (67%) |
| Female                                | 22 (33%) |
| <b>Clinical Diagnosis</b>             |          |
| Chronic LRTI                          | 24 (36%) |
| Acute LRTI in COPD                    | 21 (31%) |
| Ventilator-associated pneumonia (VAP) | 13 (19%) |
| Hospital-acquired pneumonia (HAP)     | 9 (13%)  |
| <b>Smoking History</b>                |          |
| Current smoker                        | 31 (46%) |
| Non-smoker                            | 21 (32%) |
| Ex-smoker                             | 15 (23%) |

LRTI=Lower Respiratory Tract Infection;  
COPD=Chronic Obstructive Pulmonary Disease;  
VAP=Ventilator-associated Pneumonia; HAP=Hospital-acquired Pneumonia

Table 3: Antimicrobial Resistance Profile of Bacterial Isolates (n=43)

| Antibiotic | <i>A. baumannii</i><br>15 (35%) | <i>K. Pneumonia</i><br>9 (21%) | <i>P. Aeruginosa</i><br>6 (14%) | <i>Burkholderia</i><br>5 (11%) | <i>E. coli</i><br>3 (8%) | MRSA<br>5 (11%) | Ref.     |
|------------|---------------------------------|--------------------------------|---------------------------------|--------------------------------|--------------------------|-----------------|----------|
| AMP        | NT                              | IR                             | IR                              | NT                             | 3 (100%)                 | 5 (100%)        | CLSI     |
| AMC        | IR                              | 7 (77%)                        | IR                              | NT                             | 2 (67%)                  | 5 (100%)        | CLSI     |
| CLO        | NT                              | NT                             | NT                              | NT                             | NT                       | 5 (100%)        | CLSI     |
| CAP        | 7 (46%)                         | 1 (11%)                        | 2 (33%)                         | 2 (40%)                        | 1 (33%)                  | 0 (0%)          | CLSI     |
| CAZ        | 14 (93%)                        | 6 (66%)                        | 2 (33%)                         | 2 (40%)                        | 2 (67%)                  | NT              | CLSI     |
| CIP        | 12 (80%)                        | 7 (77%)                        | 4 (67%)                         | NT                             | 2 (67%)                  | 3 (60%)         | CLSI     |
| CLI        | NT                              | NT                             | NT                              | NT                             | NT                       | 1 (20%)         | CLSI     |
| COT        | 10 (66%)                        | 7 (77%)                        | 2 (33%)                         | 0 (0%)                         | 2 (67%)                  | 2 (40%)         | CLSI     |
| CRO        | 14 (93%)                        | 6 (66%)                        | IR                              | NT                             | 2 (67%)                  | NT              | CLSI     |
| DOX        | 5 (33%)                         | 2 (22%)                        | IR                              | NT                             | 1 (33%)                  | 1 (20%)         | CLSI     |
| ERY        | NT                              | NT                             | NT                              | NT                             | NT                       | 2 (40%)         | CLSI     |
| GEN        | 11 (73%)                        | 4 (44%)                        | 4 (67%)                         | NT                             | 1 (33%)                  | 1 (20%)         | CLSI     |
| AK         | 10 (66%)                        | 3 (33%)                        | 4 (67%)                         | NT                             | 1 (33%)                  | 1 (20%)         | CLSI     |
| IMP        | 12 (80%)                        | 5 (55%)                        | 4 (67%)                         | NT                             | 1 (33%)                  | NT              | CLSI     |
| MEM        | 12 (80%)                        | 5 (55%)                        | 2 (33%)                         | 0 (0%)                         | 1 (33%)                  | NT              | CLSI     |
| LEV        | 11 (73%)                        | 7 (77%)                        | 4 (67%)                         | 2 (40%)                        | 2 (67%)                  | NT              | CLSI     |
| TZP        | 14 (93%)                        | 6 (66%)                        | 4 (67%)                         | NT                             | 2 (67%)                  | NT              | CLSI     |
| Colistin*  | 1 (6%)                          | 1 (11%)                        | 4 (67%)                         | IR                             | 0 (0%)                   | NT              | CLSI-BMD |
| LNZ        | NT                              | NT                             | NT                              | NT                             | NT                       | 0 (0%)          | CLSI     |
| VAN        | NT                              | NT                             | NT                              | NT                             | NT                       | 0 (0%)          | CLSI     |

