World Journal of

Experimental Biosciences

Volume 12, Number 2: 49 - 52

ISSN: 2313-3937

2024

Research article

Emerging Patterns of Meropenem Resistance in *Pseudomonas aeruginosa* from Burn Patients: Epidemiological Data from Central Iraq

Rusul Hasham Ahmed^{1,2}*

ABSTRACT

Infected burns are among the most serious clinical cases with high mortality rates, especially when infected with multidrug-resistant (MDR) bacteria. Pseudomonas aeruginosa infection in burns significantly contributes to the high mortality associated with bacterial burn infections. This study aimed to conduct a bio-surveillance of burn cases infected with *P. aeruginosa* and their resistance to meropenem. A total of 305 burn cases were examined, with samples collected from the burn and wound hospital in Baghdad. Of these, 180 samples came from skin and soft tissue infections (SSTIs) associated with systemic sepsis, 100 from SSTIs, and 25 from minor burn injuries. *P. aeruginosa* was isolated and identified using biochemical methods. The Kirby–Bauer disk diffusion method was used to assess the response of the bacterial isolates to meropenem. Results showed that out of 82 *P. aeruginosa* infection cases. The percentage of isolates resistant to meropenem was 62.19%, sensitive was 34.14%, and those with intermediate response was 3.6%. The highest resistance to meropenem was observed in SSTIs with systemic sepsis. The study concludes that the incidence of *P. aeruginosa* infection is high, and resistance to meropenem is correlated with the severity of the infection.

Keywords: Antibiotics, Burn, Meropenem, *Pseudomonas aeruginosa*.

Citation: Ahmed RH. (2024) Emerging Meropenem Resistance Patterns of *Pseudomonas aeruginosa* in Burn Patients: Epidemiological Evidence from Central Iraq. *World J Exp Biosci* **12**: 49-52.

Received November 02, 2024; Revised December 08, 2024; Accepted: December 24, 2024; Published: December 30.

1. INTRODUCTION

Burn injuries are a big public health issue worldwide, especially in developing countries, because inadequate healthcare facilities and the lack of provision of infection control measures delay the management of complications [1]. Infectious diseases are the most public and serious complications in burn patients, which seriously contribute to longer hospital stays, increased healthcare costs, and higher rates of morbidity and mortality [2]. There are various pathogens responsible for burn wound infections. *Pseudomonas aeruginosa* is one of the most common opportunistic bacteria. It has resistance to a wide spectrum of antibiotics and a high potential to develop resistant mechanisms, making it a challenging pathogen in medical institutions [3].

The nature of burn wounds is highly conducive to *P. aeruginosa* biofilm formation and colonization of biotic and abiotic surfaces, leading to chronic infections [4]. The pathogen's high effectiveness and exposure to the widespread use of antibiotics have led to the emergence of multidrug-resistant (MDR), extensively drugresistant (XDR), and even pan-drug-resistant (PDR) strains [5]. These resistant strains decrease the effectiveness of traditionally used antibiotics like cephalosporins, aminoglycosides, carbapenems, and fluoroquinolones, making colistin highly important, despite its significant toxicity [6].

Burn injuries are common in Iraq because of local accidents, occupational trauma, and war exposure [7]. Despite the high prev-

Department of Biology, College of Science, University of Baghdad, Baghdad, Iraq Full list of author information is available at the end of the article.

Copyright: ©. Rusul Hasham Ahmed. This is an open-access article distributed under the terms of the Creative Commons Attribution. International License (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.

^{*} Correspondence: Rusul Hasham Ahmed. E-mail: rusul.ahmed1202@sc.uobaghdad.edu.iq.

alence of burn injuries, monitoring antimicrobial resistance (AMR) patterns of *P. aeruginosa* among burn patients in central Iraq remains limited. Insufficient use of antibiotics results from the failure to monitor and standardize treatment protocols, leading to the development of drug resistance. Understanding local epidemiological and resistance of *P. aeruginosa* is important for rising active infection control policies and antibiotic treatment quidelines in the hospitals [8].

