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*Research Article*

# Clinical Features Associated with *A. baumannii* BSI Mortality Clinical Features Associated with *Acinetobacter baumannii* Bloodstream Infections Mortality in a Tertiary Hospital in Southern Brazil

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## Abstract

Introduction: *Acinetobacter baumannii* Bloodstream Infections (BSIs) are associated with high mortality and increasing antimicrobial resistance, particularly in Intensive Care Units (ICUs). The COVID-19 pandemic further intensified these challenges by increasing the frequency and severity of healthcare-associated infections.

Objective: This study aimed to characterize the epidemiological and clinical features of patients with *A. baumannii* BSI in a Brazilian tertiary hospital and identify risk factors associated with mortality.

Methods: We conducted a retrospective study from March 2020 to May 2023 at the University Hospital of Londrina, Paraná, Brazil. Patients with at least one peripheral blood culture positive for *A. baumannii* were included. Epidemiological, microbiological and clinical data were collected and stratified by survival outcome. Antimicrobial susceptibility was determined using the VITEK 2® system and interpreted according to CLSI guidelines. Statistical analyses were performed using SPSS v25.0, with significance set at $p < 0.05$.

Results: A total of 261 patients with *Acinetobacter baumannii* bloodstream infections were analyzed. The vast majority of isolates (94.2%) were resistant to meropenem. The overall in-hospital mortality rate was 70.5%. Several factors were significantly associated with increased mortality. Among comorbidities, diabetes (OR = 2.71; $p = 0.006$) and systemic arterial hypertension (OR = 1.88; $p = 0.025$) were both linked to higher risk of death. In terms of invasive procedures, the presence of indwelling urinary catheters (OR = 4.70; $p < 0.001$), enteral nutrition tubes (OR = 4.70; $p < 0.001$), orotracheal intubation (OR = 3.32; $p < 0.001$) and the need for hemodialysis (OR = 3.81; $p < 0.001$) were all significantly associated with fatal outcomes. Septic shock was present in 67.4% of patients and had a particularly strong association with mortality (OR = 12.8; $p < 0.001$). Prior use of certain antimicrobials, particularly third-generation cephalosporins (OR = 2.66; $p = 0.002$) and carbapenems (OR = 1.95; $p = 0.016$), also contributed to an increased risk of death. Coinfection with COVID-19, identified in 43.3% of cases, was another significant risk factor for poor outcomes (OR = 1.91; $p = 0.022$). Patients with COVID-19 had shorter hospital stays and a higher 30-day mortality rate (73.4%) compared to those without COVID-19 (54.7%).

Conclusion: This study highlights a high mortality rate associated with *A. baumannii* BSIs, driven by antimicrobial resistance, comorbidities, invasive procedures and septic complications. The COVID-19 pandemic exacerbated these trends. Early identification, targeted empirical therapy and effective infection control are essential to improving outcomes.

**Keywords:** *Acinetobacter baumannii*; Bloodstream Infection; Antimicrobial Resistance; Carbapenem-Resistant; COVID-19; Mortality; Epidemiology

## Introduction

Hospital-acquired Bloodstream Infections (BSI) are a major cause of morbidity and mortality, with *Acinetobacter baumannii* being one of the most concerning pathogens due to its high mortality rates reaching up 43% in ICU settings and 16% in other wards, making this pathogen the one of the major leading causes of death among nosocomial BSI [1]. *A. baumannii* is also notable for its extensive antimicrobial resistance, driven by both intrinsic and acquired mechanisms. Multidrug-resistant (MDR) and carbapenem-resistant *A. baumannii* (CRAB) are highly disseminated worldwide. As a result, individuals infected with extensively resistant strains are at increased risk of severe illness and death, with bloodstream infections leading to worse clinical outcomes and fewer effective treatment options [2].

Several risk factors are associated with *A. baumannii* BSI, for example invasive procedures, prolonged ICU stays, prior antibiotic use, especially carbapenems and underlying health conditions like cancer or immunosuppression. The COVID-19 pandemic further amplified these risks, with high rates of co-infection reported among critically ill patients [1]. Although several studies have reported a high incidence of *A. baumannii* BSI, as well as a high mortality rate from these infections in the last few years, it is important to maintain constant epidemiological surveillance studies. Therefore, this study aims to perform an epidemiological characterization of patients hospitalized with *A. baumannii* BSI, identifying factors associated with the outcome of these infections.

