Original Article

**Associated factors of Acinetobacter baumannii complex in hospitalized patients: A case-control study**

Débora Fiorentin Vandresen¹, Léia Carolina Lucio¹,², Roberto Shigueyasu Yamada¹, Ana Paula Vieira¹,², Franciele Ani Caovilla Follador¹,², Volmir Pitt Benedetti³, Kérley Pereira Bento Casari¹,², Cleide Viviane Buzanello Martins²,⁴, Guilherme Welter Wendt¹, Lirane Elize Defante Ferreto¹,²

¹ Health Sciences Center, Western Paraná State University (UNIOESTE), Francisco Beltrão, Brazil
² Postgraduate Program in Applied Health Sciences, Western Paraná State University (UNIOESTE), Francisco Beltrão, Brazil
³ Faculty of Pharmacy, Paranaense University (UNIPAR), Francisco Beltrão, Brazil
⁴ Western Paraná State University (UNIOESTE), Toledo, Brazil

**Abstract**

**Introduction:** Acinetobacter baumannii complex are microorganisms of critical priority of resistance, being associated with higher costs and negative outcomes for hospitalized patients. Thus, the study aimed to analyse the factors associated with A. baumannii complex infection in various hospital sectors.

**Methodology:** This is a case-control study that included patients hospitalized from January 2017 to June 2019. Demographic, microbiological and clinical variables were collected from each patient. All cases had positive culture results for A. baumannii complex resistant to more than three classes of antimicrobials. Carbapenem-resistance was examined by the disk diffusion test, while the broth microdilution method was used to determine the susceptibility to colistin.

**Results:** A. baumannii complex infection was mostly present in ICU (74.2%) than in other hospital areas. The bacteria was also linked with the length of hospitalization until the results for the culture (OR = 1.13; 95% CI: 1.06 – 1.21; p < 0.001) and with pneumonia associated with mechanical ventilation (OR = 4.48; 95% CI: 1.55 – 13.00; p = 0.006). Moreover, patients exposed to infection with multidrug-resistant A. baumannii complex had higher risks of death (OR = 3.25; 95% CI: 1.06 – 9.91; p = 0.039).

**Conclusions:** This study provides evidence that A. baumannii complex infection is associated with the number of days of hospitalization up to culture positivity, pneumonia associated with the use of mechanical ventilation and death. Infections appear to be more critical in ICU when compared to other areas. Taken together, these findings could support hospital infection surveillance programs, as well as prevention measures to reduce mortality rates and other complications.

**Key words:** Acinetobacter baumannii complex; hospital infection; multiple bacterial pharmacoresistence.

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**Introduction**

Acinetobacter baumannii complex (A. baumannii) has contributed to the increase in healthcare-associated infections (HAIs), creating major problems for public health. The higher costs of health institutions are, at least in part, consequences of lengthy hospitalizations. In addition A. baumannii raises morbidity and mortality rates in hospital services [1,2]. For instance, it has been estimated that the hospital cost linked to HAIs is $651/day and the costs related to intensive care unit (ICU) are $1,780/day; in Brazil, this cost can be up to three times higher in patients with infections than in those without infections [3].

The carbapenem-resistant bacterium A. baumannii, together with Pseudomonas aeruginosa, Klebsiella pneumoniae and Escherichia coli are critical in the context of health institutions [4]. As a colonizing microorganism, A. baumannii causes infections in ICU patients on invasive device and in those in antimicrobials treatment [5]. In the early 1970s, these microorganisms were controlled by aminoglycosides, nalidixic acid, and ampicillin. However, this scenario is no longer the same. Currently, most strains have demonstrated resistance to the vast majority of antimicrobial classes, including 3rd and 4th generation cephalosporins and carbapenems, which have already been considered an excellent treatment option [6]. According to Gazel and Otkun, appropriate doses of colistin, combined with other antibiotics, are available to clinicians dealing with patients infected with with
carbapenem-resistant *A. baumannii* complex, notwithstanding data reporting on cases of colistin resistance and heteroresistance [7].

In the light of the critical importance of microbial resistance and the limited information of risks associated with *A. baumannii* in various hospital sectors, research efforts for better understanding this pathogen are needed, especially in developing countries. Consequently, the aim of the investigation was to analyse the factors associated with *A. baumannii* infection in hospitalized patients.

**Methodology**

This study adopted a case-control design and was approved by the Western Paraná University Research Ethics Committee (n. 3.441114). Cases were all the patients with positive cultures for *A. baumannii* complex resistant to three classes of antimicrobials admitted from January 2017 to June 2019. A total of 29 patients satisfied these criteria. In the other hand, samples for the controls consisted of patients admitted to the hospital who did not present positivity for *A. baumannii*. Two controls were assigned for each case. In addition, controls were matched with cases by age (same age ± 5 years), year of hospitalization, sex, and sector of hospitalization, totaling 58 patients (see Supplementary Table 1). The hospital unit is located in the municipality of Francisco Beltrão, PR, Brazil.

