RESEARCH PAPER

Prevalence of blaKPC Gene in Carbapenem-Resistant Klebsiella pneumoniae Isolated from Clinical Samples of a Tertiary Care Hospital

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Background: Carbapenem-resistant *Klebsiella pneumoniae* (CRKP) is a critical World Health Organization priority pathogen. Although *bla* KPC remains a major carbapenemase globally, the relative contribution of KPC compared with other mechanisms varies across regions and directly influences diagnostic strategies and use of newer β-lactam/β-lactamase inhibitor combinations. This study assessed the prevalence and clinical correlates of the *blaKPC* gene in *K. pneumoniae* isolates from a tertiary-care hospital with a high burden of carbapenem resistance.

Methods: In this cross-sectional laboratory-based study, 220 non-duplicate clinical *K. pneumoniae* isolates were collected over a 12-month period from blood, urine, pus, and other specimens. Demographic and ward data were retrieved from laboratory records. Antimicrobial susceptibility to carbapenems was determined using standard methods in accordance with contemporary guidelines. Carbapenemase production was screened using the Carba NP test. Detection of *blaKPC* was performed by polymerase chain reaction.

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INTRODUCTION

Klebsiella pneumoniae is a major cause of healthcare-associated bloodstream, respiratory, and urinary tract infections worldwide. Recent global analyses indicate that K. pneumoniae infections are responsible for a substantial proportion of deaths and years of life lost attributable to antimicrobial resistance (AMR), with carbapenem-resistant K. pneumoniae (CRKP) emerging as one of the most lethal Gram-negative pathogens [1,2].

In recognition of this threat, the 2024 World Health Organization (WHO) Bacterial Priority Pathogens List ranks carbapenem-resistant and third-generation cephalosporin-resistant K. pneumoniae among the highest-priority organisms for research, surveillance, and infection-prevention efforts [3].

The prevalence of CRKP has increased sharply in hospital settings, particularly in low- and middle-income countries. A recent systematic review estimated that nearly one-third of hospital-acquired K. pneumoniae infections globally are carbapenem-resistant, with especially high burdens reported from South and East Asia [4]. These infections are typically multidrug-resistant, are associated with prolonged hospitalisation and complex combination therapy, and confer markedly higher mortality compared with carbapenem-susceptible infections [1,2,4]. The growing convergence of carbapenem resistance with hypervirulent lineages further amplifies the clinical impact and outbreak potential of this pathogen [1,5].

Carbapenem resistance in K. pneumoniae is mediated predominantly by carbapenemase enzymes. Among these, K. Pneumonia carbapenemases (KPCs) have played a pivotal role since their first description in the mid-1990s, driving large hospital outbreaks and regional epidemics, particularly in the Americas and parts of Europe [5]. However, the global carbapenemase landscape is heterogeneous and dynamic. Contemporary studies highlight important geographical differences, with KPC, NDM, and OXA-48-like enzymes variously predominating across regions and sometimes co-circulating within the same healthcare system [5,6]. This heterogeneity has major implications for empirical therapy, infection-control policies, and the deployment of

newer β-lactam/β-lactamase inhibitor combinations that are primarily active against KPC producers.

Accurate characterisation of underlying resistance mechanisms is therefore essential. Phenotypic tests such as Carba NP and related assays are widely used for rapid detection of carbapenemase activity, but they cannot reliably distinguish between different carbapenemase families [7]. Molecular methods targeting *bla*KPC and other carbapenemase genes, or broader genomic approaches, provide the necessary resolution but are not universally available and must be tailored to local epidemiology to be cost-effective [4,7]. Recent reports of hypervirulent, carbapenemase producing K. pneumoniae clones identified through WHO surveillance networks underscore the importance of understanding which specific genes circulate in a given setting [5,8].Many institutions report very high levels of phenotypic carbapenem resistance, yet the extent to which this is driven by KPC, metallo-β-lactamases, OXA-48-like enzymes, or non-enzyme mechanisms (e.g., ESBL/AmpC plus porin loss) has not been systematically evaluated. Against this background, the present study aimed to determine the prevalence of the *blaKPC* gene among clinical K. pneumoniae isolates in a tertiary-care hospital with a high burden of carbapenem resistance, and to examine its association with basic demographic, clinical, and phenotypic characteristics. Understanding whether KPC represents a major or minor resistance mechanism in this context is crucial for rationalising molecular diagnostics, informing antimicrobial stewardship, and guiding the local use of KPC-targeted agents.

