

RESEARCH ARTICLE

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Limited Therapeutic Options in *bla*_{NDM} and *bla*_{OXA-48} producing Carbapenem-resistant *Klebsiella pneumoniae*: Insights from a Cross-sectional Study

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Abstract

Carbapenem-resistant *K. pneumoniae* (CRKP), listed in the WHO 2024 priority, hydrolyzes β -lactam antibiotics, especially carbapenems, posing a significant challenge. Carbapenems are the last resort antibiotics for severe Gram-negative infections and are associated with increased mortality in ICUs and IPDs. This cross-sectional study at a tertiary hospital (April 2023-December 2024) included 375 multidrug-resistant (MDR) *K. pneumoniae* isolates with ertapenem MIC ≥ 8 μ g/mL. Carbapenemase genes were detected via conventional PCR. Bivariate analysis examined clinical correlations, while MIC_{50/90} assessed resistance. The most common carbapenemase genes were *bla*_{NDM} (48.26%) and *bla*_{OXA-48} (37.86%), followed by *bla*_{KPC} (13.6%). Co-occurrence of genes was also reported. Twelve of seventeen clinical variables were significantly associated with gene presence ($p < 0.05$). Ertapenem, imipenem, and meropenem had MIC_{50/90} ≥ 8 μ g/mL, indicating high resistance. Tigecycline showed better sensitivity, with MIC_{50/90} of 0.5/2 μ g/mL (*bla*_{NDM}) and 2/2 μ g/mL (*bla*_{OXA-48}). Fosfomycin MIC₉₀ in *bla*_{OXA-48} isolates ranged up to 256 μ g/mL. The study highlights high *bla*_{NDM} and *bla*_{OXA-48} prevalence, their clinical associations, and limited therapeutic options. Tigecycline remains most effective *in vitro*, but pharmacokinetic concerns exist. These findings emphasize the need for antimicrobial stewardship and molecular surveillance.

Keywords: Carbapenemases, *Klebsiella pneumoniae*, Intensive Care Unit, Multidrug-resistant

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INTRODUCTION

Klebsiella pneumoniae is a Gram-negative, opportunistic pathogen commonly involved in both community- and hospital-acquired infections, including pneumonia, urinary tract infections (UTIs), bloodstream infections, and wound infections.¹ Its capacity to acquire resistance genes, survival on hospital surfaces, and dissemination through plasmid transfer makes it a significant healthcare challenge. The World Health Organization (WHO) has listed carbapenem-resistant *K. pneumoniae* (CRKP) as a “critical priority pathogen”, highlighting the urgent need for global surveillance and new treatment options.²⁻⁴

Carbapenems such as imipenem, meropenem, and ertapenem are considered last-resort antibiotics for treating multidrug-resistant Enterobacteriales, primarily strains that produce extended-spectrum β -lactamases (ESBLs).^{2,4} The effectiveness of carbapenems has also been significantly reduced due to the emergence of carbapenemase-producing organisms. These enzymes, such as *K. pneumoniae* carbapenemase (KPC), OXA-48-like oxacillinas, IMP (Imipenemases), VIM (Verona integron-encoded metallo- β -lactamase), and NDM (New Delhi metallo- β -lactamase), hydrolyze carbapenems and other β -lactam antibiotics. The spread of these resistance genes through plasmids has accelerated their global dissemination.^{5,6}

CRKP prevalence varies significantly by region. In India, *bla*_{NDM} and *bla*_{OXA-48} are most common, with hospital studies showing rates of 45%-65%.⁵⁻⁷ China reports a high prevalence of KPC and NDM, with rates of up to 60%-70% in tertiary centers.^{8,9} In Europe, prevalence exceeds 40% in countries such as Greece and Italy, while it stays below 5% in northern regions.^{2,10-12} In contrast, the United States has a lower prevalence (<10%), with KPC remaining the most common carbapenemase.¹³ This worldwide variation underscores the impact of regional antibiotic use, infection-control strategies, and genetic exchange processes on the epidemiology of CRKP.