Data were extracted from laboratory reports and epidemiological surveillance records of the Hospital Infection Control Commission (ICC). In all sectors of the hospital, a routine of service was established for this study. Hence, all patients who presented eligible criteria as reported by a physician underwent examinations to verify the presence of bacterial infection. The collected material (biological material and surveillance culture) was sent to a laboratory contracted by the hospital and double checked by the Central State Laboratory (LACEN), responsible for classifying all the isolates as *A. baumannii* complex. The samples were sown in specific medium for the development of microorganisms (MacConkey and blood agar) and incubated for 24 hours at 35°C in a bacteriological greenhouse in the microbiology sector.

The identification for *A. baumannii* was performed by manual methods: cytochrome oxidase reaction, glucose fermentation, motility, arginine dihydrolase activity, lysine decarboxylation and Gram staining. The confirmation of manual identification was performed through Vitek 2 (bioMérieux®, Marcy-l’Étoile, France) and the presence of the *bla*OXA23 gene was carried out using PCR.

The susceptibility profile of *A. baumannii* isolates were determined by the disk diffusion method. For this technique, a dilution was used on a scale of 0.5 McFarland through the dilution of three to five colonies in 5 mL of trypticase soybean broth (Laborclin®, Pinhais, PR, Brazil), being incubated at 37°C until reaching the scale corresponding to 1.5x10⁸CFU/mL. Subsequently, with the aid of a sterile swab, sowing was performed in Mueller-Hinton Agar and antimicrobial discs were applied: amikacin (30μg), ampicillin/sulbactam (10-10μg), cefepime (30μg), ciprofloxacin (5μg), gentamicin (10μg), imipenem (10μg), meropenem (10μg), doxycycline (30μg), and ceftriaxone (30μg). After being incubated for 24 hours at 37°C, the inhibition zones were read according to recommended standards [7]. These discs were again obtained from Laborclin®, Pinhais, PR, Brazil. Broth dilution method was used for testing colistin resistance and heteroresistance following the ISO 20776-1 guidelines and results were interpreted according to the Clinical and Laboratory Standards Institute (CLSI) [8]. For these experiments, colistin sulfate salt was used (Laborclin®, Pinhais, PR, Brazil) along with cation-adjusted Mueller-Hinton agar (Laborclin®, Pinhais,
PR, Brazil) starting with 128 mg/L of colistin. Serial dilutions were performed (50μL), inoculated (5×10^6 CFU/mL), and incubated at 35°C for 16–20 hours.

Figure 1 describes the flowchart of the process for selecting cases and controls. After the selection of cases and controls, the following variables were then examined: length of stay in the sector until culture positivity, type of hospital admission (i.e., referral from another hospital or direct from the community), hospitalization sector (ICU and surgical clinic), diagnosis at admission, use of invasive device (type of probe, central and peripheral catheter, intubation), use of antimicrobials, surgical procedure, and patient outcome (hospital discharge/death). Microbiological data examined included microorganism isolates, antimicrobial resistance profile, isolation site, resistance genes, and phenotypic tests.

Absolute (n) and relative (%) frequencies were used to describe the characteristics of the patients and the resistance profile of A. baumannii. For detailing the variables, measures of central tendency (mean and

Table 1. Clinical data of patients and genetic characteristics of A. baumannii isolates, of the 29 patients with positive culture for A. baumannii.

