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ORIGINAL ARTICLE

Ventilator-associated pneumonia: incidence, microbial etiology and antimicrobial resistance profile

Pneumonia associada à ventilação mecânica: incidência, etiologia microbiana e perfil de resistência antimicrobiana

Neumonía asociada a ventilador: incidencia, etiología microbiana y perfil de resistencia antimicrobiana

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ABSTRACT

Background and Objectives: Infections caused by multi-drug resistant microorganisms have a great clinical and economic impact. The present study proposed to determine and assess ventilator-associated pneumonia (VAP) incidence in an Intensive Care Unit (ICU), to establish the profile of hospitalized patients and to determine the frequency of microorganisms isolated as well as their antimicrobial resistance profile. **Methods**: A descriptive, documental study, with a quantitative approach, carried out at a teaching hospital. Participants were all individuals admitted to the General ICU who developed VAP in 2018 and 2019. **Results**: During the study, 146 patients were diagnosed with VAP, with an incidence of 23.66/1000 patient-days on mechanical ventilation. The median age of patients was 52.5 years and most of them were man. One hundred and eight microorganisms were isolated in cultures, the majority being gram-negative bacteria. Non-fermenting bacteria were the most frequent (n=46; 42.6%), followed by enterobacteria (n=42; 38.9%). *Staphylococcus aureus* was the most frequent microorganism among gram-positive (n=17; 15.7%). The most frequent multi-drug resistant bacteria were *Acinetobacter baumannii* and *Enterobacter* spp. No microorganism showed colistin and vancomycin resistance. Patients infected with multi-drug resistant bacteria were hospitalized longer when compared to other patients. **Conclusions**: VAP incidence was high. The knowledge of the etiologic agents of VAP and their antimicrobial resistance profile is fundamental to support the elaboration of institutional treatment protocols as well as assist in empirical antibiotic therapy.

Keywords: *Cross Infection. Pneumonia Ventilator-Associated. Intensive Care Units. Bacterial Drug Resistance.*

RESUMO

Justificativa e Objetivos: As infecções causadas por microrganismos multirresistentes têm grande impacto

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clínico e econômico. O presente estudo propôs determinar e avaliar a incidência de pneumonia associada à ventilação mecânica (PAV) em uma Unidade de Terapia Intensiva (UTI), estabelecer o perfil dos pacientes internados e determinar a frequência de microrganismos isolados, bem como seu perfil de resistência antimicrobiana. **Métodos:** Estudo descritivo, documental, com abordagem quantitativa, realizado em um hospital universitário. Participaram todos os indivíduos admitidos na UTI Geral que desenvolveram PAV em 2018 e 2019. **Resultados:** Durante o estudo, 146 pacientes foram diagnosticados com PAV, com incidência de 23,66/1000 pacientes-dia em ventilação mecânica. A idade mediana dos pacientes foi de 52,5 anos e a maioria era do sexo masculino. Cento e oito microrganismos foram isolados em culturas, sendo a maioria bactérias gram-negativas. As bactérias não fermentadoras foram as mais frequentes (n=46; 42,6%), seguidas das enterobactérias (n=42; 38,9%). *Staphylococcus aureus* foi o microrganismo mais frequente entre os Gram-positivos (n=17; 15,7%). As bactérias multirresistentes mais frequentes foram *Acinetobacter baumannii* e *Enterobacter spp.* Nenhum microrganismo apresentou resistência à colistina e vancomicina. Pacientes infectados com bactérias multirresistentes ficaram mais tempo internados quando comparados a outros pacientes. **Conclusões:** A incidência de PAV foi alta. O conhecimento dos agentes etiológicos da PAV e seu perfil de resistência antimicrobiana é fundamental para subsidiar a elaboração de protocolos institucionais de tratamento, bem como auxiliar na antibioticoterapia empírica.