Values are presented as number (%) of resistant isolates. High resistance (=60%); \*=Colistin by broth microdilution only (CLSI M07 12th ed.); IR=Intrinsic Resistance; NT=Not Tested. AK=Amikacin; AMC=Amoxicillin-clavulanic acid; AMP=Ampicillin; CAP=Chloramphenicol; CAZ=Ceftazidime; CIP=Ciprofloxacin; CLI=Clindamycin; CLO=Cloxacillin; COT=Co-trimoxazole; CRO=Ceftriaxone; DOX=Doxycycline; ERY=Erythromycin; GEN=Gentamicin; IMP=Imipenem; LEV=Levofloxacin; LNZ=Linezolid; MEM=Meropenem; TZP=Piperacillin-tazobactam; VAN=Vancomycin. Cefoxitin resistant isolates were classified as methicillin resistant *Staphylococcus aureus* (MRSA= resistant to all  $\beta$ -lactams including penicillin, cephalosporins, carbapenems and monobactams)

56% for gentamicin. Meropenem and imipenem showed comparable carbapenem resistance rates (55%), precluding monotherapy with either agent in the majority of isolates. *Pseudomonas aeruginosa* exhibited 67% resistance (4 isolates) to levofloxacin, ciprofloxacin, gentamicin, amikacin, imipenem, and piperacillin-tazobactam. Notably, 4 of 6 isolates (67%) were colistin-resistant by broth microdilution. All MRSA isolates were susceptible to vancomycin and linezolid; 60% showed resistance to ciprofloxacin, while 40% showed resistance to co-trimoxazole and erythromycin (Table 3).

## DISCUSSION

Lower respiratory tract infections remain a major cause of morbidity and mortality, particularly among hospitalized adults, where antimicrobial resistance can substantially complicate treatment. In the present study, Gram-negative bacteria accounted for the majority of respiratory isolates, with *Acinetobacter baumannii*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* being the predominant pathogens. These organisms exhibited high levels of resistance to several commonly used antimicrobial agents, including

fluoroquinolones,  $\beta$ -lactams, aminoglycosides, and carbapenems. The predominance of resistant Gram-negative organisms in this study highlights the challenges faced in selecting appropriate empirical therapy for hospitalized patients with lower respiratory tract infections. The findings also emphasize the importance of obtaining adequate respiratory specimens and performing antimicrobial susceptibility testing to support subsequent treatment decisions, particularly in patients with prior antibiotic exposure or healthcare-associated infections.

*A. baumannii* was the most frequently isolated organism in the present study (35%) and demonstrated extensive resistance to  $\beta$ -lactam antibiotics, fluoroquinolones and carbapenems. The high level of resistance observed across multiple antimicrobial classes indicates a substantial degree of antimicrobial resistance among the *A. baumannii* isolates recovered from these hospitalized patients. In particular, the high resistance to carbapenems is concerning because these agents are important therapeutic options for serious infections caused by Gram-negative organisms. Similar findings have been reported from tertiary care hospitals in Pakistan, where *A. baumannii* has emerged as an important cause of

healthcare-associated infections with limited antimicrobial susceptibility. Jabeen et al. reported widespread multidrug resistance among bloodstream isolates of *A. baumannii*, while Shah et al. also identified high antimicrobial resistance rates among clinical isolates recovered from hospitalized patients in Peshawar, supporting the persistence of this organism as an important nosocomial pathogen in Pakistan.<sup>14,20</sup> The consistency of these observations across different Pakistani healthcare settings suggests that substantial antimicrobial resistance among *A. baumannii* is not restricted to a single institution. The predominance of this organism and its broad resistance profile in the present study therefore support the need for continued local susceptibility surveillance and culture-guided antimicrobial selection.

