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"TO STUDY THE MOLECULAR CHARACTERIZATION OF BLANDM-1 RESISTANT GENES IN CARBAPENEM RESISTANCE *KLEBSIELLA PNEUMONIA* CLINICAL ISOLATES IN ADULT ICU PATIENTS"

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ABSTRACT

BACKGROUND: *K.pneumoniae* is a gram-negative bacterium belonging to the *Enterobacteriaceae* family. This microorganism is a part of the healthy microbiome of individuals and colonizes many parts of the body. The incidence of carbapenem-resistant *Klebsiella pneumoniae* (CRKP) infections is increasing globally. In India, around 65% of *K. pneumoniae* isolates are resistant to carbapenem antibiotics. The bla_{NDM} is the predominant carbapenem-resistant gene in CRKP isolates.

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AIM AND OBJECTIVE: To Study the Molecular Characterization of blaNDM-1 Resistant genes in Carbapenem Resistance *Klebsiella Pneumonia* Clinical isolates.

MATERIAL AND METHODS: This was a cross sectional study carried out for a period of 1 year i.e, during 2023 to 2024at K.G.M.U, Lucknow . Samples like urine, sputum, ET tube, pleural fluid, pus, CSF, blood and Ascitic fluid were included in this study. Carbapenemase resistance was detected phenotypically by MHT, mCIM and eCIM methods and genotypically by using PCR where the DNA extraction was done and the resistant gene blaNDM-1 was confirmed by PCR assay.

RESULT:A total of 350 isolates of *K. pneumoniae* were collected from patients, with 127(36.28%) identified as CRKP. There were 30 (57.69%) isolates obtained from male and 22(42.30%) were obtained from female, while the maximum number of patients belong to the age group <50 years and maximum patients were engaged as Student/Housewife/Retired (44.09%) followed by Clerical/Shopkeeper/Farmer (36.22%) and others. In our study,it was also observed that, in phenotypic test 81.88% were positive for M-CIM while 77.95% were positive for E-CIM and in genotypic test there were 86.61 % positive for NDM-1.

CONCLUSION: The study highlighted the existence of carbapenemase-producing *K. pneumoniae*, particularly in blaNDM-1, in patients with comorbidities. Our findings emphasize the importance of the molecular characterization of resistance-determinant-carrying bacterial pathogens as a part of infection control and prevention in hospital settings.

KEYWORDS: MDR, *K.pneumoniae*, ESBL, CRKP, Gene, PCR

INTRODUCTION

Carbapenems are classified as antibiotics in the β-lactam class. With a five-member ring structure and a fused β-lactam ring, carbapenems are different from penicillin in that they are unsaturated and have a carbon atom instead of the sulphur atom that Penicillin has. Antibiotics in the carbapenem class have a wide range of activities. Carbapenem antibiotics are currently used to treat infections brought on by Gram-negative bacteria that are resistant to a number of medications [1].

K. pneumoniae, described by Edwin Klebs in 1875, is a gram-negative bacterium belonging to the *Enterobacteriaceae* family. This microorganism is part of the healthy microbiome of individuals and colonizes many parts of the body. Despite its role as a healthy component of

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the microbiome, it can cause severe infections in critically ill patients, newborns, immunocompromised individuals or those with other risk factors in healthcare establishments. Antibiotics such carbapenems are widely used to treat infections, especially those caused by *Enterobacteriaceae*, a producer of extended-spectrum β-lactamase (ESBL); however, the use or misuse of such antibiotics has contributed to the appearance of isolates resistant to carbapenems [1].

Carbapanem-resistant *K. pneumoniae* (Cr-KPN) is a pathogen that affects people worldwide, with prevalence in low, middle and upper income countries. Resistance to carbapenem is mediated by two primary mechanisms. First, Cr-KPN is able to produce β-lactamases with the ability to hydrolyze cephalosporins such *AmpC* cephalosporinase e.g. DHA-1 and CMY-2 or ESBL e.g. CTX-M-2 in combination with decreased membrane permeability in the cell wall [2,3].

An increasing trend of Carbapenem-resistant Enterobacterales (CRE) infections, has been reported in the last decade . It is a major public health problem that poses a serious global threat to humanity. CRE isolates are most often spread via cross-transmission in hospital settings from person to person in contact with infected or colonized individuals, especially in ICU settings. Certain infections caused by CRE isolates result from the unhygienic and unsterilized use of medical devices such as IV catheters, urinary catheters, implants, or through wounds caused by road traffic accidents (RTA) injuries or surgeries [3].

The second mechanism is mediated by the production of a β-lactamases capable of hydrolyzing most β-lactams antibiotics including carbapenems. According the Ambler classification it belongs to class A (*K. pneumoniae* carbapenemase, KPC), class B or metallo-β-lactamases (MBL) (New Delhi metallo-β-lactamases, NDM) and class D (OXA-48-like carbapenemases) [4].

