JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Original Article

A meta-analysis of the correlation between carbapenem antibiotic use and the incidence of carbapenem-resistant *Pseudomonas aeruginosa*

Cheng Tang[1], Yaosheng Mei[2], Hang Fang[1], Wei Wang[1], Meiyan Lv[1]

[1] Department of Clinical Laboratory, The First People's Hospital of Yongkang, Yongkang City, Zhejiang Province, 321300, China
[2] Department of Cardiology, The First People's Hospital of Yongkang, Yongkang City, Zhejiang Province, 321300, China

Abstract

Introduction: This meta-analysis evaluates the correlation between carbapenem antibiotic use and the incidence of carbapenem-resistant *Pseudomonas aeruginosa* (CRPA).

Methodology: A comprehensive literature search conducted across multiple databases yielded seven clinical experimental studies involving 4,417 patients. The primary outcomes assessed were the risk factors associated with CRPA infection, drug resistance rates, and the comparison of resistance rates between meropenem (MEM) and imipenem (IPM). The Newcastle-Ottawa Scale (NOS) was used to assess study quality, and Egger's test and funnel plots were used to assess publication bias.

Results: The NOS scores for the included studies ranged between 6 and 8, indicating their generally high quality. The analysis indicated that prior carbapenem use significantly increased the risk of CRPA infection (OR = 1.866, 95% confidence interval [CI]: 1.164–2.993, $p = 0.010$). The drug resistance rates of *P. aeruginosa* to carbapenems ranged between 21.07% and 37.90%. There was no significant difference in drug resistance rates between MEM and IPM (risk ratio = 1.09, 95% CI: 0.99-1.21, $p = 0.517$).

Conclusions: With drug resistance rates between 21.07% and 37.90%, these findings suggest that carbapenem use is associated with an increased risk of CRPA infection, highlighting the need for the judicious use of these antibiotics in clinical practice.

Key words: Meta-analysis; carbapenem antibiotic; carbapenem-resistant *Pseudomonas aeruginosa*; drug resistance rates.

J Infect Dev Ctries 2025; 19(9):1377-1383. doi:10.3855/jidc.20950

(Received 12 October 2024 – Accepted 23 January 2025)

Introduction

Pseudomonas aeruginosa is a ubiquitous gram-negative bacterium known for its remarkable adaptability and intrinsic resistance to multiple antibiotics [1]. It is a leading cause of nosocomial infections, particularly in immunocompromised patients and those with severe underlying diseases [2]. The concept of heteroresistance, wherein a subset of the bacterial population exhibits resistance to an antibiotic while the majority remains susceptible, adds another layer of complexity to the phenomenon of carbapenem resistance in *P. aeruginosa* [3]. This heterogeneity in resistance profiles can lead to treatment failures and complicate the interpretation of susceptibility testing results [4]. The emergence and spread of carbapenem-resistant *P. aeruginosa* (CRPA) strains has become a global health concern, posing significant challenges in clinical treatment and infection control [5].

Carbapenems, including meropenem (MEM) and imipenem (IPM), are often considered the last line of defence against multidrug-resistant gram-negative bacteria [6]. However, the increasing prevalence of CRPA threatens the efficacy of these crucial antibiotics [7]. The mechanisms of carbapenem resistance in *P. aeruginosa* are complex and multifactorial, involving the production of carbapenemases, efflux pump overexpression, and alterations in outer membrane proteins [8].

The relationship between carbapenem use and the development of resistance in *P. aeruginosa* has been extensively studied and yielded conflicting findings [9]. Although some studies have reported a strong association between prior carbapenem exposure and the emergence of CRPA [10], others have found contradictory results suggesting that prior antibiotic use was not associated with the acquisition of high-MEM-level-resistant *P. aeruginosa* [11]. Despite the growing body of research on CRPA, there remains a need for a comprehensive analysis of the available evidence to elucidate the relationship between carbapenem use and the incidence of resistance. Previous meta-analyses have focused on specific aspects of CRPA, such as

treatment outcomes or risk factors for acquisition, but few have specifically addressed the correlation between carbapenem use and resistance development [12,13]. Understanding this relationship is crucial for developing effective antibiotic stewardship programmes and preventing the further spread of resistance.

