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International Journal of Medical Science and Dental Health (ISSN: 2454-4191)
Volume 11, Issue 09, September 2025
Doi: https://doi.org/10.55640/ijmsdh-11-09-20

Prevalence Of Carbapenem Resistant Pseudomonas Aeruginosa Isolated from Wound Infection and The Genes Responsible for Carbapenemase Production in Najaf Hospitals

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Received: 11 August 2025, **accepted:** 16 September 2025, **Published Date:** 30 September 2025

Abstract

Background: *Pseudomonas aeruginosa* is one of the most prevalent opportunistic human pathogens among Gram-negative bacteria, it is linked to nosocomial infections such as burn and wound infections. The rise of carbapenem-resistant *P. aeruginosa* (CRPA) is a major therapeutic challenge. The objective of the current study is to specify the frequency carbapenem resistant *P. aeruginosa* and the associated carbapenemase genes in *P. aeruginosa* isolated from wound infection.

Methods: During the study period, 300 swabs were collected from patients who had wound infections. *P. aeruginosa* were identified using standard bacteriological and biochemical methods. The Kirby-Bauer disk diffusion method was utilized to investigate the antibiotic susceptibility of using 17 antimicrobial drugs. Multi-druge resistance(MDR) and Extensive-druge resistance (XDR) were identified using international guideline. Extended-spectrum-beta-lactamase (ESBL) production were screened using ceftazidime, ceftriaxone, cefotaxime and aztreonam antibiotics by disk diffusion method. Carbapenem resistance isolates were characterized using imipenem and/or meropenem antibiotics resistance and the double disk diffusion test was used to confirm its production. PCR analysis was conducted to identify ESBL and carbapenem resistance genes ($bla_{\text{CTX-M}}$, bla_{TEM}, bla_{SHV}, bla_{OXA}, bla_{KPC}, bla_{IMP}, bla_{VIM}, bla_{SIM}, bla_{NDM}, bla_{GIM}, bla_{SPM}, $bla_{\text{OXA-48}}$).

Results: from 300 swabs specimen *P. aeruginosa* isolates were identified in 40 (13.3%) specimens. Antibiotic susceptibility test revealed 13(32.5%) isolates were carbapenem resistant *P. aeruginosa*, and the highest resistant was to β-lactam class and cephalosporin antibiotics. The results showed 17(42.5%) of isolates were MDR and 23(57.5%) were XDR. PCR assay revealed that $bla_{\text{CTX-M}}$ was found in 22(55%) and bla_{OXA} was noticed in 27 (67.5%) of *P. aeruginosa*

isolates. Among 13 CRPA isolates, 1(7.6%) isolate had bla_{OXA-48}, 2(15.3%) isolates had bla_{IMP}, bla_{SIM} and bla_{VIM} for each, 3(23%) carry bla_{GIM}, and 4 (30.7%) had bla_{NDM}. While bla_{SPM} and bla_{KPC} were not found in any isolate.

Conclusion: wound infections showed high rate of XDR and CRPA driven by diverse carbapenem resistance genes, indicating dangerous public health concern

Keywords: *Pseudomonas aeruginosa*, Carbapenem Resistant genes, ESBL

Introduction

Pseudomonas aeruginosa is an opportunistic pathogen that cause a wide range of endogenous and exodogenous infections. Endogenous infection, like pneumonia and bacteremia, often arise from colonization sites such as the gastrointestinal tract in neutropenic patients or the endotracheal tube in intubated pateints, whereas, exogenous infections include urinary tract infection, burn wound infections, conjunctivitis, and keratitis. [1] *P. aeruginosa* is well-known for its intrinsic resistance to many antibiotics classes and capacity to cause resistance even during a treatment course.[2] Resistance primarily arises from chromosomal mutations or horizontal acquisitions of resistance genes via mobile genetic elements like plasmid and integrons. Key mechanisms of this acquired resistance include overexpression of efflex pumps, reduced outer membrane permeability, and production of enzymes such as beta-lactamases and carbapenemases.[1] According to epidemiological research, infections brought on by *P. aeruginosa* resistant organisms raise morbidity, mortality.

Carbapenem are broad spectrum beta-lactam antibiotics they are typically regarded as the final resort for antibiotic therapy, specifically for extended spectrum beta-lactamase (ESBL) producing microorganisms [3]. Carbapenemases are a subclass of beta-lactamases like cephalosporins and other beta-lactam antibiotics, which can hydrolyze carbapenem antibiotics [4].There are three main classes of carbapenemase which are clinically isolated from carbapenem resistant *Enterobacteriaceae*: Class A, which mainly has KPC (*Klebsiella pneumoniae* carbapenemase); Class B which has IMP (Imipenemase metallo-beta-lactamase), NDM (New Delhi Metallo-beta-lactamase), and VIM (Verona integron-encoded-metallo-beta-lactamase) and Class D that has OXA (Oxacillinase) and many of its variants like OXA-48, OXA-162 and OXA0181 [4; 5; 6]. Gram-negative bacteria resistance to carbapenem is increasing and growing, particularly in nosocomial infections such as *P. aeruginosa* [3;7;8]. Nosocomial isolates of *P. aeruginosa* may be resistant to most antibiotics, resulting in extensive drug resistant (XDR) strain multidrug resistant (MDR) [8; 9; 10].

Carbapenem resistant bacteria can abundant because they frequently switch to MDR strain [3]. *P. aeruginosa* can develop carbapenem resistant by a verity of ways [7; 8; 11]. The most crucial mechanism is the ability to create carbapenemase since the majority of carbapenemase genes might be present on transferable genetic elements and spread rapidly across bacteria.

