

Original Research Article

Study of carbapenem resistance in patients admitted to MICU in a tertiary care hospital

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ABSTRACT

Background: Carbapenem Resistance is defined as gram negative bacteria that are resistant to one or all of the following carbapenems: ertapenem, meropenem, imipenem or doripenem. Recognizing the risk of resistance to carbapenem especially in the most vulnerable patients and the early detection of specific carbapenem-resistance mechanisms are critical to reducing the risk of mortality, length of hospitalization and associated costs. So, this study is done to detect carbapenem resistance in patients admitted in MICU.

Methods: A Retrospective study was carried out for one year from period of January 2023-January 2024 in the Department of Microbiology, Government Medical College, Aurangabad. Total 1941 samples were received from patients admitted in the medical intensive care unit (MICU). The isolates were identified using standard microbiological methods. Antimicrobial susceptibility was performed using the Kirby-Bauer disc diffusion technique and interpreted as per CLSI 2023 standards.

Results: Out of 1941 samples, total gram-negative isolates were 775 (40%), 478 samples were sterile and rest were gram positive organism. Out of gram-negative organism *Acinetobacter baumannii* (26.58%), *Escherichia coli* (11.74%), *Klebsiella pneumoniae* (32.25%) and *Pseudomonas aeruginosa* (29.41%) were isolated. In case of *Acinetobacter*, Carbapenem resistant is high and is around 90%, in *Escherichia coli* it is 74%, in *Klebsiella* and *Pseudomonas* it is 83% and 44% respectively.

Conclusions: In our study *Acinetobacter baumannii* shows high carbapenem resistance. The efficient ways to avoid infection include strict adherence to infection prevention and control practices like hand hygiene techniques and bundle care approach.

Keywords: Carbapenem resistance, Carbapenems, Gram negative bacilli, MICU

INTRODUCTION

According to the centers for disease control and prevention (CDC), CRE is defined as either Enterobacterales that produce a carbapenem or Enterobacterales that test resistant to at least one carbapenem antibiotic (i.e., minimum inhibitory concentrations of ≥ 4 $\mu\text{g/ml}$ for doripenem, meropenem and imipenem and ≥ 2 $\mu\text{g/ml}$ for ertapenem).¹ The five-membered β -lactam ring of carbapenems is different from that of penicillin in that it is unsaturated and contains a carbon atom instead of a

sulphur atom. For the most part, this special molecular structure provides exceptional stability against β -lactamases, particularly extended spectrum β -lactamases (ESBLs).^{2,12}

Classes A, B, C and D are the four main classes of β -lactamases identified by the Ambler categorization system, which is based on amino acid homology. While class B β -lactamases (metallo-beta-lactamases or MBLs) need zinc to function, classes A, C and D β -lactamases (serine β -lactamases) all share a serine residue in their

active site. Because they are healthcare-associated pathogens, Enterobacterales belonging to classes A, B and D are clinically significant and impart carbapenem resistance.¹

The Carbapenem group of drugs comprises ertapenem, imipenem, meropenem and doripenem. Carbapenem resistance is developed by inadequate carbapenem binding to penicillin binding protein, which is followed by porin loss, overexpression of efflux pumps and overproduction of expanded spectrum beta lactamases. The gene that produces carbapenemase is located on transposons and is easily transferred horizontally to other Enterobacteriaceae and Non-Enterobacteriaceae, such as *Pseudomonas* and *Acinetobacter* species. This increases the risk of resistance spreading among susceptible isolates. The resistance to carbapenem is plasmid mediated.³

Carbapenem-resistant bacteria, particularly CRE, are emerging and spreading quickly, posing a major threat to public health. Rapid spread and a high death rate are linked to these CRE infections. Given the substantial increase in CRE prevalence, early identification is crucial.⁴

Therefore, the main goal is to investigate carbapenem resistance in MICU patients in order to manage treatment, stop the spread of infections and lower mortality and morbidity.

METHODS

A one-year retrospective study was conducted in the Department of Microbiology at Government Medical College, Aurangabad, between January 2023 and January 2024. Total 1941 samples were received from patients admitted in the medical intensive care unit. The isolates were obtained from various clinical specimens like sputum, urine, tracheal aspirate and blood.

