VENTILATOR-ASSOCIATED PNEUMONIA: CLINICAL AND BACTERIOLOGICAL ASPECTS OF PATIENTS AT UNIVERSITY HOSPITAL OF LONDRINA

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VENTILATOR-ASSOCIATED PNEUMONIA: CLINICAL AND BACTERIOLOGICAL ASPECTS OF PATIENTS AT UNIVERSITY HOSPITAL OF LONDRINA

ABSTRACT: Objective: To determine the incidence and bacteriology of microorganisms isolated from endotracheal aspirates (EA) of patients with VAP. **Methods**: Patients admitted to the ICU from June 1, 2017 to May 31, 2019 were considered. Of the 1017 patients in whom EA cultures were performed, 555 were diagnosed with some type of pneumonia. From the ones considered, 235 developed VAP and 170 developed non-ventilator associated pneumonia. Finally, only 153 VAP positive patients met all diagnostic inclusion criteria. **Results**: The most frequent microorganisms identified were *Acinetobacter baumannii* (67), *Pseudomonas aeruginosa* (25), *Staphylococcus aureu*s (35) and *Klebsiella pneumoniae* (34). Most clinical isolates were extensively resistant to antibiotics (XDR). The mean age of the patients was

42 ± 69 years old (p-value=0.004), 160 (68.1%) were male, 203 (86.4%) had late-onset VAP and 164 (69.9%) died. VAP proved to be a major problem in ICU patients at the University Hospital of Londrina. **Conclusion**: Knowledge of epidemiological and microbiological data from patients with VAP assists in proposing measures for the identification, prevention and control of healthcare-related infections.
Keywords: Ventilator-Associated Pneumonia; Bacteriology; Intensive Care Unit.

QUADRO DE CONTRIBUIÇÕES DO ESTUDO

INTRODUCTION

Ventilator-associated pneumonia (VAP) is a type of pneumonia that develops in patients with mechanical ventilation (MV). VAP is the most common nosocomial infection among patients admitted in hospitals particularly for Intensive Care Unit (ICU) [1–3].

Despite recent advances in diagnosis, preventative measures and the approval of new antibiotics therapies, VAP remains a major concern and burden to the healthcare system, resulting in increased hospital length of stay, treatment costs, and mortality rates [2–4].

Several factors may be involved in VAP pathogenesis, such as aging, male gender, the excessive use of antibiotics, underlying diseases, low level of consciousness, prolonged MV, the need for reintubation after extubation, patient's position, infections in other organs, tracheostomy, bronchoscopy, aspiration of oropharyngeal secretions, loss of natural protective mechanisms of the airways, and direct pathogen inoculation during intubation [3,4]. The diagnosis of VAP is usually based on clinical, radiographic, and microbiological findings. Several pathogens may be involved in VAP although *Acinetobacter baumannii, Pseudomonas aeruginosa, Staphylococcus aureus, Klebsiella pneumoniae* and *Escherichia coli* are the most common. These microorganisms are generally multi-drug-resistant (MDR) and highly virulent, making their early detection extremely important [3,5].

VAP is a common complication for patients with acute respiratory failure requiring MV. These patients usually develop the infection 48 hours or longer after the intubation[4]. Early-onset VAP is usually less severe, being established during the first 4 days of MV and being more likely to be caused by antibiotic-sensitive bacteria. On the other hand, late-onset VAP occurs within five days or more after the initiation of MV; it is usually caused by MDR pathogens and is associated with difficulties among the choice of the most appropriate therapy strategies [2].

Regarding the increased detection of MDR pathogens in critical care units and since the newer antibiotics in the past decade have not brought down the mortality associated with VAP, this study aimed to determine the incidence, bacteriology, the sensitivity profile of microbial isolates from endotracheal aspirates (EA), and the resistance profile including MDR isolates, as well as risk factors, and outcome of patients with or without VAP in a tertiary care university hospital.

METHODS

STUDY DESIGN AND DATA SOURCE

This was a retrospective cross-sectional study of VAP, conducted over two years (June 1, 2017– May 31, 2019) in ICUs of a tertiary care university hospital.