The NDM carbapenemase was reported from *K. pneumoniae* and *Escherichia coli* in 2009, similar to other member of MBL it requires of zinc for hydrolysis of β-lactam antibiotics and their activity could be inhibited by ethylenediaminetetraacetic acid (EDTA) as chelating agent.[5] KPC–producer *K. pneumoniae* (KPC-Kp) is a pathogen with a high capacity for clonal expansion and exchange of mobile genetic elements (MGEs) promoting increased resistance. KPC-Kp among their capacities to generate resistance can also persist in human reservoirs and create biofilms, which provide protection from hospital disinfection protocols [5,6]

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In India, *bla*$_{NDM}$ is the most prevalent carbapenemase gene, and now *bla*$_{OXA-48}$ and co-expression of both *bla*$_{NDM}$ and *bla*$_{OXA-48}$ genes are increasingly reported. Timely detection of CRKP infection and epidemiology of carbapenem-resistant genes are vital to optimize antibiotic therapies and develop infection control policies [7].

In the current study, carbapenem resistant isolates are frequently isolated from clinical sample. There is no current protocol for screening for CRE in ICU patients. Hence, the present study was planned to determine the proportion of rectal colonization with Carbapenem resistant Enterobacterales in one of our hospital ICU and to determine the associated risk factors for such colonization.

MATERIAL& METHODS

This was a cross sectional study carried out for a period of 1 year i.e, during 2023 to 2024 at K.G.M.U, Lucknow, India. A total of 350 rectal swab samples were collected from adult patients admitted to the ICUs on days one, three, and five of their ICU stay. These samples were transported to the Central laboratory of the Microbiology Department at KGMU for further processing and analysis. Informed consent was obtained from patients, their relatives, or attendants prior to data collection.

Inclusion criteria:

1.Patients aged 18 years and above admitted to the intensive care unit (ICU).

2. A total of 350 *K. pneumoniae* strains isolated from clinical specimens (urine, blood, pus, sputum, endotracheal secretion, bronchoalveolar lavage fluid, CSF and tracheal aspiration) were included in the study.

Exclusion criteria

1.Anal atresia or other conditions preventing the collection of a rectal swab sample on the day of screening.

2. Lack of consent from the adult patient, caretaker, legal guardian, or relative.

3. Other bacterial strains isolated from the study samples were not included in the analysis. Stool samples were excluded from the study as they could contain *K. pneumoniae* as normal flora from the human intestine.

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Ethical considerations:

The Ethical clearance was duly obtained from KGMU, Lucknow where the work plan of this study was accepted [Registration No.-ECR/262/Inst/UP/2013/RR-19]

Bacterial identification

It was performed by standard culture and biochemical tests. The Kirby-Bauer's test was used to determine the antimicrobial susceptibility testing for cefotaxime (CTX, 30 µg), cefoxitin (CX, 10 µg), ceftazidime (CAZ, 30 µg), amikacin (AK, µg), piperacillin/tazobactam (PT, 100/10 µg), gentamicin (GM, 10 µg), ciprofloxacin (CIP, 5 µg), meropenem (MRP, 10 µg), imipenem (IMP, 10 µg), and ertapenem (ETP, 10 µg) (Himedia, India) according to the CLSI guidelines 2022. *K. pneumoniae* isolates that exhibit resistance to any one of the carbapenems used in this study were considered as CRKP and they were further screened for phenotypic and genotypic confirmatory tests.

Investigating antibiotic resistance by disk diffusion

Using the Clinical and Laboratory Standards Institute (CLSI) guidelines , an antibiogram assay was performed on the isolated *K. pneumoniae* colonies. The antibiotic discs contained ampicillin (30 µg), cotrimoxazole (25 µg), cefixime (5 µg), cefotaxime (30 µg), ceftriaxone (30 µg), ceftazidime (30 µg), gentamicin (10 µg), amikacin (30 µg), tetracycline (30 µg), doxycycline (30 µg), minocycline (30 µg), tigecycline (15 µg), ciprofloxacin (5 µg), levofloxacin (5 µg), ampicillin/sulbactam (100/10 µg), piperacillin/tazobactam (100/10 µg), imipenem (10 µg), meropenem (10 µg), ertapenem (10 µg), doripenem (10 µg), aztreonam (30 µg), colistin (10 µg), and fosfomycin (200 µg) (Mast Diagnostics, United Kingdom). The minimum inhibitory concentration (MIC) of imipenem, meropenem, and colistin for isolates resistant to carbapenems was determined by using E-test (Liofilchem, Italy) according to the 2022 CLSI guidelines [8].

Phenotypic Detection Method

Detection of carbapenemase

To recognize carbapenemase-positive isolates, the samples were subjected to the modified Hodge test (MHT), modified carbapenem inactivation method (mCIM), and EDTA-modified carbapenem inactivation method (eCIM) procedures according to the CLSI guidelines 2022[9].

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Genotypic Detection Method

Genetic Analysis of MDR *Klebsiella pneumoniae* Isolates

Detection of Antibiotic Resistance Genes the *K. pneumoniae* isolates were screened for the carbapenemase gene of Screening of Ertapenem, Meropenem , Imipenem disc and NDM-1 using a PCR assay [10].