Inclusion criteria

All samples (sputum, urine, tracheal aspirate and blood) received from MICU was included in the study.

Exclusion criteria

Samples received from OPD and other wards were excluded from the study.

The isolates were identified using standard conventional biochemical testing methods. Following identification, Kirby-Bauer disc diffusion testing was used to test the isolates for antimicrobial susceptibility. The drugs which are used by Kirby-bauer disc diffusion method were Gentamicin (10 mcg), Ampicillin (10 mcg), Cefuroxime 30mcg), Cefotaxime (30 mcg), Ceftazidime (30 mcg), Amikacin (30 mcg), Ciprofloxacin (5 mcg), Imipenem (10 mcg), Meropenem (10 mcg), ertapenem (10 mcg). Screening for carbapenem resistance was done using

meropenem (10 µg) and imipenem (10 µg) and ertapenem (10 µg) disc by Disc diffusion testing.

The antibiotic discs were procured from Hi-Media. The zone diameters were interpreted as per CLSI 2023. *E. coli* ATCC 25922 was used as control for the Kirby-Bauer disc diffusion method. Following are the zone diameters according to CLSI 2023 shown in Table 1.

Ethical approval

Ethical approval was taken before the start of study.

RESULTS

Out of 1941 samples, total gram-negative isolates were 775 (40%), 478 samples were sterile and rest were gram positive organism as shown in Figure 1.

Out of gram-negative organism *Acinetobacter baumannii* (26.58%), *Escherichia coli* (11.74%), *Klebsiella pneumoniae* (32.25%) and *Pseudomonas aeruginosa* (29.41%) were isolated as shown in Figure 2.

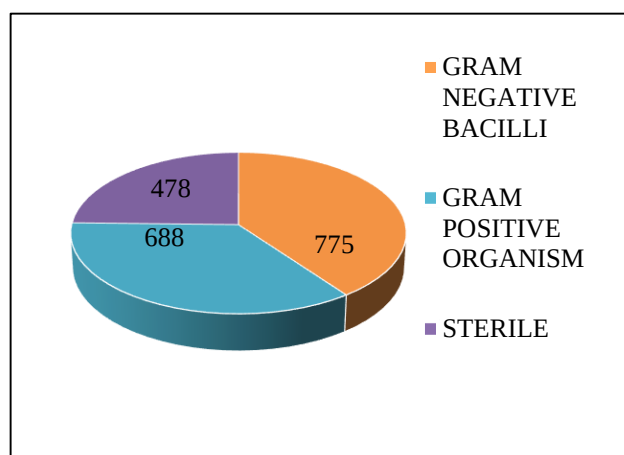


Figure 1: Number of isolates from different samples.

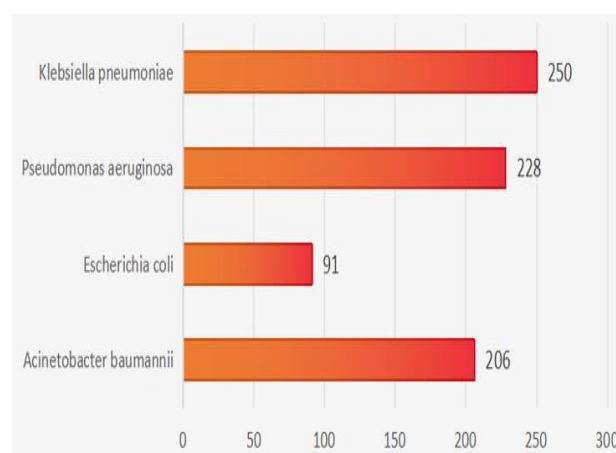


Figure 2: Number of gram-negative organisms isolated.

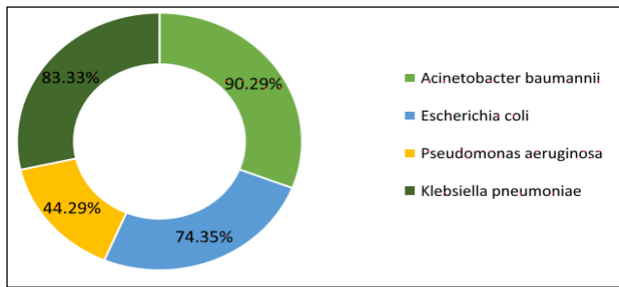


Figure 3: Percentage of carbapenem resistance.