The lack of rapid, accurate diagnostic tests for detecting carbapenemases makes treatment more difficult, often leading to delays in administering effective therapies. As a result,

clinicians are usually forced to rely on last-resort antibiotics like colistin, fosfomycin, or tigecycline drugs that can be toxic or have inconsistent success rates, with growing reports of resistance.^{8,9} These treatment challenges increase patient morbidity and mortality and promote the development of pan-drug-resistant bacteria.^{14,15}

In this context, thorough hospital-based surveillance is essential. This study—carried out at a single tertiary-care centre—utilized various baseline clinical and microbiological data, such as infection type, comorbidities, ICU admissions, bacterial co-infections, and minimum inhibitory concentration (MIC_{50/90}) values, to characterize carbapenemase-producing multidrug-resistant *Klebsiella pneumoniae* (MDR-CRKP). The primary objective is to determine the prevalence and genetic diversity of carbapenemase genes among MDR-CRKP strains isolated from intensive care units and inpatient environments. Since the analysis is based on data from a single centre, its findings might not be entirely applicable to other hospitals or regions. Nonetheless, they offer valuable local insights that can support antimicrobial stewardship and infection-control efforts while also enhancing overall understanding of CRKP epidemiology.

MATERIALS AND METHODS

This cross-sectional study was conducted from April 2023 to December 2024. It included all clinical samples received from various inpatient departments (ICU) and intensive care units (ICUs) within the Department of Microbiology at the Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, India. Informed consent from the patients was collected at the time of specimen collection and ethical approval was obtained from the Institutional Ethics Committee vide letter number MMIMSR/IEC/2427.

Inclusion and exclusion criteria

Samples from ICUs and various IPDs (e.g., Medicine, Surgery, Neurosurgery, Paediatric, Respiratory Medicine, Urology, Obstetrics and Gynaecology) were included in the study. In contrast, samples from Outpatient departments (OPDs) and repeated organisms from the same patient were excluded from the study.

Sample processing

All clinical specimens were initially examined by direct microscopy using Gram staining or wet-mount techniques to identify inflammatory cells and microorganisms.

Samples, except blood, were inoculated on routine media, such as Blood Agar and MacConkey Agar, and then incubated at 37 °C for 24-48 hours under aerobic conditions.

For blood cultures, approximately 5-7 mL of venous blood was collected under sterile conditions and placed into BACTEC culture bottles, which were then loaded into the BD BACTEC FX40 automated system for continuous monitoring over five days. Bottles that indicated a positive result were Gram-stained and subcultured onto Blood and MacConkey agar plates, then incubated at 37 °C for 24 hours. Blood culture bottles that showed no signal after five days were deemed culture-negative.

Identification of bacteria and antibiotic sensitivity testing

A bacterial suspension was prepared by emulsifying well-isolated colonies in 3 mL sterile saline in a 12 × 75 mm polystyrene test tube. Using the DensiCHEK Plus turbidity meter (BioMerieux, India), turbidity was adjusted to 0.5 McFarland. The interval between preparing the bacterial inoculum and loading the VITEK cards did not exceed 30 minutes.

Bacteria were identified by the VITEK-2 Compact System utilizing Gram-negative (GN) identification cards. Antimicrobial susceptibility testing (AST) was performed using the N405 and N235 AST cards, following the Clinical and Laboratory Standards Institute (CLSI) guidelines and the manufacturer's protocols.¹⁶ The minimum inhibitory concentrations (MIC) of an antibiotic that may inhibit 50% and 90% of bacterial isolates were calculated as MIC₅₀ and MIC₉₀.¹⁷

Categorization of multidrug-resistant isolates

MDR organisms are resistant to at least one agent in at least three antimicrobial categories.¹⁸

Carbapenemase screening

An isolate showing an MIC ≥8 µg/mL of ertapenem was collected.¹⁵

DNA extraction

All MDR isolates showing MIC ≥8 µg/mL of ertapenem were collected, and DNA extraction was performed using Geno Sen's Genomic DNA extraction kit according to the manufacturer's instructions. The extracted DNA was stored at -20 °C.

Polymerase chain reaction conditions

Conventional PCR was used to identify: bla_{KPC}, bla_{NDM}, bla_{VIM}, bla_{IMP}, and bla_{OXA-48}, following previously published techniques reported by Booq et al.¹⁹ (Table 1). The PCR products were evaluated through electrophoresis at 80 V for 45 minutes in a 2% agarose gel, with bands visualized using a UV transilluminator.