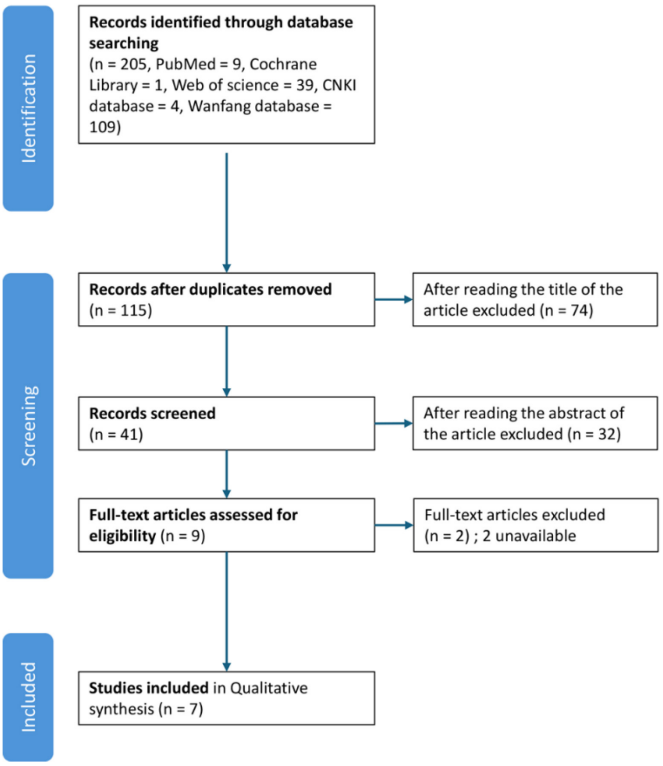
This meta-analysis aims to evaluate the link between carbapenem antibiotic use and the incidence of CRPA. By synthesising data from high-quality clinical studies, it seeks to provide a clearer understanding of CRPA infection risk factors, the prevalence of carbapenem resistance in *P. aeruginosa,* and the resistance rates of different carbapenem antibiotics. The findings will contribute to guiding antibiotic prescription and infection control strategies employed in the management of *P. aeruginosa* infections.

Methodology

Search Strategy

A comprehensive literature search was conducted across multiple databases to identify relevant studies investigating the correlation between carbapenem antibiotic use and the incidence of CRPA. The databases searched included PubMed, the Cochrane Library, Web of Science, China National Knowledge Infrastructure (CNKI), and Wanfang. The search terms used were '*Pseudomonas aeruginosa*', 'carbapenems heteroresistance', 'drug resistance', 'carbapenems', and 'antibiotics', as well as their Chinese equivalents. Relevant literature was searched from inception to September 2024.

Figure 1. Flow chart of literature screening.



Inclusion and Exclusion Criteria

Studies were included if they met the following criteria: (1) a clinical experimental research design; (2) an investigation of carbapenem use and CRPA incidence; (3) the reporting of at least one of the following outcomes: risk factors for CRPA infection, drug resistance rates or a comparison of resistance rates between different carbapenems; and (4) full-text availability. Studies were excluded if they were non-clinical, did not focus on *P. aeruginosa* or carbapenem resistance, or did not report relevant outcome measures. Duplicate literature was also excluded.

Study Selection and Data Extraction

Two independent reviewers screened the titles and abstracts of the identified studies. Full texts of potentially eligible studies were then assessed for inclusion. Disagreements were resolved through discussion or consultation with a third reviewer. Data extraction was performed using a standardised form that included study characteristics (e.g. author, year, sample size, and study design), the types of carbapenems studied, the quality control strains used, and outcome measures.

Quality Assessment

The quality of the included studies was assessed using the Newcastle-Ottawa Scale (NOS) for clinical experimental studies. This scale evaluates studies based on selection, comparability, and outcome assessment. Studies with scores of 6 or higher were considered to be of high quality [14].

Statistical Analysis

Meta-analyses were conducted using RevMan 5.3 software. The primary outcomes assessed were the risk factors associated with CRPA infection, drug resistance rates, and the comparison of resistance rates between MEM and IPM. For dichotomous outcomes (drug resistance rates), risk ratios (RRs) with 95% confidence intervals (CI) were computed. For continuous outcomes, mean differences or standardised mean differences were calculated as appropriate. Random effects models were used in anticipation of heterogeneity among the studies. Heterogeneity was assessed using the I^2 statistic, with values >50%

Table 1. Basic characteristics of included literature.