Materials and Methods

Study design and setting

This was a cross-sectional, laboratory-based study conducted in the microbiology department of a tertiary-care teaching hospital. The study included consecutive, non-duplicate *K. pneumoniae* isolates recovered from clinical specimens over a 12-month period. Only the first isolate per patient was included to avoid over-representation of colonisation or persistent infection.

Isolate selection and clinical data

All clinical specimens submitted for routine culture (blood, urine, pus, respiratory samples, and other sterile body fluids) were processed in VITEK -2 for identification and antimicrobial susceptibility. Out of these samples Klebsiella pneumoniae were collected for the study, basic demographic and clinical data were extracted from laboratory request forms: patient age, sex, inpatient ward (medical, intensive care unit [ICU], surgical, gynaecology/obstetrics, other), and specimen type (blood, urine, pus, other).

Identification and susceptibility testing

Bacterial Identification Antimicrobial susceptibility testing to carbapenems (meropenem, imipenem, ertapenem) was carried out using automated method VITEK 2. Klebsiella pneumoniae isolates showing resistance to carbepenem drugs i.e. Imipenem, meropenum and ertapenem were taken for the study to detect blaKPC gene.

Detection of *bla*KPC gene

The *bla*KPC gene was amplified from the plasmid DNA extracted from all the resistant isolates of K. pneumoniae. PCR amplification was performed using the primers for *bla*KPC i.e., forward primer: 5'ACG ACG GCA TAG TCA TTT GC 3′ and reverse primer: 5′ CAT TCA AGG GCT TTC TTG CTGC 3′ with amplicon of 538 base pairs PCR mixture of total volume 25 µl was prepared which consisted of 3 µl of template DNA, 0.5 µl each of forward and reverse primer and 21 µl of PCR master mix. The thermal cycling conditions for amplification was initial denaturation at 95 °C for 15 minutes followed by 32 cycles of denaturation at 94 °C for 30 seconds, annealing at 58 °C for 90 seconds and extension at 72 °C, followed by final extension at 72 °C for 10 minutes. The amplified PCR products were analyzed in 1.2% agarose gel stained with ethidium bromide.

Ethical considerations

The study used residual clinical specimens and anonymised laboratory data. No patient-identifiable information was recorded. The protocol complied with the Declaration of Helsinki and was approved by the institutional ethics committee, which granted a waiver of informed consent because of the retrospective, laboratory-based design.

Statistical analysis

Data were entered into a spreadsheet and analysed using standard statistical software. Age was non-normally distributed (Shapiro–Wilk $p<0.001$) and is presented as median with interquartile range (IQR). Categorical variables are described as counts and percentages. Comparisons between bla-KPC-positive and -negative isolates were made using the Mann–Whitney U test for age and Fisher's exact test for categorical variables because of sparse cells and small numbers of positives.

Effect sizes were calculated to aid interpretation: rank-biserial correlation (r) for age, Cramér's V for multi-category variables (sample type, ward), and

odds ratios with 95% confidence intervals for binary comparisons (sex, age group, carbapenem resistance, Carba NP). A p-value <0.05 was considered statistically significant. Multivariable logistic regression was attempted to identify independent predictors of *bla*KPC positivity, but it did not converge because only four isolates carried the gene; these results are therefore not reported.

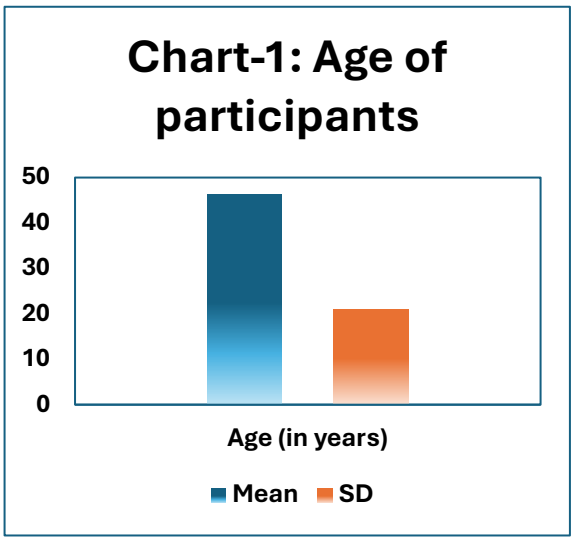
RESULT

In our study, we have collected Klebsiella pneumoniae isolates from 220 samples from different wards such as RICU, Medicine ward, respiratory ward, Oncology ward, ICU, Neurosurgery ward, MICU, temp Ward, Gastroenterology ward, PICU, HDU, Ortho ward, ENT ward, Surgical oncology ward, plastic surgery ward, gynaecology ward, ICU-CTVS, INPR, Nephrology ward, and KTU kidney transplant Unit.