## Material and Methods

### *Study Design*

A retrospective study was conducted at Hospital Universitário de Londrina in Londrina, PR, Brazil. Patients with positive peripheral blood culture for *A. baumannii* identified between March 2020 and May 2023 were evaluated. This study was approved by the Research Ethics Committee of the State University of Londrina under CAAE number: 28316819.0.0000.523.

### *Microbiology Identification and Susceptibility Test*

Positive peripheral blood cultures were detected by BD BACTEC FX40 (Becton Dickinson, United States). Then, microbial identification and antimicrobial susceptibility testing were performed by the automated system VITEK 2® (bioMérieux, France). The results of antimicrobial susceptibility testing were interpreted according to the criteria of the Clinical and Laboratory Standards Institute (CLSI) [3].

### *Data Collection and Statistical Analysis*

Clinical and epidemiological data was obtained using patient's digital medical records. Data such as age, sex, length of hospital stay, comorbidities, invasive devices, complications, other positive cultures and previous use of antimicrobials were collected. Patients were divided into two groups according to the outcome: survived or died.

The incidence of *A. baumannii* BSI was calculated by incidence density per 1,000 patient-days. For statistical analysis, the IBM Statistical Package for the Social Sciences (SPSS) software, version 25.0, was used. Categorical data were evaluated by the chi-square test; the difference between groups was determined as significant when $p < 0.05$. The degree of association between the variables and the outcome was assessed through the Odds Ratio (OR) and 95% confidence interval (95% CI).

## Results

Between January 2014 and December 2023, a total of 8,202 *A. baumannii* isolates were obtained. The distribution of isolates over the years is shown in Fig. 1. During this period, 4,784 (58.3%) isolates were obtained from tracheal aspirates, followed by 857 (10.4%) from tissue and secretions, 796 (9.7%) from urine, 514 (6.3%) from peripheral blood, 91 (1.1%) from liquor and other body fluids and 13 (0.2%) from other materials. Among patients with *A. baumannii* infections, 5,696 (69.4%) were from patients admitted to the ICU, while 2,506 (30.6%) from patients in general wards. Of all isolates, 334 (4.1%) were susceptible to meropenem, while 7,876 (96.1%) were resistant to carbapenems. Among the resistant isolates, 350 (4.3%) were also resistant to both carbapenems and polymyxins.

From 2020 to 2023, we observed an increase in the incidence density of *A. baumannii* BSI per 1,000 patient-days (Fig. 2). During this period, 261 *A. baumannii* isolates were recovered from peripheral blood cultures.

Among the *A. baumannii* isolates obtained from peripheral blood cultures, 94.2% of the isolates were resistant to meropenem. The resistance rates to ciprofloxacin, amikacin and gentamicin were 94.6%, 91.2% and 84.1%, respectively. Furthermore, 8.9% were resistant to polymyxin, 10 of which were also resistant to carbapenems (Fig. 3). The mortality rate was significantly higher in infections caused by CRAB ($p = 0.044$), as well as in those caused by isolates resistant to amikacin and gentamicin ($p = 0.033$ and $p = 0.012$, respectively).

Demographical and clinical data from patients with *A. baumannii* BSI are described in Table 1. The average age of patients was 58 years and most patients (58.6%) were male. Furthermore, patients with *A. baumannii* BSI presented positive peripheral blood culture after an average of 13 days from hospital admission. Most patients had at least one underlying condition, with systemic arterial hypertension (44.4%) and diabetes (24.1%) being the most common. Both conditions were associated with an increased risk of mortality ($p = 0.025$; OR = 1.88 and $p = 0.006$; OR = 2.71, respectively). Additionally, 113 (43.3%) patients had a COVID-19 diagnosis. Most patients required invasive procedures such as Central Venous Catheters (CVC) (90.8%), Indwelling Urinary Catheters (IUC) (88.1%) and Mechanical Ventilation (MV) (85%). Among the invasive devices, IUC ($p < 0.001$; OR = 4.70), enteral nutrition tubes ($p < 0.001$; OR = 4.70) and orotracheal intubation ($p < 0.001$; OR = 3.32) were significantly associated with mortality. Patients with BSI also had positive cultures for *A. baumannii* in tracheal secretions (62.8%), urine (19.5%) and tissue samples (8.43%). During hospitalization, 154 (67.4%) patients with *A. baumannii* BSI developed septic shock and the majority of these patients (83.7%) died ($p < 0.001$; OR = 12.8). Prior antibiotic use was common, with 97% of patients receiving at least one antimicrobial, the most frequently used drugs were carbapenems (65.5%), piperacillin-tazobactam (44.4%), polymyxins (36.4%) and third-generation cephalosporins (33.3%), which was associated with higher risk of mortality ($p = 0.002$; OR = 2.66). After the identification of *A. baumannii* in peripheral blood culture, the most commonly used drugs were polymyxins (46%), carbapenems (33.3%), colistin (20.7%) and aminoglycosides (18%). The average hospital length of stay was 38.3 ± 34.3 days. Patients who died had a shorter hospital stay (30.8 ± 28.7 days) compared to those who were discharged (56.3 ± 39.5 days). Similarly, patients with COVID-19 had a shorter hospitalization duration (31 ± 26.6 days) compared to those without COVID-19 (43.9 ± 38.3 days) (Fig.4). The overall in-hospital mortality rate was 70.5% (184/261), with 62.8% (164/261) dying within 30 days after the identification of *A. baumannii* in peripheral blood culture. COVID-19 patients were 1.91 times more likely to die than to be discharged ($p = 0.022$) Among COVID-19 patients, the mortality rate increased to 77.9% (88/113), with 73.4% (83/113) dying within 30 days. In contrast, the 30-day mortality rate for non-COVID-19 patients was 54.7% (81/148).