Palavras-chave: *Infecção Cruzada. Pneumonia Associada ao Ventilador. Unidades de Terapia Intensiva. Resistência Bacteriana a Medicamentos.*

RESUMEN

Justificación y Objetivos: Las infecciones causadas por microorganismos multirresistentes tienen un gran impacto clínico y económico. El presente estudio se propuso determinar y evaluar la incidencia de neumonía asociada a ventilación mecánica (NAV) en una Unidad de Cuidados Intensivos (UCI), establecer el perfil de pacientes hospitalizados y determinar la frecuencia de microorganismos aislados así como su perfil de resistencia antimicrobiana. **Métodos:** Estudio descriptivo, documental, con abordaje cuantitativo, realizado en un hospital escuela. Participaron todas las personas ingresadas en UCI General que desarrollaron NAV en 2018 y 2019. **Resultados:** Durante el estudio, 146 pacientes fueron diagnosticados con NAV, con una incidencia de 23,66/1000 pacientes-día en ventilación mecánica. La mediana de edad de los pacientes fue de 52,5 años y la mayoría eran hombres. Se aislaron 108 microorganismos en cultivos, siendo la mayoría bacterias gramnegativas. Las bacterias no fermentadoras fueron las más frecuentes (n=46; 42,6%), seguidas de las enterobacterias (n=42; 38,9%). *Staphylococcus aureus* fue el microorganismo más frecuente entre los grampositivos (n=17; 15,7%). Las bacterias multirresistentes más frecuentes fueron *Acinetobacter baumannii* y *Enterobacter spp.* Ningún microorganismo mostró resistencia a colistina y vancomicina. Los pacientes infectados con bacterias multirresistentes fueron hospitalizados por más tiempo en comparación con otros pacientes. **Conclusiones:** La incidencia de NAV fue alta. El conocimiento de los agentes etiológicos de la VAP y su perfil de resistencia a los antimicrobianos es fundamental para apoyar la elaboración de protocolos de tratamiento institucionales, así como para ayudar en la terapia antibiótica empírica.

Palabras clave: *Infección cruzada. Neumonía asociada a ventilador. Unidades de cuidados intensivos. Resistencia bacteriana a los medicamentos.*

INTRODUCTION

Mechanical ventilation (MV) is one of the most important supports used in the Intensive Care Unit (ICU) to replace totally or partially patients' ventilation in acute or chronic respiratory failure treatment, through the renovation of gas exchanges and respiratory muscle comfort.[1]

Mechanically ventilated patients are at risk for pneumonia, mainly because of aspiration, due to decreased pulmonary defense through underlying diseases, the high risk of aspiration and retention of contaminated upper airway secretions, and the presence of drug-resistant microorganisms on surfaces and materials close to the environment, causing colonization in patients.[2] The tracheal tube weakens individuals' natural defenses and enables the entry of particles directly into the lower airways. Moreover, the presence of the tube and patients' state of unconsciousness compromise oral hygiene, further favoring microbial proliferation and bacteria translocation to the lower respiratory tract.[3]

Ventilator-Associated Pneumonia (VAP) can be defined as clinical or microbiological. The clinical criteria for the definition of VAP were established by the Brazilian National Health Surveillance Agency (Anvisa), and are based on the presence and number of different signs and symptoms presented by patients. VAP microbiologically defined requires a sample collection from the respiratory tract for culture or other tests.[4]

Risk factors for healthcare-associated pneumonia can be classified into modifiable or non-modifiable. Modifiable factors are related to MV duration, reintubation, tracheostomy, gastrointestinal tubes, aspiration of gastric fluids, antimicrobial agents previous use, and staying in the supine position. Non-modifiable factors are advanced age, Chronic Obstructive Pulmonary Disease (COPD), severity of hospitalization, neurological disease, and surgery.[5]

Worldwide, VAP is the second most frequent

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Healthcare-Associated Infection (HAI), with mortality ranging from 20% to 60%[2] and a cost of over US$40,000 per episode.[6] In Brazil, there is a lack of data on VAP incidence in ICUs. This happens because their notifications only became mandatory as of 2017, added to the fact that some hospitals do not follow the diagnostic protocols established by Anvisa.[2]

