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Original Article

Frequency of Ceftazidime-Avibactam Susceptibility In Specimens of Carbapenem-Resistant Pseudomonas Aeruginosa In A Tertiary Care Hospital

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ABSTRACT

Objective: To determine the frequency of Ceftazidime-Avibactam (CAZ-AVI) susceptibility in specimens of Carbapenem-resistant Pseudomonas aeruginosa (CRPA) at a tertiary care hospital.

Study Design: Analytical cross-sectional study.

Place and Duration of Study: Department of Microbiology, Combined Military Hospital (CMH), Multan, Pakistan, from Jan-Jun 2024.

Methodology: Specimens of carbapenem-resistant Pseudomonas aeruginosa were included in the study to find the susceptibility of CAZ-AVI using the standard Kirby Bauer disc diffusion method. Zones were interpreted using a Vernier caliper following Clinical Standard Institute (CLSI) 2023, where zone of CAZ-AVI ≥21 was considered as susceptible.

Results: The total sample size was 103 CRPA specimens, out of which, 47(45.60%) were found to be susceptible to CAZ-AVI with an average zone of inhibition of 16.9 ± 8.8 mm, with male patients showing more susceptibility as compared to females (51.00% vs. 40.40%). The majority 44(68.80%) of resistant cases were from inpatient department as compared to the outpatient department 12(30.80%) (*p*-value <0.001). Organisms were more susceptible in the specimens bronchioalveolar lavage sputum (87.50% and 75.00% respectively) whereas the most resistant isolates were found in Tracheal aspirate and blood specimens (100.00%) *(p*-value <0.001).

Conclusion: The study demonstrates that approximately 45.60% of carbapenem-resistant Pseudomonas aeruginosa (CRPA) isolates at a tertiary care hospital are susceptible to Ceftazidime-Avibactam (CAZ-AVI), supporting its potential role as a valuable treatment option.

Keywords: Carbapenem resistant Pseudomonas aeruginosa (CRPA), Ceftazidime avibactam (CAZ-AVI), Multi drug resistant (MDR)

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INTRODUCTION

With the irrational use of broad-spectrum antibiotics, the emergence of multidrug-resistant Pseudomonas aeruginosa isolates has become a significant health problem worldwide.[1] Infection caused by CRPA is related to high levels of morbidity and mortality[2] making it one of the leading causes of healthcare-associated infections around the world[3]. In hospitals, prolonged hospital stay, immunosuppression and an overall increase in resistance, accounts for greater healthcare costs[4] leading to complicated abdominal, bloodstream, surgical site, urinary tract and skin infections predominantly in burn patients, healthcare-associated pneumonia and ventilator-associated pneumonia in intensive care units[5]. Currently, carbapenems are considered as first-line antimicrobial agents for the treatment of severe gram-negative infections,[6] however, it is not cost-effective, has adverse effects and its excessive use in critical care units has increased the resistance of the drug to serious life-threatening infections worldwide as the resistance is attributed to the presence of enzymes called carbapenemsases which inactivate most β-lactam antibiotics[7]. Ceftazidime-avibactam was approved by the Food and Drug Administration (FDA) in 2015 for the treatment of complicated infections caused by multi-drug resistant or extended drug resistant gram-negative bacteria[8]. A review study regarding the global frequency of Carbapenem-resistant Pseudomonas aeruginosa showed the frequency to range from 16.80 to 50.00%[9] while a study conducted in Pakistan analyzed 155 CRPA strains isolated from different clinical specimens, out of which 131 (84.5%) were susceptible and 24 (15.5%) were found to be resistant[10]. The rationale of the study is to increase the evidence base for the use of Ceftazidime-avibactam (CAZ-AVI) in patients with Carbapenem-resistant

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Pseudomonas aeruginosa infection to improve patient outcomes by decreasing hospital stays and decrease the cost of treatment.

