





Original Article

Molecular epidemiology of Carbapenemase-encoding genes and comparative evaluation of carbapenem MIC with genotypic carbapenem resistance in *Klebsiella* isolates from neonatal sepsis cases

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ABSTRACT

Objectives: The objective of this study was to determine the molecular epidemiology of Carbapenemase-encoding genes in *Klebsiella* isolates from neonatal sepsis cases and comparative evaluation of carbapenem minimum inhibitory concentration (MIC) with genotypic carbapenem resistance.

Materials and Methods: One hundred cases of neonatal sepsis with blood cultures positive for *Klebsiella* spp. were included in the study. MIC for imipenem and meropenem was determined by Epsilon-meter test. Antimicrobial susceptibility testing (AST) was performed by modified Kirby Bauer disc diffusion method. All the isolates of *Klebsiella* spp. were tested for the presence of beta-lactamase *Klebsiella pneumoniae* carbapenemase (*bla*KPC), beta-lactamase New Delhi metallo-β-lactamase-1 (*bla*NDM-1), beta-lactamase imipenemase (*bla*IMP), beta-lactamase Verona imipenemase (*bla*VIM) genes by multiplex polymerase chain reaction (PCR) and uniplex PCR for beta-lactamase oxacillinase-48 (*bla*OXA-48). Comparison of individual antibiotic susceptibility between carbapenemase-encoding gene positive and negative *Klebsiella* spp. isolates was performed.

Statistical analysis: Statistical analysis was done using the Fisher's exact test. $P < 0.05$ was considered significant.

Results: The prevalence of carbapenemase-encoding genes in *Klebsiella* spp. was 16%. Most predominant carbapenemase-encoding gene was *bla*OXA-48 gene (12%) followed by *bla*NDM-1 gene (6%). Coexpression of both *bla*OXA-48 and *bla*NDM-1 was observed in 2% of isolates. All the *Klebsiella* spp. isolates harboring the carbapenemase gene (100%) had resistant MIC values for Meropenem, whereas, for imipenem, only 75% of isolates had resistant MIC values.

Conclusions: Determination of prevalence of carbapenemase-encoding genes is of paramount importance in the development of effective antibiotic policies at various levels.

Keywords: Carbapenemase-encoding genes, Carbapenem-resistant *Enterobacteriales*, OXA-48, New Delhi metallo-β-lactamase, Coexpression OXA-48 and New Delhi metallo-β-lactamase, *Klebsiella pneumoniae*

INTRODUCTION

The past two decades have witnessed an increase in the incidence and spread of multidrug-resistant organisms like Carbapenem-resistant *Enterobacteriales* (CRE). CRE poses a considerable threat to mankind as they are resistant to almost all the available beta-lactam antimicrobials, including one or more carbapenem drugs along with fluoroquinolones, and aminoglycosides. The treatment options are either very few or non-existent for this group of multidrug-resistant bacteria.^[1]

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Klebsiella pneumoniae (*K. pneumoniae*) is the most notorious member of CRE group that is frequently associated with life-threatening infections. This pathogen can be resistant to the repertoire of available antibiotics. The isolation of *K. pneumoniae* in increased frequencies from hospital environments, including intensive care units especially in developing countries is alarming.^[2-4] *K. pneumoniae* is very frequently associated with oxacillinases (OXA)-48 like and New Delhi metallo- β -lactamase (NDM) carbapenemase-encoding genes globally. Acquisition and transmission of potent transferable plasmid-encoded carbapenemases such as *Klebsiella pneumoniae* Carbapenemase (KPC), NDM, Imipenemase (IMP), Verona integron-encoded metallo-beta-lactamase (VIM), and oxacillinase-48 like enzymes is common in multi-drug resistant and hypervirulent strains of *Klebsiella* spp.^[3]