Statistical analysis

A forest plot displaying odds ratios with 95% confidence intervals and significance, along with a scatter plot of MIC₅₀ and MIC₉₀, was created in R version 4.4.3.

RESULTS

Of 612 *Klebsiella pneumoniae* isolates, 375 were MDR (Table 1). No bla_{VIM} and bla_{IMP} genes were detected in the current study. Of the 375 CRKP isolates, 159 (42.4) were from males, and 216 (57.6) were from females.

Year-wise distribution

Between 2022 and 2024, the most prevalent gene was bla_{NDM}, followed by bla_{OXA-48} and bla_{OXA-48} + bla_{NDM}. No relation was found among these parameters using bivariate analysis.

Type of infection

Non-UTI cases included bloodstream, lower respiratory tract, and wound infections. A significant association was observed between UTI cases and the bla_{NDM} gene ($p < 0.05$). While no association was established among non-UTI cases due to the small sample size.

ICU admissions

Among 138 patients, 72 patients had an ICU stay of more than 7 days, followed by 66 patients with a stay of less than 5 days. A significant

Table 1. Primers for identification of genes responsible for Carbapenem-resistance

No.	Gene	Nucleotide Sequence	Amplicon size
1.	bla_{KPC}	KPC F-CGTCTAGTTCTGCTGCTTG KPC R-CTTGTATCCTTGTAGGCG	798
2.	bla_{NDM}	NDM F-GGTTGGCGATCTGGTTTC NDM R-CGGAATGGCTCATCACGATC	621
3.	bla_{IMP}	IMP F-GGAATAGAGTGGCTTAAYCTC IMP R-GGTTTAAAYAAAACAAACCACC	232
4.	bla_{VIM}	VIM F-GATGGTGTGGTCGCATA VIM R-CGAATGCGCAGCACAG	390
5.	bla_{OXA-48}	OXA-48 F-GCGTGGTTAAGGATGAACAC OXA-48 R-CATCAAGTTAACCCAACCG	438

Table 2. Culture positivity rate and distribution of microbial isolates among various clinical samples

Total No. of Samples Processed	No Growth	Gram-Positive	With Growth (n = 4077) (40.2%)			
			Gram-negative (n = 2981) (29.4%)			<i>Candida</i> spp.
			<i>Klebsiella pneumoniae</i>	<i>Klebsiella oxytoca</i>	Other Gram-negative isolates	
10132	6055 (59.8%)	1050 (10.4%)	612 (6%)	150 (1.5%)	2219 (21.9%)	46 (0.5%)

Table 3. Distribution of *Klebsiella pneumoniae* (multidrug-resistant and carbapenem-resistant) among various clinical specimens (n = 375)

No.	Type of Sample	No. of sample (%)
1.	Urine	230 (61.3%)
2.	Respiratory secretions	40 (10.7%)
3.	Pus	37 (9.9%)
4.	Wound Swabs	35 (9.3%)
5.	Blood and sterile fluids	33 (8.8%)

association was observed between ICU admissions and the presence of bla_{OXA-48} and $bla_{OXA-48} + bla_{NDM}$.

Comorbidities

A significant association was established between diabetes mellitus and bla_{NDM} . The association between age and other genes was found to be non-significant. A significant

association was seen between other co-morbid conditions and bla_{NDM} and bla_{OXA-48} .

Bacterial co-infection

A significant association was observed between bla_{KPC} , bla_{NDM} , and bla_{OXA-48} , as well as between bla_{OXA-48} and bla_{NDM} .

MIC_{50} and MIC_{90}

Most antibiotics have an MIC_{90} of CRKP equal to the MIC_{50} , and the resistance rate was high among β -lactam combinations, fluoroquinolones, aminoglycosides, etc. Tigecycline was the most sensitive drug after Fosfomycin.