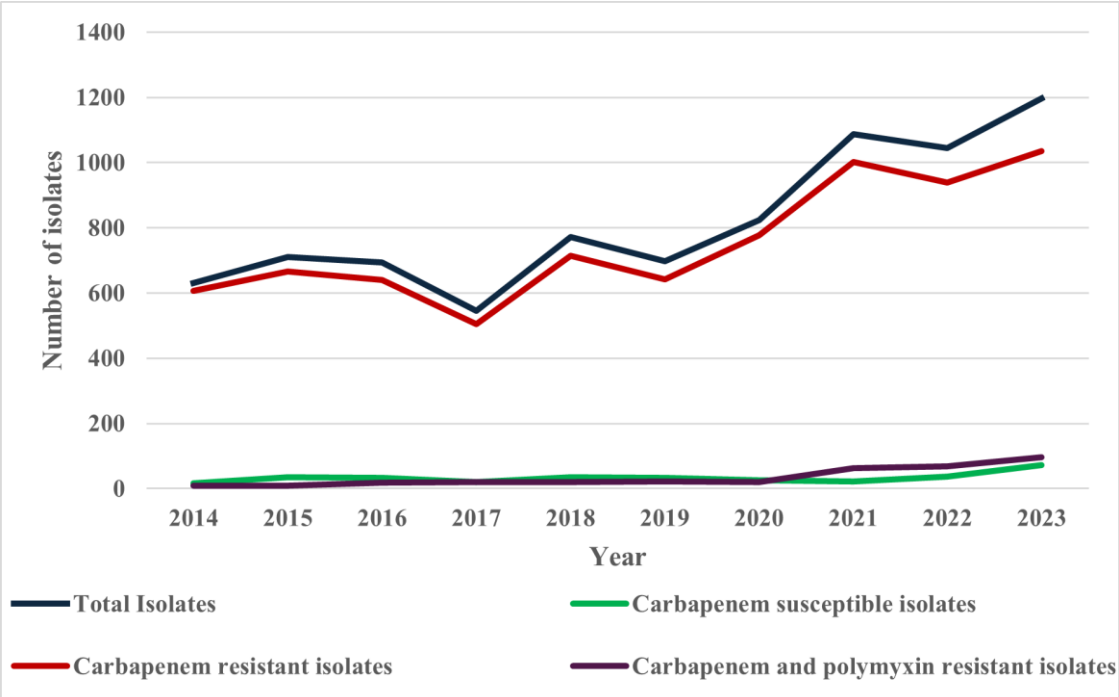


**Figure 1:** Number of *A. baumannii* isolates obtained from patients hospitalized between 2014 and 2023.

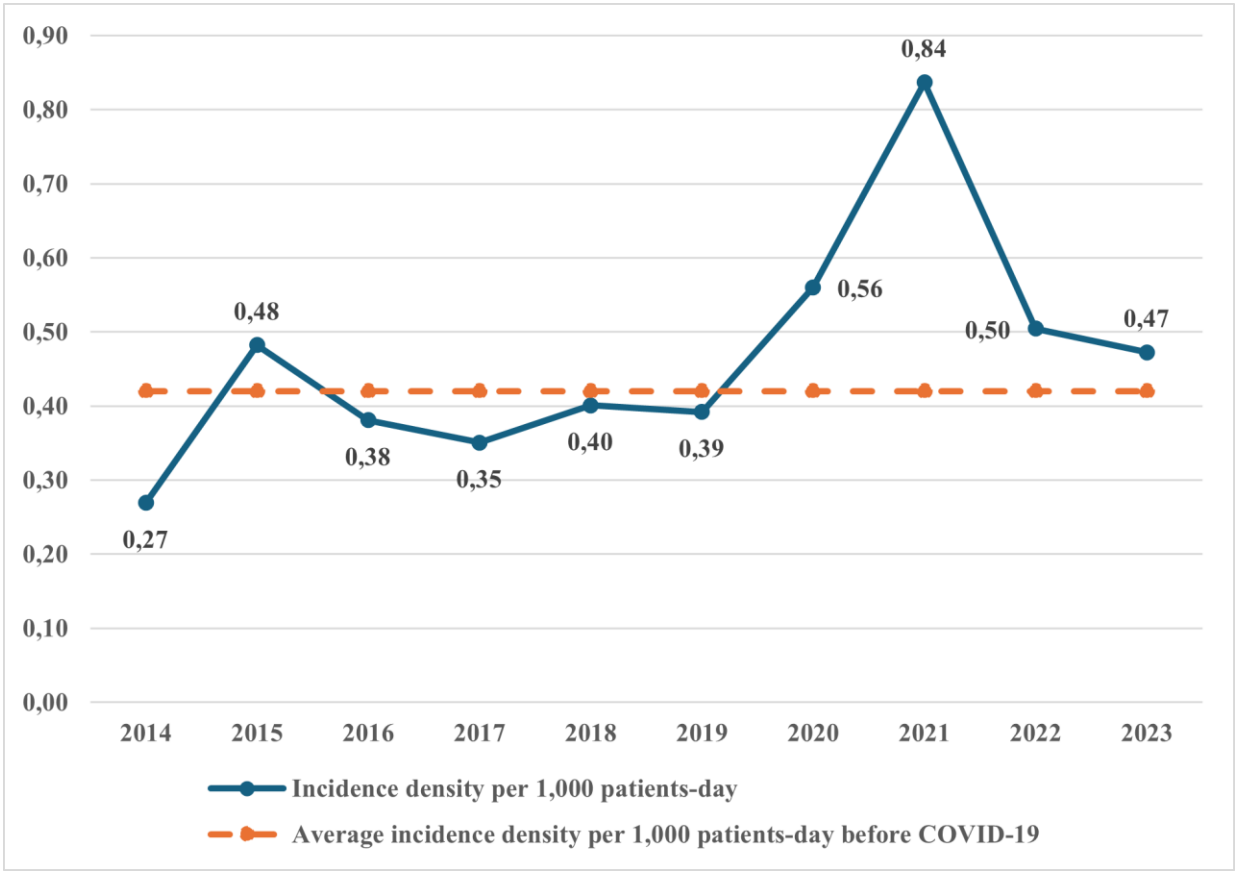


**Figure 2:** Incidence density of *A. baumannii* bloodstream