Meropenem is a broad-spectrum carbapenem antibiotic frequently used to treat severe bacterial infections, especially the burn cases caused by MDR *P. aeruginosa*. The mechanism of action of this antibiotic is inhibiting the synthesis of bacterial cell walls by binding to penicillin-binding proteins, which subsequently leads to cell lysis. This antibiotic is highly effective against different pathogenic bacterial species that cause serious infections such as sepsis, pneumonia, and complicated skin or burn wound infections [9]. The current study aims to highlight the epidemiological trends and meropenem resistance patterns of *P. aeruginosa* in the burn patients in central Iraq through a surveillance study.

2. MATERIALS and METHODS

2.1. Study Design

The present research involved a cross-sectional study conducted at a Burns Hospital in Baghdad, Iraq, from September 2023 to March 2024. This study exclusively included patients with burn injuries admitted to a specialized referral center for burn care. In this study, infected skin and soft tissue (SSTIs) were defined as erythema, swelling, heat, or purulence around the wound, accompanied by clinical signs of infection such as fever and an increased number of blood leukocytes. Colonization was defined as the presence of bacteria in the absence of clinical signs of infection.

2.2. Infection Control or Antibiotic Protocols

The cases involved in the present study received controlled systemic administration of antibiotics and used them as advised by the clinician. Infection control protocols include regular washing of the patient's body every 24–48 hours as needed, and frequent changes of central lines (every three days unless clinically advised). Sample collection and identification, including debridement, are performed upon admission and as needed afterward. The use of carbapenems (such as meropenem) is part of the empirical sepsis regimen, especially for Intensive Care Unit (ICU) patients with suspected bacterial infections, such as *P. aeruginosa*.

2.3. Isolation and Identification

The samples were collected after removing all ointments and creams covering the infected burn wound areas. They were taken from different anatomical sites of the infected burn wounds in the presence of a clinician. In cases of multiple infections, the first samples were involved in the study. The clinical samples (swabs) were transferred aseptically to the laboratory and immediately cultured on MacConkey agar, blood agar, and neutral agar. Gram staining was performed on each sample. Non-fermented colonies on MacConkey agar were cultured on cetrimide agar. Biochemical tests, including catalase and oxidase, were conducted. VITIK 2 technology was used to confirm the presence of *P. aeruginosa* isolates. The isolates were stored short-term by culturing them on nutrient agar and kept at 4°C for 2 to 3 weeks. For longer storage, isolates were preserved at −20°C in nutrient broth containing 20% glycerol [10].

2.4. Antibiotic Susceptibility Testing

The Kirby–Bauer disk diffusion method was used to identify meropenem-resistant *P. aeruginosa* (MRPA) and meropenemsensitive *P. aeruginosa* (MSPA), as well as isolates that exhibited an intermediate response to meropenem. The previous method was followed. The diameters were compared with the diameters on the Clinical and Laboratory Standards Institute (CLSI) breakpoint charts to determine the sensitivity (S), intermediate (I), and resistance (R) of bacteria to imipenem [10-11].

2.5. Statistical analysis

Statistical analyses were done using Origin software version 8.6 (OriginLab, Northampton, MA, USA). Categorical variables, including the source of infection and resistance pattern, were reported as absolute frequencies and percentages. Continuous variables were presented as mean ± standard deviation (SD). All analyses were prespecified, with no post hoc hypothesis testing.

3. RESULTS

3.1. Infection with P. aeruginosa

During the study period, 305 samples were collected from patients with burn wound infections. The number of patients infected with *P. aeruginosa* was 82, with the same isolates of *P. aeruginosa*, which were a significant contributor, accounting for 26.88% (82/305) of the bacterial isolates.

3.2. Demographics and Clinical Features

The mean age of the patients in this study was 42.1 ± 16.7 years, with an age range from 18 to 73 years. Among the isolates, 58.5% (48/82) were collected from male patients and 41.5% (34/82) from female patients. The demographic information of the studied population was summarized in Table 1.

