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Original Article

Impact of multidrug-resistant *Pseudomonas aeruginosa* bloodstream infections on mortality in oncology patients

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Abstract

Introduction: *Pseudomonas aeruginosa* (PAE) is among the most frequent causes of bloodstream infections (BSIs) in cancer patients. Resistant strains are associated with increased morbidity and mortality.

Methodology: A retrospective study was conducted at a tertiary oncology hospital in Mexico City, including all episodes of PAE-BSI. The isolates were classified as susceptible, carbapenem-resistant (CR), multidrug-resistant (MDR), or difficult-to-treat resistant (DTR).

Results: A total of 259 PAE-BSI episodes were analyzed: 202 (78.4%) susceptible, 19 (7.3%) CR, 13 (5.0%) MDR, and 25 (9.7%) DTR. Resistant strains were significantly associated with prior antibiotic use (84.2% vs. 52.5%), more extended hospital stays (18 vs. 9 days), septic shock (36.8% vs. 19.8%), and inappropriate empiric therapy (54.4% vs. 19.3%). Overall, 30-day mortality was 38.2%, rising to 47.4% in CR, 84.6% in MDR, and 76% in DTR cases; compared with 29.7% in susceptible isolates ($p < 0.001$). No mortality benefit was observed with combination therapy compared to monotherapy. Multivariate analysis indicated that age ≥ 60 years, advanced oncological status, secondary bacteremia, septic shock, invasive mechanical ventilation, inadequate source control, and carbapenem strains were independent predictors of 30-day mortality. Appropriate antimicrobial therapy was a protective factor.

Conclusions: Resistant PAE-BSI in cancer patients was associated with longer hospitalizations and a significantly increased mortality rate. Appropriate antimicrobial therapy can lead to a reduction in mortality.

Key words: *Pseudomonas aeruginosa*; bloodstream infection; cancer; mortality.

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Introduction

Bloodstream infections (BSIs) are one of the most frequent and life-threatening infections in people with cancer, and are associated with high mortality [1,2]. Timely and proper management of bacterial infections is critical, as delays in antimicrobial therapy have been proven to significantly increase adverse outcomes, particularly in immunocompromised patients [3]. *Pseudomonas aeruginosa* (PAE) is one of the most frequently isolated Gram-negative bacteria (GNB) in people with cancer, typically ranking after *Escherichia coli* and *Klebsiella pneumoniae*. PAE-BSI is associated with disproportionately high rates of morbidity and mortality in the hospital setting [4–6]. PAE exhibits numerous inherent and acquired mechanisms of antimicrobial resistance, including biofilm formation, production of inactivating enzymes, and alterations in porins and efflux pumps, which confer multidrug resistance (MDR) in some isolates [4,5]. The severity of PAE-BSI is influenced by a combination of factors, including the site of infection, antibiotic treatment, microbiological determinants, and host factors such as chemotherapy-induced neutropenia [7].

The clinical impacts of PAE-BSI with resistant strains include limiting therapeutic options, delay in appropriate antimicrobial treatment, extended hospital stays, higher treatment-associated costs, life-threatening complications, and delays in oncological treatment [8,9]. There are studies in Latin America that have described outbreaks and cohorts of BSI caused by MDR-PAE in oncologic populations; most of these reports are limited by small sample sizes, heterogeneous designs, or lack of standardized resistance classification [10,11]. To date, no study has systematically assessed the clinical characteristics and outcome in patients with PAE BSIs in Mexican oncology patients. This study describes the demographic, clinical, and microbiological characteristics, outcomes, and risk factors for 30-day mortality in a cohort of patients with cancer who presented with PAE-BSI and the impact of antimicrobial resistance on survival.