The Bacterial DNA was extracted. The primers were purchased from "**Saha gene'** and was reconstituted with sterile double distilled water based on the manufacturer's instruction.

Molecular Characterization: TheDNA extraction was performed using the boiling method as described by Holmes et al. (1981). Four to five individual pure isolated bacterial colonies were picked and dispersed in a 1.5 ml Micro Centrifuge Tube (MCT) using 200 µl of nuclease-free water. The MCTs were then placed in a water bath at 95°C for 15 minutes. Following this, centrifugation was carried out at 2000 rpm for 5 minutes, and the supernatant was transferred to a fresh MCT, serving as the DNA template for subsequent amplification. Following PCR amplification, the presence of the target gene was confirmed by electrophoresis on a 1.5% agarose gel stained with Ethidium bromide. Bands were visualized under UV light to confirm the successful amplification of blaNDM-1 gene [11].

Figure No. 1: The blaNDM primer

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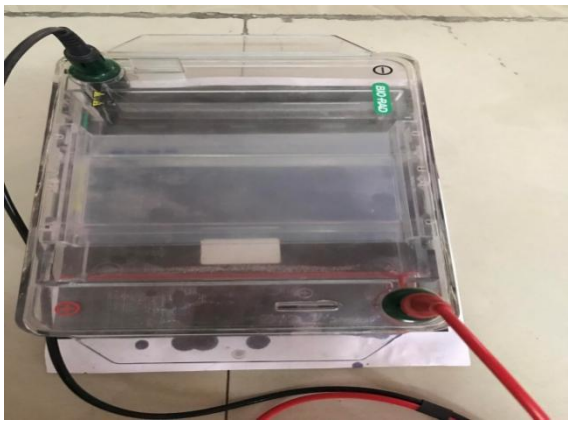

Figure No.2: Gel Electrophoresis for the DNA Extraction

The Primers

S.N.	Gene	Primer sequence (5'→3')	Size
1.	NDM-1	F: GGCGGAAGGCTCATCACGA R: CGCAACACAGCCTGACTTTC	287bp

Table No.1 : Primer used for the blaNDM-1 gene amplification

The Polymerase Chain Reaction

For the PCR amplification, 2 µl of template DNA was added to 18 µl reaction containing 10 µl of Qiagen master mix, 2 µl of primer mix (1 µl each of the respective forward and reverse primers) and 6 µl of molecular-grade water.

The cyclic conditions for blaNDM-1 gene, initial denaturation at 95 °C for 15 min, 30 cycles of 94 °C for 30 s, 59 °C for 1 min 30 s and 72 °C for 1 min 30 s were followed by extension of 72 °C for 10 min.

The PCR cycling conditions

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Step	**Program** **BlaNDM-1** **Time Temperature**	**Cycles**
Initial denaturation	15 min 95 ºC	30
Denaturation	30 s 94 ºC	
Annealing	1 min30 s 59 ºC	
Extension	1 min 30 s 72º C	
Final extension	10 min 72º C	

Table No. 2 : The PCR cycling conditions to amplify blaNDMgene fragments.

The Agarose gel preparation and visualized by Gel Doc™ EZ Gel Documentation System

The Agarose Gel Electrophoresis was performed in order to identify the Purified PCR Product which was previously identified by its amplified DNA fragments. The resulting PCR product was subjected to 1% agarose gel electrophoresis and visualized by Gel Doc™ EZ Gel Documentation System (Bio-Rad Laboratories Inc., Hercules, CA, USA). A 1 kb DNA Ladder (Thermo Fisher Scientific ™, Waltham, MA, USA) was used as the marker to evaluate the PCR product of the sample [11].

Statistical analysis

Data recorded on the report form and structured proforma were subsequently entered into a spreadsheet. Data management and analysis were performed using Microsoft Excel.