India is endemic to CRE harboring carbapenemase-encoding genes of OXA-48, such as OXA-181 and OXA-232 and NDM-1 variants, which were first described in *K. pneumoniae*.^[5,6] The sporadic outbreaks of various members of CRE possessing other carbapenemase-encoding genes such as IMP, KPC, and VIM have also been reported over recent years.^[7,8] Noticeably, the circulating carbapenemase strains of pathogenic bacteria may vary geographically or even at different locations within the same healthcare setting. Phenotypic determination of potential carbapenem resistance due to the presence of carbapenemase-encoding gene and its impact on the susceptibility to other antimicrobial agents varies widely according to the individual carbapenemase-encoding gene present.^[1] OXA-48 like carbapenemases is known to possess weak carbapenem hydrolytic activity and, thus, is likely to be missed by phenotypic detection methods.^[9,10] Therefore, the molecular identification of resistance mechanisms in circulating strains of CRE pathogens is crucial for healthcare settings to effectively manage life-threatening infections without unwarranted delay. Furthermore, the availability of information regarding the prevalent resistant strains can play an important role in containment of these infections.

Neonatal sepsis is the third leading cause of neonatal mortality. As per United Nations Children's Fund, the neonatal mortality rate in India was 21.7/1000 live births in the year 2022.^[11] Carbapenem-resistant *K. pneumoniae* is often known for frequently causing outbreaks in neonatal intensive care units (NICUs), thus warrants its molecular characterization pertaining to the presence of carbapenemase-encoding genes.^[12] Often the inadequacy of molecular diagnosis of CRE and their underlying resistance mechanisms in resource-limited settings contribute to the inadvertent spread of these resistant isolates. The growing complexities surrounding the treatment of life-threatening infections caused by CRE demands an understanding of its local epidemiology for providing adequate empirical coverage and antimicrobial resistance control initiatives.

Numerous studies have addressed the dissemination of CRE, but the data on neonatal sepsis are limited. Earlier studies reported the presence of a single carbapenemase gene in *K. pneumoniae*, but recent years have shown the emergence of coproduction of multiple carbapenemases.^[13,14] Furthermore, NDM producing *K. pneumoniae* was more prevalent previously in neonatal infections. Besides, recent years have noted a significant emergence of highly transferable OXA-48 class D carbapenemase in *Enterobacteriales*.^[15,16] Therefore, the present study attempted to determine the molecular epidemiology of Carbapenemase-encoding genes and comparative evaluation of carbapenem minimum inhibitory concentration (MIC) with genotypic carbapenem resistance in *Klebsiella* isolates from neonatal sepsis cases.

MATERIALS AND METHODS

A prospective study was conducted by the molecular laboratory of the Department of Microbiology in collaboration with NICU and the Department of Pediatrics. Post obtaining the approval from the Institutional Ethics Committee-Human Research, the study was extended for over a period of one year, starting July 2019 to June 2020. The first 100 neonates admitted to NICU with clinical signs and symptoms suggestive of neonatal sepsis who had blood cultures positive for *Klebsiella* spp. were included in the study. Sepsis screening was performed in the clinically suspected cases. The criteria included total leukocyte count ($<500/\text{mm}^3$), absolute neutrophil count ($<1800/\text{mm}^3$), immature to a total neutrophil ratio ($>20\%$), C-reactive protein ($>1 \text{ mg/dL}$), and micro erythrocyte sedimentation rate (15 mm or more in the 1st h). Sepsis screening was considered positive if any two of these parameters were positive.^[17]

All these non-duplicate *Klebsiella* spp. isolates from blood samples of neonatal sepsis patients were identified and processed further using the standard laboratory guidelines. Antimicrobial susceptibility testing (AST) was performed by modified Kirby Bauer disc diffusion method using the amikacin (30 μg), aztreonam (30 μg), azithromycin (15 μg), ceftazidime (30 μg), cefotaxime (30 μg), cefixime (5 μg), ciprofloxacin (5 μg), cotrimoxazole (25 μg), gentamicin (10 μg), imipenem (10 μg), meropenem (10 μg), and piperacillin-tazobactam (100/10 μg) antibiotic discs (HiMedia laboratories, India).