The high prevalence of *K. pneumoniae* (21%) observed in this study is also consistent with reports identifying this organism as a major respiratory pathogen in healthcare settings. Most isolates demonstrated resistance to fluoroquinolones, third-generation cephalosporins and cotrimoxazole, while more than half were resistant to carbapenems. Although molecular characterization and specific phenotypic testing were not performed in the present study, this resistance pattern is suggestive of extended-spectrum  $\beta$ -lactamase production with possible coexisting carbapenem resistance, findings that have been widely documented in Pakistani hospitals. Gondal et al. reported a significant burden of carbapenem-resistant Enterobacterales in a tertiary care hospital in Pakistan, while a systematic analysis from Southeast Asia also documented a considerable burden of multidrug-resistant *K. pneumoniae* similar to that seen in the current study.<sup>15,16</sup> The findings from the present study therefore add to the available evidence of substantial antimicrobial resistance among *K. pneumoniae* in tertiary care settings. This further reflects the limited usefulness of commonly relied-upon antimicrobial agents and reinforces the need for continued susceptibility surveillance and culture-guided treatment. An important observation in this study was the limited susceptibility of both *A. baumannii* and *K. pneumoniae* to several first-line antimicrobial agents. Although colistin retained activity against most isolates of *A. baumannii*, resistance was identified in one isolate, while one *K. pneumoniae* isolate was also resistant to colistin. Although the absolute number of resistant isolates was small, the detection of resistance is clinically significant because colistin is often reserved for infections caused by organisms with resistance to multiple other antimicrobial classes. The presence of resistance to this agent may further restrict therapeutic options when treatment alternatives are already limited. These findings underline the necessity for careful antimicrobial stewardship and routine susceptibility testing before initiating or modifying therapy. The value of culture-directed antimicrobial therapy has also been demonstrated by Altaf et al., who reported that culture and sensitivity results facilitated optimization and de-escalation of empirical

antimicrobial therapy in hospitalized patients, supporting more rational antibiotic use.<sup>21</sup> In the present setting, timely availability of susceptibility results may similarly assist clinicians in avoiding unnecessary exposure to broad-spectrum or last-resort antimicrobial agents and in tailoring treatment to the identified pathogen.

Among *P. aeruginosa* isolates, resistance to carbapenems, aminoglycosides, fluoroquinolones and piperacillin–tazobactam was common. Of particular concern, four of six isolates (67%) were resistant to colistin by broth microdilution. Although the present study did not investigate the underlying resistance mechanisms, similar findings have recently been reported in Pakistan. Ijaz et al. identified colistin-resistant *P. aeruginosa* among clinical isolates and highlighted the emergence of resistance determinants in the local setting.<sup>7</sup> The relatively high proportion of colistin-resistant *P. aeruginosa* observed in the present study is an important finding, particularly because susceptibility to this agent may become relevant when resistance to other antimicrobial classes is present. The use of broth microdilution for colistin susceptibility testing also provides greater confidence in this finding, as this method is recommended for determining susceptibility to polymyxins.<sup>11,12</sup> Continued surveillance of colistin susceptibility is therefore warranted, particularly in institutions where MDR Gram-negative organisms are frequently encountered. All Gram-positive isolates recovered in this study were methicillin-resistant *Staphylococcus aureus* (MRSA). Despite universal susceptibility to vancomycin and linezolid, resistance to ciprofloxacin was observed in 60% of isolates, indicating that fluoroquinolones are unreliable for empirical treatment when MRSA is suspected. These findings are consistent with the established epidemiology of MRSA, in which glycopeptides and oxazolidinones remain the principal therapeutic agents for serious respiratory infections. A recent network meta-analysis also demonstrated favorable clinical outcomes with linezolid in patients with MRSA pneumonia, although antibiotic selection should ultimately be guided by the patient's clinical condition and local susceptibility patterns.<sup>8,18</sup>

