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Prevalence of Carbapenemase Genes *bla*$_{OXA-48}$, *bla*$_{NDM}$, and *bla*$_{IMP}$ in Multidrug Resistant *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* Clinical Isolates from University Hospital Sharjah, UAE

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Abstract

Background: Carbapenem-resistant *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* are globally recognized as priority pathogens due to their association with multidrug resistance and limited therapeutic options. Carbapenemase genes, such as *bla*$_{OXA-48}$, *bla*$_{NDM}$, and *bla*$_{IMP}$, play a central role in the dissemination of resistance.
Methods and Results: This study investigated the prevalence and co-occurrence of these pathogens in 100 multidrug-resistant isolates collected from University Hospital Sharjah, between November 2024 and June 2025. PCR detection revealed *bla*$_{OXA-48}$ as the most prevalent gene (66.7% in *P. aeruginosa* and 65.5% in *K. pneumoniae*), followed by *bla*$_{IMP}$ (44.4% and 38.2%), and *bla*$_{NDM}$ (15.6% and 23.6%). Co-occurrence of two or more genes was observed in over 30% of isolates, and a small proportion carried all three. Approximately one-quarter of isolates tested negative for these targets, indicating alternative mechanisms of carbapenem resistance.
Conclusion: Our findings provide hospital-level molecular data from Sharjah that align with broader trends in the UAE, while highlighting the complexity of resistance-gene combinations. The results underscore the importance of ongoing molecular surveillance, monitoring of gene co-occurrence, and enhanced antimicrobial stewardship to mitigate the effects of multidrug-resistant, Gram-negative infections.(**International Journal of Biomedicine. 2025;15(4):731-735.**)

Keywords: β-lactamases • carbapenem resistance • metallo-beta-lactamase • infection control

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Abbreviations

CRE, carbapenem-resistant Enterobacterales; **IMP**, imipenemase; **KPC**, *Klebsiella pneumoniae* carbapenemase; **MBLs**, metallo-β-lactamases; **NDM**, New Delhi metallo-β-lactamase; **VIM**, Verona integron-encoded metallo-β-lactamase.

Introduction

The rapid emergence of multidrug-resistant (MDR) Gram-negative bacteria presents a significant global health challenge.[1] *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* are associated with a wide range of infections, including bloodstream infections, ventilator-associated pneumonia, urinary tract infections, and surgical site infections,[2] which have earned them a place in the WHO's list of substantial MDR pathogens in their priority list for 2024.[3] *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* possess the ability to acquire and disseminate β-lactamase genes, including carbapenemases that hydrolyze carbapenems, the last line of defence against multidrug-resistant Gram-negative infections. According to the Ambler molecular classification in 1980, β-lactamases are divided into four classes (A–D).[4] Among them, classes A, B, and D harbour the clinically

most significant carbapenemases, while class C enzymes play an indirect role.

Class A comprises serine carbapenemases such as *Klebsiella pneumoniae* carbapenemase (KPC) and, less commonly, GES-type enzymes, which are now globally disseminated in Enterobacterales.[5] Class B includes the metallo-β-lactamases (MBLs), a zinc-dependent group represented by New Delhi metallo-β-lactamase (NDM), Verona integron-encoded metallo-β-lactamase (VIM), and imipenemase (IMP), all of which confer resistance to nearly all β-lactams except monobactams.[6,7]

Class C enzymes, mainly AmpC-type cephalosporinases, are not highly efficient carbapenemases but can lead to carbapenem resistance when combined with porin loss or efflux mechanisms.[8] Finally, class D enzymes, specifically the oxacillinases, encompass the clinically significant OXA-48-like carbapenemases, which are now endemic in *K. pneumoniae* in the Middle East and North Africa.[9,10]

Recent surveillance indicates that the OXA-48 enzyme remains the most frequently detected carbapenemase globally, followed by NDM and KPC, while IMP variants continue to predominate in East Asia, particularly in Japan.[11-13] In *P. aeruginosa*, carbapenemase-mediated resistance is also escalating, with bla_{VIM} and bla_{OXA-48} being the most common, whereas bla_{IMP} and bla_{NDM} occur at lower frequencies but frequently co-exist, compounding resistance mechanisms.[14] Longitudinal studies demonstrate a significant increase in bla_{NDM} prevalence among carbapenem-resistant *P. aeruginosa* between 2021 and 2025, highlighting its expanding clinical impact.[15-18]

In the UAE, surveillance data confirm the growing clinical threat posed by carbapenem-resistant Enterobacterales (CRE). A retrospective national study analysing more than 14,500 isolates between 2010 and 2021 found that *K. pneumoniae* accounted for nearly half (48.1%) of all cases, followed by *Escherichia coli* (25.1%) and other Enterobacterales (26.8%). By 2021, resistance in *K. pneumoniae* was alarmingly high, reaching 67.6% for imipenem, 76.2% for meropenem, and 91.6% for ertapenem. bla_{NDM} and bla_{IMP} were detected across *E. coli*, *K. pneumoniae*, *P. aeruginosa*, and *A. baumannii*, often in combination with ESBL genes, while bla_{OXA-48} was notably absent.[19]

Understanding the local prevalence and interaction of carbapenemase genes is crucial for implementing effective infection control practices and antimicrobial stewardship programs. This study investigated the prevalence and co-occurrence of bla_{OXA-48}, bla_{NDM}, and bla_{IMP} genes among MDR *P. aeruginosa* and *K. pneumoniae* isolates obtained from University Hospital Sharjah in the UAE. Offering insights into the genetic architecture of resistance in this high-risk setting.