Methodology

A retrospective study was conducted from 1 January 2019 to 31 December 2024, at the Instituto

Nacional de Cancerología (INCan), a tertiary care oncology hospital for adult patients in Mexico City. The study was approved by the Institutional Review Board (INCAN/0710/2025). The information on all PAE strains isolated from blood cultures was recovered from the Laboratory's Microbiology database. Samples were inoculated and incubated for five days in BD BACTEC™ (Becton Dickinson, Franklin Lakes, NJ, USA). The isolates were identified using standard techniques and mass-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS; Bruker, Billerica, MA, USA). Antimicrobial susceptibilities were determined using the VITEK-2™ system (BioMérieux, Lyon, France). Disk diffusion was used to confirm carbapenem resistance, in accordance with the Clinical and Laboratory Standards Institute (CLSI) [12].

PAE-BSI was defined as the isolation of the organism from at least one blood culture in a patient with symptoms and/or signs of infection. Only the first episode per patient was included. The following data were recorded from the electronic chart: age; gender; malignancy type; clinical stage (divided as recent diagnosis, progression, relapse, or remission); length of hospitalization; intensive care unit (ICU) admission and length of stay; antibiotic treatment; origin of BSI; and outcome at 72 hours, 30 days, and 90 days. Empirical therapy was defined as the initial antimicrobial treatment administered within the first 48 hours after blood cultures were obtained, prior to the availability of susceptibility results. Appropriate antimicrobial treatment was considered for patients who received a treatment for which the isolate was susceptible, which was initiated within the first 48 hours of blood culture collection and continued for a minimum of 4 days. A confirmed PAE-BSI in patients was considered a hospital-acquired infection if the patient had been hospitalized for more than 48 hours, and a healthcare-associated infection if the patient had been hospitalized or received healthcare within the previous three months.

Definitions

PAE isolates were classified according to their resistance profiles as follows: susceptible, susceptibility to at least three antipseudomonal groups, including carbapenems; carbapenem-resistant (CR), resistant to one or more carbapenems with recognized antipseudomonal activity; multidrug resistant (MDR), resistant to at least one agent in three or more antipseudomonal classes; difficult to treat (DTR)-modified, resistant to antipseudomonal fluoroquinolones, piperacillin/tazobactam, antipseudomonal cephalosporins, meropenem, aztreonam, and imipenem/cilastatin.

BSIs were classified as:

Catheter-related BSI (CRBSI): signs of systemic infection, and no apparent source of infection, in addition to time to positivity (TTP) of > 2 hours, central venous catheter/venipuncture, and/or the catheter-tip culture being positive for the same organisms; and/or signs and symptoms of catheter entry-site infection with the same strain isolated from the blood [13,14].

Secondary BSI: When PAE was identified not only in blood but also in other sites such as urine, biliary fluid, bronchial aspirate, and abdominal abscess, among others.

Primary BSI: Patients with severe neutropenia (neutrophils < 500/μL) and no other source of infection.

Adequate source control was considered when the primary infection was controlled, such as removing the central line in CRBSI cases, relieving biliary or urinary obstruction, and draining abscesses, among other measures.

Statistical analysis

The Student's *t*-test or the Mann-Whitney U test was used to compare continuous variables. The Chi-square or Fisher's exact test was utilized to compare categorical variables. Analysis of variance (ANOVA) was used to compare PAE strains (susceptible, CR, MDR, and DTR). A p value ≤ 0.05 was considered statistically significant. Collinearity among variables was assessed using variance inflation factors before multivariate analysis. A multivariate Cox regression model was performed to identify risk factors for 30-day mortality. Hazard ratios (HR) with 95% confidence intervals (95% CI) were calculated. Data were analyzed using Stata (version 14; StataCorp, College Station, TX, USA).

Results

A total of 26,745 blood cultures were performed over the 6-year study period: 4,076 (15.2%) were reported as positive. GNB were identified in 2,955 (72.5%) blood cultures, and 278 isolates were PAE (9.4% of all GNB and 6.8% of all the positive blood cultures). Seven were excluded due to incomplete data and 12 due to duplication, leaving 259 in the study.

BSI was classified as secondary in 135 patients (52.1%), primary in 83 (32.1%), and catheter-related in 42 (15.8%). Among all isolates, 17% were resistant to ceftazidime, 17.4% to ciprofloxacin, 14.3% to piperacillin/tazobactam, 20.9% to carbapenems, 10.3% to amikacin, and 0.8% to colistin.