infections per 1,000 patient-days between 2014 and 2023.

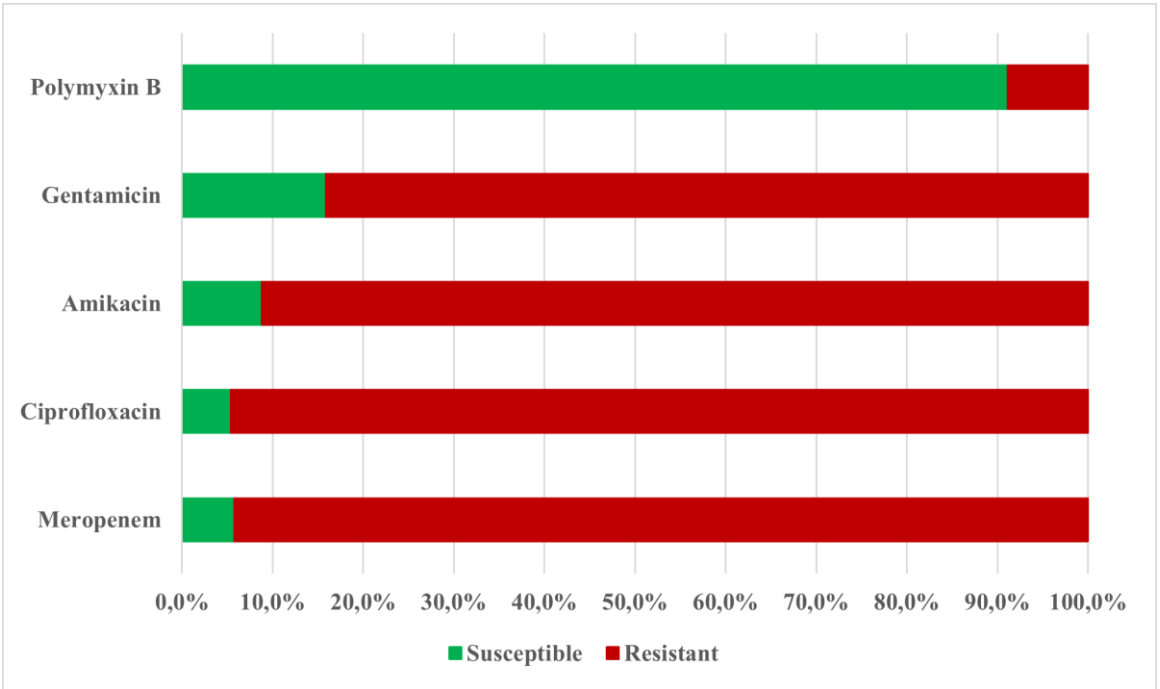


**Figure 3:** Antimicrobial susceptibility test of *A. baumannii* isolates obtained from peripheral blood culture between 2020 and 2023.