Author (year)	Type of study	Total number	Type of Carbapenems	Quality control strain	Exposure factors	NOS score
Ma 2019 [15]	Clinical experimental research	169	Meropenem, Imipenem	ATCC27853	The comorbid conditions, invasive procedures, detection of multiple pathogens	7
Yuan 2017 [16]	Clinical experimental research	179	-	CRPA, CSPA	Stay in Department of Neurosurgery, prior carbapenem use, peripherally inserted central catheter, nasal feeding, and mechanical ventilation	7
Xiong 2013 [17]	Clinical experimental research	2521	Imipenem	PA	drug resistance, multi-drug resistance, pan-resistant strains	6
He 2012 [18]	Clinical experimental research	1238	Imipenem	PA	the rate of resistance to imipenem	6
Fei 2010 [19]	Clinical experimental research	162	Meropenem, Imipenem	PA	the rate of resistance to imipenem	6
Howard-Anderson 2022 [20]	Clinical experimental research	143	-	CRPA	the rate of resistance to imipenem	7
Bergen P 2011 [21]	Clinical experimental research	5	Meropenem, Imipenem	ATCC27853	drug resistance, multi-drug resistance, pan-resistant strains	8

indicating substantial heterogeneity. Publication bias was evaluated using Egger's test and funnel plots.

Results

Study Selection and Characteristics

An initial database search identified 205 records (109 from Wanfang, 47 from CNKI, 39 from Web of Science, 9 from PubMed, and 1 from the Cochrane Library). After removing duplicates, 115 records remained for screening. Following a title and abstract review, 74 articles were excluded, leaving 41 for full-text assessment. Ultimately, seven clinical experimental studies met the inclusion criteria and were included in the meta-analysis (Figure 1).

The seven included studies involved a total of 4,417 patients or isolates. Sample sizes ranged between 5 and 2,521. The studies investigated various types of carbapenems, with MEM and IPM being the most common. The quality control strain ATCC27853 was used in two studies, and NOS scores for the included studies ranged between 6 and 8, indicating their generally high quality (Table 1).

Risk Factors for Carbapenem-Resistant Pseudomonas aeruginosa Infection

Two studies reported risk factors associated with CRPA infection using logistic regression analysis. Ma *et al*. (2019) [15] found that prior carbapenem use was associated with an increased risk of CRPA infection, although the result was not statistically significant (OR = 1.268, $p = 0.529$). Yuan *et al.* (2017) [16] reported a significant association between prior carbapenem use and CRPA infection (OR = 1.866, 95% CI: 1.164–2.993, $p = 0.010$) (Table 2).

Other risk factors identified in these studies included comorbid conditions, invasive procedures, the detection of multiple pathogens, stays in the department of neurosurgery, peripherally inserted central catheter use, nasal feeding, and mechanical ventilation. However, these factors were not consistently reported across the studies, precluding meta-analysis.

Drug Resistance Rates

Three studies reported the drug resistance rates of *P. aeruginosa* to carbapenems. Xiong *et al.* (2013) [17] found a resistance rate of 21.07% among 782 isolates ($p < 0.05$). He *et al.* (2012) [18] reported a higher resistance rate of 37.90% among 1,238 isolates. Fei *et al.* (2010) [19] observed a resistance rate of 31.70% among 102 isolates ($p < 0.01$) (Table 3).

The variation in resistance rates across these studies may be attributed to differences in study populations, geographical locations, and the carbapenems studied. The overall trend suggests a high prevalence of carbapenem resistance in *P. aeruginosa*, ranging between approximately one-fifth and over one-third of isolates.

Table 2. Risk factors (Prior carbapenem use) associated with carbapenem-resistant P. *aeruginosa* infection by logistic stepwise regression analysis.

Author (year)	OR	*p*	95% CI
Ma 2019	1.268	0.529	-
Yuan 2017	1.866	0.010	1.164-2.993

Table 3. The comparison of PA separation rate and drug resistance rate.