The past decade has seen carbapenem resistant *Enterobacteriaceae* become a significant in resistance [12], with reported prevalence considered to be extremely high distributed throughout the world [13; 14; 15]. As well as having a high risk of rapid spread [16]. The increase of Enterobacteriaceae capable of producing carbapenemase poses a risk to the progress made in modern medicine [17], and poses a threat to healthcare globally in terms of patient safety [18]. This research purposed to specify the frequency of antimicrobial resistance patterns for carbapenem resistant and genes responsible for carbapenemase production in *P. aeruginosa* isolated from injured skin infection.

Material and Methods

This descriptive analytical study was carried out in Al-Najaf provinces Al-Sader Medical city. Between July 2023 and March 2024. Three hundred swab specimens from patients who clinically suspected having a wound infection. The specimens were sent a way to the microbiology lab. The *P. aeruginosa* isolates from wound swab had been determined by using standard biochemical tests and microbiological methods and confirmed by Vitek2 compact system. The disk agar diffusion method (Kirby-Bauer) was applied to evaluate the antibiotic susceptibility pattern of the isolates, based on the Clinical and Laboratory Standards Institute (CLSI) recommendations using the antibiotic disks listed in

Table (1). All susceptibility results were interpreted using the common values carried out CLSI 2023[19]

To detected the production of ESBLs, all *P. aeruginosa* isolates were explored for susceptibility to cefotaxime, ceftazidime and ceftriaxone (30mg/disk) using disk diffusion sensitivity test. Potential ESBL producers were identified if the zone diameter for cefotaxime was ≤ 26mm, ≤ 21 mm for ceftazidime, and ≤ 23 mm for ceftriaxone. The double disk diffusion test (DDT) was performed using a standard phenotypic detection of carbapenem resistance. In this research, the resistance to carbapenem has been characterized as resistance to at least one of the two carbapenem antibiotics tested: meropenem and imipenem, consistent to the CLSI 2023 suggestions for improvement. Isolates exhibiting a zone of inhibition≤ 19 mm in diameter for meropenem and/or imipenem have been classified as carbapenem resistant.

Screening of genes associated with antibiotic resistance

The genomic DNA extraction carried out according to the instructions established by the manufacturing origin (Magen, China) A biophotometer plus (Nanodrop) was used to determine the yield and purity of a DNA sample. To prepare for PCR, the extracted DNA was frozen at -20 ºC. The present study used monoplex PCR assay patterns. Use 12.5 µl PCR master mix, reverse primers (10µM) and 2 µl of forward, and 2 µl (10-250 ng) of extracted DNA. For obtaining the PCR 25 µl reaction mixture, 6.5 of deionize water, prepered using the manufacturing (Promga) protocol kit. PCR conditions had been carried out in T3000 thermocycler (Biometra, USA). After a brief spinning to ensure proper mixing of the contentes, all the carbapenem resistant *P. aeruginosa* were screening for genes (bla_{OXA}, bla_{CTX-M}, bla_{TEM}, bla_{SHV}, bla_{KPC}, bla_{IMP}, bla_{VIM}, bla_{SIM}, bla_{NDM}, bla_{GIM}, bla_{SPM}, bla_{OXA-48}) responsible for carbapenemase production, the primer sequence and PCR conditions was described elsewhere reference [20-25]. Amplicons have been evaluated using 1.5% agarose gel electrophoresis with 1X TBE buffer and stained with ethidium bromide. Microsoft Office Excel 2019 was used for certain calculations in the current study, and chi-square calculator was used for statistical analysis. Statistical significance was established for *p-values* below a significant threshold of 0.05.

Results

Out of 300 wound specimens had been cultured, there 238(79.3%) of wound swabs were found to have growth bacteria present, in compare, 62 (20.6%) had non growing bacteria. Out of 238 bacterial isolates, the Gram-negative bacterial growth frequency was 174(73.1%), while the Gram-positive bacterial growth frequency was 64 (26.9%), with 40(22.9%) being identified as *P. aeruginosa* based up on standard biochemical tests and colonial characteristics of *P. aeruginosa* and confirmed by Vitek2 compact system (bioMérieux, France) test.

Antimicrobial susceptibility for *P. aeruginosa* isolates

As indicated in the table 1, the 17 antibiotic disk resistance profile belong to 8 classes of antibiotics. The high resistance rate to cefotaxime (90%), cefixime (85%), ceftriaxone (82.5%), followed by cefepime, ciprofloxacin (77.5%), and followed by piperacillin (67.5%), Tobramycin(65%). While highest sensitivity of *P. aeruginosa* has been to Colistin and Amikacin (62.5%), imipenem (60%), meropenem (57%). According to the resistance profile, 17(42.5%) of isolates were conceded as MDR and 23(57.5%) XDR.