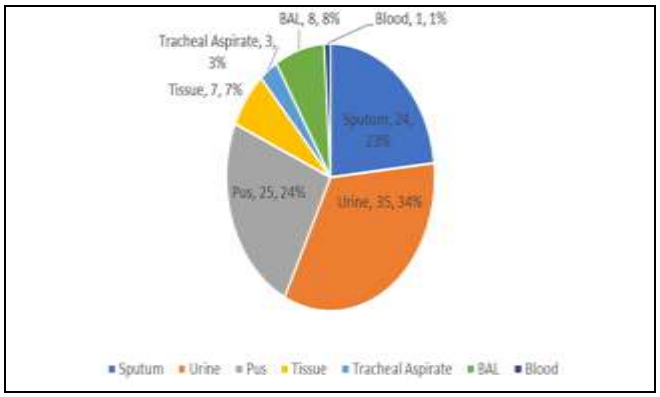

Figure-1: Frequency of CRPA Specimen (n=103)
**BAL: Bronchoalveolar Lavage*

METHODOLOGY

This analytical cross-sectional study was conducted in Department of Microbiology, Combined Military Hospital (CMH) Multan, Pakistan, over a duration of six months, from January to June 2024. Ethics approval was obtained from the Institutional Ethics Committee Letter Number : (04/2024).

Inclusion Criteria: All microbiological samples (blood, urine, pus) positive for Carbapenem resistant Pseudomonas aeruginosa, from either gender, with age ranging from 18 to 65 years, admitted or outdoor patients, were included in the study.

Exclusion Criteria: Samples of the patients which were recurrent and duplicate samples of Carbapenem-resistant Pseudomonas aeruginosa were excluded from the study.

A sample size of 103 patients was calculated through the World Health Organization (WHO) sample size calculator using the formula for single proportion, keeping the frequency of Pseudomonas aeruginosa susceptibility to Ceftazidime-avibactam as 84.50%, desired precision 7.00% and level of confidence as 95.00%12. Patient characteristics including age (years), gender (male/female), type of specimen, and indoor/outdoor cases were noted. Kirby-Bauer disk diffusion method was used to determine the antibiotic susceptibility of Pseudomonas aeruginosa by preparing inoculum of 0.5 Mc Farland standard. The suspension was streaked on Muller Hinton agar and antibiotic discs were applied as per standard guidelines. Plates were incubated at 37 degrees for 24 hours and results were interpreted according to CLSI 2023 with Vernier caliper in Carbapenem resistant cases. Ceftazidime-avibactam (CAZ-AVI) discs were applied, and results were interpreted according to CLSI guidelines. A zone of ≥21 was considered susceptible and zone of < 20 was considered as resistant. Descriptive statistics were calculated for qualitative and quantitative variables in the form of mean ± standard deviation (SD) and frequency and percentages using Statistical Package for Social Sciences version 23.00. Relation of CAZ-AVI susceptibility with age groups and type of specimen was assessed through chi-square. Pearson Correlation was used to find the realtionship of age and CAZ-AVI Zone of Susceptibility in CRPA Isolates test taking p-value < 0.05 as significant.

RESULTS

Out of a total of 103 specimens, 47(45.60%) were found to be susceptible to CAZ-AVI with an average zone of inhibition of 16.90 ± 8.80. Male patients showed more susceptibility to CAZ-AVI as compared to female patients (51.00% vs. 40.40%). The majority of resistant cases were from the inpatient department 44(68.80%) as compared to the outpatient department (n=12, 30.80%) with a significant *p*-value (<0.001) as shown in Table-I.

Table-I: Location-wise CAZ-AVI Susceptibility in CRPA Isolates (n=103)

Location	Resistant n (%)	Susceptible n (%)	*p*-value
IPD	44(68.80%)	20(31.30%)	<0.001
OPD	12(30.80%)	27(69.20%)	
Total	56(54.40%)	47(45.60%)	

**CAZ-AVI: Ceftazidime-avibactam,*
CRPA: Carbapenem-resistant pseudomonas aeruginosa,
IPD: Inpatient department,
OPD: Outpatient department

The majority of susceptible cases belonged to the age group of 14-25 years whereas the majority of the resistant cases belonged to the age group of 60-77 years as shown in Table-II.