RESULTS

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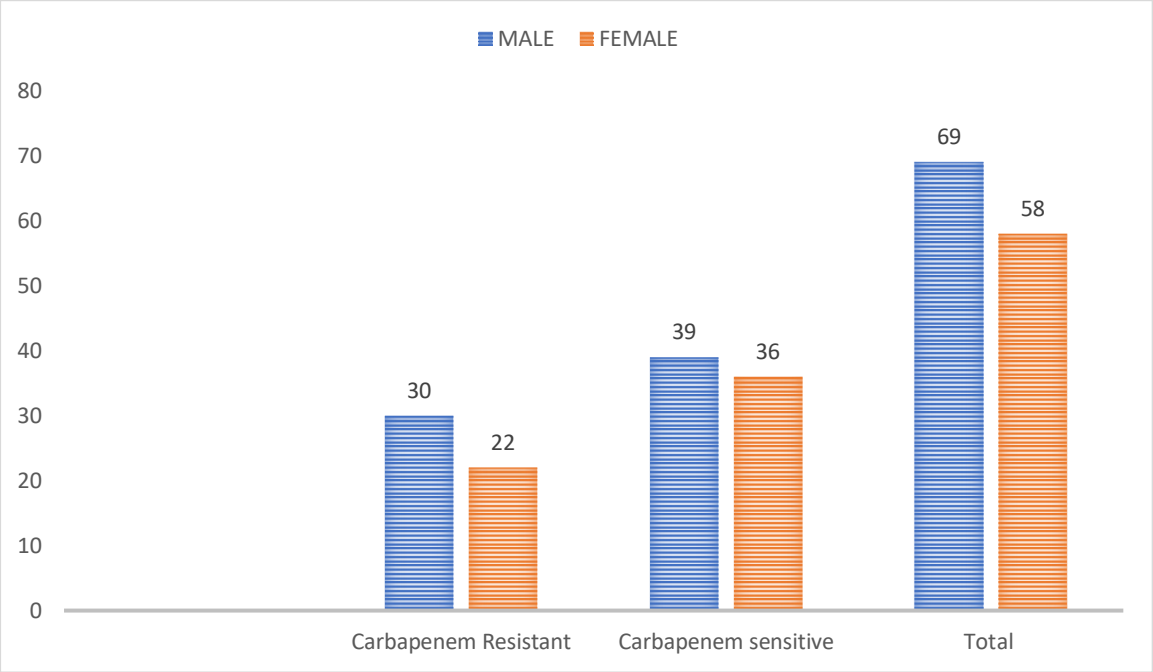
A total of 350 isolates of *K. pneumoniae* were collected from patients, with 127(36.28%) identified as CRKP. There were 30 (57.69%) isolates obtained from male and 22(42.30%) were obtained from female.This study showed the Carbapenem resistance is maximum in male than in female as shown in table 3 and graph no. 1.

	Male	Female
Carbapenem Resistant	**30**	**22**
Carbapenem sensitive	**39**	**36**
Total	**69**	**58**

Table No. 3: Gender wise distribution (n-127)



Graph No. 1 : Graphical Representation of Gender wise distribution (n- 127)

In the our study, we found that the maximum carbapenem resistance 46.15% (N=24) was present in the age group > 50 yrs old followed by the age group 41-50 yrs, 19.23%(N=10) respectively as shown in Graph.2 and Table 4.

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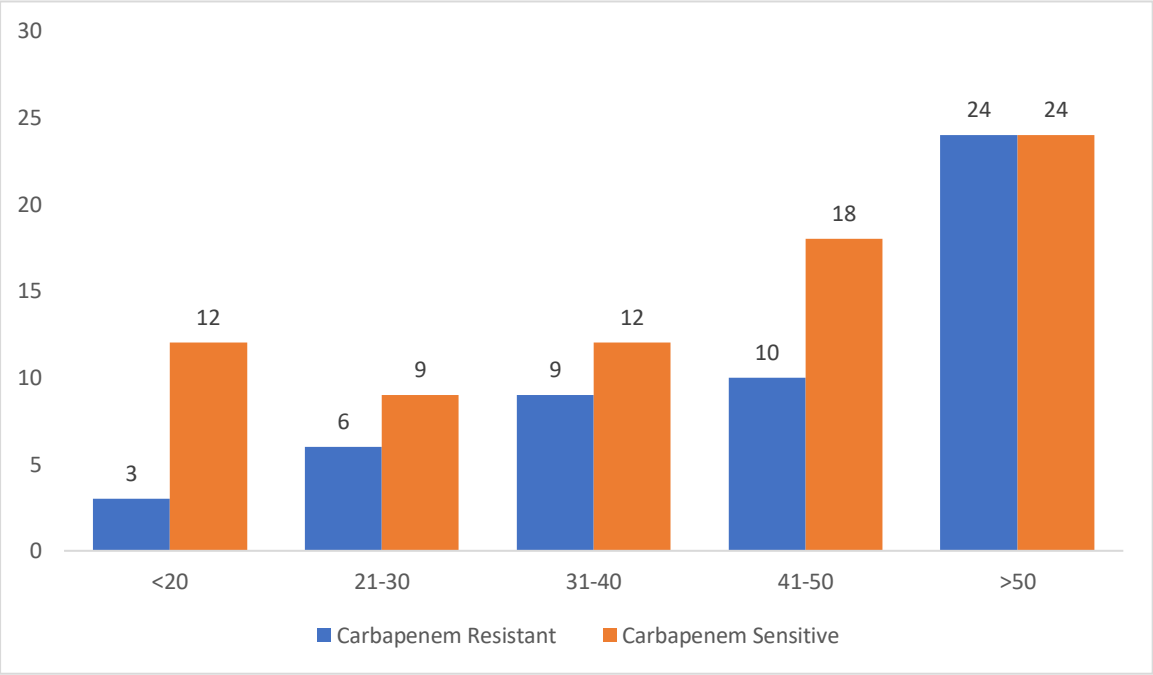
	Carbapenem Resistant	Carbapenem Sensitive
<20	3	12
21-30	6	9
31-40	9	12
41-50	10	18
>50	24	24

Table No. 4: Age wise distribution (n-127)



Graph No. 2 : Graphical Representation of Age wise distribution(n-127)

In our study total 127 *K. pneumoniae* strains were collected from clinical samples such as sputum (n =15), urine (n = 12), blood (n = 5), pus (n= 6) and other clinical samples as shown in Graph no. 3.