Author (year)	PA	Drug resistance rate (%)	*p*
Xiong (2013)	782	21.07	< 0.05
He (2012)	1238	37.90	-
Fei (2010)	102	31.70	< 0.01

Comparison of Resistance Rates between Meropenem and Imipenem

Three studies provided data comparing drug resistance rates between MEM and IPM. The meta-analysis revealed no significant difference in resistance rates between these two carbapenems (RR = 1.09, 95% CI: 0.99-1.21, p = 0.517). There was no significant heterogeneity among the studies (I^2 = 0.0%, p = 0.517) (Figure 2).

A forest plot (Figure 2) illustrates the individual and pooled risk ratios for drug resistance between MEM and IPM. The study by He *et al.* (2012) [18] contributed the most weight (92.62%) to the analysis, likely due to its larger sample size relative to the other included studies.

Publication bias was assessed using a funnel plot (Figure 3) and Egger's test. The funnel plot appeared relatively symmetrical, and Egger's test revealed no significant publication bias (p = 0.472) (Figure 4).

Discussion

This meta-analysis examined seven clinical experimental studies to assess carbapenem resistance in *P. aeruginosa*. The findings revealed varying resistance rates to carbapenems (mainly MEM and IPM) ranging between 21.07% and 37.90% and indicating a widespread issue. Prior carbapenem use was identified as a potential risk factor for CRPA infections, although other risk factors were inconsistently reported across studies. A comparison of resistance rates between MEM and IPM showed no significant difference, suggesting similar resistance profiles for both drugs. Overall, this study highlights the significance of carbapenem resistance as a concern and underscores the need for continued monitoring and prudent management of antibiotic use.

Figure 3. Funnel plots of Drug resistance between MEM and IPM.

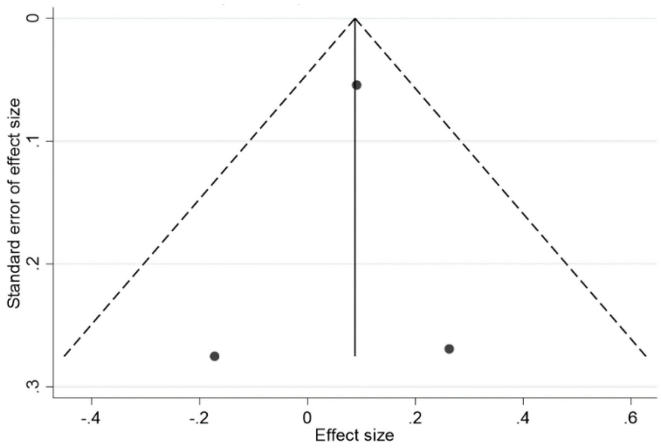
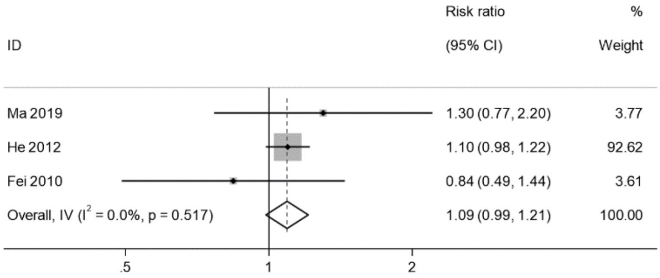


Figure 2. Forest plots of Drug resistance between MEM and IPM.



Risk Factors for Carbapenem-Resistant Pseudomonas aeruginosa Infection

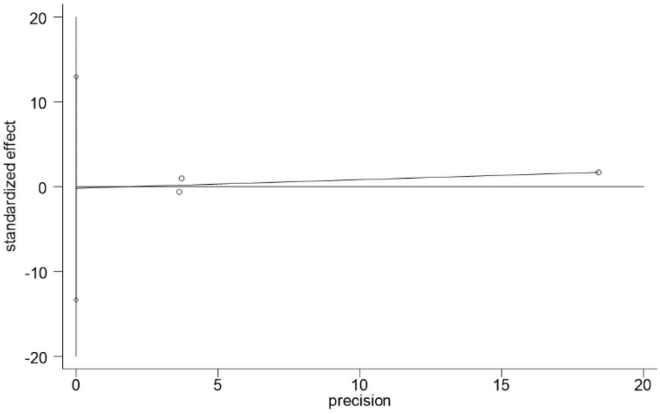
The analysis of risk factors for CRPA infection revealed that prior carbapenem use was significantly associated with an increased risk of developing CRPA infection. This finding aligns with previous studies suggesting that antibiotic exposure, particularly to broad-spectrum agents such as carbapenems, can exert selective pressure that favours the emergence of resistant strains [22].