Table 1. Demographic and clinical features of the clinical cases involved in the study

	Variable	Values		
1.	Range of age	18-73 Years		
2.	Mean age	42.1 ± 16.7 Years		
3.	Gender male/female ratio	1.411		
4.	Kind of burn	Thermal (85.24%), electrical (13.11%), chemical (1.6%)		
5.	ICU admission	62.29%		
6.	Total Body Surface Area (TBSA)	11%–25%: 65.5 % 26%–50%: 29. 5% > 50%: 4.9%		

3.3. Clinical Sources and Distribution

SSTIs emerged as the primary clinical source of *P. aeruginosa*, accounting for 59.01% of cases, excluding those with sepsis. While the prevalence of sepsis was 32.78%. However, the low-burn wound infection was 8.19%. Interestingly, most *P. aeruginosa* isolates were isolated from the first group of patients. 62.7% were traced back to patients in the intensive care unit (ICU), highlighting the nosocomial nature of these infections. Furthermore, the total body surface area (TBSA) of 26%–50% showed the highest rate of *P. aeruginosa* infection compared to the others Table 2.

3.4. Meropenem Resistance Patterns

The Kirby–Bauer disk diffusion method was used to identify meropenem resistance patterns among 82 *P. aeruginosa* isolates

from 305 cases of infected burn wounds. High resistance levels were observed in cases of SSTIs with sepsis, followed by cases of SSTIs without sepsis. The present study showed that 62.19% of the isolates were resistant, while 34.14% of *P. aeruginosa* isolates were sensitive to meropenem (Table 2).

Table 2. Distribution of *P. aeruginosa* isolates and their meropenem susceptibility patterns among burn patients with different clinical conditions. Percentages represent the proportion of cases out of 305 total burn patients. Resistant, sensitive, and intermediate isolates were determined based on CLSI guidelines. SSTIs = skin and soft tissue infections.

	Percentag es of cases (305 cases)	No of cases that isolated P. aeruginosa	No of resistant isolates to meropene m	No of sensitive isolates to meropenen	No of Intermediate
SSTIs with sepsis	59.01%	49	30 (36.58%)	18 (21.95 %)	1 (1.2 %)
SSTIs without sepsis	32.78%	31	20 (24.39%)	9 (10.97 %)	2 (2.44 %)
Low burn infectio n	8.19%	2	1 (1.2 %)	1 (1.2 %)	0 (0%)
Total	100%	82	51 (62.19 %)	28 (34.14 %)	3 (3.65 %)

4. DISCUSSION

The findings of this study offer valuable epidemiological data on the burden of *P. aeruginosa* infections and their resistance to meropenem among burn patients in central Iraq. The high rate of *P. aeruginosa* isolated from burn wounds confirms its dominance as an opportunistic pathogen in post-burn infections, consistent with global reports that identify these bacterial isolates as a leading cause of morbidity and mortality in burn units [12]. Burn wounds create an ideal environment for *P. aeruginosa* colonization due to broken skin barriers, necrosis, and compromised immune responses, making infections in burn patients especially difficult to treat [13].

The 62.19% rate of resistance to meropenem that was observed is of concern and highlights the rising trend of multidrug-resistant (MDR) and extensively drug-resistant (XDR) P. aeruginosa strains in burn and wound hospitals. Such high levels of resistance have also been described in other Middle Eastern and North African nations, where overuse and empirical use of carbapenems have led to selective pressure and the development of resistance [14]. Meropenem, a previously effective therapy for severe P. aeruginosa infections, is losing its effectiveness and represents a serious therapeutic problem. Resistance mechanisms include metallo- β -lactamases (MBL) production, overexpression of efflux pumps, loss of outer membrane porins, and biofilm formation, which entraps the bacteria and limits the penetration of antibiotics, thereby supporting survival in burn wounds [15].

The resistance was significantly highest in SSTI with systemic sepsis (36.58%), showing a direct proportionality between the severity of infection and resistance. Severe systemic infections demand extended hospitalization and higher dosage of antibiotics, and thus might favor more resistant pathogens [16].

Less resistant infections were found in cases of minor burns, indicating that the emergence and selection of resistant isolates depend on the severity and duration of the infection. Given that delayed or ineffective therapy greatly increases fatal outcomes in MDR *P. aeruginosa* infections, the high mortality rate of infected

patients further emphasizes the clinical significance of antibiotic resistance [17]. These results highlight the importance of implementing efficient antimicrobial stewardship programs in Iraqi burn hospitals. To control the outbreak of resistant strains that infect the burn wounds. It is critical to closely follow up the resistant isolates to carbapenems and strictly adhere to infection control guidelines. Alternative therapies, such as phage therapy, combination antibiotic therapy, and the use of novel antipseudomonal agents, should be considered [18]. Furthermore, molecular research on the genes and mechanisms underlying resistance would provide important insights for focused interventions.