Table1: Antibiotic susceptibility test of *Pseudomonas aeruginosa* isolated from wound infection (n= 40)

Antibiotic class	Antimicrobial agent	No. (%) isolates exhibited		
		Resistant	Intermediate	Sensitive
Ampicillin	Piperacillin	27(67.5)	6(15)	7(17.5)
Beta-lactamase inhibitor	Piperacillin-tazobactam	16 (40)	3(7.5)	21(52.5)
Cephems	Ceftazidime	15(37.5)	9(22.5)	16 (40)
	Ceftriaxone	33(82.5)	4(10)	3 (7.5)
	Cefotaxime	36(90)	2(5)	2 (5)
	Cefepime	31(77.5)	0(0)	9 (22.5)
	Cefixime	34(85)	1(2.5)	5 (12.5)
Monobactams	Aztreonam	25(62.5)	6(15(	9 (22.5%)

Carbapenem	Imipenem	11(27.5)	4(10)	23 (57.5)
	Meropenem	13(32.5)	3(7.5)	24 (60)
Aminoglycosides	Amikacin	14(35)	1(2.5)	25(62.5)
	Gentamicin	16(40)	1(2.5)	23(57.5)
	Tobramycin	26(65)	3(7.5)	11 (27.5)
Quinolones	Ciprofloxacin	31(77.5)	4(10)	5 (12.5)
	Levofloxacin	18(45)	0(0)	22(55)
	Norfloxacin	20(50)	7(17.5)	13(32.5)
Lipopeptides	Colistin	15(37.5)	0(0)	25(62.5%)

Screening for Extended Spectrum Beta-Lactamase production

The existence of ESBLs was examined in every *P. aeruginosa* isolates by using initial screening test, 100% displayed resistance to cephalosporins, the results showed that cefotaxime had an 90%, ceftriaxone 82.5%, aztreonam 62.5% and ceftazidime 37.5%. double disk diffusion test used confirmatory techniques on all isolates that showed antibiotic resistance to any the third generation cephalosporins and aztreonam examined. However, based on the double disk diffusion test, 9 isolate was found to be ESBL producer.

Phenotypic evaluation of resistance to carbapenem

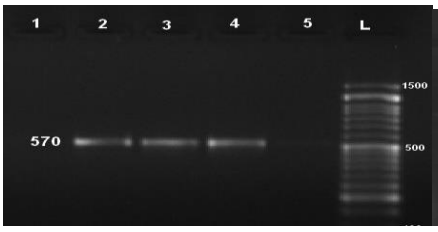
In accordance to the CLSI (2023) standards, carbapenem resistance was defined in this study as resistance to meropenem, imipenem and at least one of the two carbapenem antibiotics tested. An isolate was considered carbapenem resistant if it was exhibited a zone of inhibition for imipenem and/or meropenem that was less than 19 mm in diameter. Overall, 40 isolates were screened in the current study with 13(32.5%) of *P. aeruginosa* were reported to resist to at least one of carbapenems by disk diffusion method. Further than the 13 carbapenem reduce susceptibility isolates, 13 (32.5%) were resistant to meropenem and 11(27.5%) isolates have been resistant to imipenem.

Detection of ESBLs genes

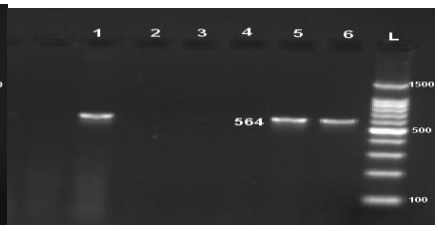
The occurence of ESBL genes in all *P. aeruginosa* isolates were evaluated using conventual PCR. When *P. aeruginosa* isolates were resistant to all third generation cephalosporines and aztreonam were analyzed, the results revealed that the most common gene among isolates was bla_{OXA}, which detected in 27(67.5%) of the isolates, then bla_{CTX-M} which was found in 22(55%) of the isolates. No isolates had bla_{SHV} and bla_{TEM}

Molecular investigation and distribution of carbapenem genes

All 13 carbapenem resistant *P. aeruginosa* isolates were investigated by PCR for the existence gene determinants encoding carbapenem genes (bla_{KPC}, bla_{IMP}, bla_{VIM}, bla_{SIM}, bla_{NDM}, bla_{GIM}, bla_{SPM}, bla_{OXA-48}). The results indicated that presence only 1(7.6%) *P. aeruginosa* isolate have the bla_{OXA-48} as well as, 2(15.3%) isolates have bla_{IMP}, bla_{SIM} and bla_{VIM}, 3(23%) carry bla_{GIM}, 4 (30.7%) have bla_{NDM} as shown in figure (1). While bla_{SPM} and bla_{KPC} were not found in any isolate. The existence of combined genes among *P. aeruginosa* isolates two or more genes were recognized, three of carbapenem genes were present in 4 isolates, and two of carbapenem genes were present in 10 isolates



Figuer1-A



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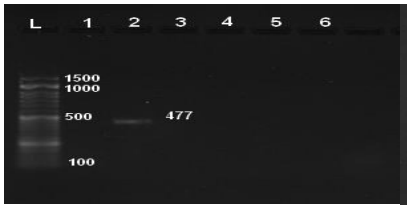

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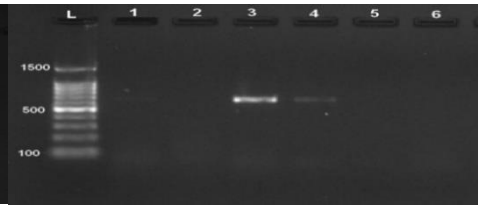

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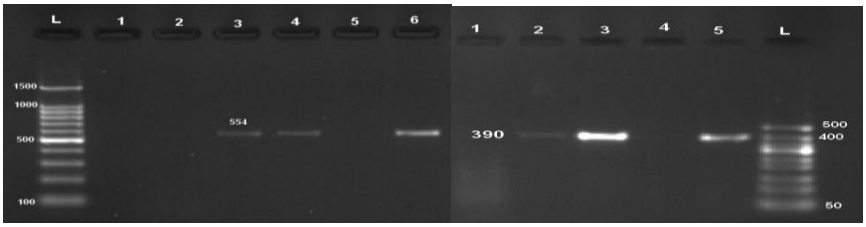
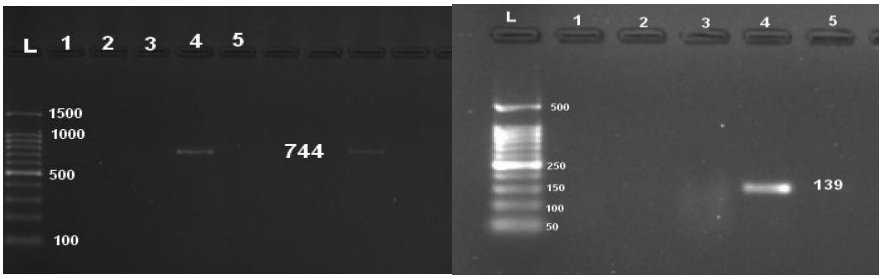