Based on a report of endotracheal culture results from June 1, 2017, to May 31, 2019, generated by the Labhos program, an active search was performed to get the records of patients submitted to EA cultures and who had any sort of pneumonia, whether or not associated with mechanical ventilation. From medical records, data were collected according to diagnosis date, isolation of microorganisms and EA culture date, invasive procedures performed in each patient, hospitalization unit, age, patients risk factors, use of antibiotics, input diagnosis, and outcome. This study was approved by the Ethics and Research Committee of the State University of Londrina (CAAE: 43013315.8.0000.5231).

CRITERIA FOR DIAGNOSIS OF VENTILATOR-ASSOCIATED PNEUMONIA AND EXCLUSION CRITERIA

The diagnosis of VAP was based on clinical and microbiological guidelines, following the criteria below:

1. MV for more than 48 h;

2. Detection of new, persistent or progressive infiltrate shadow in the chest X-ray;

3. And the presence of fever (temperature >38ºC); or white cell count >12000/mL or <4000/mL; or altered level of consciousness in patients older than 70 years;

4. And/or the emergence of purulent discharge or changes in its characteristics or increased respiratory discharge; a declining ratio of partial pressure to the inspired fraction of oxygen (PaO_2/FiO_2ratio <240) or increased need for oxygen supply; no snoring or stenosis; the onset or worsening of cough, dyspnea or tachypnea;

5. Diagnosis confirmation by performance of a quantitative culture of the EA and observing $\geq 10^6$ CFU/mL[2,6].

All patients with clinical and radiological signs suggestive of pneumonia at admission, and who did not meet the criteria for diagnosis of VAP mentioned above, were excluded from the study, as well as patients younger than 15 years old.

DEFINITIONS FOR ACQUIRED RESISTANCE

Isolates that showed resistance to at least one agent in three or more antimicrobial classes were classified as multi-drug resistant (MDR). Extensively drug-resistance (XDR) was defined as susceptibility to only one or two antimicrobial classes, and pan drug-resistance (PDR) as resistance to all agents in all antimicrobial classes [7].

STATISTICAL ANALYSIS

Categorical variables were expressed as absolute number (n) and percentage (%) while continuous variables were expressed as mean (± standard deviation) or median (interquartile range), for normal and non-normal distributions, respectively. To assess data normality, the Kolmogorov–Smirnov test was performed and the logarithmic (Ln) transformation of continuous data was adopted when the variables did not present a normal distribution. Categorical variables were compared by the Chi-square test. Quantitative continuous variables were compared using Student's t-test and Mann–Whitney U test, for parametric and non-parametric results, respectively. P-values <0.05 were considered as statistically significant. Analyses were carried out using SPSS software (version 22.0).

RESULTS

Of the 1017 patients in whom at least one EA culture was performed, during the two years analyzed (June 1, 2017– May 31, 2019), only 555 were diagnosed with some type of pneumonia, of which 405 were ICU patients over 16 years old. Of the 405 patients, 235 patients developed VAP and 170 developed non-ventilator associated pneumonia (non-VAP), but only 153 attended all the diagnostic criteria applied in this study [Figure 1, Table 1]. A total of 58.0% (n=235) of ICU patients had VAP, of which 33.6% (n=136) were in ICU I, 17.3% (n=70) in ICU II, and 7.1% (n=29) in burn intensive unit care (BICU).

The clinical outcome of patients with VAP was similar to those of with non-VAP. However, the number of patients with VAP was slightly higher. The average age among the 235 patients was 57 years (42 ± 69 years; p-value=0.004). Of 235 patients with VAP, 160 (68.1%) were males and 75 (31.9%) were females (p-value=0.339; RR: 1.091; 95% confidence interval [CI]: 0.808–1.856; odds ratio: 1.225). In total, 32 (13.6%) patients had early-onset VAP and 203 (86.4%) had late-onset, (p-value=0.360; odds ratio: 0.751; 95% CI: 0.406–1.389; RR: 1.189). There were a total of 66 (28.1%) survivors and 164 (69.9%) non-survivors (p-value=0.528; odds ratio: 1.209; 95% CI: 0.786–1.860; RR: 1.085). As admissions diagnosis, 11 (4.7%) patients had abdominal cavity disease (p-value=0.093), 45 (19.1%) vascular and cardiac disease (p-value=0.748), 62 (26.4%) fractures and trauma (p-value=0.015), 24 (10.2%) burns (p-value=0.499), 14 (6%) neurological disease (p-value=0.583), 12 (5.1%) respiratory/pulmonary disease (p-value=0.139), 8 (3.4%) tumor/cancer (p-value=0.708), 15 (6.4%) infections (p-value=0.321), and 44 (18.7%) were diagnosed with other comorbidities (p-value=0.862) [Table 1].