| No. | Gender/age | Time of hospital stay until culture positivity | Length of hospitalization | Diagnosis at hospitalization | Sensitivity | Outcome | Sample | MIC for polymyxin (mg/L) | Resistance gene |
|-----|------------|-----------------------------------------------|---------------------------|----------------------------|-------------|---------|---------|------------------------------|----------------|
| 1   | F/26       | 45                                            | 89                        | Cholelithiasis              | AMI, DOX    | Discharge | Tracheal aspirated      | 0.125           | Oxa_23               |
| 2   | M/14       | 15                                            | 36                        | Pancreatitis                | AMI, SUT, DOX | Discharge | Tracheal aspirated      | 0.25            | Oxa_23               |
| 3   | F/18       | 44                                            | 85                        | Trauma                      | AMI, SUT    | Discharge | Tracheal aspirated      | 0.125           | Oxa_23               |
| 4   | M/58       | 2                                             | 27                        | Pneumonia                   | AMI, DOX, ASB | Discharge | Tracheal aspirated      | 0.25            | Oxa_23               |
| 5   | F/76       | 7                                             | 41                        | Pneumonia                   | AMI, SUT    | Death     | Wound                | 0.125           | Oxa_23               |
| 6   | M/60       | 28                                            | 55                        | Renal failure               | AMI, ASB, DOX | Discharge | Tracheal aspirated      | 0.125           | Oxa_23               |
| 7   | M/60       | 28                                            | 55                        | Renal failure               | AMI, DOX    | Discharge | Urine                | 0.125           | Oxa_23               |
| 8   | M/72       | 3                                             | 65                        | Trauma                      | AMI, ASB, DOX | Discharge | Urine                | 0.25            | Oxa_23               |
| 9   | M/87       | 60                                            | 95                        | Sepsis                      | AMI, ASB, DOX | Death     | Urine                | <0.125          | Oxa_23               |
| 10  | M/82       | 22                                            | 36                        | Renal failure               | AMI, ASB, DOX | Death     | Urine                | 0.25            | Oxa_23               |
| 11  | M/72       | 13                                            | 70                        | Ischemic cardiomyopathy     | AMI, ASB, DOX | Discharge | Tracheal aspirated      | <0.125          | Oxa_23               |
| 12  | M/20       | 13                                            | 39                        | Trauma                      | AMI, LVX, ASB, DOX | Discharge | Tracheal aspirated      | <0.125          | Oxa_23               |
| 13  | F/76       | 6                                             | 10                        | Pneumonia                   | AMI, SUT, DOX | Death     | Tracheal aspirated      | 0.125           | Oxa_23               |
| 14  | F/37       | 18                                            | 47                        | Diabetes                    | AMI, SUT, DOX | Discharge | Tracheal aspirated      | 0.125           | Oxa_23               |
| 15  | F/37       | 18                                            | 47                        | Diabetes                    | AMI, SUT, DOX | Discharge | Urine                | 0.125           | Oxa_23               |
| 16  | M/72       | 14                                            | 27                        | Trauma                      | AMI, ASB, DOX, LVX | Death     | Tracheal aspirated      | 1.00            | Oxa_23               |
| 17  | M/38       | 9                                             | 22                        | Trauma                      | AMI, ASB    | Discharge | Tracheal aspirated      | 0.125           | Oxa_23               |
| 18  | M/68       | 1                                             | 4                         | Pneumonia                   | AMI, ASB, DOX, LVX | Death     | Tracheal aspirated      | 0.25            | Oxa_23               |
| 19  | M/57       | 6                                             | 13                        | Coronary artery disease     | AMI, ASB, DOX | Death     | Tracheal aspirated      | 0.125           | Oxa_23               |
| 20  | F/31       | 27                                            | 48                        | Trauma                      | DOX, ASB    | Discharge | Sputum               | <0.125          | Oxa_23               |
| 21  | M/88       | 15                                            | 16                        | Urinary tract infection     | DOX, ASB    | Discharge | Urine                | 0.25            | Oxa_23               |
| 22  | M/47       | 11                                            | 23                        | Stroke                      | DOX         | Death     | Tracheal aspirated      | 0.25            | Oxa_23               |
| 23  | F/82       | 11                                            | 17                        | Sepsis                      | DOX, ASB    | Death     | Tracheal aspirated      | 0.125           | Oxa_23               |
| 24  | F/82       | 13                                            | 17                        | Sepsis                      | DOX, ASB    | Death     | Tracheal aspirated      | 0.125           | Oxa_23               |
| 25  | M/52       | 20                                            | 50                        | Trauma                      | DOX         | Discharge | Tracheal aspirated      | 0.125           | Oxa_23               |
| 26  | M/29       | 15                                            | 43                        | Trauma                      | DOX         | Discharge | Tracheal aspirated      | 2.00            | Oxa_23               |
| 27  | M/58       | 31                                            | 31                        | Sepsis                      | DOX         | Death     | Wound                 | 0.25            | Oxa_23               |
| 28  | M/58       | 23                                            | 31                        | Sepsis                      | DOX         | Death     | Wound                 | 0.25            | Oxa_23               |
| 29  | F/67       | 10                                            | 10                        | Respiratory failure         | DOX, ASB    | Death     | Tracheal aspirated      | 0.25            | Oxa_23               |

Doxycycline (DOX), Ampicillin/Sulbactam (ASB), Amikacin (AMI) and LevoFlaxcin (LVX) samples were not tested for the sensibility test for the Rectal Swab samples.
median) and dispersion (standard deviation and interquartile amplitude) were used. The normality of data was inspected by the Kolmogorov-Smirnov test. Comparisons of variables with normal distribution were performed with student’s t-test for independent samples. Mann-Whitney’s test was used when data were not normal. In addition, categorical variables were compared with Chi-square test. Variables that presented p < 0.20 in these analyses were included in binary logistic regression models. Analyses were performed in SPSS (Chicago, IL, version 25).