Materials and Methods

Study Design and Setting

This cross-sectional, laboratory-based study was conducted from November 2024 to June 2025 at University Hospital Sharjah in the United Arab Emirates. A total of 100 non-duplicate MDR clinical isolates, comprising 45 *Pseudomonas aeruginosa* and 55 *Klebsiella pneumoniae,* were obtained from clinical specimens, including blood, urine, sputum, wound swabs, and other sterile body fluids.

Identification and Antimicrobial Susceptibility Testing

All isolates were identified and subjected to antibiotic susceptibility testing using the VITEK® 2 Compact system (bioMérieux, France).

DNA Extraction

Genomic DNA was extracted using the G-spin Total DNA Extraction Kit from iNtRON Biotechnology, Korea, according to the manufacturer's instructions. The DNA's concentration and purity were assessed with a NanoDrop™ 2000 spectrophotometer (Thermo Fisher Scientific).

PCR Amplification of Carbapenemase Genes

PCR amplification targeting the OXA-48, IMP, and NDM genes using the primers listed in Table 1 was performed under optimized thermal cycling conditions. Each 25 µL reaction mixture contained 12.5 µL of GoTaq® Green Master Mix (Promega), 1 µL of each primer (10 µM), 2 µL of DNA template, and nuclease-free water. The thermal cycling process started with an initial denaturation at 95°C for 5 minutes, followed by 35 cycles of denaturation at 95°C for 30 seconds, annealing at variable temperatures for 30 seconds, and extension at 72°C for 1 minute, ending with a final extension at 72°C for 10 minutes (Table 2). PCR products were analyzed using 1.5% agarose gel electrophoresis and stained with ethidium bromide. Electrophoresis was conducted at 100V for 45 minutes, and bands were visualized under UV light using a Bio-Rad GelDoc XR+ Imaging System.

Statistical Analysis

Data were entered and analyzed using Microsoft Excel 2021. Descriptive statistics were used to summarize gene frequencies and co-occurrence patterns. Categorical variables were expressed as counts and percentages.

Table 1.

Primer sequences used for PCR detection of bla_{OXA-48}, bla_{IMP}, and bla_{NDM}

Gene	Sequence (5' – 3')	Length (bp)	Reference
bla_{OXA-48}	F GCGTGGTTAAGGATGAACAC R CATCAAGTTCAACCCAACCG	1080	20
bla_{IMP}	F GAAGGYGTTTATGTTCATAC R GTAMGTTTCAAGAGTGATGC	188	22
bla_{NDM}	F GGTTTGGCGATCTGGTTTTC R CGGAATGGCTCATCACGATC	621	23

Table 2.

PCR amplification parameters for each target gene.

Target Gene	Initial Denaturation	Cycles	Annealing Temperature	Extension (per cycle)	Final Extension
bla_{OXA-48}	94 °C for 6.5 min	35×	52 °C for 45 sec	72 °C for 1 min	72 °C for 5 min
bla_{IMP}	95 °C for 3.5 min	34×	48 °C for 45 sec	72 °C for 1 min	72 °C for 5 min
bla_{NDM}	95 °C for 3.5 min	34×	58 °C for 45 sec	72 °C for 1 min	72 °C for 5 min

Results

Among the 100 multidrug-resistant isolates analyzed, 45 were *P. aeruginosa* and 55 were *K. pneumoniae*.

Gene Prevalence

Among the 45 *P. aeruginosa* isolates, bla_{OXA-48} was detected in 30 (66.7%), IMP in 20 (44.4%), and bla_{NDM} in 7 (15.6%). In contrast, of the 55 *K. pneumoniae* isolates, bla_{OXA-48} was present in 36 (65.5%), bla_{IMP} in 21 (38.2%), and bla_{NDM} in 13 (23.6%) (Figure 1).

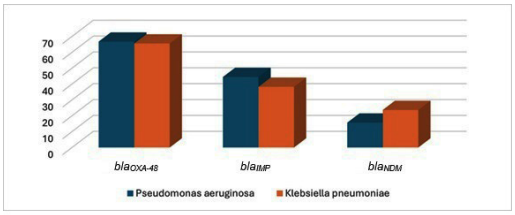

Fig. 1. *Prevalence of carbapenemase genes among multidrug-resistant clinical isolates of P. aeruginosa and K. pneumoniae. PCR detection showed* bla_{OXA-48} *as the most frequent gene in both species, followed by* bla_{IMP} *and* bla_{NDM}

Gene Co-Occurrence

The distribution of single and multiple gene positivity was as follows: In *K. pneumoniae*, the most frequent profile was single gene bla_{OXA-48} alone (29.1%), followed by bla_{OXA-48} + bla_{IMP} (21.8%), while 5.5% of isolates carried all three genes (Figure 2). In *P. aeruginosa*, the dual combination bla_{OXA-48}+ bla_{IMP} predominated (28.9%), with bla_{OXA-48} alone detected in 24.4%. Single-gene carriage of bla_{IMP} or bla_{NDM} was more frequent in *P. aeruginosa* (8.9% each) compared to *K. pneumoniae* (3.6% each). Notably, around one-quarter of isolates in both species were negative for all three genes, suggesting alternative resistance mechanisms.