The significant association reported by Yuan *et al.* (2017) underscores the importance of judicious carbapenem use in clinical practice. This result supports the notion that antimicrobial stewardship programmes should focus on optimising carbapenem prescription to mitigate the risk of resistance development [23].

Notably, Ma *et al.* (2019) reported a non-significant association between prior carbapenem use and CRPA infection. This discrepancy highlights the complex nature of resistance development and suggests that other factors may also play crucial roles in the emergence of CRPA [24].

The identification of additional risk factors such as comorbid conditions, invasive procedures, and the detection of multiple pathogens emphasises the multifactorial nature of CRPA infections. These findings suggest that a comprehensive approach to

Figure 4. Egger-test of Drug resistance between MEM and IPM.



infection prevention and control that addresses multiple risk factors may be necessary to effectively reduce the incidence of CRPA [25].

Drug Resistance Rates

The analysis of drug resistance rates revealed considerable variation across the studies, with resistance rates ranging between 21.07% and 37.90%. This variability may reflect differences in study populations, geographical locations, and local antibiotic prescription practices [26].

The observed resistance rates, indicating that a substantial proportion of *P. aeruginosa* isolates are resistant to carbapenems, are concerning. This high prevalence of resistance poses significant challenges for clinical management, as carbapenems are often considered last-resort antibiotics for multidrug-resistant gram-negative infections [27].

The variation in resistance rates across studies also highlights the importance of local surveillance programmes to monitor antibiotic resistance trends. Such programmes can provide valuable data to guide empirical antibiotic therapy and inform infection control strategies [28].

Comparison of Resistance Rates between Meropenem and Imipenem

The meta-analysis comparing resistance rates between MEM and IPM revealed no significant difference between these two carbapenems (RR = 1.09, 95% CI: 0.99, 1.21, $p = 0.517$). This finding suggests that *P. aeruginosa* exhibits similar resistance profiles to both MEM and IPM.

The lack of a significant difference in resistance rates between MEM and IPM has important clinical implications. It suggests that these carbapenems may be similarly effective (or ineffective) against *P. aeruginosa* infections, and the choice between them may depend on other factors, such as pharmacokinetics, side effect profiles, and local availability.

However, it is important to note that this analysis does not account for potential differences in minimum inhibitory concentrations or the prevalence of heteroresistance between MEM and IPM. Future studies investigating these aspects could provide more nuanced insights into the comparative efficacy of these carbapenems against *P. aeruginosa* [29].

Implications for Clinical Practice and Antibiotic Stewardship

This meta-analysis provides several implications for clinical practice and antibiotic stewardship. First, the association between prior carbapenem use and CRPA infection underscores the need for the judicious use of carbapenems, with clinicians carefully considering their necessity and exploring alternative antibiotics where appropriate. Second, the identification of multiple risk factors for CRPA infection suggests that a holistic approach to patient assessment and infection prevention is crucial, including the minimisation of invasive procedures, the optimisation of comorbidity management, and the implementation of strict infection control measures [30]. The variability in resistance rates across the studies highlights the importance of local antimicrobial resistance surveillance, with hospitals and healthcare systems developing and regularly updating antibiotic prescription guidelines based on local resistance patterns [31,32]. While not directly addressed in this meta-analysis, the concept of heteroresistance in *P. aeruginosa* emphasises the need for improved diagnostic methods and potentially more aggressive treatment strategies for suspected resistant infections [33]. Finally, given the high resistance rates observed, research into effective combination therapies for CRPA infections, including investigations into synergistic antibiotic combinations and novel therapeutic approaches, should be prioritised.