5. Conclusion

In the present study, a highly important result of the meropenem resistance rate (62.19%) was reported; the findings demonstrate the substantial burden of *P. aeruginosa* infections among burn patients in central Iraq. The current study showed that the severity of burn infection is associated with infection with *P. aeruginosa* that is resistant to meropenem. Thus, the current study demonstrates that *P. aeruginosa* is a significant risk to burn patients in Iraq and that complex infections.

Acknowledgments

We would like to thank the staff members of the Clinical Laboratory at the Department of Biology, College of Science, University of Baghdad, Baghdad, Iraq. We would also like to thank the clinical laboratory at the Central Public Health Laboratories in Baghdad, Iraq. Moreover, special thanks to the staff members of the Burn and Wound Hospital, Baghdad, Iraq.

Funding information

This work received no specific grant from any funding agency.

Conflict of interest

The authors declare that they have no conflict of interest.

Ethical Approval

This study was approved by the Ethics Committee of the University of Baghdad (CSEC/0984/0102; September 04, 2023). Since it was a retrospective analysis of routinely collected clinical data, individual patient consent was waived in accordance with national ethical guidelines.

Author contributions

Rusul H. Ahmed: Resources; Methodology, Supervision; Validation; Roles/Writing, Writing—review, Investigation; Project administration; Roles/Writing—original draft; and Writing—review & editing.

REFERENCES

- [1] Jordan KC, Di Gennaro JL, von Saint André-von Arnim A, Stewart BT. (2022) Global trends in pediatric burn injuries and care capacity from the World Health Organization Global Burn Registry. Front Pediatr 10:954995. doi: 10.3389/fped.2022.954995. PMID: 35928690; PMCID: PMC9343701.
- [2] Roy S, Mukherjee P, Kundu S, Majumder D, Raychaudhuri V, Choudhury L. (2024) Microbial infections in burn patients. Acute Crit Care 39(2):214-225. doi: 10.4266/acc.2023.01571. Epub 2024 May 24. PMID: 38863352; PMCID: PMC11167422.
- Tchakal-Mesbahi A, Metref M, Singh VK, Almpani M, Rahme LG. (2021) Characterization of antibiotic resistance profiles in *Pseudomonas aeruginosa* isolates from burn patients. *Burns* 47(8):1833-1843. doi: 10.1016/j.burns.2021.03.005. Epub 2021 Mar 17. PMID: 33795157; PMCID: PMC8590735.

- [4] de Sousa T, Hébraud M, Alves O, Costa E, Maltez L, et al. (2023) Pereira JE, Martins Â, Igrejas G, Poeta P. Study of Antimicrobial Resistance, Biofilm Formation, and Motility of Pseudomonas aeruginosa Derived from Urine Samples. Microorganisms 11(5):1345. doi: 10.3390/microorganisms11051345. PMID: 37317319; PMCID: PMC10224020.
- [5] Kadivarian S, Rostamian M, Dashtbin S, Kooti S, Zangeneh Z, et al. (2023) High burden of MDR, XDR, PDR, and MBL producing Gram negative bacteria causing infections in Kermanshah health centers during 2019-2020. Iran J Microbiol 15(3):359-372. doi: 10.18502/ijm.v15i3.12896. PMID: 37448672; PMCID: PMC10336284.
- [6] Ontong JC, Ozioma NF, Voravuthikunchai SP, Chusri S. (2021) Synergistic antibacterial effects of colistin in combination with aminoglycoside, carbapenems, cephalosporins, fluoroquinolones, tetracyclines, fosfomycin, and piperacillin on multidrug resistant Klebsiella pneumoniae isolates. PLoS One 16(1):e0244673. doi: 10.1371/journal.pone.0244673. Erratum in: PLoS One. 2021 May 14;16(5):e0251994. doi: 10.1371/journal.pone.0251994. PMID: 33406110; PMCID: PMC7787437.
- [7] Baiee HA, Ismaiel IS, Al-Charrakh AH. (2024) Microbiological Profile of Burn Accidents Among Patients Admitted to Imam Al-Sadiq Teaching Hospital in Babylon, Iraq. Hilla University College J. Med Sci 2(1): 15-19. doi.org/10.62445/2958-4515.1006.
- [8] Nagavci B, Schwingshackl L, Martin-Loeches I, Lakatos B. (2024) Utilization of expert opinion in infectious diseases clinical guidelines-A meta-epidemiological study. PLoS One 19(6):e0306098. doi: 10.1371/journal.pone.0306098. PMID: 38935698; PMCID: PMC11210760.
- [9] Khalil MA, El Maghraby GM, Sonbol FI, Allam NG, Ateya PS, Ali SS. (2021) Enhanced Efficacy of Some Antibiotics in Presence of Silver Nanoparticles Against Multidrug Resistant Pseudomonas aeruginosa Recovered From Burn Wound Infections. Front Microbiol 12:648560. doi: 10.3389/fmicb.2021.648560. PMID: 34616370; PMCID: PMC8488261.
- [10] Ghafil JA, Al-Sudani KSF, Ibrahim SBM, Alshahrani AM, Zgair AK. (2024) Relationship between biofilm formation of Pseudomonas aeruginosa and susceptibility to rifaximin and ofloxacin. Pak J Pharm Sci 37(6):1609-1614. PMID: 39923153.