Variables	Ventilator-Associated Pneumonia		p-value
	No (n: 170)	**Yes** (n: 235)	
Age (years), median (range)[a]	64 (46 – 75)	57 (42 – 69)	0.004
Sex, n (%)			
Males	108 (63.5)	160 (68.1)	0.339
Females	62 (36.5)	75 (31.9)	
Diagnostic on hospital admission, n (%)			
Abdominal cavity disease	17 (10)	13 (5.6)	0.093
Vascular and cardiac	34 (20)	44 (18.7)	0.748
Fractures and trauma	27 (15.9)	61 (26.0)	0.015
Burns 21	(12.4)	24 (10.2)	0.499
Neurological	8 (4.7)	14 (6.0)	0.583
Respiratory/pulmonar	15 (8.8)	12 (5.1)	0.139
Tumor/Cancer	7 (4.1)	8 (3.4)	0.708
Infections	7 (4.1)	15 (6.4)	0.321
Others	33 (19.4)	44 (18.7)	0.862
Clinical profile, n (%)			
Early-onset	18 (10.6)	32 (13.6)	0.360
Late-onset	152 (89.4)	203 (86.4)	
Clinical outcome, n (%)			
Survivors	57 (33.5)	71 (30,2)	0.479
Non-survivors	113 (66.5)	164 (69.9)	
Risk fator, n (%)			
IUC	39 (22.9)	33 (14)	0.021
CVC	22 (12.9)	23 (9.8)	0.319
IBC	44 (25.9)	67 (28.5)	0.558
DLC	55 (32.4)	57 (24.3)	0.072
OTI	41 (24.1)	64 (27.2)	0.480
ETI	107 (62.9)	153 (65.1)	0.654
TQT	12 (7.1)	28 (11.9)	0.106
Others Catheters	15 (8.8)	19 (8.1)	0.791
Antibiotic therapy during infection, n (%)			
Penicillins	100 (58.8)	136 (57.9)	0.848
1st, 2nd, 3rd generation cephalosporins	4 (2.4)	19 (8.1)	0.014
4rd generation cephalosporins	11 (6.5)	12 (5.1)	0.558
Carbapenems	92 (54.1)	146 (62.1)	0.106
Quinolones	13 (7.6)	33 (14.0)	0.045
Glycopeptides	102 (60.0)	139 (59.1)	0.863
Aminoglycosides	20 (11.8)	25 (10.6)	0.722
Macrolides/Lincosamides	6 (3.5)	15 (6.4)	0.201
Sulfamethoxazole-trimethoprim	0 (0.0)	5 (2.1)	0.056
Polymyxin	83 (48.8)	125 (53.4)	0.362
Other antibiotics	52 (30.6)	46 (19.6)	0.011
Antifungal agentes	1 (1.2)	4 (1.7)	0.666

Table 1: Analysis of demographic and clinical characteristics of patients with ventilator-associated pneumonia.

Continuous variables were expressed as median (inter-quartile range) and categorical variables were expressed as absolute number (n) and percentage (%).[a]Logarithmic transformation (Ln).

IUC: indwelling urinary catheter; CVC: central venous catheter; IBC: indwelling bladder catheters; DLC: double-lumen catheter; OTI: orotracheal intubation; ETI: endotracheal intubation; TQT: tracheotomy.