Limitations and Future Directions

Several limitations of this meta-analysis should be acknowledged. First, the number of included studies was relatively small, potentially limiting the generalisability of its findings. Second, heterogeneity in the study designs, populations, and outcome measures may have affected the results.

Additionally, this meta-analysis focused primarily on clinical outcomes and did not extensively explore the molecular mechanisms of carbapenem resistance in *P. aeruginosa*. Future research should aim to integrate clinical, microbiological, and molecular data to provide a more comprehensive understanding of CRPA.

Future research directions should encompass a range of critical areas to address the growing challenge of CRPA. Large-scale, prospective studies are needed to investigate the temporal relationship between carbapenem use and CRPA emergence and provide valuable insights into the dynamics of resistance development. Novel diagnostic methods for the early detection of carbapenem resistance, including heteroresistance, should be investigated to improve the timely and accurate identification of resistant strains. Additionally, research should focus on evaluating combination therapies and alternative treatment

strategies for CRPA infections to explore potential synergistic effects and novel approaches to combat these challenging infections.

Conclusions

The high prevalence of carbapenem resistance in *P. aeruginosa*, ranging between 21.07% and 37.90%, emphasises the need for effective countermeasures. The lack of a significant difference in resistance between MEM and IPM suggests that the choice of carbapenem should be based on factors other than antimicrobial activity. This analysis underscores the importance of judicious carbapenem use, infection control, and ongoing resistance surveillance to effectively manage CRPA infections.

Availability of data and materials

All data generated or analysed during this study are included in this article. Further inquiries can be directed to the corresponding author.

Authors contributions

Tang C conceived of the study, Mei YS and Fang H participated in its design and data analysis and statistics and Wang W and Lv MY helped to draft the manuscript. All authors read and approved the final manuscript.

Corresponding author

Meiyan Lv
Department of Clinical laboratory,
The First People's Hospital of Yongkang
No.599 Jinshan West Road, Yongkang City,
Zhejiang Province, 321300, China
Tel: +86 13738969268
Email: lmy2024lmy@163.com

Conflict of interest

No conflict of interest is declared.

References

1. Mohanty S, Baliyarsingh B, Nayak SK (2020) Antimicrobial resistance in *Pseudomonas aeruginosa*: a concise review. Antimicrob Resist One Health Perspect 1: 1-14. doi: 10.5772/intechopen.88706