- [11] CLSI. (2018) Performance standards for antimicrobial disk susceptibility tests, M02, 13th ed. Clinical and Laboratory Standards Institute, Wayne, PA.
- [12] Kambouris AR, Brammer JA, Roussey H, Chen C, Cross AS. (2023) A combination of burn wound injury and Pseudomonas infection elicits unique gene expression that enhances bacterial pathogenicity. mBio 14(6):e0245423. doi: 10.1128/mbio.02454-23. Epub 2023 Nov 6. PMID: 37929965; PMCID: PMC10746159.
- [13] Sanya DRA, Onésime D, Vizzarro G, Jacquier N. (2023) Recent advances in therapeutic targets identification and development of treatment strategies towards Pseudomonas aeruginosa infections. *BMC Microbiol* 23(1):86. doi: 10.1186/s12866-023-02832-x. PMID: 36991325; PMCID: PMC10060139.
- [14] Al-Orphaly M, Hadi HA, Eltayeb FK, Al-Hail H, Samuel BG, et al. (2021) Epidemiology of Multidrug-Resistant Pseudomonas aeruginosa in the Middle East and North Africa Region. mSphere 6(3):e00202-21. doi: 10.1128/mSphere.00202-21. PMID: 34011686; PMCID: PMC8265635.
- [15] Laxminarayan R, Matsoso P, Pant S, Brower C, Røttingen JA, et al. (2016) Access to effective antimicrobials: a worldwide challenge. *Lancet* 387(10014):168-75. doi: 10.1016/S0140-6736(15)00474-2. Epub 2015 Nov 18. PMID: 26603918.
- [16] Avent ML, McCarthy KL, Sime FB, Naicker S, Heffernan AJ, et al. (2022) Evaluating Mono- and Combination Therapy of Meropenem and Amikacin against Pseudomonas aeruginosa Bacteremia in the Hollow-Fiber Infection Model. *Microbiol Spectr* 10(3):e0052522. doi: 10.1128/spectrum.00525-22. Epub 2022 Apr 20. PMID: 35442072; PMCID: PMC9241727.
- [17] Frem JA, Doumat G, Kazma J, Gharamti A, Kanj SS, et al. (2023) Clinical predictos of mortality in patients with Pseudomonas aeruginosa infection. PLoS One 18(4):e0282276. doi: 10.1371/journal.pone.0282276. PMID: 37115776; PMCID: PMC10146515.
- [18] Kunz Coyne AJ, El Ghali A, Holger D, Rebold N, Rybak MJ. (2022) Therapetic Strategies for Emerging Multidrug-Resistant Pseudomonas aeruginosa. *Infect Dis Ther* 11(2):661-682. doi: 10.1007/s40121-022-00591-2. Epub 2022 Feb 12. PMID: 35150435; PMCID: PMC8960490.

Author affiliation

- 1. Department of Biology, College of Science, Baghdad, Iraq.
- 2. Al-Turath University, Baghdad, Iraq.

ORCID:

Rusul H. Ahmed: https://orcid.org/0009-0000-3251-7539