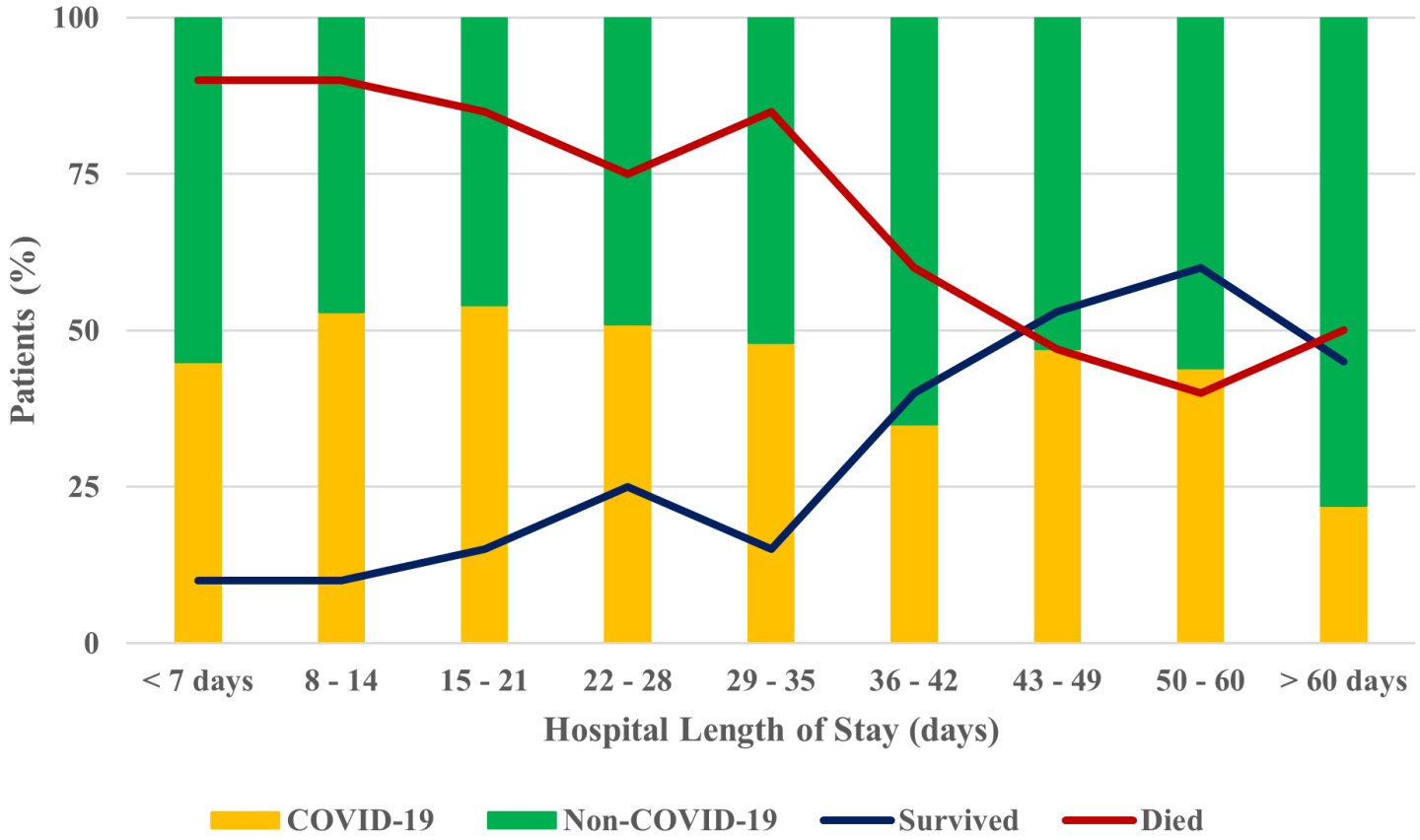


**Figure 4:** Hospital length of stay and outcomes of patients with *A. baumannii* BSI, with and without COVID-19 diagnosis.

| Characteristics | Died N = 184 (70.5%) | Survived N = 77 (29.5%) | *p* value | OR (95% CI) |
|---|---|---|---|---|
| **Age** | | | | |
| Mean ± SD[a] | 58.4 ± 17.3 | 44.3 ± 22.1 | | |
| **Male sex** | 99 (53.8%) | 54 (70.1%) | **0.015** | 2.04 (1.14 – 3.57) |
| **Hospital length of stay** | | | | |
| Mean number of days ± SD[a] | 30.8 ± 28.7 | 56.3 ± 39.5 | | |
| **Comorbidities** | | | | |
| Diabetes | 53 (28.8%) | 10 (13.0%) | **0.006** | 2.71 (1.30 – 5.66) |
| Systemic arterial hypertension | 90 (48.9%) | 26 (33.8%) | **0.025** | 1.88 (1.08 – 3.27) |
| Smoking | 36 (19.6%) | 14 (18.2%) | 0.796 | * |
| Alcoholism | 22 (12.0%) | 7 (9.1%) | 0.502 | * |
| Chronic obstructive pulmonary disease | 16 (8.7%) | 4 (5.2%) | 0.332 | * |
| Autoimmune disease | 7 (3.8%) | 2 (2.6%) | 0.626 | * |

| Characteristics | Died N = 184 (70.5%) | Survived N = 77 (29.5%) | *p* value | OR (95% CI) |
|---|---|---|---|---|
| Chronic kidney failure | 15 (8.2%) | 5 (6.5%) | 0.646 | * |
| Cancer | 6 (3.3%) | 2 (2.6%) | 1.000 | * |
| **Invasive procedure** | | | | |
| Indwelling urinary catheter | 172 (93.5%) | 58 (75.3%) | **<0.001** | 4.70 (2.15 – 10.3) |
| Central venous catheter | 169 (91.8%) | 68 (88.3%) | 0.367 | * |