Table 1. Demographic and clinical characteristics of 259 patients with *Pseudomonas aeruginosa* bloodstream infection.

Characteristics	Susceptible (n = 202, 78%)	Resistant (n = 57, 22%)	*p* value
Male gender	103 (51)	33 (57.9%)	0.357
Age (years)[a]	53 (38–64)	49 (33–61)	0.161
Hematological malignancy	76 (37.6)	25 (43.9)	0.394
Underlying conditions			
Diabetes	30 (14.9%)	12 (21.1)	0.262
Hypertension	44 (21.8)	11 (19.3)	0.686
PLHIV[b]	8 (3.7)	2 (3.51)	0.876
Obesity	1 (0.5)	0 (0)	0.595
Chronic kidney disease	2 (1)	4 (7)	0.008
COPD[c]	2 (19)	1 (1.8)	0.634
HSCT[d]	6 (2.9)	2 (3.5)	0.836
Type of cancer			
Leukemia	23 (11.4)	16 (28.1)	
Lymphoma	47 (23.8)	8 (14)	
Multiple myeloma/plasmacytoma	5 (2.5)	3 (5.3)	
Cervical	15 (7.4)	3 (5.3)	
Pancreas and biliary ducts	15 (7.4)	11 (19.3)	
Colorectal	14 (6.4)	5 (8.8)	
Breast	12 (5.9)	0	
Skin and soft tissue	11 (5.5)	0	
Head and neck	10 (5)	3 (5.3)	
Sarcomas	6 (3)	0	0.021
Ovarian	5 (2.5)	1 (1.8)	
Intestinal	5 (2.5)	1 (1.8)	
Liver	5 (2.5)	1 (1.8)	
Testes	5 (2.5)	0 (0)	
Esophagus/stomach	4 (1.2)	2 (3.5)	
Germinal	3 (1.5)	0 (0)	
Prostate	2 (1)	2 (3.5)	
Bladder/Kidney	2 (1)	1(1.8)	
Lung	2 (1)	0	
Other[e]	11 (5.5)	0	
Clinical state			
Recent diagnosis	114 (56.4)	27 (47.4)	
Progression	59 (29.2)	10 (17.5)	0.004
Relapse	18 (8.9)	9 (15.8)	
Remission	11 (5.5)	11 (19.3)	
Previous antibiotic[f]	106 (52.5)	48 (84.2)	< 0.001
Days of antibiotics[a]	7 (5–9)	10 (7–24)	< 0.001
Previous hospitalization[f]	112 (55.5)	40 (70.2)	0.046
Previous surgery[f]	39 (19.3)	12 (21.1)	0.770
Previous chemotherapy[g]	123 (60.9)	21(36.8)	< 0.001
Severe neutropenia	78 (38.6)	28 (49.1)	0.154
Type of bacteremia			
Primary	68 (33.7)	15 (26.3)	
Secondary	102 (50.5)	33 (57.9)	0.277
Catheter-related	32 (15.8)	9 (15.8)	
Source of secondary bacteremia[h]			
Urinary tract infection	40 (38.8)	4 (11.8)	
Biliary tract	21 (20.4)	14 (41.2)	
Pneumonia	19 (18.5)	7 (20.6)	0.008
Soft tissue	14 (13.6)	3 8.8)	
Abdominal sepsis	8 (6.8)	6 (17.7)	
Septic shock	40 (19.8)	21 (36.8)	0.007
Intensive care unit admission	25 (12.4)	22 (38.6)	< 0.001
Mechanical ventilation	16 (7.9)	14 (24.6)	< 0.001
Appropriate antimicrobial therapy	163 (80.7)	26 (45.6)	< 0.001
Combined antimicrobial therapy	39 (17.4)	23 (40.4)	< 0.001
Death at 72 hours	25 (12.4)	18 (31.6)	< 0.001
Death at 30 days	58 (28.7)	37 (64.9)	< 0.001
Death at 90 days	87 (43.1)	43 (75.4)	< 0.001

[a] Median (interquartile range); [b] PLHIV: people living with HIV; [c] COPD: chronic obstructive pulmonary disease; [d] HSCT: hematopoietic stem cell transplantation; [e] Other: 3 Kaposi sarcoma: 2 endometrium: 1 peritoneum: 1 vaginal: 1 neuroendocrine: 1 medulloblastoma: 1 vulvar: and 1 myelodysplastic syndrome; [f] During the previous 90 days; [g] During the last 30 days; [h] Analysis was performed in the 135 patients with secondary BSI.