2. Tacconelli E, Carrara E, Savoldi A, Harbarth S, Mendelson M, Monnet DL, Pulcini C, Kahlmeter G, Kluytmans J, Carmeli Y, Ouellette M, Outterson K, Patel J, Cavaleri M, Cox EM, Houchens CR, Grayson ML, Hansen P, Singh N, Theuretzbacher U, Magrini N (2018) Discovery, research, and development of new antibiotics: The WHO priority list of antibiotic-resistant bacteria and tuberculosis. Lancet Infect Dis 18: 318-327. doi: 10.1016/S1473-3099(17)30753-3.
3. El-Halfawy OM, Valvano MA (2015) Antimicrobial heteroresistance: An emerging field in need of clarity. Clin Microbiol Rev 28: 191-207. doi: 10.1128/CMR.00058-14.
4. Assoni L, Milani B, Carvalho MR, Nepomuceno LN, Waz NT, Guerra MES, Converso TR, Darrieux M (2020) Resistance mechanisms to antimicrobial peptides in Gram-positive bacteria. Front Microbiol 11: 593215. doi: 10.3389/fmicb.2020.593215.
5. Castanheira M, Mendes RE, Gales AC (2023) Global epidemiology and mechanisms of resistance of *Acinetobacter baumannii*-calcoaceticus complex. Clin Infect Dis 76 Suppl 2: 166-178. doi: 10.1093/cid/ciad109.
6. Suay-García B, Pérez-Gracia MT (2019) Present and future of carbapenem-resistant *Enterobacteriaceae* (CRE) infections. Antibiotics 8: 122. doi: 10.3390/antibiotics8030122.
7. Kazmierczak KM, Rabine S, Hackel M, McLaughlin RE, Biedenbach DJ, Bouchillon SK, Sahm DF, Bradford PA (2016) Multiyear, multinational survey of the incidence and global distribution of metallo-β-lactamase-producing *Enterobacteriaceae* and *Pseudomonas aeruginosa*. Antimicrob Agents Chemother 60: 1067-1078. doi: 10.1128/AAC.02379-15.
8. Shahzad N, Aslam B, Arshad M (2020) Carbapenem resistance: Mechanisms and drivers of global menace. In: Hashmi MZ, editor. Antibiotics and antimicrobial resistance genes in the environment. Amsterdam: Elsevier. 123-145.
9. Zhao Y, Lin Q, Liu L, Ma R, Chen J, Shen Y, Feng S (2020) Risk factors and outcomes of antibiotic-resistant *Pseudomonas aeruginosa* bloodstream infection in adult patients with acute leukemia. Clin Infect Dis 71 Suppl 4: 386-393. doi: 10.1093/cid/ciaa1522.
10. Lautenbach E, Synnestvedt M, Weiner MG, Bilker WB, Vo L, Schein J, Kim M (2010) Imipenem resistance in *Pseudomonas aeruginosa*: Emergence, epidemiology, and impact on clinical and economic outcomes. Infect Control Hosp Epidemiol 31: 47-53. doi: 10.1086/649021.
11. Eagye KJ, Kuti JL, Nicolau DP (2009) Risk factors and outcomes associated with isolation of meropenem high-level-resistant *Pseudomonas aeruginosa*. Infect Control Hosp Epidemiol 30: 746-752. doi: 10.1086/603527.
12. Onorato L, Macera M, Calò F, Cirillo P, Di Caprio G, Coppola N (2022) Beta-lactam monotherapy or combination therapy for bloodstream infections or pneumonia due to *Pseudomonas aeruginosa*: A meta-analysis. Int J Antimicrob Agents 59: 106512. doi: 10.1016/j.ijantimicag.2021.106512.
13. Chen G, Xu K, Sun F, Sun Y, Kong Z, Fang B (2020) Risk factors of multidrug-resistant bacteria in lower respiratory tract infections: A systematic review and meta-analysis. Can J Infect Dis Med Microbiol 2020: 7268519. doi: 10.1155/2020/7268519.