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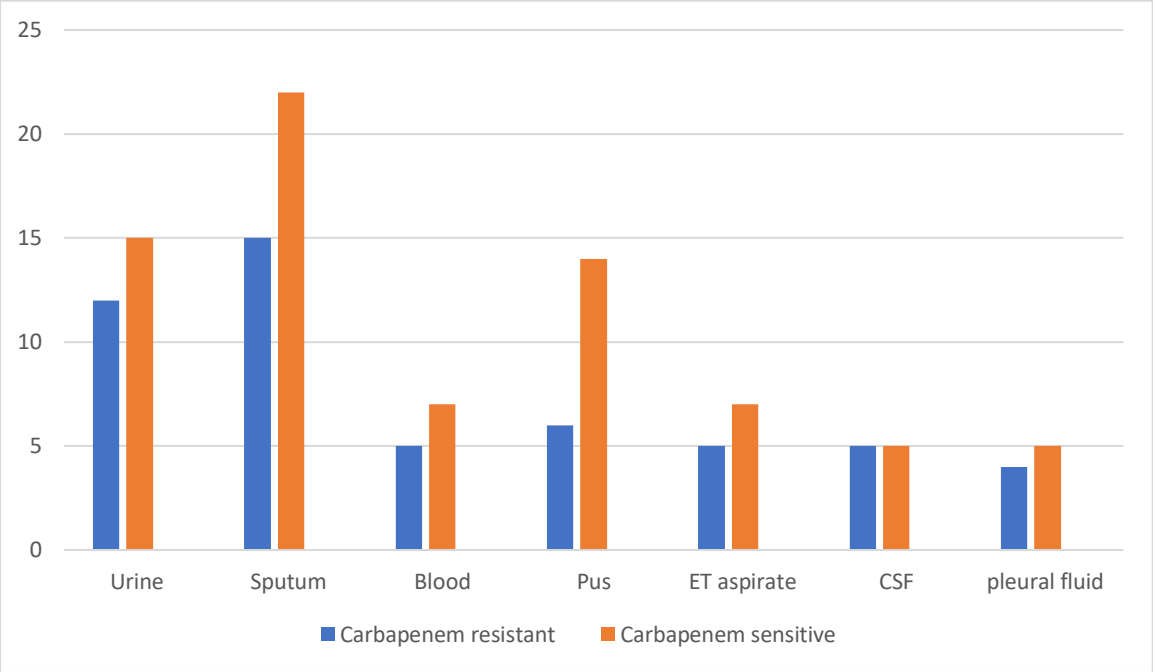
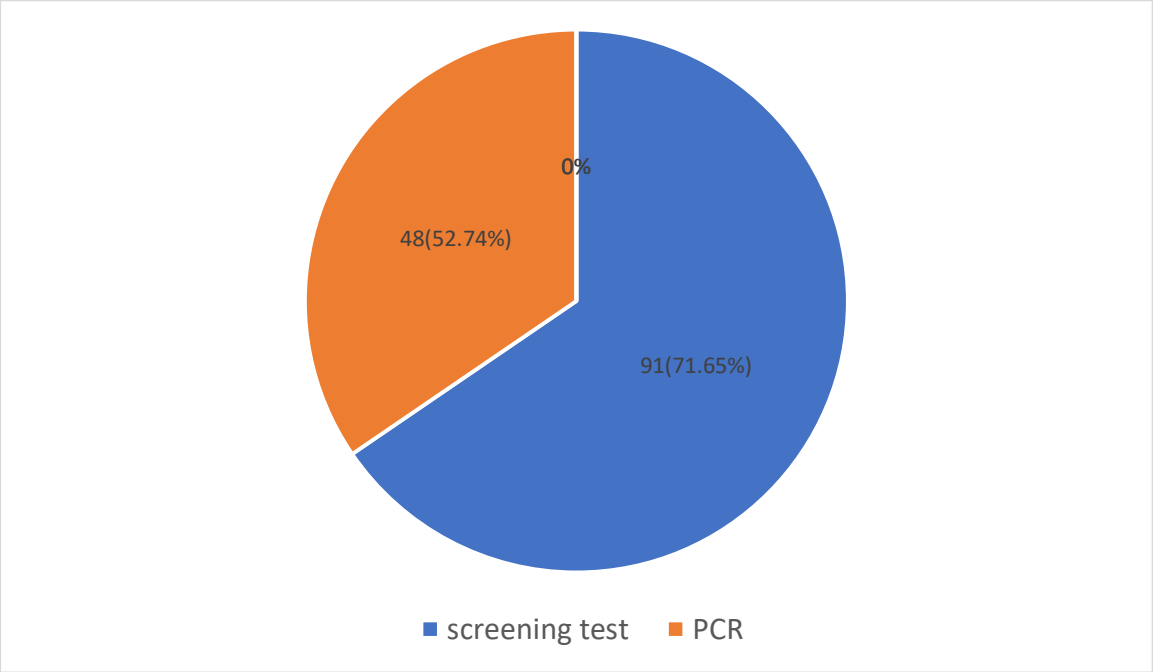