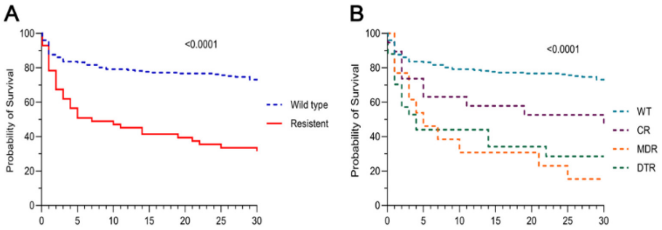
From the entire sample, 202 strains were classified as susceptible (78.4%), 19 (7.3%) CR, 13 (5%) MDR, and 25 (9.7%) DTR (there were 57 resistant strains, 21.6% of the entire sample). The resistance trend over the 6 years shows that susceptible strains remained between 72% and 80%. The year with the highest number of DTR strains was 2019, whereas CR strains showed a significant increase in 2024. (Figure 1).

When patients with resistant vs. susceptible strains were compared, it was noted that they had a history of receiving antibiotics within the previous 90 days more frequently (84.2% vs. 52.5%) and a history of prior hospitalization (70.2% vs. 55.5%). Also, patients with PAE-resistant strains had longer hospital stays (18 days vs. 9 days), more admissions to the ICU (38.6% vs. 12.4%), developed septic shock (35.8% vs. 19.8%), required mechanical ventilation (24.6% vs. 7.9%), and received inappropriate antibiotic treatment (54.4% vs. 19.3%), compared with those with susceptible strains. Other clinical data are shown in Table 1.

When the patients were classified into susceptible, CR, MDR, and DTR, it was noted that those with susceptible strains had received chemotherapy more frequently during the prior month (60.9%), compared with CR (42.1%), MDR (30.8%), and DTR (36%); $p < 0.001$. The primary source of secondary bacteremia differed between groups: the urinary tract was the source in susceptible strains and the biliary tract in resistant strains. Combined antimicrobial treatment was more common in patients with resistant strains (Supplementary Table 1).

Mortality at 30 days was 38.2%, being 29.7% in susceptible, 47.4% in CR, 84.6% in MDR, and 76% in patients with DTR strains ($p < 0.001$; Figure 2).

Figure 2. Kaplan-Meier survival curve. Mortality at 30 days in patients with Pseudomonas aeruginosa bloodstream infection. A. Comparison in susceptible (wild type) and resistant strains. 2B. Comparison of susceptible (WT), carbapenem-resistant (CR), multidrug-resistant (MDR), and difficult-to-treat (DTR) strains.



There was no statistically significant difference in 30-day mortality between patients receiving combination therapy and those receiving monotherapy (22.5% vs. 26.3%, respectively). The univariate risk factors for 30-day mortality were septic shock, invasive mechanical ventilation, carbapenem-resistant strain, and inadequate source control. Appropriate antimicrobial therapy was a protective factor. In the multivariate Cox regression analysis, independent predictors of 30-day mortality included older age (aHR 1.02, 95% CI 1.00–1.03), advanced oncological status (aHR 1.67, 95% CI 1.07–2.61), secondary bacteremia (aHR 2.24, 95% CI 1.12–4.50), septic shock (aHR 2.94, 95% CI 1.68–5.14), invasive mechanical ventilation (aHR 1.93, 95% CI 1.03–3.64), infection by CR strains (aHR 1.87, 95% CI 1.11–3.16), and inadequate source control (aHR 2.60, 95% CI 1.45–4.67). Appropriate antimicrobial therapy remained independently protective (aHR, 0.35; 95% CI, 0.21–0.58; $p < 0.001$; Table 2).