Minimum Inhibitory Concentration (MIC for imipenem and meropenem was determined by Epsilon-test using Imipenem Ezy MIC[™] Strip (IPM) (0.002–32 $\mu\text{g/mL}$) and Meropenem Ezy MIC[™] Strip (MRP) (0.002–32 $\mu\text{g/mL}$) (HiMedia Laboratories, India). *K. pneumoniae* ATCC BAA-1705 and *K. pneumoniae* ATCC BAA-1706 were used as positive and negative controls. For both the antibiotics, imipenem and meropenem, isolates were considered susceptible (MIC $\leq 1 \mu\text{g/mL}$), intermediate (MIC of 2 $\mu\text{g/mL}$), and resistant (MIC $\geq 4 \mu\text{g/mL}$) after incubation of 18 h at 35–

37°C. The AST and interpretation of results were performed as per Clinical and Laboratory Standards Institute guidelines.^[18]

The deoxyribonucleic acid (DNA) was extracted (HIPURATM bacterial genomic DNA purification kit from HiMedia laboratories, India) by spin-column procedure. All the isolates of *Klebsiella* spp. were tested for the presence of beta-lactamase *Klebsiella pneumoniae* carbapenemase (*bla*KPC), beta-lactamase New Delhi metallo- β -lactamases-1 (*bla*NDM-1), beta-lactamase imipenemase (*bla*IMP), beta-lactamase Verona imipenemase (*bla*VIM) genes by multiplex polymerase chain reaction (PCR) and uniplex PCR for beta-lactamase oxacillinase-48 (*bla*OXA-48) using the primer sequences for target genes mentioned in Table 1.^[19,20]

Cycling conditions for *bla*KPC, *bla*NDM-1, *bla*IMP, and *bla*VIM genes Multiplex PCR: ^[19] For amplification, 30 cycles were done at 94°C for 1 min, 54°C for 1 min, and 72°C for one and a half minutes followed by a final extension step of 5 min at 72°C.

Cycling conditions for *bla*OXA-48 gene Uniplex PCR:^[20] For amplification, initial denaturation at 94°C for 10 min; 30 cycles of 94°C for 40 s, 60°C for 40 s, and 72°C for 1 min followed by a final elongation step at 72°C for 7 min. The annealing temperature was optimal at 57°C.

The amplified products were then run on 1.5% Agarose gel (HiMedia laboratories India) at 100 Volts for 45 min to 1 h and viewed under UV light (G: BOX, SynGene). The gel was then photographed using GeneSnap from SynGene [Figure 1].

Statistical analysis

Comparison of individual antibiotic susceptibility between carbapenemase-encoding gene positive and negative *Klebsiella* spp. isolates was performed using the Fisher's exact test. *P*-values were calculated for the analysis of the difference in antibiotic susceptibility between carbapenemase-encoding gene positive and negative *Klebsiella* spp. Isolates. Relevant frequencies and percentages were calculated.

RESULTS

Distribution of carbapenemase-encoding genes among *Klebsiellas* spp. isolates

The overall prevalence of carbapenemase-encoding genes in *Klebsiella* spp. isolates from blood samples of neonatal sepsis cases admitted in NICU was 16% (16/100). The distribution of various carbapenemase-encoding genes is shown in Table 2 and Figure 2. The most predominant carbapenemase-encoding gene was *bla*OXA-48 gene (12%), followed by *bla*NDM-1 gene (6%). None of the isolates harbored carbapenemase-encoding genes of *bla*IMP, *bla*VIM, and *bla*KPC. The coexpression of both *bla*OXA-48 and *bla*NDM-1 was observed in 2% of isolates.

Comparative distribution of carbapenemase-encoding genes in different MIC cutoff categories of imipenem and meropenem

Comparative distribution of carbapenemase-encoding genes in different MIC cutoff categories of imipenem and meropenem among *Klebsiellas* spp. isolates from blood samples of neonatal sepsis cases admitted in NICU are shown in Table 3. All the *Klebsiella* spp. isolates harboring the carbapenemases gene (100%) had resistant MIC values for meropenem (≥ 4 μ g/mL), whereas, for imipenem, only 75% of isolates had resistant MIC values (≥ 4 μ g/mL). For imipenem, 18.7% of carbapenemase-encoding genes harboring *Klebsiella* spp. had susceptible (≤ 1 μ g/mL) and 6.25% had intermediate MIC values. Out of three isolates with susceptible MIC values for imipenem, two were harboring *bla*OXA-48 (MIC 0.19 μ g/mL and 0.25 μ g/mL), and one had *bla*NDM-1 gene (MIC 0.75 μ g/mL). The isolate with intermediate MIC harbored *bla*OXA-48 gene (MIC 2 μ g/mL). A significant association was observed between the presence of carbapenemase-encoding genes and MIC values for imipenem and meropenem ($P < 0.001$ and $P = 0.016$, respectively).