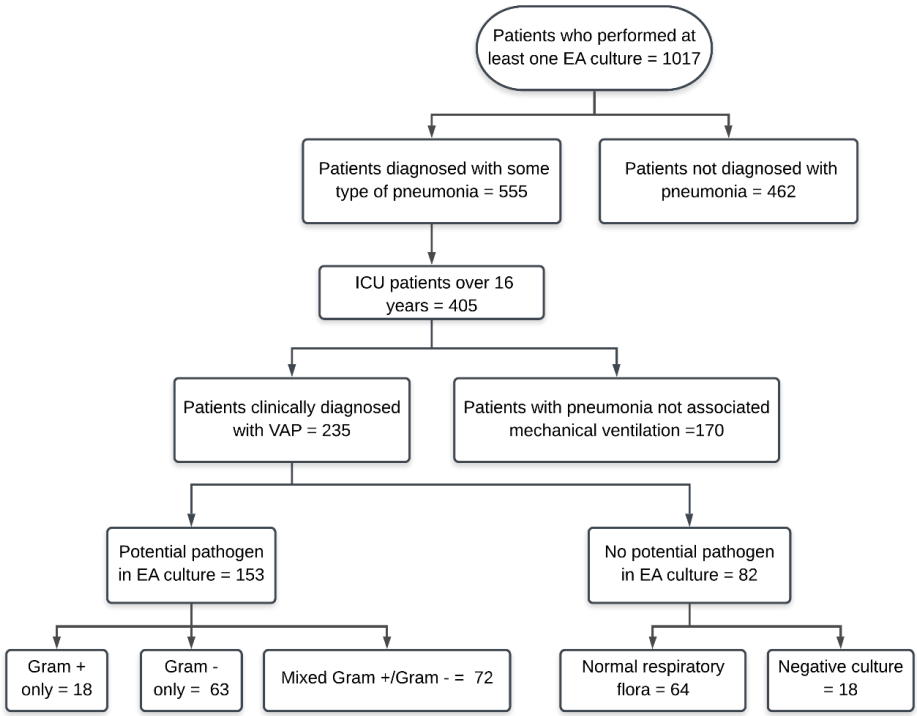

Figure 1: Bacteriological characteristics of EA samples obtained in the study period.

Of total, 33 (14%) patients used indwelling urinary catheter (IUC) (p-value=0.021), 23 (9.8%) central venous catheter (CVC) (p-value=0.319), 67 (28.5%) indwelling bladder catheter (IBC) (p-value=0.558), 57 (24.3%) double-lumen catheter (DLC) (p-value=0.072), 64 (27.2%) orotracheal intubation (OTI) (p-value=0.480), 153 (65.1%) endotracheal intubation (ETI)

(p-value=0.654), 28 (11.9%) tracheotomy (TQT) (p-value=0.106) and 19 (8.1%) other catheters (p-value=0.791) [Table 1].

All patients were treated with multiple antibiotics of different classes (penicillins, carbapenems, piperacillin-tazobactam, colistin, cephalosporins, glycopeptides, aminoglycosides, macrolides, sulfamethoxazole-trimethoprim, polymyxin, quinolones and/or others) used simultaneously. Furthermore, 136 (57.9%) patients were treated with penicillins

(p-value=0.848), 19 (8.1%) first/second/third generation cephalosporins (p-value=0.014), 12 (5.1%) 4th generation cephalosporins (p-value=0.558), 146 (62.1%) carbapenems (p-value = 0.106), 33 (14.0%) quinolones (p-value=0.045), 139 (59.1%) glycopeptides (p-value=0.863), 25 (10.6%) aminoglycosides (p-value=0.722), 15 (6.4%) macrolides/lincosamides (p-value=0.201), 5 (2.1%) sulfamethoxazole-trimethoprim (p-value=0.056), 125 (53.4%) polymyxin (p-value=0.362), 46 (19.6%) other antibiotics (p-value=0.011) and 4 (1.7%) antifungal agents (p-value=0.666) [Table 1].

The mortality was similar to what has been reported in previous studies and it may be due to severe infections or morbid state of the patients (Huang, et al., 2018). In addition, we found risk factors which were related to the VAP mortality 164 (69.8%), including elevated numbers of leukocytes (p-value= 0.024), neutrophils (p-value= 0.040), and other inflammatory cells and sepsis 120 (4.3%), p-value=0.012 [table 2].