Figure 1. Trend in resistance of 6 major anti-pseudomonal drugs over the 6-year study period.

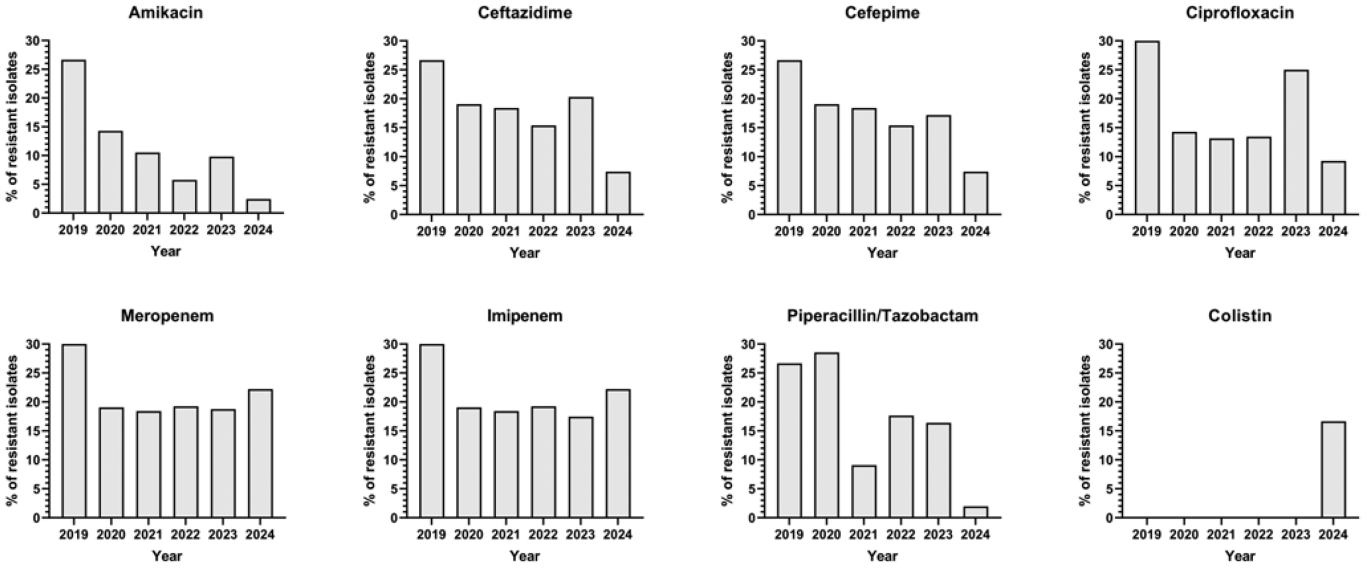


Table 2. Univariate and multivariate analysis for mortality at 30 days in 259 patients with *Pseudomonas aeruginosa* bloodstream infection.

Variable	Univariate		Multivariate	
	HR (95% CI)	*p* value	aHR (95% CI)	*p* value
Age (years)	1.01 (0.99–1.02)	0.216	1.02 (1.0–1.03)	0.027
Advanced oncological status	1.51 (0.98–2.33)	0.06	1.67 (1.07–2.61)	0.023
Catheter related-bacteremia	0.41 (0.18–0.92)	0.031	1.44 (0.52–3.96)	0.483
Secondary bacteremia	0.95 (0.60–1.51)	0.834	2.24 (1.12–4.5)	0.023
Severe neutropenia	1.44 (0.94–2.22)	0.095	1.70 (0.06–3.01)	0.067
Septic shock	4.14 (2.66–6.44)	< 0.001	2.94 (1.68–5.14)	< 0.001
Invasive mechanical ventilation	5.98 (3.62–9.89)	< 0.001	1.93 (1.03–3.64)	0.041
Carbapenem-resistant strain	3.43 (2.2–5.35)	< 0.001	1.87 (1.11–3.16)	0.019
Inadequate source control	2.17 (1.4–3.37)	0.001	2.6 (1.45–4.67)	0.001
Appropriate antimicrobial therapy	0.27 (0.18–0.42)	< 0.001	0.35 (0.21–0.58)	< 0.001