Results

Out of the 87 patients here included, seven cases are from 2017, 10 cases from 2018, and 12 cases in 2019, with their respective controls. The incidence of *A. baumannii* was 0.09%, 0.12% and 0.28% in 2017, 2018 and 2019, respectively. All samples from the case samples revealed *A. baumannii* complex with *bla*OXA23 gene and resistant to carbapenems. Colistin resistance and heteroresistance was not detected (all isolates had colistin minimum inhibitory concentration below 2 mg/L). Moreover, there was a higher number of cases with *A. baumannii* in the ICU and among males (Supplementary Table 1). Clinical characteristics of cases are shown in Table 1, showing that the tracheal aspirate sample presented most results of *A. baumannii* isolates.

Table 2 shows the general characteristics of the sample. Cases presented longer hospitalization time

|                          | Cases (n = 29) | Controls (n = 58) | p     |
|--------------------------|---------------|------------------|-------|
| **Age**                  |               |                  |       |
| Mean                     | 56.0          | 56.8             | 0.877 |
| SD                       | 22.2          | 22.5             |       |
| **Length of stay until the realization of the culture** |               |                  |       |
| Mean                     | 18.2          | 6.1              | < 0.001 |
| SD                       | 13.6          | 8.8              |       |
| **Year**                 |               |                  | 1.000 |
| 2017                     | 7             | 14               |       |
| 2018                     | 10            | 20               |       |
| 2019                     | 12            | 24               |       |
| **Hospitalization sector** |             |                  | 1.000 |
| ICU                      | 21            | 42               |       |
| Medical and surgical clinics | 8           | 16               |       |
| **Type of hospital admission** |         |                  | 0.033 |
| Transfer from another health unit | 20          | 26               |       |
| Community                | 9             | 32               |       |
| **Diagnosis of admission** |            |                  | 0.816 |
| Respiratory tract disease | 2            | 4                |       |
| Trauma                   | 8             | 23               |       |
| Cardiovascular disease   | 5             | 11               |       |
| Sepsis                   | 5             | 5                |       |
| Respiratory disorder     | 5             | 8                |       |
| Genitourinary system disease | 4          | 7                |       |
| **Use of invasive device** |          |                  | 0.062* |
| Yes                      | 29            | 49               |       |
| No                       | 0             | 9                |       |
| **Antimicrobial use**     |               |                  | 0.425 |
| Yes                      | 24            | 42               |       |
| No                       | 5             | 16               |       |
| **Surgical procedure**   |               |                  | 1.000 |
| Yes                      | 5             | 11               |       |
| No                       | 24            | 47               |       |
| **Patient outcome**      |               |                  | 0.013 |
| Death                    | 13            | 10               |       |
| Discharge                | 16            | 48               |       |
| **Isolated site**        |               |                  | < 0.001 |
| Tracheal aspirated       | 20            | 12               |       |
| Others                   | 9             | 46               |       |

* Not included in the regression analyses due to the absence of cases without invasive device usage.
until the culture for *A. baumannii* (p < 0.001) and higher transfer rate from another health unit (p = 0.038). All cases made use of invasive device. In addition, we observed a higher relative number of deaths (p = 0.013) and a higher samples from tracheal aspirate (p < 0.001) in cases compared to the controls. No difference related to the diagnosis of admission, the use of antimicrobials and the submission to surgical procedure was observed. The mortality rate in patients with *A. baumannii* in 2017, 2018 and 2019 was 143, 400 and 667 cases per 1000 inhabitants, respectively.

With the exception of one variable (i.e., use of invasive device), variables with p < 0.20 were taken into a logistic regression model (Table 3). Each additional day between hospitalization and the performance of the culture increases by 11% the chance of developing infection with multidrug-resistant *A. baumannii*. Deaths were more common in patients with *A. baumannii*. In addition, it was evaluated that ventilator-associated pneumonia was almost eight times more frequent in cases compared to controls.

**Discussion**

Despite the increase in the reports of outbreaks of *A. baumannii* in Brazil, research on its risk factors in different hospital sectors is rare [6]. *A. baumannii* is an etiological agent responsible for endemic diseases in hospital environments, being a microorganism that stands out as a cause of nosocomial infections, especially in ICU. It has the capacity to rapidly acquire resistant-genes, which results in a threat in the use of antibiotics [9,10]. Epidemiological data of *A. baumannii* isolates in hospitals are needed in order to implement prevention strategies, as well as to improve hospital infection programs (especially those focusing on antimicrobials).

In the present study, 72.4% of the isolates of *A. baumannii* were detected in the ICU, which means that only about one in four of positive cultures for this microorganism occurred in other hospital wards. Data on the prevalence of this microorganism in the various hospital sectors are still limited, and most of available literature investigated the presence of multidrug-resistant bacteria in ICU. Interestingly, Ciello and Araujo (2016) reported a prevalence of 22.8% of this microorganism in ICU, also noting great numbers of isolates in the emergency room (ER) [11]. In the current study, no isolates of *A. baumannii* were found in ER. Moreover, data from a reference hospital in Spain indicated that *A. baumannii* was the microorganism with the highest incidence in HAI, and the infections it caused in ICU accounted for 35.4% of HAI [12].