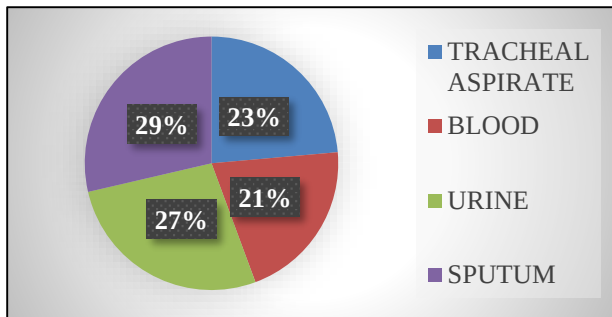


Figure 4: Specimen wise distribution of carbapenem resistant strains.

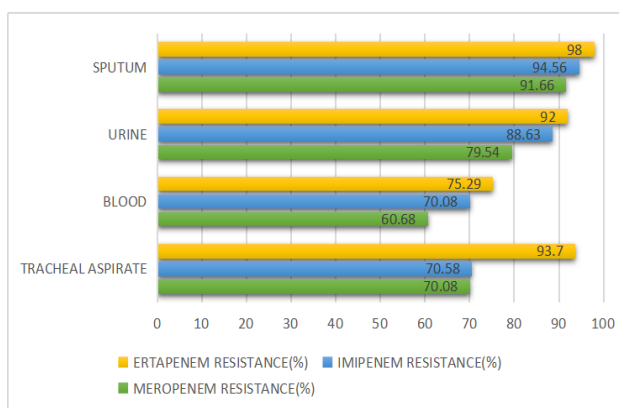


Figure 5: Detailed carbapenem resistant drugs in various sample.

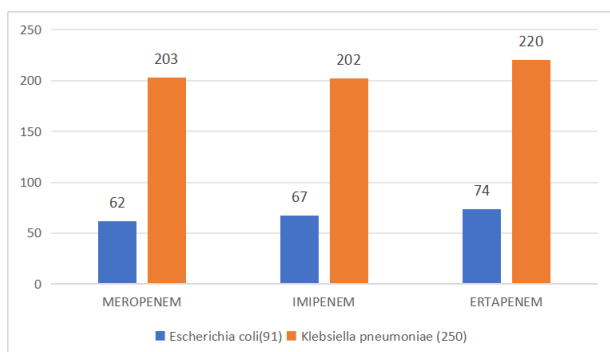


Figure 6: Comparison of carbapenem resistance in *Escherichia coli* and *Klebsiella pneumoniae*.

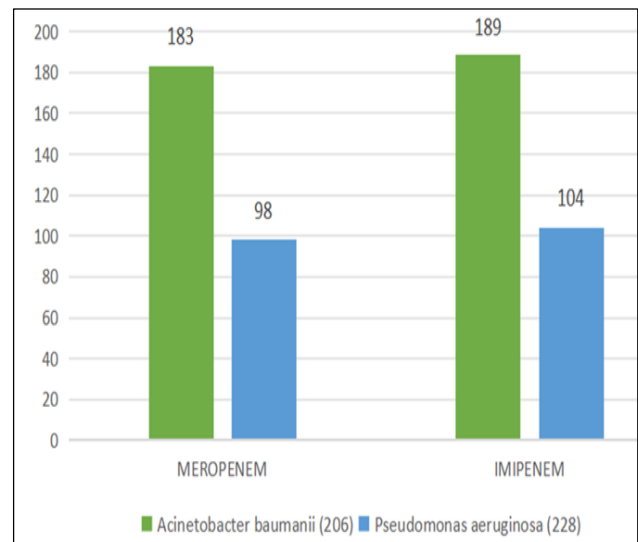


Figure 7: Comparison of carbapenem resistance in *Acinetobacter baumannii* and *Pseudomonas aeruginosa*.

In case of *Acinetobacter*, carbapenem resistance is high and is 90.29%, in *Klebsiella* it is 83.33%, in *Escherichia coli* and *Pseudomonas* it is 74.35% and 44.29% respectively as shown in Figure 3.