In this study, we have included participants of all age group and the average age of participants was 46.25 ± 21.13 (± SD) years (Table-1 and Chart-1).

Table-1: Age of participants.

	Mean	SD
Age (in years)	46.25	21.13

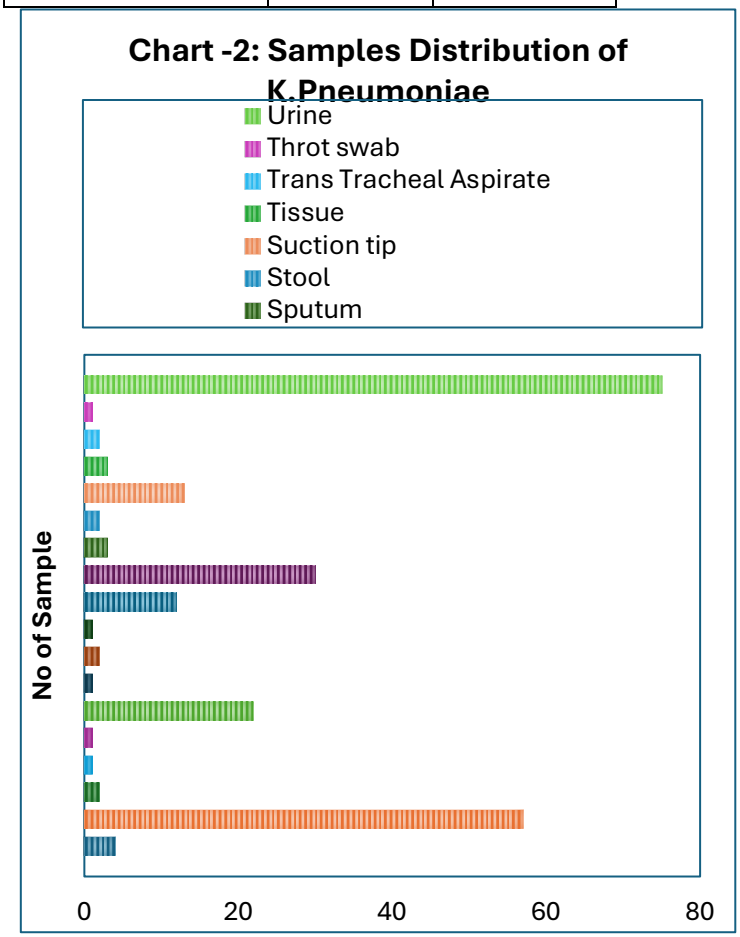


DISTRIBUTION OF SUBJECTS BASED ON SAMPLE TYPE:

In this study, 4 BAL samples, 57 blood sample, 2 bone marrow, 1 CSF, 1 Drain tip, 22 ET aspirate, 1 fluid, 2 IAF, 1 Nasal pack ear pack, 12 pic line, 30 Pus, 3 Sputum, 2 stool, 13 suction tip, 3 tissue, 2 trans tracheal aspirate, 1 throat swab and 75 urine samples showing the growth of Klebsiella pneumoniae were taken from different wards (Table-2 and chart-2)

Table-2: Distribution of sample positive for the growth of Klebsiella pneumoniae.