Table-II: Age Distribution and CAZ-AVI Susceptibility in CRPA Isolates (n=103)

Age Group	Resistant n (%)	Susceptible n (%)	*p*-value
14-25	1(8.30%)	11(91.70%)	<0.001
26-39	4(17.40%)	19(82.60%)	
40-59	20(60.60%)	13(39.40%)	
60-77	31(88.60%)	4(11.40%)	
Total	56(54.40%)	47(45.60%)	

**CAZ-AVI: Ceftazidime-avibactam, CRPA: Carbapenem-resistant pseudomonas aeruginosa*

Moreover, a significant correlation (*p*-value <0.005) was found between age and zone of susceptibility with intermediate strength of association (r = -.58). This showed that with advancing age there was a decrease in the sensitivity to CAZ-AVI as shown in Table III.

Table-III: Correlation of Age and CAZ-AVI Zone of Susceptibility in CRPA Isolates (n=103)

Variable		Zone of Susceptibility
Age	r value	-0.58
	p value	<0.001

**r = correlation coefficient,*
CAZ-AVI: Ceftazidime-avibactam,
CRPA: Carbapenem-resistant pseudomonas aeruginosa

A significant association was found between the zone of susceptibility and specimen type (*p*-value <0.001). The most susceptibility was noted in BAL and sputum (87.50% and 75.00% respectively) samples whereas the most resistant isolates were of tracheal aspirate and blood (100.00%) as shown in Table IV.

Table-IV: Distribution of Specimen Type and CAZ-AVI Susceptibility in CRPA Isolates (n=103)

Specimen Type	Resistant n (%)	Susceptible n (%)	*p*-value
Sputum	6(25.00%)	18(75.00%)	<0.001
Urine	19(54.30%)	16(45.70%)	
Pus	21(84.00%)	4(16.00%)	
Tissue	5(71.40%)	2(28.60%)	
Tracheal Aspirate	3(100.00%)	0(0.00%)	
BAL	1(12.50%)	7(87.50%)	
Blood	1(100.00%)	0(0.00%)	
Total	56(54.40%)	47(45.60%)	

**CAZ-AVI: Ceftazidime-avibactam,*
CRPA: Carbapenem-resistant pseudomonas aeruginosa,
BAL: Bronchoalveolar Lavage

DISCUSSION

In this study susceptibility of Ceftazidime-avibactam in MDR Carbapenem resistant Pseudomonas aeruginosa came out to be 45.60%. A study conducted in Turkey noted that multi-drug resistant and extensive drug resistant, Pseudomonas aeruginosa was one of the leading causes of death in hospitals particularly in ICUs.[12] Another study showed greater susceptibility to CAZ-AVI than our study at 84.50%[13] showing that this drug responded more in developed countries than under developed countries, probably due to lack of good hospital care and infection control measures in under-privileged countries. Another European study showed the frequency of MDR Pseudomonas aeruginosa as 30.20% whereas in this study it was 56.00%. The susceptibility was low in Pakistan due to advising antibiotics when necessary and strict compliance of infection control strategies[14]. A study noted the susceptibility of Ceftazidime-avibactam in South America to be 86.00% whereas it was 46.00% in this study[15]. A study conducted in Sub-Saharan Africa showed the resistance of Pseudomonas aeruginosa as 14.00% which was found to be less resistant[16]. In a study conducted in Qatar, 205 samples were taken, out of which 68.80% were found to be susceptible to ceftazidime avibactam with the organism most commonly isolated from respiratory samples (44.00%)[17], however in this study, organism was isolated mostly from urine (34.00%).[18] A study conducted in Iran predominately showed that the sensitivity of respiratory samples was found to be 85.00%[19] whereas in our study, bronchoalveolar lavage was 87.50% followed by sputum 75% with respiratory samples being more susceptible to ceftazidime in both the studies. The frequency of Ceftazidime-Avibactam (CAZ-AVI) in the treatment of Carbapenem-Resistant Pseudomonas aeruginosa (CRPA) is increasing drastically. Keeping this in view Ceftazidime-avibactam could be novel therapeutic option, particularly in the context of multidrug-resistant organisms where treatment options are too limited.