Discussion

In this 6-year retrospective study, resistant PAE strains accounted for 21.6% of BSIs and were strongly associated with increased 30-day mortality. There was a prevalence of CR-PAE strains of 20.9%, MDR 5%, and DTR 10%; lower than results from other studies on oncological populations, which have documented rates ranging from 26% to 38% for CR, 10% to 67% for MDR, and 4% to 35.9% for DTR [5–7,15–18]. These rates were also lower than those reported by a Mexican surveillance network group, which reported MDR-PAE in 29.7% of cases [19]. A notable finding is the decrease in DTR strains observed over the study period, indicating an improvement in the local stewardship efforts.

When comparing each antibiotic separately with the two epidemiological surveillance networks in Mexico, resistance percentages were lower: for ciprofloxacin (17.4% vs. 20.3%), piperacillin/tazobactam (14.3% vs. 18.4%), ceftazidime (17% vs. 21.3%), meropenem (20.9% vs. 28.9%), and amikacin (10.3% vs. 17.2%) [20,21].

In this study, the biliary tract was the most frequent site of infection with resistant isolates (41%), likely due to the high proportion of pancreatic and biliary tract neoplasms, which can cause biliary obstruction and necessitate biliary catheter replacement. In other studies, the primary source of infection was identified as the urinary tract [22,23].

The history of previous antimicrobials was related to resistant strains; these findings have been documented in other studies, particularly with carbapenem use within 90 days [6]. Septic shock was more prevalent in patients with resistant strains compared with those with susceptible strains (36.8% vs. 19.8%). This finding aligns with a previous study, which reported septic shock in 33.8% of resistant vs. 21.1% of susceptible cases [24].

PAE-BSI is associated with high mortality rates, ranging from 17% to 40% in oncology patients [6,15–18], which is higher than that of other GNB (21%) [9,18]. In this cohort, an overall 30-day mortality rate of 38.2% was observed, which was increased in patients with resistant isolates (64.9%) vs. susceptible (28.7%), consistent with previous studies reporting mortality rates of 24 to 34% for CR and 20 to 35% for MDR isolates [16,25].

Another finding was that in this cohort, 27% of patients received inadequate antimicrobial therapy, a higher proportion among patients with resistant vs. susceptible isolates (54.4% vs. 19.3%), as has been described in other studies (65.8% vs. 18.8%, respectively) [15]. Those who received inappropriate therapy had a 48.5% mortality rate, compared with 13.7% among those who received appropriate treatment, similar to the results of other studies [17, 26,27]. The impact of combination therapy could not be assessed; therefore, large-scale, multicenter, prospective studies are needed to yield more precise results. Current guidelines recommend monotherapy for most CR-PAE infections and combination therapy in specific cases [28–30]. The current analysis identified factors associated with 30-day mortality in patients with PAE-BSI, including advanced oncological disease, septic shock, mechanical ventilation, inadequate source control, and the presence of a carbapenem-resistant strain. Conversely, appropriate antimicrobial therapy significantly reduced mortality, underscoring the importance of timely and adequate management in this population of immunocompromised patients.

The main strengths of the study are that it is the first study in Mexico to evaluate the clinical impact and 30-day mortality associated with multidrug-resistant PAE-BSI in oncology patients. The number of patients included provides sufficient data to identify independent predictors of mortality and to describe trends in resistance. However, this study has some limitations. First, the study was conducted at a single-center hospital dedicated to oncology care, which limits the generalizability of the findings to other healthcare settings. Second, given its retrospective design, residual

unmeasured confounding could not be excluded; a further prospective, multicenter design would allow for more robust associations. The DTR definition was adapted to exclude aztreonam, since susceptibility testing for this agent could not be performed, and it is not available in Mexico. The European Committee on Antimicrobial Susceptibility Testing (EUCAST) and the Clinical and Laboratory Standards Institute (CLSI) recommend broth microdilution as the reference method for colistin susceptibility testing, but the reliability of the results is limited because it was not available at the institution. Lastly, genotypic characterization of resistance mechanisms was not performed; incorporating genotypic data in future studies could enhance understanding of the epidemiology and spread of resistant PAE.