Graph No. 3: Graphical Representation of Sample wise distribution

Out of which, 71.65%(n=91)of total *Klebsiella* isolates were carbapenem resistant by Kirby-Bauer disc diffusion but 52.74% (48/91) of *Klebsiella* isolates were confirmed for Carbapenemase production by PCR as shown in Graph. 4.



Graph No.5: Carbapenem production screening by (Ertapenem/ Meropenem /Imipenem disc) and Confirmatory by PCR Assay.

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In this table it was observed that, Male dominance was more in study population (49.27%). while the maximum number of patients belong to age group <50 years and Maximum patients were engaged as Student/Housewife/Retired (44.09%) followed by Clerical/Shopkeeper/Farmer (36.22%), only 5 (3.93%) was professional, 4 (3.14%) Semiskilled worker, 6 (4.72%) were semi-professionals and 7 (5.51%) was Unskilled worker.

	No.	Percentage (%)
Student/Housewife/Retired	59	44.09%
Clerical/Shopkeeper/Farmer	46	36.22%
Professional	5	3.93%
Semiskilled worker	4	3.14%
semi-professionals	6	4.72%
Unskilled worker	7	5.51%

Table No.5: Occupation wise distribution of *Klebsiella pneumoniae* isolates.

Among these isolates, Ertapenem resistance was observed in 87 (68.5%), Meropenem resistance in 88 (69.2%), and Imipenem resistance in 86 (67.7%) isolates. As depicted in table 6.

Antimicrobial resistance	No.	Percentage (%)
Ertapenem resistance	87	68.5%
Meropenem resistance	88	69.2%
Imipenem resistance	86	67.7%

Table No. 6 : Antimicrobial resistance profile of *Klebsiella pneumoniae* isolates .

Phenotypic tests M-CIM and E-CIM positive rates of patients with CRE isolates (n=127) were 82.20% and 80.36% respectively. Among patients with CRE isolates NDM-1 gene was expressed in 86.61%, as depicted in Table 6.

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SN	Test	CRE (n=127)	
		Number	**Percentage**
I	**Phenotypic test**		
	M-CIM positive	104	81.88%
	E-CIM positive	99	77.95%
II	**Genotypic test**		
	NDM-1 positive	110	86.61%

Table 7: Phenotypic and Genotypic Characteristics among CRE Colonizers (n=127)

In this table, it was observed that, In phenotypic test 81.88% were positive for M-CIM while 77.95% were positive for E-CIM and in genotypic test, 86.61 % were positive for NDM-1.

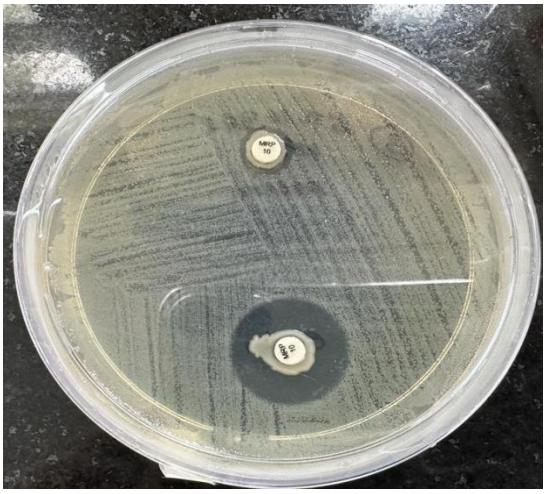

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Figure No 3: mCIM Positve phenotypic test in CRE isolates.

Figure No.4: eCIM Positve phenotypic test in CRE isolates.

Figure No.5 : The DNA extraction of blaNDM gene detection

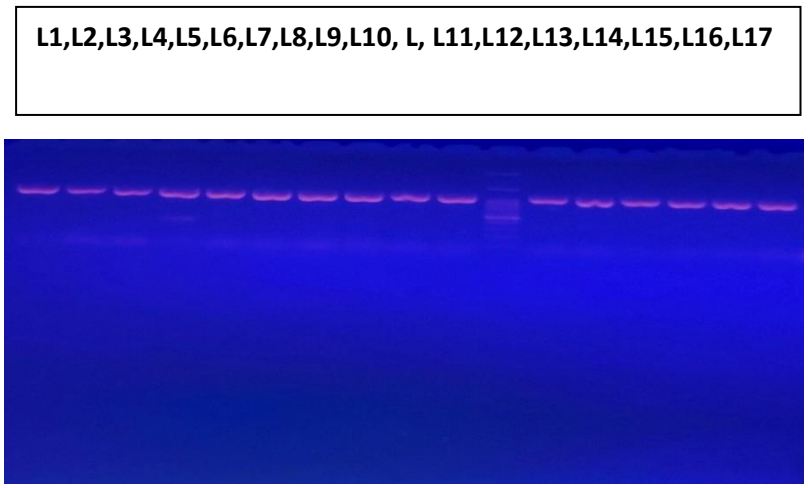

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Figure No.6: Showing positive band for NDM-1 Gene 287 bp