Regarding the infectious etiology, microorganisms can vary greatly according to the institution. Brazilian studies show that the microorganisms predominantly isolated from cultures of tracheal secretions are gram-negative bacteria, mainly *Acinetobacter baumannii* and *Pseudomonas aeruginosa*, in addition to gram-positive ones, such as methicillin-resistant *Staphylococcus aureus* (MRSA).[5,7]

Infections caused by multi-drug resistant bacteria are complex therapeutics, as the antimicrobial options available for treatment are restricted. As a result, there is a great clinical and economic impact related to patients' hospital stay, which causes an increase in morbidity and mortality rates in ICUs and higher hospital costs.[6]

Considering the above, this study aims to determine and assess VAP incidence in a General ICU of a teaching hospital, to characterize the profile of hospitalized patients and to determine the frequency of microorganisms isolated in cultures, as well as their antimicrobial resistance profile. From this perspective, this work will help the hospital under study, in order to work/elaborate/improve prevention measures related to VAP health care in ICUs and, consequently, reduce its incidence and severity. In addition to promoting quality care with less impact on morbidity and mortality, length of stay and increased costs for the institution. Another aspect of great importance is that knowledge of the main microorganisms and their antimicrobial resistance profile will help in the empirical treatment of patients with VAP.

METHODS

Study Design and Setting

This is a descriptive, documental, and retrospective study, with a quantitative approach, carried out at a public teaching hospital with 238 beds, located in the state of Paraná. This hospital has a General ICU with 14 beds, being a center for the region in high complexity in the areas of traumatology, neurology, vascular surgery, and high-risk pregnancy.

Participants and Data Collection

Participants were all individuals admitted to a General ICU, from January 2018 to December 2019, who developed VAP throughout the hospitalization period. Patients admitted to Neonatal and Pediatric ICUs were not included in the study. The diagnostic criteria for VAP were those determined by Anvisa.[2,4]

Data collection was carried out after approval of the study by the local Ethics Committee, under Certificate of Presentation for Ethical Consideration 50066815.8.0000.0107 and Opinion 4,030,375 of May 15, 2020. Data were retrieved from Microsoft Office Excel® databases from the Hospital Infection Control Service (HICS), prepared and provided by residents of the Nursing Residency Program in the Health Surveillance and Infection Control specialty. To complement the data, Electronic Patient Records (EHR) were accessed through the Philips Tasy management system.

The variables selected for analysis from HICS were sex, age, hospitalization unit, VAP classification, clinical outcome, type of microorganism, and bacterial sensitivity to antimicrobials. The identification of microorganisms isolated in cultures and antimicrobial susceptibility tests were performed using the VITEK® 2 system. The cut-off points for determining resistance were those defined by the European Society of Clinical Microbiology and Infectious Diseases.[8] The definition of multi-drug resistance was according to the Magiorakos et al. criteria, in which a microorganism is considered multi-drug resistant due to the absence of sensitivity to at least one antimicrobial agent in three or more drug categories.[9]

The variables collected in the Philips Tasy system were comorbidities, nasogastric tube (NGT) and nasoenteral tube (NET) use, tracheostomy, reintubation, starting of MV, time on MV, date of admission to the General ICU, hospital length of stay, and ICU length of stay.

Data analysis

For data analysis, Microsoft Office Excel®, version 2010, and jamovi, version 1.8.4.0, were used, which enabled the analyzes, through descriptive statistics, mainly through central tendency measures, such as median, using absolute and relative frequencies, which were later presented in tables and graphs for better understanding. VAP incidence was calculated using a ratio, where the numerator was the number of episodes of VAP in the study period and the denominator was the number of patients on MV per day in the same period, multiplying the result by 1,000. To assess the association between bacterial multi-drug resistance and mortality, the chi-square test was used, set at 5% significance level with $p \leq 0.05$ being statistically significant. To assess the association between bacterial multi-drug resistance and hospital or ICU length of stay, the Mann-Whitney U test was used.