| Enteral nutrition tube | 162 (88.0%) | 47 (61.0%) | **<0.001** | 4.70 (2.48 – 8.90) |
| Orotracheal intubation | 157 (85.3%) | 49 (63.6%) | **<0.001** | 3.32 (1.79 – 6.17) |
| Tracheostomy | 58 (31.5%) | 21 (27.3%) | 0.496 | * |
| Blood transfusion | 49 (26.8%) | 27 (35.1%) | 0.180 | * |
| Drain | 19 (10.3%) | 5 (6.5%) | 0.328 | * |
| Hemodialysis | 92 (50.0%) | 16 (20.8%) | **<0.001** | 3.81 (2.05 – 7.10) |
| **Septic shock** | 154 (83.7%) | 22 (28.6%) | **<0.001** | 12.8 (6.83 – 24.1) |
| **COVID-19** | 88 (47.8%) | 25 (32.5%) | **0.022** | 1.91 (1,09 – 3.33) |
| **Tracheal secretion culture** | 118 (64.1%) | 46 (59.7%) | 0.503 | * |
| **Urine culture** | 39 (21.2%) | 12 (15.6%) | 0.297 | * |
| **Tissue culture** | 11 (6.0%) | 11 (14.3%) | 0.228 | * |
| **Previous use of antimicrobials** | | | | |
| Ampicillin sulbactam | 11 (6.0%) | 5 (6.5%) | 1.000 | * |
| Sulfamethoxazole trimethoprim | 8 (4.3%) | 1 (1.3%) | 0.289 | * |
| Piperacillin tazobactam | 88 (47.8%) | 28 (36.4%) | 0.089 | * |
| Ceftazidime avibactam | 9 (4.9%) | 8 (10.4%) | 0.101 | * |
| 1st and 2nd Gen. Cephalosporins | 1 (0.5%) | 2 (2.6%) | 0.209 | * |
| 3rd Gen. Cephalosporins | 72 (39.1%) | 15 (19.5%) | **0.002** | 2.66 (1.41 – 5.02) |
| 4th Gen. Cephalosporins | 12 (6.5%) | 9 (11.7%) | 0.162 | * |
| Fluoroquinolones | 24 (13.0%) | 10 (13.0%) | 0.990 | * |
| Polymyxin | 71 (38.6%) | 24 (31.2%) | 0.256 | * |
| Aminoglycosides | 29 (15.8%) | 19 (24.7%) | 0.090 | * |