Table 1: Primer sequence for target genes.

S. No.	GENES	FP/RP	PRIMER SEQUENCE (5'-3')	SIZE (bp)
1.	NDM-1	FP RP	GCATAAGTCGCAATCCCCG CTTCCTATCTCGACATGCCG	237
2.	VIM	FP RP	GTTTGGTCGCATATCGCAAC AATGCGCAGCACCAGGATAG	382
3.	IMP	FP RP	GAAGGCGTTTATGTTTCATAC GTAAGTTTCAAGAGTGATGC	578
4.	KPC	FP RP	TCGAACAGGACTTTGGCG GGAACCAGCGCATTTTTGCG	201
5.	OXA-48	FP RP	GCTTGATCGCCCTCGATT GATTTGCTCCGTGGCCGAAA	281

NDM-1: New Delhi metallo- β -lactamase-1, VIM: Verona integron-encoded metallo-beta-lactamase, IMP: Imipenemase, KPC: *Klebsiella pneumoniae* Carbapenemase, OXA-48-like: Oxacillinases, FP: Forward Primer, RP: Reverse Primer, bp: Base pair

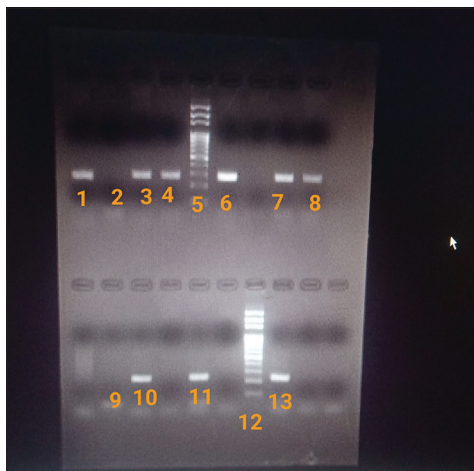


Figure 1: Gel electrophoresis showing bands of DNA and 100bp DNA ladder in GeneSnap software. 1: Positive control for *bla*NDM-1 gene; 2,9: Negative control (Distilled water); 5, 12: DNA ladder; 3,4,6,7,8: Test (positive for *bla*NDM-1 gene); 10: Positive control for *bla*OXA-48 gene; 11,13: Test (positive for *bla*OXA-48 gene). *bla*NDM-1: beta-lactamase New Delhi metallo- β -lactamases-1, *bla*OXA-48: Oxacillinases.

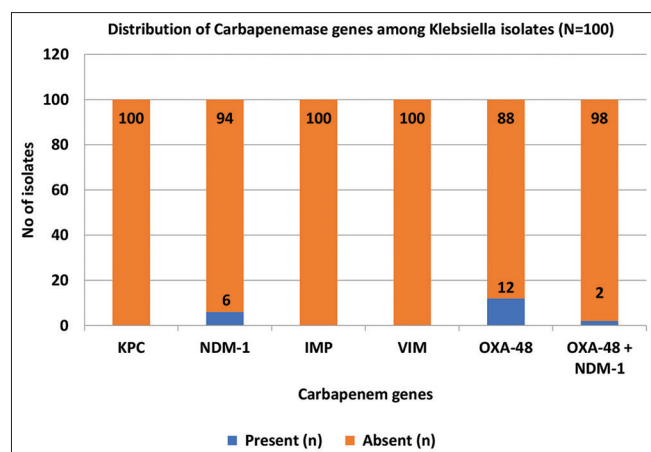


Figure 2: Prevalence of carbapenemase-encoding genes in *Klebsiella* spp. isolates from blood samples of neonatal sepsis cases admitted in neonatal intensive care unit ($n = 100$). n : Specify total number of tested isolates, KPC: *Klebsiella pneumoniae* Carbapenemase, NDM-1: New Delhi metallo- β -lactamase-1, IMP: Imipenemase, VIM: Verona integron-encoded metallo-beta-lactamase, OXA-48-like: Oxacillinases.