Variables	Non-survivors	Survivors	p-value
Gender, male n (%)	178 (64,3)	85 (70,2)	0.488
PAV, n (%)	164 (69.8)	71 (30,2)	0,479
C-reactive protein (mg/l)	142,0 (78,4 - 219,0)	159,4 (80,5 - 232,4)	0.578
Leukocytes (/mm3)	12770 (9240 – 17760)	11585 (9055 – 14681)	0.024
Band (/mm3)	554 (118 – 1660)	553 (142 – 984) 0.310	
Neutrophils (/mm3)	9200 (6298 – 13050)	1940 (5980 – 11009)	0.040
Lymphocytes (/mm3)	1263 (807 – 1762)	1192 (878 – 1799)	0.890
Monocytes (/mm3)	588 (385 – 888)	608 (430 – 832)	0.894
Eosinophils (/mm3)	120 (0 – 448)	171 (0 – 343)	0.784
Platelets (/mm3)	243 (154 – 321)	228 (170 – 319)	0.855
Lactate (mmol/L)	1,80 (1,40 – 2,50)	1,70 (1,30 – 2,30)	0.103
Sepsis (yes/no)	120 (43,3)/ 144 (52,0)	45 (37,2)/ 71,4 (58,7)	0,012

Table 2: Univariate comparison between non-survivors and survivors.

Continuous variables presented as medians & interquartile ranges (25th - 75th percentile) (Mann-Whitney test used for analysis). Categorical variables presented as absolute numbers (n) and percentages (Chi-square test used for analysis).

With the results obtained from EA cultures, patients with VAP were grouped according to whom presented only Gram-positive, only Gram-negative, and mixed Gram-positive/negative, displaying no bacterial growth or only normal respiratory flora (NRF). Of 153 patients, 98 (64.4%) with VAP had only one pathogen, being the most common *Acinetobacter baumannii* with 41 (27.0%) isolates, *Pseudomonas aeruginosa* with 12 (7.9%), *Staphylococcus aureus* with 18 (11.8%) and *Klebsiella pneumoniae* with 11 (7.2%). Of the 64 patients who did not meet the VAP microbiological criteria, 43 (67.2%) were colonized by the main VAP causing organisms, and the number of infections by these organisms was higher than colonization [Table 3, Figure 1].

Organism	n= 153 (%)
Acinetobacter baumannii	41 (27.0)
Acinetobacter baumannii + Klebsiella pneumoniae	7 (4.6)
Acinetobacter baumannii + Pseudomonas aeruginosa	5 (3.3)
Acinetobacter baumannii + Escherichia coli	1 (0.7)
Acinetobacter baumannii+ Staphylococcus aureus	3 (2.0)
Acinetobacter baumannii + Enterobacter asburiae	1 (0.7)
Acinetobacter baumannii + Enterobacter cloacae	4 (2.6)
Acinetobacter baumannii + Enterobacter aerogenes	1 (0.7)
Acinetobacter baumannii + Stenotrophomonas maltophilia	1 (0.7)
Acinetobacter baumannii + Serratia marcens	2 (1.3)
Acinetobacter baumannii + Streptococcus sanguinis	1 (0.7)
Pseudomonas aeruginosa	12 (7.9)
Pseudomonas aeruginosa + Proteusmirabilis + Klebsiella penumoniae	1 (0.7)
Pseudomonas aeruginosa + Klebsiella pneumoniae	4 (2.6)
Pseudomonas aeruginosa + Serratia marcescens	2 (1.3)
Staphylococcus aureus	18 (11.8)
Staphylococcus aureus + Escherichia coli	3 (2.0)
Staphylococcus aureus + Klebsiella pneumoniae	4 (2.6)
Staphylococcus aureus + Klebsiella peumoniae + Streptococcus agalactiae	1 (0.7)
Staphylococcus aureus + Klebsiella pneumoniae + Stenotrophomonas maltophilia	1 (0.7)
Staphylococcus aureus + Streptococcus penumoniae	1 (0.7)
Staphylococcus aureus + Stenotrophomonas maltophilia	2 (1.3)
Staphylococcus aureus + Proteus mirabilis	1 (0.7)
Staphylococcus aureus + Klebsiella oxytoca	1 (0.7)
Escherichia coli	2 (1.3)
Klebsiella pneumoniae	11 (7.2)
Klebsiella pneumoniae + Escherichia coli	1 (0.7)
Klebsiella pneumoniae + Serratia marcescens	1 (0.7)
Klebsiella pneumoniae + Enterobacter cloacae	1 (0.7)
Klebsiella pneumoniae + Enterobacter cloacae+ Streptococcus anginosus	1 (0.7)
Klebsiella pneumoniae + Stenotrophomonas maltophilia	1 (0.7)
Stenotrophomonas maltophilia	5 (3.3)
Serratia marcescens	5 (3.3)
Serratia marcescens + Citrobacter freundii	1 (0.7)
Serratia marcescens + Citrobacter koseri	1 (0.7)
Enterobacter cloacae	2 (1.3)
Enterobacter aerogenes	2 (1.3)