The length of hospitalizations is directly related to increased chances of developing *A. baumannii* infection [11]. The chance of developing an infection by this microorganism in the present study increases by 11% each day of hospitalization, corroborating past evidence linking a higher chance of developing multidrug-resistant bacteria infections the longer the length of hospital stay [1]. *A. baumannii* infection in ICU is not limited to the length of hospitalization, being also associated with higher patient density and higher healthcare professionals density. *A. baumannii* infections lead to significantly higher costs for the health system (i.e., medications, consultations, and laboratory testing) when compared to other bacteria [13]. Indeed, previous reports have shown a link between *A. baumannii* infections and longer hospitalizations. The length of hospital stay until culture positivity for *A. baumannii* found in the literature (i.e., 24.8 days) [14] seems slightly above that identified in this study (i.e., 18.2 days). Moreover, there is a positive relationship between *A. baumannii* infection and invasive procedures, use of wide-spectrum antibiotics, immunosuppression, and the ICU environment, which itself contributes to the natural selection of microorganisms [15].

It was also observed that patients transferred from other hospital units were more likely to develop *A. baumannii* infections than patients who came directly

| Table 3. Predictors of positive culture for *A. baumannii* in hospitalized patients. |
|----------------------------------|---------------|----------------|----------------------------------|----------------|
|                                   | **OR** (95% CI) | **p**        | **OR adj (95% CI)** | **p**        |
| **Length of stay until the realization of the culture** |
| Transfer from another health unit  | 1.11 (1.05-1.18) | < 0.001 | 1.11 (1.04-1.18) | < 0.001 |
| Community                          | 1              |            |                    |           |
| **Type of hospital admission**     |
| Death                              | 3.90 (1.43-10.60) | 0.014 | 4.39 (1.20-15.99) | 0.025 |
| Discharge                          | 1              |            |                    |           |
| **Patient outcome**                |
| Death                              | 3.90 (1.43-10.60) | 0.014 | 4.39 (1.20-15.99) | 0.025 |
| Discharge                          | 1              |            |                    |           |
| **Isolated site**                  |
| Tracheal aspirated                 | 8.52 (3.10-23.42) | 0.001 | 7.68 (2.33-25.30) | 0.001 |
| Others                             | 1              |            |                    |           |

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from the community, reinforcing that this bacterium remains within the hospital environment. Nonetheless, studies have identified the presence of this bacterium in environments outside the hospital, including samples from food slaughterhouses [16–18]. The presence of this microorganism - especially the one containing the blaOXA23 gene - in the community represents significant health risk because its dissemination increase community and nosocomial infections, contributing to higher rates of antimicrobial resistance.

Reports on A. baumannii strains carrying the blaOXA23 gene resistant to carbapenems are especially found in isolates from biological samples of ICU patients [19–21]. A study conducted in five Brazilian states showed a 94.2% prevalence of the carbapenem-resistant blaOXA23 gene [22], which is very similar to data here reported (i.e., found in all cases). The production of carbapenemase belonging to class D β-lactamases, also called oxacilinses (OXAs), are responsible for A. baumannii resistance to carbapenems [23]. In addition to Brazil, these carbapenemases have already been detected elsewhere (i.e., Europe, Asia, North and Latin America). This widespread dissemination of OXA-type is facilitated by the presence of insertion sequences and transposons, increasing the potential of its propagation [24,25].

Recent evidence indicate that some patients infected with A. baumannii might require colistin treatment [7]. However, in our study, colistin resistance and heteroresistance was not detected since colistin minimum inhibitory concentrations were below 2 mg/L in all isolates. Moreover, no prior cases of hospitalized patients infected with A. baumannii presenting with colistin resistance were documented in our city.

Indeed, the regularity in which samples of A. baumannii are reported corroborates the endemic feature of this bacteria in the hospital environment. In the present study, similarly to what has been reported by Souza and collaborators [26], A. baumannii proved to be more aggressive, hence increasing mortality. A high mortality rate might be explained by an ability of the bacteria in developing resistance to multiple drugs, as well as its capacity to resist the desiccation of abiotic surfaces and in forming biofilms (hence colonizing and invading human epithelial cells) [27,28]. In this study, a mortality rate of 45.5% was found between January 2017 to June 2019, which is lower when compared to the rate of 59% reported in Brazil [9]. An important difference is that, in our study, all the strains contained the gene blaOXA51. In Neves and collaborators’ investigation, only 51.2% of the strains had this same gene. However, all strains had the expression of the gene blaOXA51 (an intrinsic enzyme related to nosocomial infections) [8]. In addition, the current study indicated that mortality rates were increasing over the three years. Hence, from 2017 to 2018, there was an increase of 179.72%. As for the period of 2018 to 2019, a mortality increase of 66.75% was found.