L corresponds to the DNA Ladder; L1- L10 are the sample positive for blaNDM-1 gene; L11 corresponds to the Positive Control for blaNDM-1 gene ; L12-L16 corresponds to the sample positive for blaNDM-1 gene; L17 is the Negative Control gene for blaNDM-1 gene

The risk factor analysis for rectal colonization with CRE in ICU patients showed several significant associations. Hospital admission within the past three months, prior hospital admissions within the last year, and the use of antibiotics before admission, Additionally, the use of ventilator support, central line support, and Foley's catheter were significantly associated with CRE colonization. These findings highlight the importance of considering prior healthcare exposure and invasive procedures when assessing the risk of CRE colonization in ICU patients.

Table 8: Duration of ICU Stay analysis of patients for Rectal colonization with CRE v/s Non CRE.

S.N	Duration of ICU stay (Days).	Total patients stay in ICU. (350)	CRE= (127)		NON CRE= (223)	
			NO	%	NO	%
1	<7 days	90	24	26.6	78	86.6
2	7-21 days	220	91	41.3	102	46.3
3	>21 days	40	12	30	43	107

In this table it was observed that the maximum number of CRE were isolated from the patient's hospital stay was > 7 days (41.3%).

Among various antibiotics used, Cefepime showed the highest resistance with 91.93% of NDM-1 positive isolates being resistant, followed closely by Ampicillin (90.16%) and

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Cefazoline (89.43%). Other antibiotics with high resistance rates include Ceftriaxone (88.97%), and Amoxiclav (81.30%), Azthreonam (80.64%), Cotrimoxazole (80.31%), and Ciprofloxacin (80.15%).Moderate resistance was observed for antibiotics like Levofloxacin (69.29%) and Cefoxitine (74.8%). The lowest resistance rates were seen in Piperacillin & Tazobactam (67.71%), Gentamicin (54.33%), and Tobramycin (60.62%). As shown in table 9.

Table 9: Antimicrobial susceptibility pattern of NDM-I positive CRE colonizer (n=127) obtained.

SN	Antimicrobial agent	Total NDM-I positive isolates (127)	NDM-I positive isolates	
			No. of resistant isolates	**%**
1	Ampicillin	122	110	90.16
2	Amoxiclav	123	100	81.30
3	Piperacillin & Tazobactam	127	86	67.71
4	Ceftriaxone	127	113	88.97
5	Cefepime	124	114	91.93
6	Cefoxitine	125	101	80.8
7	Cefazoline9	123	110	89.43
8	Amikacin	126	76	60.31
9	Gentamycin	127	69	54.33
10	Ciprofloxacin	126	101	80.15
11	Cotrimoxazole	127	102	80.31
12	Azthreonam	124	100	80.64
13	Tobramycin	127	77	60.62
14	Levofloxacin	127	88	69.29

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In this table, it was observed that, Piperacillin and Tazobactam, Levofloxacin, Amoxicillin, Ampicillin, Ceftriaxone, Cefoxitine, and Cefazoline antibiotics showed varying degrees of resistant across different bacterial species, with generally higher resistance rates observed in CRE compared to non CRE.

DISCUSSION

The emergence of CRKP presents a significant challenge to worldwide public health, posing a substantial obstacle to effective clinical infection management [12-16].This study sought to explore the drug resistance profile and epidemiological features of CRKP at the CMC, with the overarching goal of implementing effective measures to curb the spread of CRKP infections among pediatric patients.

The high prevalence of CRKP complicates the management of nosocomial infections, underscoring the urgency for a reassessment of current infection control protocols and antibiotic stewardship strategies. The predominant risk factors commonly associated with CRE infection include the utilization of indwelling medical devices, previous exposure to antibiotics, and admission to the ICUs. Urinary catheters and central venous catheters, frequently utilized in healthcare settings to address diverse medical needs and ensure critical patient care, establish an optimal environment for bacterial colonization. Moreover, prior antibiotic exposure is identified as another key risk factor driving the emergence and spread of CRE infections. All patients included in our study had a history of previous hospitalization and prior antibiotic use. Enhanced infection control measures, including stringent adherence to hand hygiene protocols, judicious use of indwelling medical devices, and implementation of antimicrobial stewardship programs to optimize antibiotic use, are essential for controlling the spread of CRE[13].