LIMITATIONS OF STUDY

A key limitation of this study is its single-center, cross-sectional design, which may limit the generalizability of CAZ-AVI susceptibility patterns to other hospitals or regions with different antibiotic-use practices. The sample size, although adequate for descriptive analysis, may not fully capture the heterogeneity of CRPA isolates across different wards and specimen types. Additionally, susceptibility was assessed only by disc diffusion without confirmatory methods such as minimum inhibitory concentration (MIC) testing or molecular characterization of resistance mechanisms, which could affect the precision and interpretability of the reported resistance rates.

CONCLUSION

The study demonstrates that approximately 45.60% of carbapenem-resistant Pseudomonas aeruginosa (CRPA) isolates at a tertiary care hospital are susceptible to Ceftazidime-Avibactam (CAZ-AVI), supporting its potential role as a valuable treatment option in this setting. These findings highlight the need for routine CAZ-AVI susceptibility testing and careful source-guided empiric therapy in CRPA infections.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

FR & IUK: Data acquisition, data analysis, critical review, approval of the final version to be published.

RMN & FTZ: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

FA & TA: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Lee YL, Ko WC, Hsueh PR. Geographic patterns of carbapenem-resistant Pseudomonas aeruginosa in the Asia-Pacific region: results from the Antimicrobial Testing Leadership and Surveillance (ATLAS) program, 2015–2019. Antimicrob Agents Chemother 2022; 66: e0200021. https://doi.org/10.1128/aac.02000-21
2. Horcajada JP, Montero M, Oliver A, et al. Epidemiology and treatment of multidrug-resistant and extensively drug-resistant Pseudomonas aeruginosa infections. Clin Microbiol Rev 2019; 32 : e00031-19. https://doi.org/10.1128/CMR.00031-19
3. Mirzaei B, Bazgir ZN, Goli HR, et al. Prevalence of multi-drug resistant (MDR) and extensively drug-resistant (XDR) phenotypes of Pseudomonas aeruginosa and Acinetobacter baumannii isolated in clinical samples from Northeast of Iran. BMC Res Notes 2020; 13: 434. https://doi.org/10.1186/s13104-020-05224-w
4. Zaragoza R, Vidal-Cortés P, Aguilar G, et al. Update of the treatment of nosocomial pneumonia in the ICU. Crit Care 2020; 24: 371. https://doi.org/10.1186/s13054-020-03091-2
5. Mosley JF, Smith LL, Parke CK, et al. Ceftazidime-avibactam (Avycaz): for the treatment of complicated intra-abdominal and urinary tract infections. P T 2016; 41: 479–484, 489–490.
6. Cassini A, Högberg LD, Plachouras D, et al. Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modelling analysis. Lancet Infect Dis 2019; 19: 56–66. https://doi.org/10.1016/S1473-3099(18)30605-4
7. Van Duin D, Arias CA, Komarow L, et al. Molecular and clinical epidemiology of carbapenem-resistant Enterobacterales in the USA (CRACKLE-2): a prospective cohort study. Lancet Infect Dis 2020; 20: 731–741. https://doi.org/10.1016/S1473-3099(19)30755-8