RESULTS

From January 2018 to December 2019, 146 patients were diagnosed with VAP in the General ICU, and of these, seven had two episodes of infection during hospitalization. VAP incidence was 23.66/1000 patient-days on MV.

Patients' hospital length of stay ranged from 8 to 116 days (median=28 days) and the ICU length of stay, from 2 to 61 days (median=16 days). Most patients with VAP admitted to the ICU came from neurosurgery (n=68; 46.5%), followed by general surgery (n=23; 15.7%) and gastroenterology (n=19; 13.0%) units. Of the 146 patients, 63 (43.2%) died throughout the hospitalization period.

The age of patients diagnosed with VAP ranged from 13 to 89 years, with a median age of 52.5 years. Regarding sex, men were more affected (n=95; 65.0%). Most

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patients had some comorbidity (71.5%), such as diabetes, dyslipidemia, COPD, alcohol consumption and smoking, with hypertension being the most frequent (41.0%). Patients were also submitted to invasive procedures classified as modifiable risk factors, such as tracheostomy (60.9%), NET (54.1%) and NGT (49.3%) use, reintubation (17.1%), and MV, whose time ranged from three to 73 days (median=13 days).

Considering the VAP classification, 93 of them (60.8%) were microbiologically defined and 60 (39.2%) were clinically defined. Of the 93 positive cultures, 15 (16.1%) showed growth of two different microorganisms. A total of 108 microorganisms were isolated from all cultures, with the majority being gram-negative bacteria (n=88; 81.5%). Non-fermenting bacteria were the most frequent (n=46; 42.6%), followed by enterobacteria (n=42; 38.9%). Among the gram-positive bacteria, isolated species were *Staphylococcus aureus* (n=17; 15.7%) and *Streptococcus pneumoniae* (n=2; 1.9%). In only one sample *Candida albicans* was observed (0.9%).

Concerning non-fermenting bacteria, there was a significant frequency of *A. baumannii* strains resistant to imipenem (82.3%), meropenem (82.3%), ciprofloxacin (82.3%), ceftazidime (64.7 %), and cefepime (70.5%) (Figure 1). *P. aeruginosa* strains showed greater resistance to ceftriaxone (85.0%) and imipenem (40.0%). Both microorganisms were sensitive to polymyxins. *Stenotrophomonas maltophilia* isolates showed sensitivity to all tested antimicrobials, and *Burkholderia cepacia* strains showed resistance to ciprofloxacin (100%) and piperacillin-tazobactam (50.0%).

Among enterobacteria, no resistance to carbapenems and colistin was observed. However, 80.9% of isolates showed resistance to ampicillin, 50.0% to ampi-

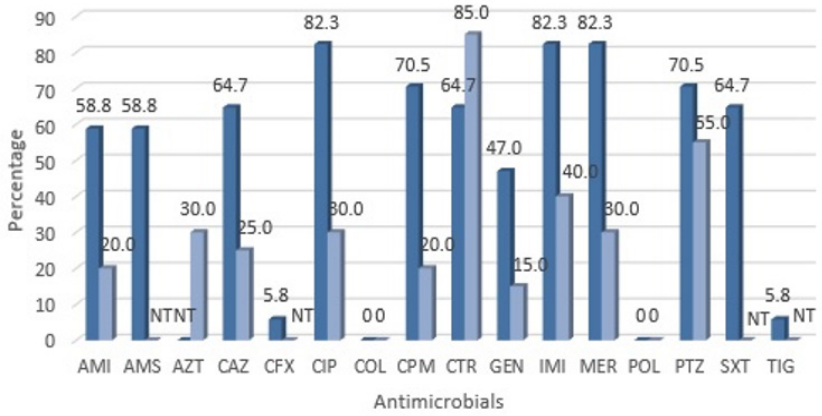

Figure 1. Antimicrobial resistance profile of non-fermenting bacteria isolated from patients with ventilator-associated pneumonia in a General ICU in the city of Cascavel, Paraná, in 2018 and 2019.