DISCUSSION

K. pneumoniae causes serious community-acquired and healthcare-associated infections. Carbapenems are a last-resort antibiotic for treating severe Gram-negative bacterial infections,

Table 4. Baseline Characteristics and their association with genes conferring Carbapenem-resistance

Variables	All (n = 375) (%)	<i>bla</i> _{KPC} (n = 51) (%)	<i>bla</i> _{NDM} (n = 181) (%)	<i>bla</i> _{OXA-48} (n = 142) (%)	<i>bla</i> _{OXA-48} + <i>bla</i> _{NDM} (n = 61) (%)	<i>bla</i> _{KPC} + <i>bla</i> _{NDM} (n = 2) (%)	<i>bla</i> _{KPC} + <i>bla</i> _{OXA-48} (n = 4) (%)
Year-Wise Distribution							
2022	112 (29.8)	12 (23.5)	48 (26.5)	38 (26.7)	17 (27.8)	0	1 (25)
2023	125 (33.3)	16 (31.3)	62 (34.2)	47 (33)	21 (34.4)	1 (50)	1 (25)
2024	138 (36.8)	23 (45)	71 (39.2)	57 (40.1)	23 (37.7)	1 (50)	2 (50)
Type of Infection							
UTI	230 (61.3)	34 (66.6)	138 (76.2)	88 (61.9)	42 (68.8)	2 (100)	3 (75)
Non-UTI	145 (38.6)	17 (33.3)	43 (23.7)	54 (38)	19 (31.1)	0	1 (25)
ICU Admission	275 (73.3)	38 (74.5)	148 (81.7)	124 (87.3)	35 (57.3)	1 (50)	2 (50)
Comorbidities							
Diabetes Mellitus	115 (30.6)	18 (35.2)	66 (36.4)	54 (38)	19 (31.1)	2 (100)	1 (25)
Age (>55)	155 (41.3)	19 (37.2)	75 (41.4)	57 (40.1)	26 (42.6)	0	2 (50)
Other	105 (28)	14 (27.4)	40 (22)	31 (21.8)	16 (26.2)	0	1 (25)
Co-morbid Conditions*							
Bacterial co-infection#	145 (38.6)	41 (80.3)	119 (65.7)	112 (78.8)	46 (75.4)	1 (50)	2 (50)

Other Co-morbid Conditions*- Hypertension, Chronic obstructive pulmonary disease (COPD), and malignant conditions **Bacterial co-infection#**- Co-infection with *Escherichia coli*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii* complex, *Citrobacter freundii*, *Proteus* spp., *Providencia* spp., and *Enterobacter cloacae* complex

Odds Ratios of Variables Associated with Carbapenemases

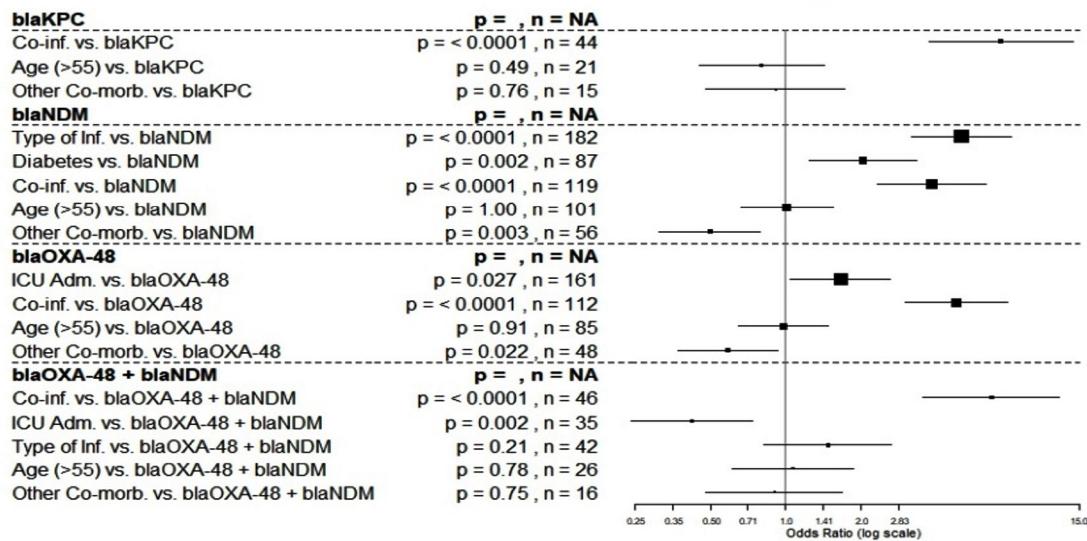


Figure 1. Forest plot showing odds ratios of variables associated with carbapenemases with their 95% confidence intervals and significance