A. baumannii infection constituted a risk factor for ventilator-associated pneumonia (VAP). Albeit community-acquired VAP attributed to A. baumannii has been reported worldwide, it appears more common in tropical and subtropical locations, such as Brazil and other developing countries [29,30]. Remarkably, even with all the evidence linking A. baumannii to negative outcomes, mechanisms involved in infections by this micorganism are not fully understood [31]. Some tentative explanations include its capacity for biofilm formation, the presence of pili, and its degree of hydrophobicity as main contributing factors for adherence to plastics, including catheter surfaces, endotracheal tubes and several other biomaterials [32,33]. In addition, it should also be noted that A. baumannii presents itself commensally in the skin, in digestive tract and respiratory tracts. The ophopharynx is one of the predominant sites of colonization of this bacterium, since the mucins present in the oral cavity serve as receptors for this bacterial species [15].

Notwithstanding presenting important data, results from this study must be considered in the light of its limitations. First, issues regarding the use of retrospective analysis shall be take into account as the quality of the data was dependent on the records that were made in the hospital. Moreover, laboratory findings from the diffusion disc test were submitted to genetic analyses to explore the presence of the blaOXA23 gene. However, the diffusion disc test is has limitations (i.e., may present lability and alteration in inadequate concentrations) [34].

**Conclusion**

This investigation suggested that A. baumannii is endemic in this health service. Longer hospitalizations, the occurrence of transfers from other hospital services and pneumonia associated with mechanical ventilation were significant risk factors for the development of A. baumannii resistant to carbapenem. Moreover, 72.4% of cases of A. baumannii were detected in the ICU, which means than only about one in four of positive cultures for this microorganism occurred in other hospital wards. These information might support tailored strategies for preventing infections in health institutions.
References

1. Sinésio MCT, Magro MC, Carneiro TA, Silva KGN (2018) Risk factors for healthcare-associated infections in intensive care units. Cogitare Enferm 23: e53826.

2. Leoncio JM, Almeida V, Ferrari RAP, Capobiangio JD, Kerbauy G, Tacla MTGM (2019) Impact of healthcare-associated infections on the hospitalization costs of children. Rev Esc Enferm USP 53: e03486–e03486.

3. Barros LM, Bento JNC, Caetano JÁ, Moreira RAN, Pereira FGF, Frota NM, De Araújo TM, Soares E (2012) Prevalence of microorganisms and antimicrobial susceptibility of nosocomial infections in an intensive care unit of a public hospital in Brazil. J Basic Appl Pharm Sci 33: 429-435. [Article in Portuguese].

4. Weber BS, Harding CM, Feldman MF (2016) Pathogenic Acinetobacter: from the cell surface to infinity and beyond. J Bacteriol 198: 880–887.

5. Huang H, Chen B, Liu G, Ran J, Lian X, Huang X, Wang N, Huang Z (2018) A multi-center study on the risk factors of infection caused by multi-drug resistant *Acinetobacter baumannii*. BMC Infect Dis 18: 11.

6. Scarcella AC, Scarcella AS, Beretta ALRZ (2017) Infection related to health assistance associated to *Acinetobacter baumannii*: literature review. RBAC 49: 18–21. [Article in Portuguese].

7. Gazel D, Otkun M (2017) Investigation of colistin heteroresistance and some factors affecting heteroresistance in carbapenem-resistant *A. baumannii* strains. Mediterr J Infect Microb Antimicrob 6: 1.

8. Clinical and Laboratory standard institute (CLSI) (2015) Performance standards for antimicrobial disk diffusion susceptibility tests, 25th informational supplement. CLSI document M100-S25 (1-56238-989-0).

9. Neves FC, Clemente WT, Lincopan N, Paião ID, Neves PR, Romanelli RM, Lima SS, Paiva LF, Mourão PHO, Nobre-Junior VA (2016) Clinical and microbiological characteristics of OXA-23-and OXA-143-producing *Acinetobacter baumannii* in ICU patients at a teaching hospital, Brazil. Braz J Infect Dis 20: 556–563.

10. Apalata T, Vasaikar S, Okute GE, Songca S (2019) Prevalence and molecular analysis of multidrug-resistant *Acinetobacter baumannii* in the extra-hospital environment in Mthatha, South Africa. Braz J Infect Dis 23: 371–380.

11. del Cielo G, Araújo MC (2016) Epidemiological profile of carbapenem-resistant *Acinetobacter baumannii* in a hospital in the countryside of Minas Gerais. Rev Fam Ciclos Vida E Saúde No Contexto Soc 4: 201–207.

12. Jover-Saenz A, Barcenilla-Gaite F, Barbé-Illa E, Garcia-González M, López-Salcedo R, Castellana-Perelló D, Garrido-Calvo S, Porcel-Pérez J (2005) Nosocomial infection by multiresistant pathogens during one year in a secondary hospital: clinical and epidemiological analysis. An. Med. Interna 22: 59–64. [Article in Spanish].