AMI - amikacin; AMS - ampicillin-sulbactam; AZT - azithromycin; CAZ - ceftazidime; CFX - cefuroxime; CIP - ciprofloxacin; COL - colistin; CPM - cefepime; CTR - ceftriaxone; GEN - gentamicin; IMI - imipenem; MER - meropenem; POL - polymyxin B; PTZ - piperacillin-tazobactam; SXT - trimethoprim-sulfamethoxazole; TIG - tigecycline; NT - not tested.

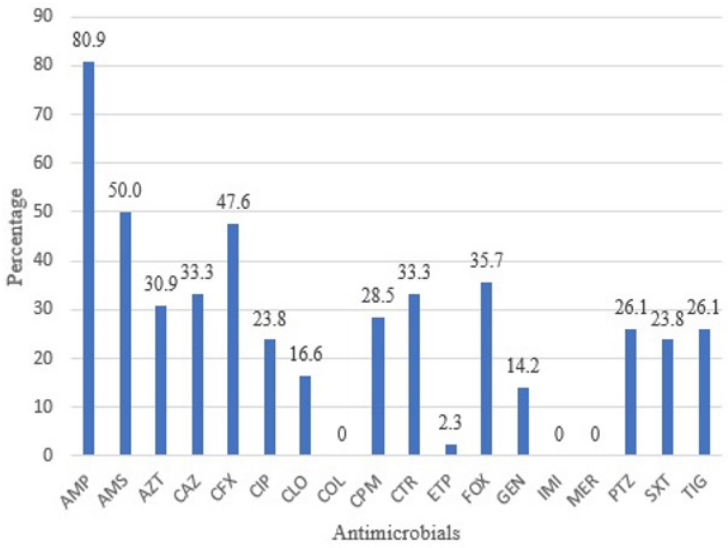

Figure 2. Antimicrobial resistance profile of enterobacteria isolated from patients with ventilator-associated pneumonia in a General ICU in the city of Cascavel, Paraná, in the years 2018 and 2019.

AMP - ampicillin; AMS - ampicillin-sulbactam; AZT - azithromycin; CAZ - ceftazidime; CFX - cefuroxime; CIP - ciprofloxacin; CLO - chloramphenicol; COL - colistin; CPM - cefepime; CTR - ceftriaxone; ETP - ertapenem; FOX - cefoxitin; GEN - gentamicin; IMI - imipenem; MER - meropenem; PTZ - piperacillin-tazobactam; SXT - trimethoprim-sulfamethoxazole; TIG - tigecycline.

cillin-sulbactam, and 47.6% to cefuroxime (Figure 2).

As for *S. aureus* isolates, 88.8% showed resistance to penicillin, 41.1% to azithromycin, 41.1% to erythromycin, 23.6% to clindamycin, 17.7% to oxacillin, and 11.8% to ciprofloxacin. Considering the 107 bacterial isolates obtained from the cultures, 49 (45.8%) were classified as multi-resistant. The most frequent multi-drug resistant bacteria were *A. baumannii* (87.5% of resistant strains) and *Enterobacter* spp (80% of resistant strains) (Table 1). There was no statistically significant association between bacterial multi-drug resistance and patient mortality (p=0.482) (Table 2). Patients infected with multi-drug resistant bacteria were hospitalized for longer when compared to other patients, with medians of 34 and 27 days, respectively (p=0.067). ICU length of stay was also longer among patients with multi-drug resistant bacteria (medians of 20 and 16 days; p=0.144).

Table 1. Etiological agents of ventilator-associated pneumonia in patients admitted to a General ICU in the city of Cascavel, Paraná, in the years 2018 and 2019.