8. Tiseo G, Brigante G, Giacobbe DR, et al. Diagnosis and management of infections caused by multidrug-resistant bacteria: guideline endorsed by SIMIT, SITA, GISA, AMCLI and SIM. Int J Antimicrob Agents 2022; 60: 106611. https://doi.org/10.1016/j.ijantimicag.2022.106611
9. Nordmann P, Poirel L. Epidemiology and diagnostics of carbapenem resistance in Gram-negative bacteria. Clin Infect Dis 2019; 69: S521–S528. https://doi.org/10.1093/cid/ciz824
10. Farooq L, Memon Z, Ismail MO, et al. Frequency and antibiogram of multi-drug resistant Pseudomonas aeruginosa in a tertiary care hospital of Pakistan. Pak J Med Sci 2019; 35: 1622–1627. https://doi.org/10.12669/pjms.35.6.930
11. Pagani L, Mantengoli E, Migliavacca R, et al. Multifocal detection of multidrug-resistant Pseudomonas aeruginosa producing the PER-1 extended-spectrum β-lactamase in Northern Italy. J Clin Microbiol 2004; 42: 2523–2529. https://doi.org/10.1128/JCM.42.6.2523-2529.2004
12. Özlem KO, Tığlı GA, Özen HN, et al. Evaluation of ceftazidime-avibactam susceptibility in carbapenem-resistant Klebsiella pneumoniae and Pseudomonas aeruginosa isolates. J Med Palliat Care 2022; 4: 625–629. https://doi.org/10.47582/jompac.1372443
13. Pérez A, Gato E, Pérez-Llarena J, et al. High incidence of MDR and XDR Pseudomonas aeruginosa isolates obtained from patients with ventilator-associated pneumonia in Greece, Italy and Spain as part of the MagicBullet clinical trial. J Antimicrob Chemother 2019; 74: 1244–1252. https://doi.org/10.1093/jac/dkz030
14. Karlowsky JA, Kazmierczak KM, Valente ML, et al. In vitro activity of ceftazidime-avibactam against Enterobacterales and Pseudomonas aeruginosa isolates collected in Latin America as part of the ATLAS global surveillance program, 2017–2019. Braz J Infect Dis 2021; 25: 101647. https://doi.org/10.1016/j.bjid.2021.101647
15. Wise MG, Karlowsky JA, Hackel MA, et al. In vitro activity of ceftazidime-avibactam against clinical isolates of Enterobacterales and Pseudomonas aeruginosa from sub-Saharan Africa: ATLAS Global Surveillance Program 2017–2021. J Glob Antimicrob Resist 2023; 35: 93–100. https://doi.org/10.1016/j.jgar.2023.08.022
16. Sid MA, Abdel HH, Hassan AA, et al. Evaluation of in vitro activity of ceftazidime/avibactam and ceftolozane/tazobactam against MDR Pseudomonas aeruginosa isolates from Qatar. J Antimicrob Chemother 2019; 74: 3497–3504. https://doi.org/10.1093/jac/dkz379
17. Özlem KO, Tığlı GA, Özen HN, et al. Evaluation of ceftazidime-avibactam susceptibility in carbapenem-resistant Klebsiella pneumoniae and Pseudomonas aeruginosa isolates. J Med Palliat Care 2022; 4: 625–629. https://doi.org/10.47582/jompac.1372443
18. Koca Ö, Tığlı GA, Özen HN, Çekin Y, Seyman D. Evaluation of ceftazidime-avibactam susceptibility in carbapenem-resistant Klebsiella pneumoniae and Pseudomonas aeruginosa isolates. J Med Palliat Care 2023; 4: 625–629. https://doi.org/10.47582/jompac.1372443
19. Mirzaei B, Bazgir ZN, Goli HR, et al. Prevalence of multi-drug resistant (MDR) and extensively drug-resistant (XDR) phenotypes of Pseudomonas aeruginosa and Acinetobacter baumannii isolated in clinical samples from Northeast of Iran. BMC Res Notes 2020; 13: 434. https://doi.org/10.1186/s13104-020-05224-w