Comparative distribution of susceptibility to various antimicrobial agents in *Klebsiella* spp. isolates with and without genotypic carbapenem resistance

Table 4 shows the comparative distribution of susceptibility to various antimicrobial agents in *Klebsiella* spp. isolates with and without genotypic carbapenem resistance. Resistance to amikacin, aztreonam, ceftazidime, cefotaxime, cefixime, ciprofloxacin, cotrimoxazole, gentamicin, imipenem,

Table 2: Distribution of carbapenemase-encoding genes in *Klebsiella* spp. isolates from blood samples of neonatal sepsis cases admitted in NICU ($n=100$).

Carbapenemase-encoding gene/s	Present (%)	Absent (%)
KPC	0	100
NDM-1	6	94
IMP	0	100
VIM	0	100
OXA-48	12	88
Coexpression of <i>bla</i> OXA-48 and <i>bla</i> NDM-1	2	98
Total	16	82

KPC: *Klebsiella pneumoniae* Carbapenemase, NDM: New Delhi metallo- β -lactamase, IMP: Imipenemase, VIM: Verona integron-encoded metallo-beta-lactamase, OXA-48-like: Oxacillinases, NICU: Neonatal intensive care unit. n : Total number of tested isolates.

meropenem, and piperacillin-tazobactam were higher among *Klebsiella* spp. isolates harboring the carbapenemase gene. The difference in the susceptibility among two groups of *Klebsiella* spp. isolates with genotypic carbapenem resistance and *Klebsiella* spp. isolates without genotypic carbapenem resistance were statistically significant for all the tested antibiotics ($P < 0.05$) except amikacin ($P > 0.05$).

DISCUSSION

Neonatal sepsis remains the third leading cause of neonatal mortality. The bacteriological profile responsible for neonatal sepsis varies geographically. The most frequent offenders of early-onset sepsis and late-onset sepsis in developing nations like India are *K. pneumoniae* and *Staphylococcus aureus*.^[21] The production of carbapenemases by *Enterobacterales* isolates especially *Klebsiella* spp., associated with invasive infections, gut colonization, or hospital-acquired infections, has been detected across the globe.^[22,23] These superbugs causing infections in vulnerable newborns are present everywhere, including the birth canal, incubators, hands of healthcare workers, and even the medical equipment like nasogastric tubes. Premature or low-birth-weight infants needing extended hospital stay or dependency on life support systems have significantly elevated risk of infection by these pathogens. The carbapenemase producers play a significant role in triggering outbreaks by transferring plasmid-encoded carbapenemase genes, thus posing an exceptionally difficult challenge in the containment of these infections.^[24] Many Indian studies have documented the high prevalence of bloodstream infections caused by multidrug resistant *Klebsiella* spp. isolates in high-risk settings of NICUs.^[25,26]

The predominant mechanism of resistance in the present study was the presence of *bla*OXA-48 (12%) followed by *bla*NDM-1 (6%). The coexpression of both *bla*OXA-48 and *bla*NDM-1 was observed in 2% of isolates. However, another

Table 3: Comparative distribution of carbapenemase-encoding genes in different MIC cutoff categories of imipenem and meropenem among *Klebsiella* spp. isolates from blood samples of neonatal sepsis cases admitted in NICU ($n=100$).

Carbapenemase Genes ($N=100$)	IMIPENEM n (%)			MEROPENEM n (%)		
	Susceptible ($\leq 1 \mu\text{g/mL}$)	Intermediate ($2 \mu\text{g/mL}$)	Resistant ($\geq 4 \mu\text{g/mL}$)	Susceptible ($\leq 1 \mu\text{g/mL}$)	Intermediate ($2 \mu\text{g/mL}$)	Resistant ($\geq 4 \mu\text{g/mL}$)
Present ($n=16$)	3 (18.7)	1 (6.25)	12 (75)	0	0	16 (100)
Absent ($n=84$)	56 (66.6)	16 (19)	12 (14.3)	40 (47.6)	17 (20.2)	27 (32.1)
Total ($n=100$)	59 (59)	17 (17)	24 (24)	40 (40)	17 (17)	43 (43)

MIC: Minimum inhibitory concentration, NICU: Neonatal intensive care unit, n : Total number of tested isolates

Table 4: Comparative distribution of susceptibility to various antimicrobial agents in *Klebsiella* spp. isolates with and without genotypic carbapenem resistance ($n=100$).