Microorganisms	FREQUENCY N (%)
Gram-positive bacteria	
Staphylococcus aureus	17 (15.7)
Streptococcus pneumoniae	2 (1.9)
Gram-negative bacteria	
Pseudomonas aeruginosa	20 (18.5)
Acinetobacter baumannii	16 (14.8)
Klebsiella pneumoniae	11 (10.2)
Stenotrophomonas maltophilia	7 (6.5)
Enterobacter aerogenes	6 (5.6)
Escherichia coli	6 (5.6)
Enterobacter cloacae	5 (4.6)
Serratia spp	4 (3.7)
Enterobacter sp	3 (2.8)
Klebsiella oxytoca	3 (2.8)
Burkholderia cepacia	2 (1.9)
Proteus mirabilis	2 (1.9)
Acinetobacter lwoffii	1 (0.9)
Citrobacter koseri	1 (0.9)
Enterobacter gergoviae	1 (0.9)
Fungus	
Candida albicans	1 (0.9)
Total	108 (100)

DISCUSSION

The ICU environment is a place characterized by patients with critical clinical conditions. These sites have the highest incidences of HAI, with VAP being the most frequent infection.[10] In this study, VAP incidence was 23.66/1000 patient-days on MV, a high incidence when compared to other studies.[11,25] In the state of Paraná, in 2018, VAP incidences in ICUs of public and private hospitals were 18.47 and 14.49/1000 patient-days on MV, respectively.[11] Higher incidences have repercussions on public health concerns, since they increase hospital length of stay, costs, and mortality rates.[5]

The median hospital length of stay for patients who developed VAP was 28 days, which is a very worrying finding, since staying in the hospital is an important risk factor for infections, due to the increased chance of colonization by microorganisms, resulting from greater exposure and risk of cross-infection.[12] A Spanish study with 316 patients from six ICUs of a hospital in Barcelona showed that hospitalization of five days or more was the most prevalent risk factor for VAP by multi-drug resistant microorganisms.[13] In a study conducted at a teaching hospital in the city of São Paulo, the hospital length of stay of patients who developed or did not develop VAP during

Table 2. Distribution of antimicrobial multi-drug resistant isolates in patients with ventilator-associated pneumonia admitted to a General ICU in the city of Cascavel, Paraná, in the years 2018 and 2019.

	MULTI-DRUG RESISTANCE			
Microorganisms	**YES N (%)**	**DEATH N (%)**	**NO N (%)**	**DEATH N (%)**
Gram-positive bacteria				
Staphylococcus aureus	3 (17.6)	0 (0.0)	14 (82.4)	5 (35.7)
Streptococcus pneumoniae	0 (0.0)	0 (0.0)	2 (100)	1 (50.0)
Gram-negative Bacteria				
Acinetobacter baumannii	14 (87.5)	6 (42.8)	2 (12.5)	0 (0.0)
Enterobacter spp	12 (80.0)	3 (25.0)	3 (20.0)	1 (33.3)
Pseudomonas aeruginosa	8 (40.0)	4 (50.0)	12 (60.0)	5 (41.6)
Klebsiella pneumoniae	6 (54.5)	3 (50.0)	5 (45.5)	2 (40.0)
Escherichia coli	3 (50.0)	2 (66.6)	3 (50.0)	1 (33.3)
Serratia spp	2 (50.0)	1 (50.0)	2 (50.0)	1 (50.0)
Klebsiella oxytoca	1 (33.3)	1 (100)	2 (66.7)	0 (0.0)
Stenotrophomonas maltophilia	0 (0.0)	0 (0.0)	7 (100)	4 (57.1)
Burkholderia cepacia	0 (0.0)	0 (0.0)	2 (100)	1 (50.0)
Proteus mirabilis	0 (0.0)	0 (0.0)	2 (100)	0 (0.0)
Acinetobacter lwoffii	0 (0.0)	0 (0.0)	1 (100)	0 (0.0)
Citrobacter koseri	0 (0.0)	0 (0.0)	1 (100)	0 (0.0)
Total	49 (45.8)	20 (40.8)	58 (54.2)	21 (36.2)