Figuer1-E **Figuer1**-F



Figuer1-G **Figuer1**-H

Figuer1: Polymerase chain reaction (PCR) amplicons obtained from the genomic DNA of *Pseudomonas aeruginosa* were analyzed using agarose gel electrophoresis. Panel (A) demonstrates amplification with **blaSIM-specific primers**; a molecular size ladder ranging from 100 to 1500 bp was employed, and positive bands at 570 bp were detected in lanes 1, 2, and 4. In panel (B), amplification was performed with **blaOXA primers**, producing a 564 bp fragment that was observed in lanes 1, 5, and 6, using the same size marker range. Panel (C) shows the results obtained with **blaGIM primers**, where products of 477 bp appeared in lanes 3, 4, and 6. Amplification using **blaNDM primers** is presented in panel (D); fragments of 621 bp were visible in lanes 3 and 5, with a 100–1500 bp marker. Panel (E) corresponds to **blaCTX-M amplification**, producing a 554 bp band in lanes 3, 4, and 6. For **blaVIM primers**, as illustrated in panel (F), lanes 2, 3, and 5 exhibited distinct 390 bp amplicons, with a 50–500 bp molecular marker used for comparison. In panel (G), amplification with **blaOXA-48 primers** yielded a band of 744 bp exclusively in lane 4. Finally, panel (H) depicts **blaIMP-specific amplification**, where a 139 bp product was identified in lane 4 using the 50–500 bp ladder.

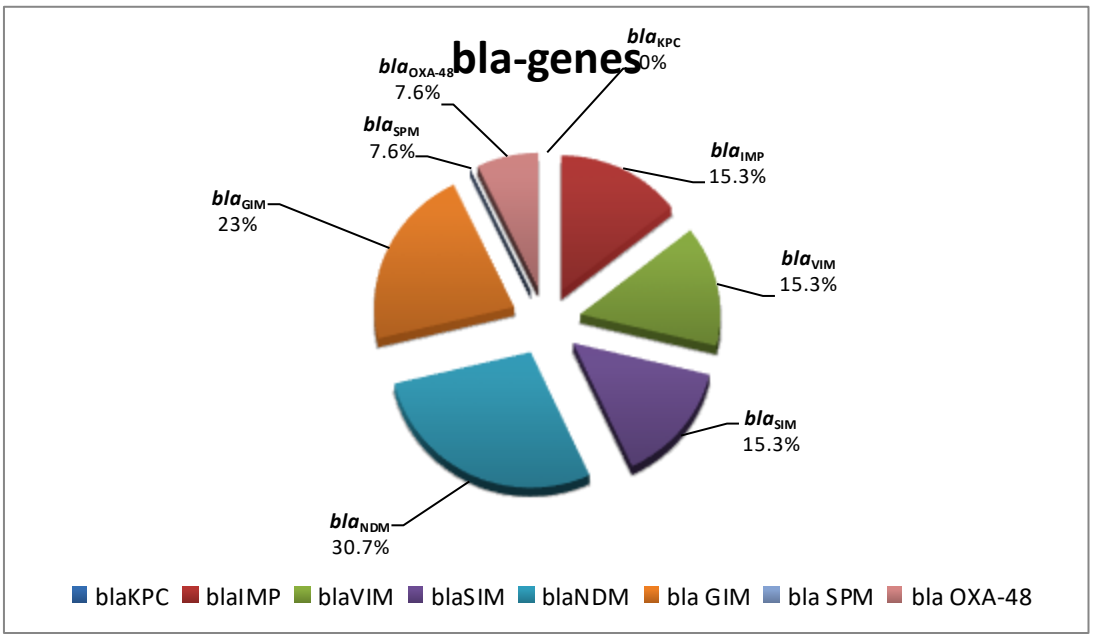


Figure 2: Dissemination of carbapenem genes in *P. aeruginosa*

Discussion

Pseudomonas aeruginosa is a widely spread community as well as in the hospital environments, which are currently among the most significant infections linked to healthcare in hospitals. *P. aeruginosa* has the potential to cause infections that are acquired in the community [26; 27; 28]. In our analysis of 300 clinical specemens from pateints with wound infections, 238(79.3%) show positive bacterial growth, while 62(20.7%) showed negative culture. The negative growth could be due to the presence of anaerobic bacteria or other causative agents of infection [29]. Among the 238 bacterial isolates, Gram-negative bacteria predominated, constituting 174(73.1%) of the isolates, compared to 64(26.9%) were Gram-positive bacteria.

This high proportion of Gram-negative isolates is consistant with findings from similar studies in Saudi Arabia that found 64.4% were Gram-negative and Gram-positive bacteria was 35.6% [30]. Additionally, research conducted in Egypt revealed that gram negative bacteria have been more common than gram positive bacteria [31]. Li *et al*., 2021 found that the prevalence rate of Gram-positive bacteria was 55.8% while the prevalence of Gram-negative was 42.9% [32]. The difference in the demographic features of participants may be connected to the diversity of outcomes. As well as hospitalization and the procedures performed after hospitalization are known to increase the risk of acquiring gram negative infection, the high concentrations of Gram-negative isolates in this study may be explained by the inclusion of only hospitalized clients [33].