Antimicrobial ($\mu\text{g/disc}$)	PCR Positive isolates ($n=16$)		PCR Negative isolates ($n=84$)		P-value
	Sensitive n (%)	Resistance n (%)	Sensitive n (%)	Resistance n (%)	
Amikacin (30)	6 (37.5)	10 (62.5)	53 (63)	31 (36.9)	0.093
Aztreonam (30)	0 (0)	16 (100)	44 (52.3)	39 (46.4)	0.0001
Ceftazidime (30)	1 (6.25)	15 (93.75)	31 (36.9)	53 (63)	0.018
Cefotaxime (30)	1 (6.25)	15 (93.75)	32 (38)	52 (61.9)	0.0178
Cefixime (5)	1 (6.25)	15 (93.75)	33 (39.2)	51 (60.7)	0.009
Ciprofloxacin (5)	1 (6.25)	15 (93.75)	39 (46.4)	45 (53.5)	0.002
Cotrimoxazole (25)	1 (6.25)	15 (93.75)	44 (52.3)	40 (47.6)	0.0006
Gentamicin (10)	2 (12.5)	14 (87.5)	64 (76.1)	20 (23.8)	0.0001
Imipenem (10)*	5 (31.25)	9 (56.25)	76 (90.4)	8 (9.5)	0.0001
Meropenem (10) [^]	1 (6.25)	14 (87.5)	63 (75)	19 (22.6)	0.0001
Piperacillin-Tazobactam (100/10)**	3 (18.75)	13 (81.25)	59 (70.2)	23 (27.3)	0.0001

PCR: Polymerase chain reaction. *Imipenem – Out of 16 PCR positive *Klebsiella* isolates, 2 (12.5%) isolates had intermediate zone diameters. [^]Meropenem – Out of 16 PCR positive *Klebsiella* isolates, 1 (6.25%) isolate had an intermediate zone diameter, and among 84 PCR negative isolates, 2 (2.4%) had an intermediate zone diameter for meropenem. **Piperacillin-Tazobactam – 2 (2.4%) PCR negative *Klebsiella* Isolates had intermediate zone diameter. The P-value ≤ 0.05 was considered statistically significant”

study from India has reported *bla*OXA48-like expression in 13%, *bla*NDM in 19%, and coexpression of *bla*NDM and *bla*OXA48-like in 28% bloodstream isolates of *K. pneumoniae*.^[27] In line with our findings, this research has also reported the predominant carbapenem-encoding genes as *bla*NDM and *bla*OXA48. Laolerd *et al.*,^[28] have reported the presence of at least one of the carbapenemase genes in 77.7% of CRE isolates (predominantly *K. pneumoniae*). The same study also documented that the prevalence of *bla*NDM (71.75%) and *bla*OXA48-like (50.22%) genes among CRE isolates and coexpression of both *bla*NDM and *bla*OXA48-like genes was 32.73% among *K. pneumoniae* isolates.^[28] The differences in the distribution of *bla*NDM, *bla*OXA48, and their coexpression can be attributed to the geographical variations.

The present study documented *bla*OXA-48 carbapenem-encoding gene to be most prevalent in a tertiary care high-volume center of north India. The OXA-48-like enzymes are hidden threats as they possess a low level of carbapenem hydrolytic activity. This mechanism of resistance remains underreported by standard laboratory procedures and subsequent treatment failures.^[10] In the present study, intermediate and susceptible MIC values were also observed along with resistant MIC values

for imipenem in *bla*OXA-48 harboring isolates. This could be probably due to the absence of coresistance mechanisms in OXA-48 like producers. In the absence of other resistance mechanisms, OXA-48, like producers, can show lower or intermediate MIC values for carbapenems. Thus, their true prevalence rates are hard to estimate.^[29,30] In our study, all the carbapenemase gene-harboring isolates had resistant MIC values for meropenem. Thus, meropenem is a better predictor of carbapenemase production in comparison to imipenem.