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hospitalization were compared, with medians of 30 and 18 days, respectively, with p=0.0178.[6] As for length of stay of patients in the ICU, the median was 16 days, which is similar to that of other Brazilian studies in which the mean was 15.2 and 16 days .[5,10] There is evidence that an increase of nearly 15 days in ICU length of stay of patients affected by VAP or others HAI is common.[12]

The specialties in which a greater number of patients with VAP were observed were neurosurgery (46.5%), followed by general surgery (15.7%) and gastroenterology (13.0%). The higher number of VAP in post-surgical patients is associated with the study institution's profile, which is a reference in traumatology and other surgical specialties in the region. Similar data were observed in a study carried out in the city of Teresópolis, Rio de Janeiro, where patients with VAP were mainly submitted to neurosurgery (44%), general surgery (13.4%) and orthopedic surgery (7.9%).[14] In another study carried out in the city of São Paulo, 9.5% of patients on MV had a gastrointestinal cause of hospitalization.[6]

The mortality rate of patients with VAP was 43.2%. Brazilian studies show that mortality can vary from 32.1 to 78.8%, depending on the institution characteristics.[15-17] Regarding patients' age, the median was 52.5 years. Several studies show that patients over 40 years of age are more affected by HAI, including VAP.[7,12,14,15] In a study conducted in the city of Uberlândia, Minas Gerais, the age of patients with VAP above 60 years and miscalculations in antimicrobial therapy duration were the only statistically significant predictors of death.[18] In the present study, there was a higher frequency of VAP in males (65.0%). Similarly, another study showed that males were predominant among those diagnosed with VAP (59.3%), due to the greater number of male patients admitted to the ICU.[19] The predominance of males (80%) in most studies can be justified by the economically active age group and, consequently, greater exposure to accidents from external causes.[20] However, there are reports that reveal a balance in the frequency of HAI between sexes and studies that show a predominance in females.[6,7,12]

In view of non-modifiable risk factors, most patients had some comorbidity (71.5%). Hypertension was the most frequent comorbidity (41.0%), while 6.8% of patients had COPD. In a study carried out in the ICU of *Hospital de Clínicas de Porto Alegre*, it was found that the number of patients with VAP who had COPD was much higher (19.7%).

On the other hand, modifiable risk factors, such as tracheostomy (60.9%), presence of NET (54.1%) and NGT (49.3%), were present in a greater number of patients. In a public hospital in the city of Macapá, Amapá, 97% of patients with VAP were using NGT.[16] Furthermore, studies show that the longer the stay on MV, the greater the risk for developing VAP.[14,15] In the present study, MV duration ranged from three to 73 days (median=13 days). Mean durations longer than this, of 23.2 and 27.1 days, were observed in studies carried out in Minas Gerais and São Paulo, respectively.[6,15] Prolonged MV duration is considered an extremely important risk factor, as it compromises the natural barrier of host defense, preventing ciliary motility of the respiratory tract, and the cough reflex, which favor the establishment of microorganisms.[20]

In the present study, the most frequent microorganisms were *P. aeruginosa* (18.5%), *S. aureus* (15.7%), *A. baumannii* (14.8%), and *K. pneumoniae* (10.2%). Different Brazilian studies have shown that *P. aeruginosa* is the most frequently isolated microorganism from patients with VAP.[15,16,18] Some studies show that 81.2% of the isolated bacteria are non-fermenting, being *P. aeruginosa* (34.4%) and *A. baumannii* (34.4%) the most common species.[13,16] Similar to the current study, some reports have shown that the second most frequently isolated microorganism has been *S. aureus*, followed by enterobacteria.[15] The fungal etiology of VAP is less frequent, but some studies have shown *Candida* spp isolation in clinical samples from patients. In a multicenter study with 28 Brazilian hospitals, 2.2% of healthcare related pneumonias were caused by *Candida* spp.[22] In another study, *Candida albicans, Candida parapsilosis* and *Cryptococcus laurentii* were isolated from tracheal samples from patients in association or not with other microorganisms.[16] In the current study, in 15 (16.1%) of the 93 cultures performed, the growth of two different microorganisms was observed. Higher rates of polymicrobial infections were reported in two other studies, with values of 25% and 30.3%.[15,16]