P. aeruginosa was significant contributor among Gram-negative isolates accounting 40(22.8%) these finding were consistent with research conducted in India, where the ratio of *P. aeruginosa* was 21.8% [34]. However, distinct to the present study, earlier study from Ahmed *et al*. 2023 in Egypt showed a high rate of *P. aeruginosa* 40% [31]. In other studies, low occurrence of *P. aeruginosa* isolated from wound specimens such as Iraq percentage 15.5% [35], Ethiopia in 12.86% [36], Saudi Arabia 8.9% [30]. The infection rate from *P. aeruginosa* in wound varies significantly by context, with a reported prevalence of 16% in surgical infections and 12.8% in burn wounds [36].

Antibiotics susceptibility testing revealed high resistance rate to cefotaxime, cefixime, ceftriaxone, cefepime, piperacillin, aztreonam, tobramycin and ciprofloxacin. Other isolates showed fewer resistance rate to amikacin, colistin, meropenem, imipenem, gentamicin, levofloxacin, and piperacillin-tazobactam. The proportion of *P. aeruginosa* isolates that are resistant to antipseudomonal medications such as carbapenems, has been increasing to about 40% [37; 38]. One of the principal obstacles in the management of multidrug-resistant (*Pseudomonas aeruginosa*) infections is the emergence of resistance to antipseudomonal β-lactams, including piperacillin, ceftazidime, cefepime, aztreonam, and the carbapenem group. This problem becomes particularly critical when resistance to these agents occurs concurrently with diminished susceptibility to additional antibiotic classes, most notably aminoglycosides and fluoroquinolones [37].

Our finding in resistance pattern show both consistencies and divergences with other studies. They align with results of study conducted in India[34] by shows high sensitive to colistin, imipenem and high resistance was shown by to gentamicin, ceftazidime and meropenem. While study done by Peshattiwar shows a resistance pattern against piperacillin 41%, ciprofloxacin 46%, amikacin 36%, and gentamicin 38%. However, study in Iraq conducted by Mahmood and Hussein (2022) [35] detected that resistance rate to gentamicin 83.8%, amikacin 54%, tobramycin and ceftazidime 25% , Imipenem and levofloaxicillin 22.5%, ciprofolxacillin , aztreonam 16%, cefoxitin ,ceftriaxone and pipracillin 6.4%. Acquired beta-lactam resistance in *P. aeruginosa* can be caused by a number of processes, such as decreased outer membrane permeability, up regulation of efflux systems and beta-lactamase production [37]. MBLs and acquired ESBL are the main developing resistance in the terms of beta-lactamase synthesis *P. aeruginosa* mechanisms. When exposed to excessive and incorrected antibiotics use, genes coding for beta-lactamase enzymes undergoes constant mutations, giving rise to novel beta-lactamase with a wide range of activity [38; 39].

Molecular screening of cephalosporin-resistance isolates for ESBL genes (*blaOXA, blaCTX-M, blaSHV, blaTEM*) revealed high frequency of bla_{OXA} 67.5 %, $bla_{\text{CTX-M}}$ 55%, respectively, while bla_{SHV} and bla_{TEM} were not detected in any isolates. These data are relatively lower than other numerous studies in India performed by Hashemi et al. (2020) [40], Brazil and South Africa [41; 42], Al-Agamy in 2016 from Saudi Arabia [43]. Additionally, present study was parallel to the work of Al-dawodeyah in 2018 from Jordan which observed that the rates of $bla_{\text{CTX-M}}$ 68.9%, bla_{TEM} 18.9%, bla_{SHV} 12.5% [44]. Numerous factors,

including the quantity and origin of bacterial isolates as well as different geographic locations, may contribute to the discrepancies between these molecular results and the prevalence of resistance genes and the findings from other studies [45].

In present study eight carbapenemase genes (*bla*$_{KPC}$, *bla*$_{IMP}$, *bla*$_{VIM}$, *bla*$_{SIM}$, *bla*$_{NDM}$, *bla*$_{GIM}$, *bla*$_{SPM}$, and *bla*$_{OXA-48}$) were identified, the result showed that the frequency of carbapenem genes among carbapenem resistant *P. aeruginosa* were 7.6% have *bla*$_{OXA-48}$ as well as 15.3% isolates have (*bla*$_{IMP}$, *bla*$_{SIM}$ and *bla*$_{VIM}$), 23% carry *bla*$_{GIM}$, 30.7% have *bla*$_{NDM}$. While *bla*$_{SPM}$ and *bla*$_{KPC}$ were not found in any isolate. The result was lower than the study in China conducted by Wang and Wang (2020) [46], who found the prevalence of *bla* $_{NDM}$ 9.4% and *bla*$_{SIM}$ 6% among *P. aeruginosa*. As well as study in Iran by Ghasemian et al 2018 aimed to detected the prevalence of MBL producing *P. aeruginosa* conducted that the *bla*$_{VIM}$ and *bla*$_{IMP}$ were prevalence 12.9% and 12.5% respectively and no isolates harboring *bla*$_{NDM}$ and *bla*$_{SPM}$ [47]. However, previous study carried out in Egypt, among 22 carbapenemas-resistance *P. aeruginosa* wound infection isolates collected 27% harbored the *bla* $_{NDM-1}$ gene, 13.6% carried the *bla* $_{OXA-48}$, and none of the isolates harbored the bla KPC [48]. Further, an article published in Saudi Arabia identified a high rate of carbapenem resistance gene among carbapenemase resistance *P. aeruginosa*: *bla* $_{NDM-1}$ 15.6% , *bla* $_{OXA-48}$ 46.8%, *bla*$_{NDM}$ 37.5% while *bla*$_{KPC}$ was detected io one isolates [49]. It is uncommon to find OAX-type carbapenemases in *P. aeruginosa* carbapenem resistant OXA-48 positive *P. aeruginosa*. There have been recent reports of in Iran, Turkey, India, Sudan, and Egypt [50, 51; 52; 53]. We propose that *P. aeruginosa* gained the carbapenem resistance gene mobile genetic elements from other microbes such as *A. baumannii* and *Enterobacteriaceae* growing in burn units with