| Characteristics | Died N = 184 (70.5%) | Survived N = 77 (29.5%) | *p* value | OR (95% CI) |
|---|---|---|---|---|
| Carbapenems | 129 (70.1%) | 42 (54.5%) | **0.016** | 1.95 (1.13 – 3.38) |
| Colistin | 29 (15.8%) | 8 (10.4%) | 0.257 | * |
| Tigecycline | 27 (14.7%) | 9 (11.7%) | 0.524 | * |
| * There was no significant statistical difference.<br>aSD: Standard deviation | | | | |

**Table 1:** Demographic and clinical data stratified by mortality from patients with *A. baumannii* BSI hospitalized between 2020 and 2023.

**Discussion**

The present study reports an increase in the number of *A. baumannii* clinical isolates, mainly CRAB, obtained over 10 years. Previous studies in Brazil reported that during COVID-19 pandemics, *A. baumannii* has become one of the main causes of secondary infections, being isolated mainly from tracheal aspirate (71.2%) and blood cultures (7.2%) particularly in ICUs, a similar profile as observed in the present study [4]. Overall, carbapenem resistance is highly prevalent in this species with resistance rates exceeding 70% in some regions, such as Eastern Europe, Africa and Asia [5]. In Brazil, carbapenem resistance rates reaches up to 80%. making infections caused by this pathogen difficult to treat, leading to worse prognoses and a higher risk of mortality [6].

In this scenario, *A. baumannii* is one of the leading causes of healthcare-acquired BSI. According to ASCENSION surveillance study, CRAB is responsible for 9.6% of all BSI in Brazil [7]. We observed an increasing *A. baumannii* BSI incidence rate from 2020 onwards, especially due to the COVID-19 pandemics. However, the impact of COVID-19 on BSI varies across studies. While some studies demonstrate that there was no increase in the incidence of BSI during the pandemic period, others, such as the present study, highlight an increase or a trend towards a higher incidence of BSI after 2020 [8-11].

A previous study carried out in the same institution as this one reported that between 2006 and 2016, 92.2% of BSI *A. baumannii* isolates were resistant to meropenem, thus we observed a small increase in the rate of resistance to meropenem, that now reaches 94.2%. Moreover, we also observed an increase in the rate of resistance to amikacin (41.7% to 91.2%) and gentamicin (69.9% to 84.1%). On the other hand, the resistance rates to ciprofloxacin and polymyxin B have decreased from 100.0% to 94.6% and 10.7% to 8.9%, respectively [12]. A similar study also observed increasing rates of resistance to carbapenems (64% to 98%) and aminoglycosides (11% to 85%) between 2019 and 2022, possibly associated with prior colonization by resistant strains, extensive use of invasive devices and antimicrobials and prolonged hospitalization, highlighting a trend of increasing resistance rates in clinical isolates of *A. baumannii* worldwide [13]. According to a systematic review, global resistance rate to polymyxins is 13%, thus polymyxins remain one of the most effective antimicrobials against MDR *A. baumannii* [14]. However, due to the high consumption of polymyxin to treat CRAB infections in the last few years, several studies in different countries have reported increasing polymyxin resistance rates *A. baumannii*. Rocca and colleagues demonstrated a 10% increase in the colistin resistance rate in *A. baumannii* between 2016 and 2021 [15]. Another study also demonstrated a 37% increase in the colistin resistance rate between 2015 and 2022, reaching 42.5% in the last year. This increase poses a major global health problem, as the spread of strains resistant to these antimicrobials further limits therapeutic choices, leading to worse prognoses and higher mortality [16].