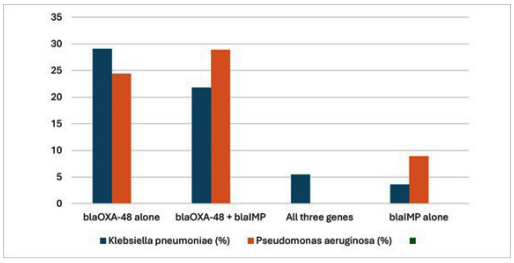

Fig.2. *Co-occurrence profiles of carbapenemase genes (*bla_{OXA-48}*,* bla_{IMP}*, and* bla_{NDM}*) among multidrug-resistant P. aeruginosa and K. pneumoniae isolates. The combination of* bla_{OXA-48} *and* bla_{IMP} *predominated in both species, while a smaller proportion carried all three genes; roughly one-quarter of the isolates were negative for all three targets, indicating the presence of alternative resistance mechanisms.*

Discussion

This study demonstrated a high prevalence of bla_{OXA-48} among both *P. aeruginosa* (66.7%) and *K. pneumoniae* (65.5%) isolates, with moderate detection of bla_{IMP} and lower but notable detection of bla_{NDM}. Gene co-occurrence was common, including isolates harbouring all three carbapenemase genes. These results underscore the dominance of bla_{OXA-48} in the UAE setting and highlight the complexity of carbapenem resistance mechanisms in clinically relevant Gram-negative pathogens.

Our findings align with reports from the Middle East and North Africa (MENA), where bla_{OXA-48} enzymes are well established as endemic.[11,20] In the UAE, Thomsen et al.[18] showed persistently high carbapenem resistance in *K. pneumoniae*, while Ragupathi et al.[19] identified bla_{NDM} and bla_{IMP} but did not detect bla_{OXA-48} in the Northern Emirates, suggesting geographic variation within the country. The recent emergence of bla_{OXA-48} in *E. coli* ST167 reported by Al-Marzooq et al.[21] further illustrates the genetic diversity of carbapenemase enzymes in the UAE. Compared to global trends, our results confirm the widespread dissemination of bla_{NDM} across Asia and the Middle East, as well as the continued prominence of bla_{IMP} in East Asia.

The predominance of bla_{OXA-48} is of particular concern, as it is often difficult to detect with routine laboratory methods and may appear susceptible in vitro, leading to inappropriate carbapenem use and therapeutic failure.[22] The co-occurrence of multiple carbapenemase genes within the same isolate raises the risk of horizontal transfer and limits the efficacy of last-line antibiotics. These findings are consistent with clinical observations from,[23] who reported high mortality rates in patients with CRE bacteremia in the UAE despite treatment with ceftazidime–avibactam and aztreonam. Together, these data highlight the urgent need for enhanced antimicrobial stewardship and optimized treatment strategies.

The detection of high rates of carbapenemase genes in both pathogens underscores the critical threat they pose to healthcare systems in the UAE. bla_{OXA-48} and bla_{NDM} are both recognized by the World Health Organization as priority resistance determinants requiring urgent attention. Our results underscore the importance of robust molecular surveillance, routine screening for gene co-occurrence, and regional collaboration in monitoring the spread of high-risk clones.

This study is limited by its sample size and single-center scope, which may not fully reflect the national distribution of resistance genes. Moreover, the absence of sequencing data restricts insights into the genetic context of these genes, such as plasmid associations or integron carriage. Finally, clinical data were not analyzed, precluding an assessment of gene presence in relation to patient outcomes.

Future research should incorporate whole-genome sequencing to explore the genetic environments of bla_{OXA-48}, bla_{NDM}, and bla_{IMP} in UAE isolates. Larger multicenter studies across the Emirates and the broader Gulf Cooperation Council (GCC) region are needed to assess epidemiological trends. Linking molecular findings to patient-level clinical outcomes will be crucial in informing treatment guidelines. Finally, investigation of novel therapeutic strategies, such as cefiderocol or optimized CAZ-AVI combinations, should be prioritized in this context.

Ethical Approval

This study was approved by the University Hospital Sharjah Research and Ethics Committee (Approval No. UHS-

HERC-176-16092025) and the Gulf Medical University Institutional Review Board (Approval No. IRB-COHS-STD-98-NOV-2024).

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Competing Interests

The authors declare that there are no conflicts of interest or competing interests regarding the publication of this paper.

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