and carbapenem resistance increases patient mortality and morbidity.^{4,20,21}

Due to its ability to survive on medical equipment and colonize patients and hospital staff asymptotically in hospitals, *K. pneumoniae* frequently causes outbreaks of epidemic proportions that are easily transmitted between wards. Consequently, plasmids harboring genes encoding carbapenem-hydrolyzing enzymes can be readily transmitted among various strains. Furthermore, a single plasmid may contain multiple resistance determinants, thereby facilitating the emergence of multidrug-resistant *K. pneumoniae* strains that contribute to highly challenging intrahospital epidemics.²² The present study assessed 375 MDR *K. pneumoniae* isolates

with an ertapenem MIC \geq 8 μ g/mL. The majority of samples collected in the current study were urine (61.33%). We investigated the genes responsible for carbapenem resistance in patients with and without urinary tract infections (UTIs), and 230 (61.3%) of the carbapenem-resistant *K. pneumoniae* isolates were derived from urine samples. Similar results were also reported in a study conducted by Pruss et al.²¹ (Tables 1-3).

Various studies recommend gene transfer as a potential trait among enterobacteriales, thereby increasing antimicrobial resistance.^{23,24} Plasmid-mediated horizontal gene transfer is a key factor in the ongoing evolution of bacterial antimicrobial resistance (AMR).²⁵ We examined the presence of carbapenemase and its association

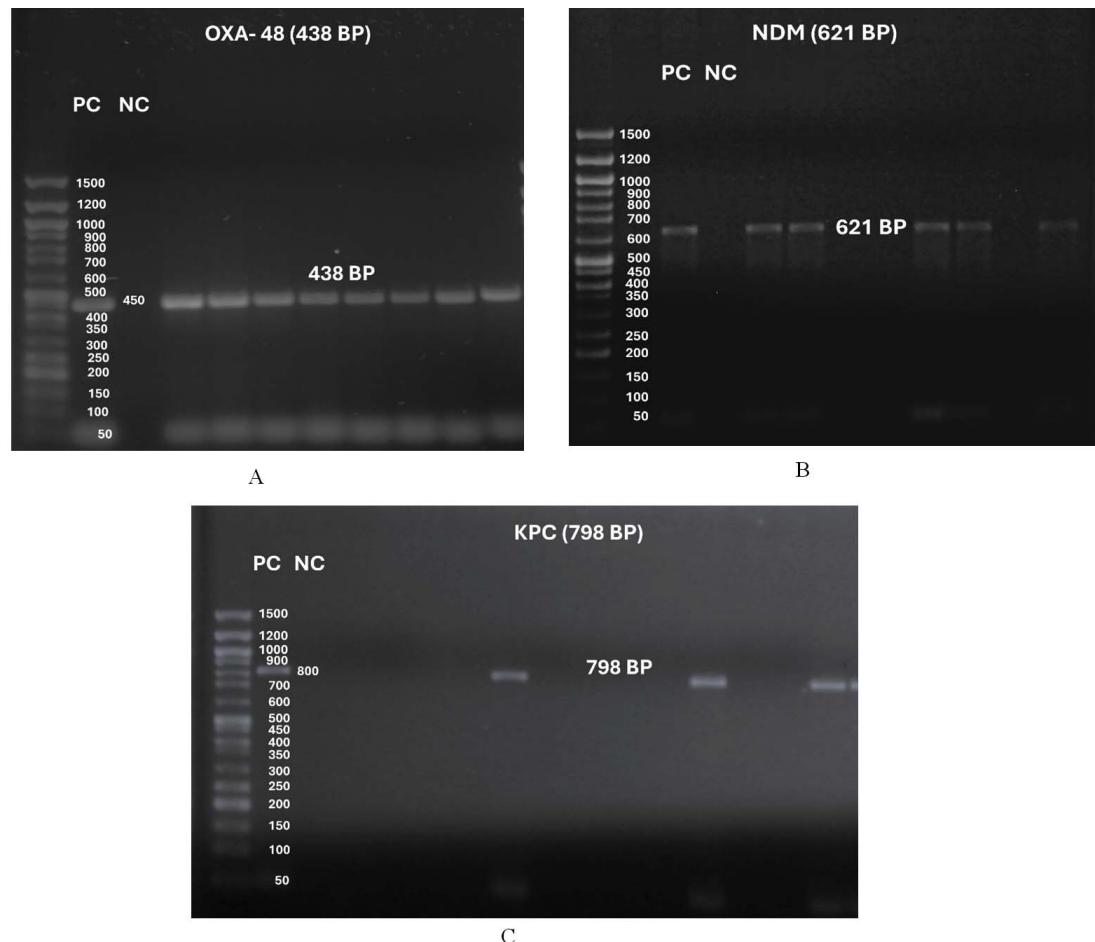
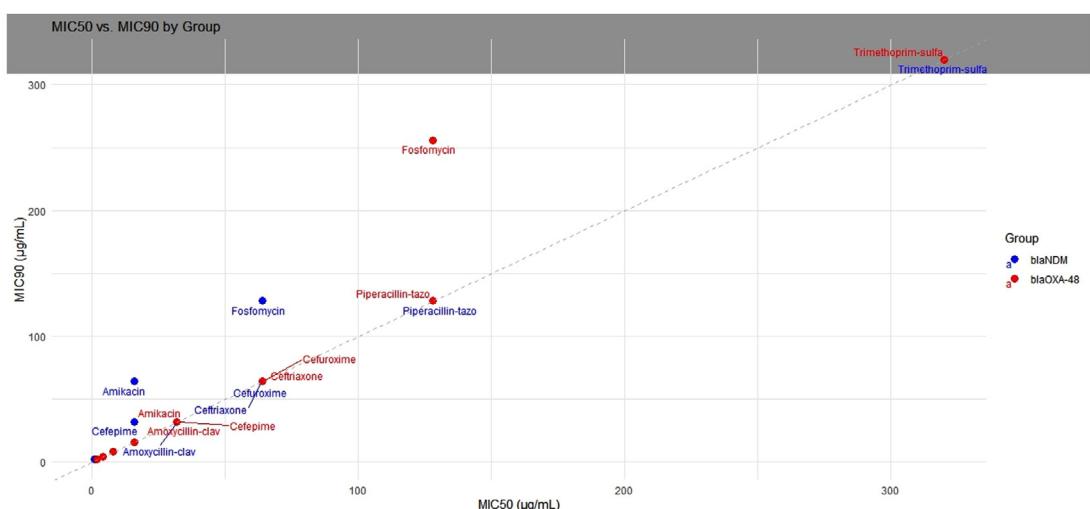