In our study we also observed 29% of isolates were recovered from sputum, 27% isolates from urine, 23% from tracheal aspirate and 21% from blood were carbapenem resistant as shown in Figure 4.

Unfortunately details regarding the outcome of the patients couldn't be studied which is one of the limitations of our study.

We also observed in sputum sample ertapenem resistance was high (98%) followed by imipenem (94.56%) and meropenem resistance (91.66%). In tracheal sample ertapenem resistance is 93.7% followed by imipenem (70.58%) and meropenem (70%) resistance.

In urine and blood sample ertapenem resistance is 92% and 75%, imipenem resistance is 88% and 70% and meropenem resistance is 79% and 60% respectively as shown in Figure 5.

In case of Enterobacterales (*Escherichia coli* and *Klebsiella pneumoniae*) ertapenem resistance is high followed by imipenem and meropenem as shown in Figure 6.

In case of non-fermenters (*Acinetobacter baumannii* and *Pseudomonas aeruginosa*) in our study meropenem resistance was high in *Acinetobacter baumannii* as compared to *Pseudomonas aeruginosa* as shown in Figure 7.

Table 1: Zone diameters of carbapenems according to CLSI 2023.

	Resistant	Intermediate	Sensitive
Enterobacterales			
Meropenem	≤19 mm	20-22 mm	≥ 23 mm
Imipenem	≤19 mm	20-22 mm	≥ 23mm
Ertapenem	≤18 mm	19-21 mm	≥ 22mm
<i>Pseudomonas aeruginosa</i>			
Meropenem	≤15 mm	16-18 mm	≥ 19mm
Imipenem	≤15 mm	16-18 mm	≥ 19mm
<i>Acinetobacter baumannii</i>			
Meropenem	≤14 mm	15-17 mm	≥18 mm
Imipenem	≤18 mm	19-21 mm	≥22 mm

DISCUSSION

Increase in the indiscriminate use of antibiotics has led to emergence of multi-drug-resistant strains. Limited treatment options are available for treating these multi-drug-resistant strains. Most of the organisms carry drug resistant gene on transposon, which can easily spread from one organism to other.⁵ In our study carbapenem resistance is high in *Acinetobacter baumannii* i.e., 90 %. This Finding is supported by another study carried out by Tempe et al.⁶ In our study, the prevalence of Carbapenem resistance was found to be more in *Klebsiella pneumoniae* (83.33%) followed by *Escherichia coli* (74.35%) and *Pseudomonas aeruginosa* (44.29%). Similar finding was observed in study done by Sharma et al.⁷

Majority of the carbapenem resistant gram-negative organism were isolated from the sputum (29%) and urine sample (27%) followed by tracheal sample (23%) and blood (21%) sample. These findings were almost similar but not exact findings to study done by Kumar et al.⁸ In study done by Alizadeh et al, imipenem, carbapenem and ertapenem resistance were also high similar to our findings as shown in Figure 5.⁹ In study done by Elbadawi et al, the carbapenem resistance was almost high and was almost similar to our findings as shown in Figure 6.¹⁰ In our study meropenem resistance was high in *Acinetobacter baumannii* as compared to *Pseudomonas aeruginosa* as shown in Figure 7 but study done by Esther et al, meropenem resistance was seen high in case of *Pseudomonas aeruginosa* which was opposite of our finding.¹³ In our study imipenem resistance was high in case of *Acinetobacter baumannii* as compared to *Pseudomonas aeruginosa*. Similar findings were noted by study done by das et al.¹⁴

The present study was a single institutional study with the limited number of patients. We have not collected the details regarding the outcome of the patients.

CONCLUSION

In conclusion, gene transfer worldwide is causing a sharp rise in carbapenem-resistant gram-negative clinical

isolates. Serious measures, including as hand hygiene, contact precautions, appropriate medical waste disposal, and limited use of intrusive devices, are required to stop the spread of these germs.¹¹ To stop carbapenem-resistance from getting worse, the use of carbapenem antibiotics should be limited. This also emphasizes how crucial it is to strictly adhere to the antimicrobial stewardship program (AMSP).

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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