13. Asim P, Naik NA, Varma Muralidhar K, Varsha AP (2016) Clinical and economic outcomes of Acinetobacter vis a vis non-Acinetobacter infections in an Indian teaching hospital. Perspect Clin Res 7: 28.

14. Dias VC, Resende JA, Bastos AN, Bastos LQ, Bastos VQ, Bastos RV, Diniz CG, Da Silva VL (2017) Epidemiological, physiological, and molecular characteristics of a Brazilian collection of carbapenem-resistant *Acinetobacter baumannii* and *Pseudomonas aeruginosa*. Microb Drug Resist 23: 852–863.

15. Lee C-R, Lee JH, Park M, Park KS, Bae IK, Kim YB, Cha C-J, Jeong BC, Lee SH (2017) Biology of *Acinetobacter baumannii*: pathogenesis, antibiotic resistance mechanisms, and prospective treatment options. Front Cell Infect Microbiol 7: 55.

16. Pomba C, Endimiani A, Rossano A, Saisal D, Couto N, Perreten V (2014) First report of OXA-23-mediated carbapenem resistance in sequence type 2 multidrug-resistant *Acinetobacter baumannii* associated with urinary tract infection in a cat. Antimicrob Agents Chemother 58: 1267–1268.

17. Poirel L, Berçot B, Millemann Y, Bonnin RA, Pannaux G, Nordmann P (2012) Carbapenemase-producing Acinetobacter spp. in cattle. Emerg Infect Dis 18: 523.

18. Wang Y, Wu C, Zhang Q, Qi J, Liu H, Wang Y, He T, Ma L, Lai J, Shen Z (2012) Identification of New Delhi metallo-

19. Castilho SRA, Godoy CS de M, Guilarde AO, Cardoso JL, André MCP, Junqueira-Kipnis AP, Kipnis A (2017) *Acinetobacter baumannii* strains isolated from patients in intensive care units in Goiânia, Brazil: Molecular and drug susceptibility profiles. PLoS One 12: e0176790.

20. França RO, Costa PS, Milanez GL, Bomfim MRQ, Gonçalves R, Farias LM, Nobre V, Santos SG (2018) Molecular association of pathogenicity and resistance to multiple antimicrobials in *Acinetobacter baumannii* strains recovered from patients with diverse infectious diseases. J Bras Patol E Med Lab 54: 288–295.

21. Royer S, Faria ALS, Seki LM, Chagas TPG, Campos PA de, Batistão DW da F, Asensi MD, Gontijo Filho PP, Ribas RM (2015) Spread of multidrug-resistant *Acinetobacter baumannii* and *Pseudomonas aeruginosa* clones in patients with ventilator-associated pneumonia in an adult intensive care unit at a university hospital, Brazil J Infect Dis 19: 350–357.

22. Rocha L, Pagano M, Campos JC, Sampaio JLM, Martins AF, Barth AL (2017) Carbapenem-resistant *Acinetobacter baumannii* in Brazil: susceptibility profile and diversity of oxacillinases. J Bras Patol E Med Lab 53:358–361.

23. Seligman R, Ramos-Lima LF, Oliveira V do A, Sanvicente C, Sartori J, Pacheco EF (2013) Risk factors for infection with multidrug-resistant bacteria in non-ventilated patients with hospital-acquired pneumonia. J Bras Pneumol 39: 339–348.

24. Opazo A, Domínguez M, Bello H, AmYES SG, González-Rocha G (2012) OXA-type carbapenemases in *Acinetobacter baumannii* in South America. J Infect Dev Ctries 6: 311–316. doi: 10.3855/jidc.2310.

25. Peleg AY, Seifert H, Paterson DL (2008) *Acinetobacter baumannii* baumannii: emergence of a successful pathogen. Clin Microbiol Rev 21: 538–582.

26. Souza ES, Belei RA, Maio-Carrilho CMD, Matsuo T, Yamada-Ogatta SF, Andrade G, Perugini MRE, Pieri FM, Dessunti EM, Kerbauy G (2015) Mortality and risks related to healthcare-associated infection. Texto Contexto Enferm 24: 220–228.

27. Cerqueira GM, Peleg AY (2011) Insights into *Acinetobacter baumannii* pathogenicity. IUBMB Life 63: 1055–1060.

28. El Kettani A, Maaloum F, Diawara I, Katfy K, Harrar N, Zerouali K, Belabbes H, Elmadgheri N (2017) Prevalence of *Acinetobacter baumannii* bacteremia in intensive care units of Ibn Rochd University Hospital, Casablanca. Iran J Microbiol 9: 318.