Table 3: Specific microorganisms in patients with ventilator-associated pneumonia.

Colistin, polymyxin, tigecycline, and amikacin showed great sensitivity to most Gram-negative isolates. For *S. aureus*, the most sensitive antibiotics were lincomycin, rifampicin, trimethoprim/sulfamethoxazole and tigecycline. Most patients had XDR isolates, 64 (95.5%) *A. baumannii* isolates were XDR, the other 3 (4.5%) were sensitive to all antimicrobials tested. Only 4 (12.0%) patients had PDR *K. pneumoniae* isolates. *P. aeruginosa* (n=11; 44.0%) and *S. aureus* (n=13; 37.1%) presented various strains sensitive to all antibiotics [Table 3, Table 4].

Organism (gram-negative)	**AK**	**CN**	**CAZ**	**CRO**	**FEP**	**IMP**	**MEM**	**PTZ**	**CIP**	**TG**	**SXT**	**POL**	**COL**
	(%)	**(%)**	**(%)**	**(%)**	**(%)**	**(%)**	**(%)**	**(%)**	**(%)**	**(%)**	**(%)**	**(%)**	**(%)**
P. aeruginosa *(25)*	22 (88)	19 (76)	21 (84)	-	19 (76)	16 (64)	16 (64)	23 (92)	18 (72)	-	-	25 (100)	25 (100)
A. baumannii (67)	21 (31)	23 (34)	4 (6)	4 (6)	4 (6)	4 (6)	4 (6)	-	5 (8)	65 (97)	5 (8)	65 (97)	65 (97)
K. *pneumoniae* (3 4)	30 (88)	17 (50)	12 (35)	10 (29)	13 (38)	20 (59)	21 (62)	13 (38)	12 (35)	24 (71)	12 (35)	29 (85)	26 (76)
Organism (gram-positive)	**BZP**	**OXA**	**DA**	**E**	**LIN**	**R**	**CIP**	**TG**	**SXT**				
	(%)	**(%)**	**(%)**	**(%)**	**(%)**	**(%)**	**(%)**	**(%)**	**(%)**				
S. aureus (35)	2 (6)	24 (67)	15 (43)	13 (37)	35 (100)	35 (100)	22 (63)	34 (97)	34 (97)				

Table 4: Drug sensitivity profile in bacteria causing ventilator-associated pneumonia

AK: Amikacin; CN: gentamicin; AMP: ampicillin; ATM: aztreonam; CAZ: ceftazidime; CRO: ceftriaxone; FEP: cefepime; IMP: imipenem; MEM: meropenem; PTZ: piperacillin/tazobactam; CIP: ciprofloxacin; LEV: levofloxacin; TG: tigecycline; SXT: Trimethoprim/sulfamethoxazole; POL: polymyxin; COL: colistin; BZP: benzylpenicillin; OXA: oxacillin; DA: clindamycin; E: erythromycin; LIN: lincomycin; R: Rifampicin;

DISCUSSION

The microbial causes of VAP are diverse. Each of the microorganisms known to cause VAP shares an ability to exploit some defect in the patient's lung defenses, resulting from the pulmonary and systemic effects of critical illness and medical therapy, the alteration of the normal host-microbial flora by illness and antibiotic therapy, and the interference with normal airway protection and clearance mechanisms due to altered consciousness and airway devices [5]. In this retrospective cross-sectional study, we investigated the organisms in patients with VAP admitted to the ICU. The incidence of VAP in our study was 23.1%. This result was similar to other studies, in which the incidence was an average 25%, depending on the diagnostic criteria used [2,8]. About 35.6% of the patients had polymicrobial VAP and 64.4% showed mono-species cultures. The main isolates found were *A. baumannii, K. pneumoniae, P. aeruginosa* and *S. aureus*. These microorganisms were isolated regardless of VAP etiology (monomicrobial or polymicrobial). These results were similar to those found by other authors.