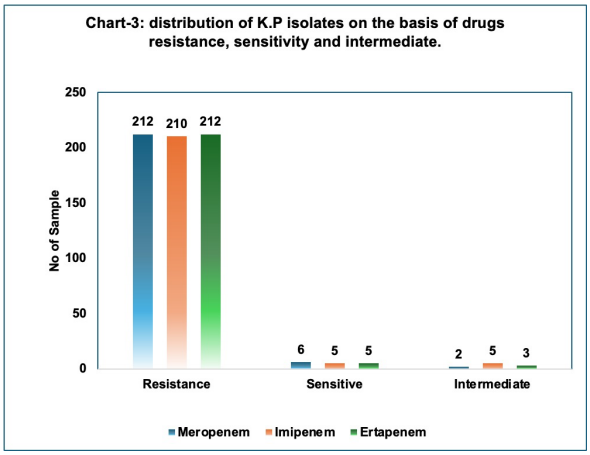
Sample Type	No of subject	sample type %
BAL	4	1.82
BLOOD	57	25.91
BONE MARROW	2	0.91
CSF	1	0.45
DRAIN TIP	1	0.45
ET aspirate	22	10.00
Fluid	1	0.45
IAF	2	0.91
Nasa pack ear pack	1	0.45
Pic Line	12	5.45
Pus	30	13.64
Sputum	3	1.36
Stool	2	0.91
Suction tip	13	5.91
Tissue	3	1.36
Trans Tracheal Aspirate	2	0.91
Throat swab	1	0.45
Urine	75	34.09
Total sample	**220**	**100.00%**



In our study, we have observed that 212 Klebsiella pneumonia isolates were resistant from the meropenem and ertapenem drugs, and 210 samples were resistant to imipenem. And 6 samples for sensitive to meropenem, and 5 samples for sensitive to ertapenem and imipenem drug. Also found 2 samples for intermediate for meropenem, 5 samples intermediate for ertapenem, and 3 samples intermediate for imipenem drug (Table-3 and chart-3).

Table-3: Distribution of KP isolates based on drug resistance, sensitivity, and intermediate.

	Meropenem		Imipenem		Ertapenem	
	No of Isolates	%	No of Isolates	%	No of Isolates	%
Resistance	212	96.36 %	210	95.45 %	212	96.36 %
Sensitive	6	2.72 %	5	2.27 %	5	2.27 %
Intermediate	2	0.90 %	5	2.27 %	3	1.36 %
Total Sample	220		220		220	



In our study, we have observed 220 isolates of K.pneumoniae from various clinical samples and their susceptibility to three carbapenem antibiotics: meropenem, imipenem, and ertapenem, categorized as resistant, sensitive, or intermediate. Among respiratory samples, 5 bronchoalveolar lavage isolates are resistant, and none are sensitive or intermediate, while endotracheal aspirates show 22 resistant isolates with no sensitive or intermediate ones. Blood has 56 resistant isolates to all three drugs, with only 1 sensitive isolate and no intermediate isolates, and bone marrow, cerebrospinal fluid, drain tip, fluid, intra-abdominal fluid, and other device-related samples each show small numbers of resistant isolates and no sensitive or intermediate ones. Pus has 27 resistant isolates and 2 sensitive ones with a few intermediate isolates, sputum has 2 resistant isolates and none sensitive, but some intermediate, and stool has 2 resistant isolates with 1 sensitive and several intermediate. Suction tips and tissue samples also show only resistant isolates, whereas throat swab has 1 resistant isolate and no others, and urine has the largest burden with 71 resistant isolates, 3 sensitive isolates, and a small number with intermediate susceptibility to each antibiotic (Table-4, 5, 6).

Table-4: Distribution of various clinical samples of K. pneumoniae and their resistance and susceptibility to three carbapenem antibiotics: meropenem, imipenem, and ertapenem.

Clinical Sample	Carbapenem Antibiotics		
	Meropenem	Imipenem	Ertapenem
BAL	5	5	5
BLOOD	56	56	56
BONE MARROW	2	2	2
CSF	1	1	1
DRAIN TIP	1	1	1
ET aspirate	22	22	22
Fluid	1	1	1
IAF	2	2	2
Nasa pack ear pack	1	1	1
Pic Line	1	1	1
Pus	27	27	27
Sputum	2	2	2
Stool	2	2	2
Suction tip	13	13	13
Tissue	3	3	3
Trans Tracheal Aspirate	1	1	1
Throat swab	1	1	1
Urine	71	71	71

Table-5: Distribution of various clinical samples showing positive growth of K.pneumoniae and their susceptibility to three carbapenem antibiotics: meropenem, imipenem, and ertapenem.