The frequent use of carbapenems and other beta-lactam antibiotics has led to increased resistance in the bacteria, and the rapid fluctuation in their susceptibility pattern challenges the treatment options for serious infections. Current guidelines from the World Health Organization recommend the use of ampicillin, extended-spectrum cephalosporins (cefotaxime), and aminoglycosides (gentamicin and amikacin) for the treatment of neonatal sepsis. This protocol is widely followed in various healthcare settings.^[31] However, the production of AmpC beta-lactamases and extended-spectrum beta-lactamases has led to increasing dependency on carbapenems as next line of treatment. Among carbapenems, meropenem is the

preferred carbapenem in neonates as the safety profiles of other carbapenems are not well documented in this patient group.^[32]

The OXA-48 producers hydrolyze penicillins with greater efficiency and carbapenems at a lower extent, sparing expanded-spectrum cephalosporins, whereas MBLs (NDM-1) are more potent, they can hydrolyze almost all available beta-lactam antibiotics, including carbapenems along with extended-spectrum cephalosporins, aminoglycosides, aztreonam, and fluoroquinolones.^[33] Optimizing treatment strategies for these infections become a challenge due to the lack of knowledge about the circulating carbapenemases. We compared the distribution of susceptibility to routine antimicrobial agents in isolates with and without genotypic carbapenem resistance. Despite the inability of OXA-48 producers to hydrolyze expanded-spectrum cephalosporins, high resistance rates (94%) to these cephalosporins were observed in our study. This additional resistance to expanded-spectrum cephalosporins among OXA-48 producers can be due to the presence of other mechanisms of resistance including coexpression of both OXA-48 and NDM-1. Imipenem was the most effective antimicrobial agent in the absence of any carbapenemase-encoding gene and amikacin was most effective in the presence of carbapenemase-encoding genes followed by imipenem. Similar results showing carbapenem drugs being most effective against *Klebsiella* were also reported in study by Mohsen et al.^[34]

Considering the widespread prevalence of multidrug-resistant *Klebsiella* spp. as a causative agent of life-threatening infections, it is crucial to understand the mechanisms of resistance behind the last resort drugs of carbapenems. Furthermore, their therapeutic utility can be largely restricted by the presence of certain carbapenemase-encoding genes.^[35] Thus, the determination of carbapenem resistance by phenotypic methods should be supplemented with genotypic assessment. The knowledge of prevailing strains of carbapenemases can aid in the implementation of antibiotic cycling and formulation of effective hospital antibiotic policies. This has the potential to significantly impact patient care in terms of reduced morbidity, mortality, and duration of hospital stay. However, further elaborative studies with larger sample sizes and diverse clinical conditions are warranted.

Carbapenems are broad-spectrum higher-level antibiotics and are often considered as last resort antibiotics. The emergence of carbapenemases is a major healthcare problem. The susceptibility of carbapenem-producing CRE to carbapenem drugs may vary depending on the molecular class of carbapenemase produced. The distribution of circulating strains is not uniform and varies geographically. Therefore, the determination of prevalence of carbapenemase-encoding genes may be of paramount importance in the development of effective antibiotic policies at various levels.

CONCLUSIONS

Early detection and knowledge of the prevalence of carbapenemase encoding genes significantly benefit patient

care by lowering morbidity, mortality, and hospitalization duration. This also impacts the formulation of combination antibiotic therapies, and hospital antibiotic policies and forms the basis of antibiotic cycling as an important component of infection control in NICU.

Ethical approval

The research/study approved by the Institutional Review Board at UCMS-Institutional Ethics Committee-Human Research (IEC-HR), number IEC-HR/2018/36/73R, dated 26/10/2018.

Declaration of patient consent

Patient's consent is not required as patients identity is not disclosed or compromised.

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Conflict of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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