In the present study, a total of 350 isolates of *K. pneumoniae* were collected from patients, with 127(36.28%) identified as CRKP. In our study, total 127 *K. pneumoniae* isolates were identified from various clinical samples.There were 30 (57.69%) isolates obtained from male and 22(42.30%) were obtained from female. The rate of isolation of the *K. pneumoniae* was more in male patients than female patients. Our study was in accordance with the study conducted by other authors Babak Pourakbari et al 2024[17] , Jane Wairimu Maina et al 2024 [18] and Alhazmi W et al. 2022[19] where more isolates were obtained from males.

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In the our study, we found that the maximum carbapenem resistance 46.15% (N=24) was present in the age group > 50 yrs old followed by the age group 41-50 yrs, 19.23%(N=10) receptively. This finding was also reported by Satyajeet k Pawan et al. (2015) [20] who observed that 41-60 age group showed maximum CRE prevalence. This finding is consistent with Alhazmi W et al. 2022 [19] were the maximum carbapenem resistance was found in 60 to 79 years = 59.7% (*n* = 114). This finding was consistent with Shibl, A et al.2013 [21] which significantly showed that old age is a risk factor associated with CRKP isolation in their study area.

In our study, total 127 *K. pneumoniae* strains were collected from clinical samples such as sputum (n =15), urine (n = 12), blood (n = 5), pus (n= 6) and other clinical samples. This finding was in accordance with a study conducted by Babak Pourakbari et al 2024[17]where the highest number of isolates were urine, with 20 cases (37%), followed by blood, which produced 15 isolates (28%). Next in frequency were isolates from bronchoalveolar lavage (BAL), accounting for 5 cases (9%), and wounds, contributing 3 cases (6%). Eye discharge yielded 2 isolates (4%), while throat, cerebrospinal fluid (CSF), sputum, and dialysis fluid, each resulted in 1 isolate (2%). And similar other finding with a study conducted by Alshahrani, A.M. et al 2022 [22]. The isolates were recovered from samples of sputum (25; 35.2%), urine (24; 33.8%), blood (12; 16.9%), wound pus (8; 11.3%), and tracheal aspirate (TIP) (2; 2.8%) and Elnaz Abbasi et al 2023 [23] in which the most infectious samples of *K. pneumoniae* were seen in urine (62, 51.2%), respiratory (48, 39.6%), wound (11, 9%), and blood infections (8, 6.6%).

In the present study, the *K. pneumoniae* was maximum resistance shown by Ampicillin 90.16%, Meropenem %and Imepenem70% both. This finding was similar to the study conducted by Alshahrani, A.M. et al 2022 [22] and Alhazmi W et al. 2022 [19] where Imipenem and Meropenem was maximum resistance to *K. pneumoniae*. This finding was similar to other study conducted by Sushma Gurung et al.2020 [24-26] where *K. pneumoniae*was observed to be resistant to ampicillin, followed by cefixime (83.3%; 20/24), cotrimoxazole (66.7%), imipenem (66.7%) and meropenem (66.7%).

In this table it was observed that the maximum number of CRE were isolated from the patient's hospital stay was > 7 days. This finding was in accordance to the study conducted by Raghdaa A Ramadan et al 2022 [27] by Recent antibiotic therapy and previous hospitalization of 5

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days or more were significant risk factors for CR *K. pneumoniae* and similarly studied by Mantzarlis et al 2013 [26] .

The lack of adequate infection control measures in our hospital raise concerns regarding the potential spread of CRKP through patient transfers, particularly from the emergency department to other wards. The detection of the bla_{NDM} gene in other clusters implies the dissemination of this resistance gene across different wards within the hospital, thereby indicating the possibility of transmission to all wards. This clonal expansion has the potential to be transmitted to patients via personnel, equipment, or contaminated surfaces [28].

Therefore, it is highly recommended to enforce rigorous infection control protocols, encompassing effective isolation measures, thorough cleaning and disinfection protocols, and strict compliance with hand hygiene practices, to control the dissemination of CRKP within the hospital setting. Effective communication and collaboration among healthcare teams are vital to ensure that patients with CRKP colonization or infection are appropriately managed during transfers, thus minimizing the risk of further dissemination [29,30].

While the bla_{NDM} gene is a significant contributor to carbapenem resistance, there are other mechanisms, such as the production of carbapenemases like KPC and OXA enzymes, as well as non-enzymatic mechanisms involving alterations in porins and efflux pumps, that can also confer resistance to carbapenems. Understanding the full spectrum of resistance mechanisms is essential for developing comprehensive strategies to combat carbapenem-resistant infections effectively.

Conclusion:

The study highlighted the existence of carbapenemase-producing K. *pneumoniae*, particularly in blaNDM-1, in patients with comorbidities. Our findings emphasize the importance of the molecular characterization of resistance-determinant-carrying bacterial pathogens as a part of infection control and prevention in hospital settings. Understanding the mechanism causing carbapenem resistance of *K. pneumoniae* has an important clinical implications and results in different prevention measurements and individualized antibiotic therapy.

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Declarations:

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