Conclusions

Resistant PAE-BSI in cancer patients was associated with longer hospitalizations and a significantly increased mortality rate. Appropriate antimicrobial therapy can lead to a reduction in mortality. It is essential to identify risk factors and consider early initiation of guideline-recommended empirical therapy for multidrug-resistant Gram-negative pathogens, particularly in patients with septic shock or when source control is expected to be delayed. The findings provide a foundation for future research, including genotypic characterization of resistant isolates and their clinical impact, the development of risk stratification tools, and the evaluation of the effect of risk-based empirical therapy on patient outcomes.

Authors' contributions

PCJ, study conception, design, and manuscript draft; IGP, CVA, ABS, MJMR, AML, data collection; ACZ, data analysis and critical review; PVF, analysis and critical review. All the authors read and approved the final manuscript.

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Conflict of interest

No conflict of interest is declared.

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Annex – Supplementary Items

Supplementary Table 1. Main characteristics of patients with *Pseudomonas aeruginosa* bloodstream infection, classified into susceptible, carbapenem-resistant (CR), multidrug-resistant (MDR), and difficult-to-treat resistant (DTR) categories.

Variable	Susceptible (n = 202, 78%)	CR (n = 19, 7.3%)	MDR (n = 13, 5%)	DTR (n = 26, 10%)	*p* value
Previous use of antibiotics [a]	106 (52.5)	16 (84.2)	10 (76.9)	22 (88)	< 0.001
History of hospitalization [a]	112 (55.5)	15 (79)	7 (53.9)	18 (72)	0.109
Previous chemotherapy [b]	123 (60.9)	8 (42.1)	4 (30.8)	9 (36)	0.013
Clinical stage					
Recent diagnosis	114 (56.4)	8 (42.1)	8 (57.1)	12 (48)	
Progression	59 (29.2)	3 (15.8)	4 (28.6)	3 (12)	0.002
Relapse	18 (8.9)	2 (10.5)	2 (14.3)	5 (20)	
Remission	11 (5.5)	6 (31.6)	0	5 (20)	
Type of bacteremia					
Primary	68 (33.7)	7 (36.8)	3 (23.1)	5 (20)	
Catheter-related	32 (15.8)	5 (26.3)	1 (7.7)	3 (12)	0.167
Secondary	102 (50.5)	7 (36.8)	9 (69.2)	17 (68)	
Source of secondary BSI					
Urinary tract infection	40 (39.2)	1 (14.3)	1 (11.1)	2 (11.7)	
Biliary tract	21 (20.6)	3 (42.9)	6 (66.7)	5 (29.4)	
Pneumonia	21 (20.6)	1 (14.3)	2 (22.2	4 (23.5)	0.008
Soft tissue	14 (13.7)	1 (14.3)	0	2(11.7)	
Abdominal	6 (5.9)	1 (14.3)	0	4 (23.5)	
Septic shock	40 (19.8)	8 (42.1)	4 (30.8%)	9 (36)	0.052
Intensive care unit admission	25 (12.4)	9 (47.4)	4 (30.8)	9 (36)	< 0.001
Appropriate empiric therapy	163 (80.7)	10 (52.6)	6 (46.2)	10 (40)	< 0.001
Combined antimicrobial therapy	39 (19.4)	9 (47.4)	4 (30.8)	10 (40)	0.008
Source control	102 (53.9)	10 (52.6)	6 (46.2)	13 (25%)	0.175
Mortality 72 h	28 (13.9)	5 (26.3)	4 (30.8)	11 (44)	0.014
30-day mortality rate	60 (29.7)	9 (47.4)	11 (84.6)	19 (76)	< 0.001
90-day mortality rate	89 (44.1)	12 (63.2)	11 (84.6)	21 (84)	< 0.001

[a] During the last three months. [b] During the last month.