Concerning antimicrobials, *A. baumannii* isolates showed greater resistance to imipenem and meropenem (82.3%), supporting a study carried out in Goiânia, where the highest frequency of resistance was for meropenem (82.8%) and imipenem (77.1%). Very worrying data since carbapenems are important antimicrobial drugs in therapy. The increase in resistance to these drugs makes treatment more difficult, limiting therapeutic options, which can extend hospital stay, increase hospital costs, and rise morbidity and mortality rates.[23]

P. aeruginosa isolates showed greater resistance to beta-lactams ceftriaxone (85%), piperacillin-tazobactam (55%), imipenem (40%), and meropenem (30%). In a study carried out at *Santa Casa de Misericórdia de Goiânia*, it was observed that *P. aeruginosa* isolates showed resistance percentages that ranged from 30% to 40% for cefoxitin, cefuroxime, imipenem, and meropenem.[23]

Among the *S. aureus* isolates, a low frequency of oxacillin resistance was observed (17.7%), when compared to penicillin (88.8%), azithromycin (41.1%), and erythromycin (41.1 %). Oxacillin resistance was also low when compared to other studies in which rates ranging from 61.9% to 80% were observed.[15,16,21]

As for enterobacteria, they showed greater resistance to ampicillin (80.9%), ampicillin-sulbactam (50.0%), and cefuroxime (47.6%). *Enterobacter* species showed resistance to a greater number of antimicrobials. Resistance to carbapenems, which, in other institutions, draws attention, in the hospital under study, did not prove to be a problem.[24] Determining the resistance profile of microorganisms in the hospital under study is extremely important for implementing protocols, since there is no protocol approved at the institution for VAP treatment.

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Knowledge of the institutional resistance profile will help in a more assertive empirical therapy, with the choice of antimicrobials with the most appropriate spectrum of action, thus avoiding the incorrect or excessive use of antimicrobials and, consequently, the emergence of multi-drug resistant microorganisms.

Considering all bacteria, the percentage of multi-drug resistant isolates was high (45.8%) and very similar to that found at *Hospital de Clínicas* of the Federal University of Uberlândia (45.6%). Multi-drug resistant bacteria rates depend on the characteristics of each institution, ranging from 27 to 59%.[16] In the present study, a correlation between bacterial multi-drug resistance and increased patient mortality was not observed. A recently published review showed that mortality in VAP cases is mainly related to the severity of the disease and underlying conditions of patients.[25]

In conclusion, it was found that VAP incidence and mortality observed in the present study were high, highlighting the need to improve preventive measures for this HAI. The most frequent microorganisms in the cultures were gram-negative, especially *A. baumannii* due to high resistance to several antimicrobials widely used in therapy, including carbapenems. In view of this, the need for new antimicrobial options, such as ceftazidime-avibactam and ceftolozane-tazobactam, became evident for VAP treatment in the ICU of the hospital under study. Knowledge of the etiological agents of VAP and their antimicrobial resistance profile is essential to support the elaboration and review of institutional treatment protocols as well as to assist in empirical antibiotic therapy.

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Flávia Allegretti Alvares: contributed to article conception, design, and writing, data analysis and interpretation.

Carla Sakuma de Oliveira: contributed to the correction of the final version of the manuscript and approval.

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Graziela Braun: contributed to article conception, planning, and design, data analysis and interpretation, correction of the preliminary and final version of the manuscript and approval of the final version.