Figure 2. Gel electrophoresis image showing DNA ladder (50 bp) along with Positive and Negative Controls and test strains: (A) bla_{OXA-48} (438 bp), (B) bla_{NDM} (621 bp) and (C) bla_{KPC} (798 bp)

Table 5. Antimicrobial susceptibility testing results of carbapenemase-producing MDR *Klebsiella pneumoniae* strains (ertapenem MIC \geq 8 μ g/mL) (n = 375)

Antimicrobial agent	All MDR & carbapenemase-producing <i>Klebsiella pneumoniae</i> (n = 375)				<i>bla</i> _{NDM} producers (n = 181)			<i>bla</i> _{OXA-48} producers (n = 142)		
	MIC calling Range	MIC ₅₀	MIC ₉₀	%R	MIC ₅₀	MIC ₉₀	%R	MIC ₅₀	MIC ₉₀	%R
Amoxycillin-clavulanic acid	\leq 4/2 - \geq 32/16	\geq 32/16	\geq 32/16	99.7	\geq 32/16	\geq 32/16	100	\geq 32/16	\geq 32/16	100
Piperacillin-tazobactam	\leq 4/4 - \geq 128/4	\geq 128/4	\geq 128/4	98.6	\geq 128/4	\geq 128/4	100	\geq 128/4	\geq 128/4	100
Ceftriaxone	\leq 0.25 - \geq 64	\geq 64	\geq 64	99.7	\geq 64	\geq 64	100	\geq 64	\geq 64	100
Cefuroxime	\leq 1 - \geq 64	\geq 64	\geq 64	100	\geq 64	\geq 64	100	\geq 64	\geq 64	100
Cefepime	\leq 0.12 - \geq 32	\geq 32	\geq 32	98.4	\geq 16	\geq 32	99.5	\geq 32	\geq 32	100
Ciprofloxacin	\leq 0.06 - \geq 4	\geq 4	\geq 4	99.7	\geq 4	\geq 4	100	\geq 4	\geq 4	100
Amikacin	\leq 1 - \geq 64	\geq 16	\geq 32	93.8	\geq 16	\geq 64	95	\geq 32	\geq 32	95
Gentamicin	\leq 1 - \geq 16	\geq 16	\geq 16	98.1	\geq 16	\geq 16	99.5	\geq 16	\geq 16	99.5
Imipenem	\leq 0.25 - \geq 16	\geq 16	\geq 16	100	\geq 16	\geq 16	100	\geq 16	\geq 16	100
Meropenem	\leq 0.25 - \geq 16	\geq 16	\geq 16	100	\geq 16	\geq 16	100	\geq 16	\geq 16	100
Fosfomycin	\leq 16 - \geq 256	\geq 64	\geq 64	91.4	\geq 64	\geq 128	92.8	\geq 128	\geq 256	96.5
Trimethoprim-sulfamethoxazole	\leq 20 (1/19)- \geq 320 (16/304)	\geq 320	\geq 320	96.8	\geq 320	\geq 320	98.9	\geq 320	\geq 320	100
Tigecycline	\leq 0.5 - \geq 8	0.5	2	51.4	\geq 1	\geq 2	69.8	\geq 2	\geq 2	80.7

%R = Resistant Percentage, MIC₅₀ and MIC₉₀: MIC of an antibiotic that may inhibit 50% and 90% of bacterial isolates

**Figure 3.** Scatter Plot of MIC₅₀ versus MIC₉₀ illustrating the relationship between MIC₅₀ and MIC₉₀ for each group of antibiotics, demonstrating the variation in resistance levels

with its occurrence (both in confirmed coinfections and carriage). In the current study, *Escherichia coli*, *Pseudomonas aeruginosa*, *Citrobacter freundii*, *Acinetobacter baumannii* complex, *Enterobacter cloacae* complex, *Proteus* spp., and *Providencia* spp. were the most commonly found organisms. Co-occurrences of bacteria were also observed in 145 cases. The study did not include Gram-positive bacteria or fungi isolated during microbiological sampling (Table 3).

According to the Ambler classification, *K. pneumoniae* mainly contains three primary types of carbapenemases: class D, also called oxacillinase-hydrolysing (OXA); class B, sometimes called metallo-beta-lactamases (MBLs); and class A, also called serine β -lactamases. The *bla_{KPC}* gene encodes *K. pneumoniae* carbapenemase (KPC), a crucial enzyme that contributed to the worldwide spread of CRKP. Carbapenemases can render resistance to all beta-lactam antibiotics, including carbapenems, monobactams, and extended-spectrum cephalosporins. Carbapenem resistance in *K. pneumoniae* was also associated with the other carbapenemases, including OXA-48, VIM, IMP, and NDM.^{1,26} Among 375 MDR *K. pneumoniae*, the majority of the genes responsible for carbapenem resistance were *bla_{NDM}* (48.26%), *bla_{OXA-48}* (37.86%), and *bla_{KPC}* (13.6%). In some bacterial isolates, co-occurrence of genes was also observed, which included *bla_{OXA-48}* + *bla_{NDM}* (16.26%), *bla_{KPC}* + *bla_{NDM}* (0.53%), and *bla_{KPC}* + *bla_{OXA-48}* (1.06%). In the current study, bivariate analysis of baseline characteristics was carried out to assess the association of different variables with the carbapenem gene, and a Forest Plot was created to establish relationships among variables, showing odds ratios along with their 95% confidence intervals and significance associated with various variables (p is significant at $p < 0.05$). Twelve out of 17 correlations were significant, demonstrating substantial effects (OR = 7.27 for Co-inf. vs. *bla_{KPC}*) and protective effects (OR = 0.42 for ICU Admission vs. *bla_{OXA-48}* + *bla_{NDM}*). Mainly, age (>55) and a few other co-morbidities displayed weaker or no relationships. Larger squares (e.g., n = 182, n = 119) indicate more robust significant findings (Figures 1 & 2 and Table 4).