Several patient-related factors identified in the present study may have contributed to the high prevalence of resistant organisms. Nearly half of the patients had received antibiotics before specimen collection, while chronic obstructive pulmonary disease, smoking and diabetes mellitus were common underlying conditions. Previous antibiotic exposure is a well-recognized risk factor for the emergence and selection of multidrug-resistant pathogens, particularly in patients with healthcare-associated respiratory infections. Likewise, chronic respiratory disease and smoking impair mucociliary clearance and local host defense, predisposing patients to recurrent infection and repeated antimicrobial exposure. These observations are consistent with previous systematic reviews and studies evaluating risk factors for

multidrug-resistant lower respiratory tract infections and support the importance of careful prescribing in high-risk populations.<sup>9,19</sup> The findings of this study have important implications for clinical practice. The high frequency of carbapenem resistance among *A. baumannii*, *K. pneumoniae* and *P. aeruginosa* indicates that empirical use of carbapenems alone may not provide adequate coverage for severe hospital-acquired lower respiratory tract infections in our institution. Instead, empirical treatment should be guided by local epidemiological data and reviewed promptly once microbiological results become available. Routine preparation and regular updating of institutional antibiograms can assist clinicians in selecting appropriate empirical therapy while supporting antimicrobial stewardship initiatives. The benefits of culture-guided de-escalation have already been demonstrated in Pakistani hospitals and should be incorporated into routine clinical practice whenever feasible.<sup>21</sup> Another notable strength of this study is the CLSI-recommended standardized methods for antimicrobial susceptibility testing, including broth microdilution for colistin, which improves the accuracy of susceptibility reporting and strengthens confidence in the observed prevalence of colistin resistance.<sup>11,12</sup> Standardized laboratory procedures are essential for generating reliable susceptibility data and ensuring comparability between institutions. In the present study, adherence to established susceptibility testing standards strengthens the reliability of the reported antimicrobial resistance findings. The current study has certain limitations. First, it was carried out at a single tertiary care hospital with a relatively small number of culture-positive isolates, which may limit the generalizability of the findings. Second, its retrospective design relied on available clinical records, restricting assessment of treatment outcomes and mortality. Third, there was no molecular characterization of resistance mechanisms, such as plasmid-mediated colistin resistance genes, carbapenemases, and extended-spectrum  $\beta$ -lactamases. Consequently, resistance mechanisms could not be confirmed at the genetic level. Future multicenter prospective studies incorporating molecular epidemiology and patient outcome data would provide a more comprehensive understanding of antimicrobial resistance patterns in lower respiratory tract infections across Pakistan.

Overall, this study provides contemporary local surveillance data demonstrating the predominance of multidrug-resistant Gram-negative pathogens among hospitalized adults with lower respiratory tract infections. The observed resistance patterns emphasize the need for continuous microbiological surveillance, evidence-based empirical prescribing and effective antimicrobial stewardship programs to preserve the efficacy of currently available antimicrobial agents.

## CONCLUSION

This study demonstrates a high burden of antimicrobial resistance among bacterial respiratory pathogens isolated from hospitalized adults with lower respiratory tract infections

at CMH Malir, Karachi. Multidrug-resistant Gram-negative organisms, particularly *Acinetobacter baumannii*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*, predominated and showed considerable resistance across several commonly used antimicrobial classes including carbapenems. Colistin resistance was also observed, particularly among *P. aeruginosa*, further highlighting the limited therapeutic options thus available. All MRSA isolates remained susceptible to vancomycin and linezolid. These findings urgently demand robust antimicrobial stewardship programs to preserve the efficacy of available antimicrobial agents, and mandatory culture-guided antimicrobial selection. Multicenter surveillance is warranted to further characterize AMR patterns across Pakistan.

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### Authors Contribution:

**Sadia Talib:** Substantial contributions to the conception or design of work  
**Syeda Hira Abid:** Supervision and project administration including oversight of the research activity planning and execution  
**Chahat Hussain:** Acquisition, analysis and interpretation of data methodology  
**Umer Adnan:** Interpretation of data and methodology  
**Shomaila Malik:** Drafting the manuscript or revising it critically for important intellectual content  
**Fatima Sana:** Data collection

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