Conclusions

Most injured skin infections are caused by Gram-negative bacteria that show a high frequency of antibiotic-resistant patterns and the presence of ESBL and carbapenem resistance genes among *P. aeruginosa* isolate andinadequate infection control practices.

Ethics Statement

The samples and patient's history information were taken after get permission to be used in this study. All protocol details of our study were approved by Faculty of Medicine, University of Kufa, Iraq.

Reference

1. Jorgensen JH, Pfaller MA,CarrollKC, Funke G,Landry ML, RichterSS,et al. Manual of clinical microbiology. 11th ed. Washington DC: American Society of Microbiology; 2015. doi: 10.1128/9781555817381.
2. Lister PD, Wolter DJ, Hanson ND. Antibacterial-resistant Pseu domonas aeruginosa: Clinical impact and complex regulation of chromosomally encoded resistance mechanisms. Clin Microbiol Rev. 2009;22(4):582–610. doi: 10.1128/CMR.00040-09.[PubMed: 19822890]. [PubMedCentral: PMC2772362].
3. Amini A , Ebrahimzadeh Namvar A. Antimicrobial resistance pattern and presence of beta-lactamase genes in Pseudomonas Iran J Basic Med Sci, Vol. 23, No.11, Nov 2020 1399 Azimi et al. Inherent and acquired carbapenem resistance mechanisms aeruginosa strains isolated from hospitalized patients, Babol Iran. J Med Bacteriol 2019;8:45-50.
4. Ambler RP. The structure of beta-lactamases. Philos Trans R Soc Lond B Biol Sci 1980;289:321-31.
5. Hall BG, Salipante SJ, Barlow M. The metallo-beta-lactamases fall into two distinct phylogenetic groups. J Mol Evol 2003;57:249-54.
6. Nordmann P, Cuzon G, Naas T. The real threat of Klebsiella pneumoniae carbapenemase-producing bacteria. Lancet Infect Dis 2009;9:228-36.
7. Bijari A, Azimi L, Fallah F, Ardebili A, Lari ER, Lari AR. Involvement of the multidrug efflux pumps in beta-lactams resistant Pseudomonas aerugionsa clinical isolates collected from burn patients in Iran. Infect Disord Drug Targets 2016;16:172-177.
8. Lari AR, Azimi L, Soroush S, Taherikalani M. Low prevalence of metallo-beta-lactamase in Pseudomonas aeruginosa isolated from a tertiary burn care center in Tehran. Int J Immunopathol Pharmacol 2015;28:384-389.
9. Armin S, Fallah F, Azimi L, Samadi Kafil H, Ghazvini K, Hasanzadeh S, et al. Warning: spread of NDM-1 in two border towns of Iran. Cell Mol Biol 2018;64:125-129.
10. Azimi L, Talebi M, Pourshafie MR, Owlia P, Rastegar Lari A. Characterization of carbapenemases in extensively drug resistance Acinetobacter baumannii in a burn care center in Iran. Int J Mol Cell Med 2015;4:46-53.

11. Mobasseri P, Azimi L, Salehi M, Hosseini F, Fallah F. Multi drug resistance profiles and expression of adeijk and abem in Acinetobacter baumannii collected from humans by Real-time PCR. J Med Bacteriol 2018;7:50-56.

12. Jean SS, Lee NY, Tang HJ, Lu MC, Ko WC, Hsueh PR. Carbapenem-Resistant Enterobacteriaceae Infections: Taiwan Aspects. Front Microbiol 2018;9:2888.

13. Livorsi DJ, Chorazy ML, Schweizer ML, Balkenende EC, Blevins AE, Nair R, et al. A systematic review of the epidemiology of carbapenem-resistant Enterobacteriaceae in the United States. Antimicrob Resist Infect Control 2018;7:55.

14. Logan LK, Weinstein RA. The Epidemiology of Carbapenem-Resistant Enterobacteriaceae: The Impact and Evolution of a Global Menace. J Infect Dis 2017;15:215:S28-S36.

15. Zhang Y, Wang Q, Yin Y, Chen H, Jin L, Gu B, et al. Epidemiology of carbapenem-resistant Enterobacteriaceae infections: report from the China CRE network. Antimicrob Agents Chemother 2018;62:e01882-17.

16. Bratu S, Landman D, Haag R, Recco R, Eramo A, Alam M, et al. Rapid spread of carbapenem-resistant Klebsiella pneumoniae in New York City: a new threat to our antibiotic armamentarium. Arch Intern Med 2005;165:1430-5.

17. Kohler PP, Melano RG, Patel SN, Shafinaz S, Faheem A, Coleman BL, et al. Emergence of Carbapenemase-Producing Enterobacteriaceae, South-Central Ontario, Canada. Emerg Infect Dis 2018;24:1674-82.