29. Dexter C, Murray GL, Paulsen IT, Peleg AY (2015) Community-acquired *Acinetobacter baumannii*: clinical
characteristics, epidemiology and pathogenesis. Expert Rev Anti Infect Ther 13: 567–573.
30. Koulenti D, Tsigou E, Rello J (2017) Nosocomial pneumonia in 27 ICUs in Europe: perspectives from the EU-VAP/CAP study. Eur J Clin Microbiol Infect Dis 36: 1999–2006.
31. Gordon NC, Wareham DW (2010) Multidrug-resistant Acinetobacter baumannii: mechanisms of virulence and resistance. Int J Antimicrob Agents 35: 219–226.
32. Ahmed MU, Farooq R, Al-Hawashim N, Ahmed M, Yiannakou N, Sayed F, Sayed AR, Lutfullah S (2015) Sensitive, resistant and multi-drug resistant Acinetobacter baumannii at Saudi Arabia hospital eastern region. Pak J Pharm Sci 28: 825–832.
33. Russo TA, Manohar A, Beanan JM, Olson R, MacDonald U, Graham J, Umland TC (2016) The response regulator BfmR is a potential drug target for Acinetobacter baumannii. MSphere 1: e00082-16.
34. Magalhães VCR, Soares VM (2018). Analysis of resistance mechanisms related to enterobacteria with decreased susceptibility to carbapenems isolated from a referral hospital in infectious diseases. Rev Bras Anal Clin 50: 278-281.

**Corresponding author**
Professor Lirane E. D. Ferreto, PhD
Director of the Public Health Research Group, Postgraduate Program in Applied Health Sciences, Western Paraná State University
Rodovia Vitório Traiano, Km2, Bairro Água Branca, Paraná – PR, CEP: 85.601-970
Tel: +55-4635200715
Email: lirane.ferreto@unioeste.br

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Annex – Supplementary Items

Supplementary Table 1. Description of matching procedures for cases (n=29) and controls (n=58) according to age, year of hospitalisation, gender, and sector of hospitalization in the institution between January 2017 to June 2019.

| Age (Cases) | Mean age ± SD (Controls) | Year of cases and controls | Gender of cases and controls | Sector of hospitalization of cases and controls |
|-------------|--------------------------|-----------------------------|-------------------------------|-----------------------------------------------|
| 26          | 24.5 ± 3.5               | 2017                        | F                            | CC2                                           |
| 14          | 18.5 ± 0.5               | 2017                        | M                            | ICU                                           |
| 18          | 18 ± 2                   | 2017                        | F                            | CC2                                           |
| 58          | 53 ± 1                   | 2017                        | M                            | CC2                                           |
| 76          | 74.5 ± 3.5               | 2017                        | F                            | CC2                                           |
| 60          | 63.5 ± 0.5               | 2017                        | M                            | ICU                                           |
| 60          | 61.5 ± 2.5               | 2017                        | M                            | ICU                                           |
| 72          | 70 ± 2.0                 | 2018                        | M                            | ICU                                           |
| 87          | 89 ± 2.0                 | 2018                        | M                            | ICU                                           |
| 82          | 83 ± 1                   | 2018                        | M                            | ICU                                           |
| 72          | 71.5 ± 2.5               | 2018                        | M                            | ICU                                           |
| 20          | 20 ± 3.0                 | 2018                        | M                            | ICU                                           |
| 76          | 81                       | 2018                        | F                            | ICU                                           |
| 37          | 41.5 ± 1.5               | 2018                        | F                            | ICU                                           |
| 37          | 34.5 ± 2.5               | 2018                        | F                            | ICU                                           |
| 72          | 71 ± 4.0                 | 2018                        | M                            | CC2                                           |
| 38          | 29.5 ± 2.5               | 2018                        | M                            | ICU                                           |
| 68          | 71 ± 3.0                 | 2019                        | M                            | CM                                            |
| 57          | 59.5 ± 0.5               | 2019                        | M                            | ICU                                           |
| 31          | 28.5 ± 0.5               | 2019                        | F                            | CC2                                           |
| 88          | 89 ± 4.0                 | 2019                        | M                            | CC1                                           |
| 47          | 47.5 ± 1.5               | 2019                        | M                            | ICU                                           |
| 82          | 86 ± 2.0                 | 2019                        | F                            | ICU                                           |
| 82          | 83.5 ± 3.5               | 2019                        | F                            | ICU                                           |
| 52          | 51.5 ± 0.5               | 2019                        | M                            | ICU                                           |
| 29          | 29.5 ± 4.5               | 2019                        | M                            | ICU                                           |
| 58          | 58 ± 1.0                 | 2019                        | M                            | ICU                                           |
| 58          | 60.5 ± 0.5               | 2019                        | M                            | ICU                                           |
| 67          | 67.5 ± 3.5               | 2019                        | F                            | ICU                                           |

M = Male; F = Female; ICU = Intensive Care Unit; CC1 = Clinical/Surgical Center 1; CC2 = Clinical/Surgical Center 2.