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Phenotypic Colistin Susceptibility Patterns among Carbapenem-Resistant Gram-Negative Bacterial Isolates in a Tertiary Care Centre in Central India

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ABSTRACT

Background:
The rapid emergence of carbapenem-resistant Gram-negative bacteria (CR-GNB) has become a major global public health concern. Colistin has re-emerged as a last-resort therapeutic option for infections caused by these multidrug-resistant pathogens. However, increasing reports of colistin resistance threaten its clinical utility.

Objectives:
To determine the phenotypic colistin susceptibility patterns among carbapenem-resistant Gram-negative bacterial isolates obtained from blood, urine, and pus samples in a tertiary care hospital.

Materials and Methods:
This hospital-based cross-sectional study was conducted in the Department of Microbiology, Index Medical College Hospital & Research Centre, Indore, from January 2022 to June 2025. A total of 312 non-duplicate carbapenem-resistant isolates were included. Colistin susceptibility was determined using the broth microdilution (BMD) method, in accordance with Clinical and Laboratory Standards Institute (CLSI) 2023 guidelines. Demographic and clinical data were analyzed using SPSS version 28.0.

Results:
Out of 312 carbapenem-resistant isolates, 56 (17.9%) were phenotypically resistant to colistin. *Klebsiella pneumoniae* constituted the predominant resistant species, followed by *Acinetobacter baumannii*. Colistin resistance was more frequently observed in blood culture isolates. The highest proportion of affected patients belonged to the 51–60-year age group. Favourable clinical outcomes were noted in 80.4% of patients with colistin-resistant infections.

Conclusion:
The notable prevalence of phenotypic colistin resistance among carbapenem-resistant isolates underscores the importance of routine MIC-based testing. Strict antimicrobial stewardship and continuous surveillance are essential to preserve the efficacy of this last-resort antibiotic.

Keywords:
Colistin resistance; Carbapenem-resistant organisms; Broth microdilution; Antimicrobial susceptibility testing; Tertiary care hospital.

INTRODUCTION

Antimicrobial resistance (AMR) has emerged as one of the most pressing threats to global health, compromising the effective treatment of a wide range of infectious diseases. Among resistant pathogens, carbapenem-resistant Gram-negative bacteria (CR-GNB) pose a particularly serious challenge due to their ability to evade multiple classes of antibiotics and cause severe, difficult-to-treat infections with high morbidity and mortality rates[1].

Carbapenems have long been considered the cornerstone for managing severe infections caused by multidrug-resistant Gram-negative organisms. However, the increasing prevalence of carbapenem resistance has forced clinicians to rely on older antibiotics such as colistin. Colistin (polymyxin E), initially introduced in the 1950s, fell out of favor due to concerns regarding nephrotoxicity and neurotoxicity[2]. Nevertheless, its potent activity against multidrug-resistant organisms, including *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa*, has led to its resurgence as a last-resort therapeutic agent[3].

The renewed use of colistin has been accompanied by a gradual but alarming rise in resistance. Colistin resistance significantly limits therapeutic options and is associated with poor clinical outcomes[4]. Accurate laboratory detection of colistin resistance is therefore critical for guiding appropriate therapy and preventing treatment failure. However, conventional susceptibility testing methods such as disc diffusion and gradient diffusion tests are unreliable for colistin due to its poor diffusion properties[5]. Consequently, broth microdilution (BMD) remains the reference standard recommended by the Clinical and Laboratory Standards Institute (CLSI)[6].

Data on colistin resistance among carbapenem-resistant isolates in India remain limited and region-specific. Understanding local resistance patterns is crucial for informed clinical decision-making and antimicrobial stewardship. The present study was undertaken to evaluate phenotypic colistin susceptibility among carbapenem-resistant Gram-negative isolates recovered from various clinical specimens in a tertiary care hospital in central India.

MATERIALS AND METHODS

Study Design and Setting

A hospital-based cross-sectional study was conducted in the Department of Microbiology, Index Medical College Hospital & Research Centre, Indore, Madhya Pradesh, India, over a period of three and a half years from January 2022 to June 2025.

Study Population

During the study period, a total of 19,074 clinical specimens comprising urine, blood, and pus samples were received for culture and antimicrobial susceptibility testing. From these, 312 non-duplicate Gram-negative bacterial isolates demonstrating resistance to at least one carbapenem were included in the study.

Inclusion and Exclusion Criteria

Inclusion criteria:

- Gram-negative isolates resistant to at least one carbapenem (imipenem, meropenem, or ertapenem)
- Isolates obtained from blood, urine, or pus samples

Exclusion criteria:

- Duplicate isolates from the same patient
- Environmental or surveillance isolates

Identification and Antimicrobial Susceptibility Testing

Bacterial identification and initial antimicrobial susceptibility testing were performed using the VITEK 2 Compact automated system (bioMérieux, France). Carbapenem resistance was defined according to CLSI 2023 breakpoints, with imipenem or meropenem MIC ≥4 µg/mL and ertapenem MIC ≥2 µg/mL[6].

Colistin Susceptibility Testing

Colistin susceptibility was determined using the broth microdilution method with cation-adjusted Mueller–Hinton broth, following CLSI recommendations. Colistin MIC values were interpreted as follows:

- MIC ≤2 µg/mL: susceptible
- MIC ≥4 µg/mL: resistant[6]

Data Collection and Statistical Analysis

Demographic and clinical data were retrieved from hospital records. Statistical analysis was performed using SPSS version 28.0. Categorical variables were expressed as frequencies and percentages.

RESULTS

Among the 312 carbapenem-resistant Gram-negative isolates analyzed, 56 (17.9%) demonstrated phenotypic resistance to colistin by broth microdilution testing. The remaining 256 isolates (82.1%) were susceptible.

Distribution of Colistin-Resistant Isolates

Klebsiella pneumoniae accounted for the highest proportion of colistin-resistant isolates, followed by *Acinetobacter baumannii* and *Pseudomonas aeruginosa*. Blood samples yielded the highest number of colistin-resistant isolates, followed by urine and pus samples.

Demographic Characteristics

The majority of patients with colistin-resistant infections belonged to the 51–60-year age group (33.9%), followed by the 41–50-year group (23.2%). A male predominance was observed.

Clinical Outcomes

Favourable outcomes were noted in 80.4% of patients with colistin-resistant infections. No significant association was observed between colistin resistance and prolonged hospital stay or repeated hospital admissions in the study population.

Discussion

The prevalence of colistin resistance observed in this study (17.9%) is a cause for concern and aligns with reports from other tertiary care centers in India and abroad[7–9]. *Klebsiella pneumoniae* emerged as the predominant colistin-resistant pathogen, consistent with its known propensity to acquire multiple resistance mechanisms[10].

The reliance on broth microdilution for colistin susceptibility testing strengthens the validity of our findings, as alternative methods are known to yield unreliable results[5]. The favourable clinical outcomes observed may reflect timely detection and judicious antimicrobial use, emphasizing the role of microbiology laboratories in guiding therapy.

The rising trend of colistin resistance underscores the urgent need for antimicrobial stewardship programs aimed at optimizing antibiotic use and preventing further resistance development[11].

CONCLUSION

This study demonstrates a significant prevalence of phenotypic colistin resistance among carbapenem-resistant Gram-negative isolates in a tertiary care hospital. Routine implementation of MIC-based colistin susceptibility testing, coupled with robust antimicrobial stewardship and continuous surveillance, is essential to preserve the effectiveness of this last-resort antibiotic.

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