18. Albiger B, Glasner C, Struelens MJ, Grundmann H, Monnet DL, European Survey of Carbapenemase-Producing Enterobacteriaceae (EuSCAPE) working group. Carbapenemase-producing Enterobacteriaceae in Europe: assessment by national experts from 38 countries, May 2015. Euro Surveill 2015;20.

19. Clinical and Laboratory Standards Institute. (2023). Performance Standards for Antimicrobial Susceptibility Testing; 33rd ed (CLSI M100–Ed33). Wayne, PA: CLSI;

20. Dallenne, C.; Da Costa, A.;Decré, D.; Favier, C. and Arlet, G. (2010). Development of a set of multiplex PCR assays for the detection of genes encoding important beta-lactamases in Enterobacteriaceae. J Antimicrob. Chemother., 65: 490-495.

21. Poirel, L.; Héritier, C.; Tolün, V. and Nordmann, P. (2004). Emergence of oxacillinase mediated resistance to imipenem in K.pneumoniae. Antimicrob. Agents Chemother., 48:15–22.

22. Gondal, A. J., Saleem, S., Jahan, S., Choudhry, N., & Yasmin, N. (2020). Novel carbapenem-resistant klebsiella pneumoniae ST147 coharboring bla NDM-1, bla OXA-48 and extended-spectrum β-lactamases from Pakistan. Infection and Drug Resistance, 2105-2115.

23. Bradford, P.A.; Bratu, S.; Urban, C.; Visalli, M.; Mariano, N. et al. (2004). Emergence of Carbapenem-Resistant Klebsiella Species Possessing the Class A Carbape- nem-Hydrolyzing KPC-2 and Inhibitor-Resistant TEM-30 β-lactamases in New York City. Clin Infect Dis., 39: 55–60.

24. Rasheed, J.K.; Jay, C.; Metchock, B.; Berkowitz, F.; Weigel, L.; Crellin, J.; Steward, C.; Hill, B.; Medeiros, A.A. and Tenover, F.C. (1997). Evolution of extended-spectrum β-lactam resistance (SHV-8) in a strain of Escherichia coli during multiple episodes of bacteremia Antimicrob. Agent Chemother., 41: 647-653.

25. Ellington MJ, Kistler J, Livermore DM, Woodford N. Multiplex PCR for rapid detection of genes encoding acquired metallo-beta-lactamases. J Antimicrob Chemother. 2007 Feb;59(2):321-2. doi: 10.1093/jac/dkl481. Epub 2006 Dec 21. PMID: 17185300.

26. Lister PD, Wolter DJ, Hanson ND. Antibacterial-resistant Pseu domonas aeruginosa: Clinical impact and complex regulation of chromosomally encoded resistance mechanisms. Clin Microbiol Rev. 2009;22(4):582–610. doi: 10.1128/CMR.00040-09.[PubMed: 19822890]. [PubMedCentral: PMC2772362].

27. Fallah F, Noori M, Hashemi A, Goudarzi H, Karimi A, Erfanimanesh S, et al. Prevalence of bla NDM, bla PER, bla VEB, bla IMP, and bla VIM Genes among Acinetobacter baumannii Isolated from Two Hospitals of Tehran, Iran. Scientifica (Cairo). 2014;2014:245162. doi: 10.1155/2014/245162. [PubMed: 25133013].

28. PoorabbasB,MardanehJ,RezaeiZ,KalaniM,Pouladfar G,AlamiMH, et al. Nosocomial Infections: Multicenter surveillance of antimicro bial resistance profile of Staphylococcus aureus and Gram negative rods isolated from blood and other sterile body fluids

in Iran. Iran J Microbiol. 2015;7(3):127–35. [PubMed: 26668699].

29. Jain SK, Barman R. Bacteriological Profile of Diabetic Foot Ulcer with Special Reference to Drug-resistant Strains in a Tertiary Care Center in North-East India. Indian J Endocrinol Metab. 2017 Sep-Oct;21(5):688-694. doi: 10.4103/ijem.IJEM_546_16. PMID: 28989875; PMCID: PMC5628537

30. Bandy A, Wani FA, Mohammed AH, Dar UF, Mallick A, Dar MR, et al. Bacteriological profile of wound infections and antimicrobial resistance in selected gram-negative bacteria. Afri Health Sci. 2022;22(4). 576-586. https://dx.doi.org/10.4314/ahs.v22i4.63

31. Ahmed EF, Rasmi AH, Darwish AMA, Gad GFM. Prevalence and resistance profile of bacteria isolated from wound infections among a group of patients in upper Egypt: a descriptive cross-sectional study. BMC Res Notes. 2023 Jun 19;16(1):106. doi: 10.1186/s13104-023-06379-y. PMID: 37337258; PMCID: PMC10280819.

32. Li, X., Cheng, Q., Du, Z., Zhu, S., & Cheng, C. (2021). Microbiological concordance in the management of diabetic foot ulcer infections with osteomyelitis, on the basis of cultures of different specimens at a diabetic foot center in china. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy, 14, 1493–1503.

33. Hassan MA, Abd El-Aziz S, Elbadry HM, Samy A, Tamer TM. Prevalence, antimi crobial resistance profile, and characterization of multi-drug resistant bacteria from various infected wounds in North Egypt. Saudi J Biol Sci 2022.

34. Bangera D, Shenoy SM, Saldanha DRM. Clinico-microbiological study of Pseu domonas aeruginosa in wound infections and the detection of metallo-β-lactamase production. Int Wound J 2016; 13:1299–1302

35. Rashid Mahmood A, Mansour Hussein N. Study of Antibiotic Resistant Genes in Pseudomonas aeroginosa Isolated from Burns and Wounds. Arch Razi Inst. 2022 Feb 28;77(1):403-411. doi: 10.22092/ARI.2021.356681.1893. PMID: 35891744; PMCID: PMC9288643.