As expected, higher mortality rates were observed in infections caused by carbapenem and aminoglycoside resistant A. baumannii, mainly because these infections are often related to treatment failure. A cohort study demonstrated that MDR *A. baumannii* infections are associated with greater risk of mortality, risk of reinfections within 30 days and longer length of hospital stay, likely due to inappropriate initial antibiotic therapy, delay to active treatment and consequent increased severity of infection [17].

Similarly, several other clinical factors were also associated with mortality. Male patients presented higher chances of not surviving, which is consistent with findings from other studies that explain this association by the need for admission to intensive care units, higher risk of infection by MDR pathogens and polymicrobial infections [18]. Diabetes and systemic arterial hypertension are underlying conditions that were associated with higher mortality, several studies have reported the association between these comorbidities and *A. baumannii* bacteremia mortality, moreover other conditions such as chronic liver and kidney diseases, smoking and immunodeficiency are also commonly associated with higher mortality in this type of infection [19-21]. The use of several invasive devices, such as Indwelling Urinary Catheters (IUC), Central Venous Catheters (CVC), Mechanical Ventilation (MV), orotracheal nutrition tubes and hemodialysis, has also been associated with higher mortality. In general, prolonged use of these devices is a risk factor for *A. baumannii* infections in hospitalized patients, a meta-analysis study showed that patients using CVC and MV were approximately 3 times more likely to develop *A. baumannii* BSI, due to the potential for biofilm formation and direct access to the bloodstream or respiratory tract [22].

In this study, septic shock was strongly associated with mortality. Other studies have also determined sepsis as an independent risk and predictor of mortality in patients with *A. baumanni* BSI, increasing the risk of mortality by approximately 3-fold. Therefore, early and effective empirical therapy is essential to reduce the likelihood of BSI progressing to septic shock [23,24]. Prior use of antimicrobials was also associated with the mortality of *A. baumannii* BSI. In our study, the use of 3$^{rd}$ and 4$^{th}$ generation cephalosporins, such as ceftriaxone and cefepime, was associated with higher mortality, but other studies mainly associate the previous use of carbapenems with higher risk in these infections, this happens because the prior use of these antimicrobials selects increasingly resistant strains that make treatment difficult, leading to therapeutic failure, worse prognoses and an increased risk of mortality [17,18]. Inappropriate empiric therapy significantly increases mortality rates in patients with CRAB infections. Studies have shown that patients who receive inadequate initial treatment have a mortality rate of up to 86% compared with 33.7% for those who receive appropriate therapy [25]. In this scenario, the main treatment for CRAB infections is the use of polymyxins or combination therapy using fluoroquinolones, aminoglycosides, ampicillin-sulbactam and carbapenems, in some cases, tigecycline is also an effective therapeutic option [17].

Overall, we observed a high mortality rate among patients with *A. baumannii* BSI, which is expected in these infections. Consistent with our findings, other studies also reported that patients with COVID-19 and *A. baumannii* coinfection had higher risk of mortality. These findings emphasize the negative impact of COVID-19 on patients with *A. baumannii* infection, highlighting risk factors common to both infections, such as prolonged ICU stays, use of multiple invasive devices and prior use of antimicrobials as empirical treatment [9,26].
Although our analysis included a wide range of potential risk factors, one limitation of the study is that this study represents a retrospective and single center analysis and may not apply to populations in other regions. Therefore, comparing our results with those from similar studies could help strengthen the development of a reliable model for predicting and reducing mortality risk factors in *A. baumannii* BSI.

**Conclusion**

This study demonstrates a significant increase in *Acinetobacter baumannii* Bloodstream Infections (BSI), particularly those caused by Carbapenem-Resistant Strains (CRAB), over the past decade. The rise in antimicrobial resistance especially to carbapenems, aminoglycosides and polymyxins has made treatment increasingly difficult, contributing to high mortality rates. The COVID-19 pandemic further exacerbated the incidence and severity of these infections, especially in ICU settings. Several clinical factors were associated with higher mortality, including male sex, underlying conditions like diabetes and hypertension, use of invasive devices, septic shock and prior antibiotic use. While this is a single-center, retrospective study, our findings are consistent with other reports and highlight the urgent need for improved infection control measures, early diagnosis and appropriate empirical therapy. Broader studies are needed to support the development of more effective strategies to reduce mortality from *A. baumannii* BSI.

**Conflict of Interest**

The authors declare that there is no conflict of interest.

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