14. Stang A (2010) Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol 25: 603-605. doi: 10.1007/s10654-010-9491-z.
15. Ma X, Li H, Lu Y, Cai Y, Zheng ZW, Zeng J, Huang B (2019) Clinical characteristics and risk factors of heterogeneous resistance to carbapenem antibiotics in *Pseudomonas aeruginosa*. J Trop Med 19: 398-403.
16. Yuan L, Ding B, Shen Z, Shi W, Xu X, Li G (2017) Clinical study of carbapenem-resistant *Pseudomonas aeruginosa* infection. Chin J Infect Chemother 17: 121-126.
17. Xu J, Huang Q, Lin Z, Liu Q (2013) Analysis of resistance rate of *Pseudomonas aeruginosa* to carbapenem antibiotics. Med Theory Pract 26: 843-846.
18. He Z, Li C, Yang Y (2012) Analysis of carbapenem resistance of 1238 *Pseudomonas aeruginosa* strains. Occup Health 28: 1216-1220.
19. Fei J, Wu L, Peng D, Tu H, Zhou M, Li C, Bao Q, Zhou T (2010) Resistance of *Pseudomonas aeruginosa* to carbapenem antibiotics. Chin J Public Health 26: 1258-1260.
20. Howard-Anderson J, Davis M, Page AM, Bower CW, Smith G, Jacob JT, Andersson DI, Weiss DS, Satola SW (2022) Prevalence of colistin heteroresistance in carbapenem-resistant *Pseudomonas aeruginosa* and association with clinical outcomes in patients: An observational study. J Antimicrob Chemother 77: 793-798. doi: 10.1093/jac/dkab461.
21. Bergen PJ, Forrest A, Bulitta JB, Tsuji BT, Sidjabat HE, Paterson DL, Li J, Nation RL (2011) Clinically relevant plasma concentrations of colistin in combination with imipenem enhance pharmacodynamic activity against multidrug-resistant *Pseudomonas aeruginosa* at multiple inocula. Antimicrob Agents Chemother 55: 5134-5142. doi: 10.1128/AAC.05028-11.
22. Mekonnen H, Seid A, Molla Fenta G, Gebrecherkos T (2021) Antimicrobial resistance profiles and associated factors of *Acinetobacter* and *Pseudomonas aeruginosa* nosocomial infection among patients admitted at Dessie comprehensive specialized hospital, North-East Ethiopia: A cross-sectional study. PLoS One 16: e0257272. doi: 10.21203/rs.3.rs-360841/v1.
23. Fabre V, Davis A, Diekema DJ, Granwehr B, Hayden MK, Lowe CF, Pfeiffer CD, Sick-Samuels AC, Sullivan KV, Van Schooneveld TC, Morgan DJ (2023) Principles of diagnostic stewardship: a practical guide from the society for healthcare epidemiology of america diagnostic stewardship task force. Infect Control Hosp Epidemiol 44: 178-185. doi: 10.1017/ice.2023.5.
24. Bassetti M, Vena A, Giacobbe DR, Castaldo N (2021) Management of infections caused by multidrug-resistant Gram-negative pathogens: Recent advances and future directions. Arch Med Res 52: 817-827. doi: 10.1016/j.arcmed.2021.09.002.
25. Yin R, Cheng J, Wang J, Li P, Lin J (2022) Treatment of *Pseudomonas aeruginosa* infectious biofilms: Challenges and strategies. Front Microbiol 13: 955286. doi: 10.3389/fmicb.2022.955286.
26. Sader HS, Mendes RE, Streit JM, Carvalhaes CG, Castanheira M (2022) Antimicrobial susceptibility of Gram-negative bacteria from intensive care unit and non-intensive care unit patients from United States hospitals (2018-2020). Diagn Microbiol Infect Dis 102: 115557. doi: 10.1016/j.diagmicrobio.2021.115557.
27. Ibrahim S, Al-Saryi N, Al-Kadmy IMS, Aziz SN (2021) Multidrug-resistant *Acinetobacter baumannii* as an emerging concern in hospitals. Mol Biol Rep 48: 6987-6998. doi: 10.1007/s11033-021-06690-6.
28. Zhanel GG, Wiebe R, Dilay L, Thomson K, Rubinstein E, Hoban DJ, Noreddin AM, Karlowsky JA (2007) Comparative review of the carbapenems. Drugs 67: 1027-1052. doi: 10.2165/00003495-200767070-00006.
29. Nicolau DP (2008) Carbapenems: a potent class of antibiotics. Expert Opin Pharmacother 9: 23-37. doi: 10.1517/14656566.9.1.23.
30. Yuan Q, Guo L, Li B, Zhang S, Feng H, Yu M, Hu H, Chen H, Yang Q, Qu T (2023) Risk factors and outcomes of inpatients with carbapenem-resistant *Pseudomonas aeruginosa* bloodstream infections in China: A 9-year trend and multicenter cohort study. Front Microbiol 14: 1137811. doi: 10.3389/fmicb.2023.1137811.
31. Fwoloshi S, Chola U, Nakazwe R, Tatila T, Mateele T, Kabaso M, Muzyamba T, Mutwale I, St Clair Jones A, Islam J, Chikatula E, Mweemba A, Mbewe W, Mulenga L, Aiken AM, Menon JA, Bailey SL, Knight GM (2023) Why local antibiotic resistance data matters - Informing empiric prescribing through local data collation, app design and engagement in Zambia. J Infect Public Health 16 Suppl 1: 69-77. doi: 10.1016/j.jiph.2023.11.007.
32. Torumkuney D, Kundu S, Vu GV, Nguyen HA, Pham HV, Kamble P, Keles N (2022) Country data on AMR in Vietnam in the context of community-acquired respiratory tract infections: Links between antibiotic susceptibility, local and international antibiotic prescribing guidelines, access to medicines and clinical outcome. J Antimicrob Chemother 77 Suppl 1: 26-34. doi: 10.1093/jac/dkac214.
33. Ma W, Li J, Wang D, Yu C, Sun S (2019) In vitro interaction of various antibiotic combinations recommended by Chinese consensus statement against carbapenem-resistant *Pseudomonas aeruginosa*. Lett Appl Microbiol 69: 198-203. doi: 10.1093/femsle/fnz198.