Misuse of antibiotics, which has gone unchecked for many years, has led to one

of the most significant global health risks. The development of antibiotic resistance in organisms such as CRKP has become an obstacle to physicians treating severe infections. The strongest indication of increased evolutionary rates in these infections is their response, which enables them to evade antibiotic action and demonstrates their exceptional adaptation. Both colistin and tigecycline exhibit good *in vitro* activity against CRKP; however, resistance during therapy remains a serious health concern.²¹ Multidrug-resistant and extremely drug-resistant strains arise from their immense genetic potential.²² The MDR strains were sensitive to tigecycline but highly resistant to cephalosporins, carbapenems, aminoglycosides, β -lactam combinations, and fluoroquinolones. A scatter plot of MIC_{50} versus MIC_{90} was generated. The points (32, 32), (64, 64), (128, 128), and so on lie on the 1:1 line, indicating consistent resistance (e.g., to amoxicillin-clavulanate and ceftriaxone). Tigecycline values were (1, 2) for *bla_{NDM}* and (2, 2) for *bla_{OXA-48}*, both of which are near or on the line, indicating minimal variation. Fosfomycin at (64, 128) for *bla_{NDM}* and (128, 256) for *bla_{OXA-48}* is located above the line, indicating a greater spread of resistance, notably in *bla_{OXA-48}*. The dotted grey line extends diagonally from (0, 0) to the top-right, intersecting at $\text{MIC}_{50} = \text{MIC}_{90}$ (Figure 3 and Table 5).

The current study shows higher resistance to antibiotics such as cephalosporins, β -lactam combinations, aminoglycosides, and fluoroquinolones, thereby limiting their effectiveness. To enhance clinical outcomes, it is crucial to develop new therapies and dosing strategies without delay. Despite the intricate and varied causes of urinary tract infections, the bacteria's ability to adhere has accelerated the development of non-antibiotic alternative anti-adhesion treatments.^{27,28} The findings of this study further emphasize the importance of optimizing infection control measures and antibiotic stewardship practices, especially considering the prevalence of *bla_{NDM}* and *bla_{OXA-48}*. Recommended strategies encompass active surveillance, rapid identification of carriers, strict contact precautions, and improved environmental sanitation within intensive care units. Routine screening in regions prone to outbreaks can

prevent covert transmission. It is imperative to update treatment protocols, reduce carbapenem usage, and promote the adoption of carbapenem-sparing therapies. Regular analysis of antibiograms and the integration of molecular resistance data are vital in mitigating the dissemination of resistant CRKP strains. These targeted interventions are essential within a single-center setting, where transmission dynamics and antibiotic utilization significantly influence resistance patterns.

CONCLUSION

In our study, *bla*_{NDM} and *bla*_{OXA-48} were the most frequent carbapenemase genes. Co-occurrence of genes was also seen in many isolates, and the majority of bacteria harbouring multiple genes had co-infection, which may be attributed to the transfer of genetic material. Out of the seventeen relationships analysed, twelve were found to be significant. Tigecycline showed the highest sensitivity in this study; however, its therapeutic use has limitations.

Limitations

This study, being single-centric, only represents data within the region, and representativeness is relatively high. The current study had limitations, including the multiple variables in the APACHE II score and other comorbid conditions in ICU patients, which would have provided a better understanding, but were not considered due to data unavailability. Also, in the current study, various CRKP resistance mechanisms and Sequence type (ST) typing studies were not done; to fill the gap in the current study, Multilocus sequence typing (MLST) genotyping will be carried out for all CRKP strains, and whole genome sequencing will be carried out when required in the future.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

RK, NK and HK conceptualized the study. RK, HK, SC and SK performed data collection and analysis. RK, HK and RB wrote the manuscript. NK, BKA and RB reviewed and edited the manuscript. All authors read and approved the final manuscript for publication.

FUNDING

None.

DATA AVAILABILITY

All datasets generated or analyzed during this study are included in the manuscript.

ETHICS STATEMENT

This study was approved by the the Institutional Ethics Committee, Maharishi Markandeshwar Institute of Medical Sciences & Research Mullana, Ambala, India, vide letter number MMIMSR/IEC/2427.

INFORMED CONSENT

Written informed consent was obtained from the participants before enrolling in the study.

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