A. baumannii was the most commonly detected isolate in EA cultures of VAP patients, alone and/or associated with others microorganisms: 41 cultures had only *A. baumannii* (27.0%), 7 with *A. baumannii + K. pneumoniae* (4.6%), 5 with *A. baumannii + P. aeruginosa* (3.3%), 3 with *A. baumannii + S. aureus* (2.0%), 4 with *A. baumannii + E. cloacae* (2.6%), and 7 had *A. baumannii* associated with another pathogen (4.6%). Similar results were found in several studies related to the incidence of *A. baumannii* in intensive care unit (ICU) patients, especially in patients who had VAP [9–11].

No statistically significant difference was observed between the VAP and non-VAP groups regarding gender, clinical profile and deaths ($p>0.05$). For entry diagnosis, only patients diagnosed with fractures/trauma showed significant differences between VAP and non-VAP ($p<0.05$). Among the risk factors, only the IUC was significant ($p<0.05$), in which the relative value of patients with this invasive procedure was higher in non-VAP patients (22.9%). Moreover, a significant difference in the use of first/second/third generation carbapenems and other antibiotics ($p<0.05$) was observed. As age also showed a statistically significant result ($p<0.05$), it can be considered a risk factor for VAP. Although no significant statistical results were given, it was possible to observe the prevalence of late-onset VAP (n=203, 84.4%), and also the prevalence of death (n=164, 69.9%) in patients with VAP. Several studies have shown late-onset VAP as a risk factor for increased mortality [2,8,12–14]. However, in this study, this fact was not analyzed.

We observed differences in the prevalence of VAP in female (n=75, 31.9%) and male (n=160, 68.1%) patients. Several studies discuss the male gender as an independent risk factor for VAP [2,8,15]. According to Wu et al., 2019, it is believed that these differences in VAP risk are related to divergences in sex hormones and the distribution of infectious pathogens, as well as effects of gender-related genetic polymorphisms on immune responses, and differences in complications in men and women.

VAP accounts for at least a quarter of infections that occur in critically ill patients, accounting for about half of antimicrobial prescriptions in mechanically ventilated patients [2]. A total of 95.5% (n=64) of *A. baumannii* were classified as XDR, the other 4.5% (n=3) were sensitive to all antimicrobials evaluated. WERARAK, KIRATISIN and THAMLIKITKUL in 2010, reported in their study that *A. baumannii* was the most common isolated pathogen in VAP patients and 92.3% of them were MDR or PDR. In our study, we obtained only PDR *K. pneumonia* (n=4, 11.8%). BOZORGMEHR, BAHRANI, and FATEMI in 2017, reported that 33.3% of VAP cases were caused by PDR strains and 17.5% by XDR strains, with a prevalence of *A. baumannii* and *K. pneumoniae* isolates. We also detected a prevalence of XDR isolates of *K. pneumoniae* (n=21, 61.8%). *P. aeruginosa* presented the same proportion of XDR and sensitive strains (n=11, 44.0%). *S. aureus* presented similar proportions of sensitivity (n=13, 37.1%) with MDR and XDR (both with n=11, 31.4%). Our results emphasize the correct use of antibiotics in the treatment of VAP. Previous and empirical treatments can lead to the emergence of resistance (MDR, XDR or PDR). For this reason, it is important to

be alert to the risk factors for VAP, and to the criteria for the implementation of preventive drugs. It is also important to know prevention and treatment protocols in order to reduce VAP mortality [2,8,14].

In conclusion, VAP is a major problem in hospitalized patients at the University Hospital of Londrina. Age and trauma were significant risk factors in this study. The most common patterns were from XDR organisms, especially A. baumannii, P. aeruginosa, K. pneumoniae, and S. aureus. The knowledge of epidemiological and microbiological data from patients with VAP assist in the identification, prevention, and control of healthcare-related infections by multiresistant microorganisms.

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