Sensitive for-	Carbapenem Antibiotics

	Meropenem	Imipenem	Ertapenem
Bal	0	0	0
Blood	1	1	1
Bone marrow	0	0	0
CSF	0	0	0
Drain tip	0	0	0
ET aspirate	0	0	0
Fluid	0	0	0
IAF	0	0	0
Nasa pack ear pack	0	0	0
Pic line	0	0	0
Pus	2	2	2
Sputum	0	0	0
Stool	1	1	1
Suction tip	0	0	0
Tissue	0	0	0
Trans tracheal aspirate	0	0	0
Throat swab	0	0	0
Urine	3	3	3

Table-6: Distribution of various clinical samples showing positive growth of K.pneumoniae and their intermediate susceptibility to three carbapenem antibiotics: meropenem, imipenem, and ertapenem.

Intermediate for-	Carbapenem Antibiotics		
	Meropenem	Imipenem	Ertapenem
Bal	0	0	0
Blood	0	0	0
Bone marrow	0	0	0
CSF	0	0	0
Drain tip	0	0	0
ET aspirate	0	0	0
Fluid	0	0	0
IAF	0	0	0
Nasa pack ear pack	0	0	0
Pic line	0	0	0
Pus	1	1	1
Sputum	1	1	1
Stool	1	1	1
Suction tip	0	0	0
Tissue	0	0	0
Trans tracheal aspirate	0	0	0
Throat swab	0	0	0
Urine	1	1	1

Prevalence of bla-KPC:

In our study, we have found 06 positive isolates of K.pneumoniae for *bla*KPC out of 220 samples. Where 03 isolates were positive for *bla*KPC in urine samples, collected from gynaecology (02 isolates) and medicine ward (01 isolate), and 03 positive isolates in blood samples, collected from neurosurgery ward (02) and medicine ward (01) (Table-7). And we have found the prevalence of *bla*KPC was 2.72 %.

Table-7: Prevalence of *bla*KPC

Sample	Ward	No of positive *bla*KPC isolates	Percentage (%)
Blood Sample	Medicine ward	01	0.45 %
	Neurosurgery Ward	02	0.90%
Urine Sample	Medicine ward	01	0.45 %
	Gynaecology ward	02	0.90%
Total		**06**	**2.72 %**

Discussion and conclusion

A total of 220 isolates were used to check sensitivity and resistance activity for Meropenem, Imipenem, and Ertapenem and find out the prevalence of *bla*KPC in patients who were visited or admitted to the tertiary care hospital, Dehradun. In our study, we have found 96.36 % (212/200) isolates for meropenem and ertapenem resistant, 95.45 % (210/220) isolates were resistant to imipenem drug. Only 0.91 % (2/220) isolates were intermediate for meropenem drug, 2.27 % (5/220) for imipenem, and 1.36 % (3/220) were intermediate for ertapenem drug. 2.27 % (5/220) isolates were sensitive to Imipenem and Ertapenem, and 2.72 % (6/220) isolates were sensitive to Meropenem and we have reported only 2.72 % positive *bla*KPC out of 220 samples.

Baral R. et.al were reported 91.70 % samples were resistant to meropenem, and found the prevalence of *bla*KPC was 8.33 %. This research reveals that K. pneumoniae isolates that produce MDR and KPC are more common, which makes it harder to employ antimicrobial drugs. Continuous microbiological and molecular monitoring should be used to find *bla*KPC early and stop it from spreading further. Sokhi et al. observed 66.6 % resistant for meropenem, 93.3 % for imipenem, and 100 % resistant for ertapenem drug. And his study found the positive KPC isolates were 9.3 %. Ghasemnejad and his colleague observed 67.7

% isolates for resistance to imipenem, 58.3 % for meropenem, and 46.9 % for ertapenem, and found 13.6 % positive isolates for KPC.

The exceptionally high burden of carbapenem resistance we document is consistent with recent global and regional estimates. Large systematic reviews have shown that nearly one-third of nosocomial *K. pneumoniae* infections worldwide, and an even higher proportion in South and East Asia, are carbapenem-resistant [2,8,9]. Global burden studies further rank carbapenem-resistant *K. pneumoniae* among the leading contributors to deaths associated with antimicrobial resistance [1,10].

Future research should extend molecular testing to a broader panel of carbapenemase genes and incorporate whole-genome sequencing to elucidate clonal relationships and transmission pathways. Parallel collection of detailed clinical data would enable evaluation of outcome differences between specific carbapenemase producers and inform risk stratification. In the interim, infection-control and antimicrobial stewardship programmes in similar settings should be cautious about assuming KPC predominance and should design diagnostic algorithms and treatment policies that reflect the broader diversity of carbapenem resistance mechanisms.

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