36. Abdi FA, Motumma AN, Kalayu AA, Abegaz WE (2024) Prevalence and antimicrobial resistant patterns of Pseudomonas aeruginosa among burn patients attending Yekatit 12 Hospital Medical College in Addis Ababa, Ethiopia. PLoS ONE19(3): e0289586. https://doi.org/10.1371/journal.pone.0289586

37. Walsh TR, Toleman MA, Poirel L, Nordmann P. Metallo-β-lactamases: the quiet before the storm? Clin Microbiol Rev 2005;18:306–25.

38. Shashikala RK, Srinivasan S, Devi S. Emerging resistance to car bapenem in hospital acquired Pseudomonas infection: a case of con cern. Indian J Pharmacol 2006;38:287–8.

39. Pitout JD, Revathi G, Chow BL, Kabera B, Kariuki S, Nordmann P, Poirel L. Metallo-beta-lactamase-producing Pseudomonas aeruginosa isolated from large tertiary centre in Kenya. Clin Microbiol Infect 2008;14:755–9.

40. Hashemi AB, Nakhaei Moghaddam M, Forghanifard MM, Yousefi E. Detection of blaOXA-10 and blaOXA-48 genes in Pseudomonas aeruginosa clinical isolates by multiplex PCR. J Med Microbiol Infect Dis, 2021; 9 (3): 142-147. DOI: 10.52547/JoMMID.9.3.142

41. de Almeida Silva K de CF, Calomino MA, Deutsch G, de Castilho SR, de Paula GR, Esper LMR, et al. Molecular characterization of multidrug-resistant (MDR) Pseudomonas aeruginosa isolated in a burn center. Burns 2017;43:137–43. doi:10.1016/j.burns.2016.07.002

42. Adjei CB, Govinden U, Moodley K, Essack SY. Molecular characterisation of multidrug-resistant P. aeruginosa from a private hospital in Durban, South Africa. South African. J Infect Dis 2017:1–4.

43. Al-Agamy MH, Jeannot K, El-Mahdy TS, Samaha HA, Shibl AM, Plésiat P, et al. Diversity of Molecular Mechanisms Conferring Carbapenem Resistance to Pseudomonas aeruginosa Isolates from Saudi Arabia. Can J Infect Dis Med Microbiol 2016;2016:1–7. https://doi.org/10.1155/2016/4379686.

44. Al Dawodeyah HY, Obeidat N, Abu-Qatouseh LF, Shehabi AA. Antimicrobial resistance and putative virulence genes of Pseudomonas aeruginosa isolates from patients with respiratory tract infection. Germs 2018;8:31–40. https://doi.org/10.18683/germs.2018.1130

45. Azeez, Z. F., & Al-daraghi, W. A. H. (2018). Molecular Phylogenetic Study in 16S Rrna Gene Among Acinetobacter baumannii Isolates Characteristic Producing To Esbls Genes in Burn Infection. 30(4), 579–585.

46. Wang, W., & Wang, X. (2020). Prevalence of metallo-β-lactamase genes among Pseudomonas aeruginosa

isolated from various clinical samples in China. Journal of Laboratory Medicine, 44(4), 197–203.

47. Ghasemian A, Salimian Rizi K, Rajabi Vardanjani H, Nojoomi F. Prevalence of Clinically Isolated Metallo-beta-lactamase-producing Pseudomonas aeruginosa, Coding Genes, and Possible Risk Factors in Iran. Iran J Pathol. 2018 Winter;13(1):1-9. PMID: 29731790; PMCID: PMC5929383.

48. El Menofy NG, Tawfick MM, Badawy MSEM. Molecular study of carbapenem-resistant Pseudomonas aeruginosa causing wound infection in an Egyptian tertiary hospital. J Infect Dev Ctries. 2025 Jul 28;19(7):997-1006. doi: 10.3855/jidc.19953. PMID: 40720456.

49. Khater ES, AlFaki AA (2022) Detection of carbapenem resistant Pseudomonas aeruginosa in tertiary care hospital in Saudi Arabia. Microbes Infect Dis 3: 693–702. doi: 10.21608/MID.2022.142569.1320.

50. Bahrami M, Mmohammadi-Sichani M, Karbasizadeh V. Prevalence of < em > SHV, TEM, CTX-M and < em > OXA-48 β-Lactamase Genes in Clinical Isolates of Pseudomonas aeruginosa in Bandar-Abbas, Iran. 2018, 5(4):86–90.

51. Elnour Rahma Mohamed S, Alobied A, Mohamed Hussien W, Ibrahim Saeed M. blaOXA-48 Carbapenem Resistant Pseudomonas aeruginosa Clinical Isolates in Sudan. J Adv Microbiol. 2018;10(4):1–5.

52. Borah VV, Saikia KK, Hazarika NK. First report on the detection of OXA-48 β-lactamase gene in Escherichia coli and Pseudomonas aeruginosa co infection isolated from a patient in a Tertiary Care Hospital in Assam. Indian J Med Microbiol. 2016;34(2):252–3.

53. Abdelraheem WM, Ismail DE, Hammad SS. Prevalence of blaOXA-48 and other carbapenemase encoding genes among carbapenem-resistant Pseudomonas aeruginosa clinical isolates in Egypt. BMC Infect Dis. 2024 Nov 11;24(1):1278. doi: 10.1186/s12879-024-10123-7. PMID: 39528967; PMCID: PMC11556172.