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ORIGINAL ARTICLE

Demographic and clinical associations with Hospital-Acquired Pneumonia and Ventilator-Associated Pneumonia

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ABSTRACT

Objective: to verify the association of sociodemographic and clinical characteristics with Ventilator-Associated Pneumonia and Hospital-Acquired Pneumonia. **Method**: a cross-sectional study with secondary data obtained from notification forms of Healthcare-Associated Infections that occurred between January 2017 and December 2018, whose variables were analyzed by descriptive and inferential statistics. **Results**: Ventilator-Associated Pneumonia was more frequent in individuals between 18 and 59 years old and HAP in individuals aged 60 years and older (p=0.003). As for the unit where pneumonia was diagnosed, there was a higher frequency of Ventilator-Associated Pneumonia in Intensive Care Units, Burn Treatment Centers, and Burn Intensive Care Units (p <0.001). The frequencies of death were 48.9% of the cases with Hospital-Acquired Pneumonia and 69.2% of the cases of Ventilator-Associated Pneumonia (p <0.001). There was a significant association between bacterial culture and type of pneumonia. In the Ventilator-Associated Pneumonia group, 76.0% of patients had a positive culture, compared to 56.3% in the Hospital-Acquired Pneumonia group (p<0.001). The most frequent microorganisms were *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, and *Pseudomona saeruginosa*. **Conclusion**: there was a statistically significant association between type and pneumonia and age, with more frequent Ventilator-Associated Pneumonia in young people and Hospital-Acquired Pneumonia in elderly people. There was also a significant association between type of pneumonia and the unit, with Ventilator-Associated Pneumonia being more frequent in intensive care units and burns. Death was more frequent in cases of Ventilator-Associated Pneumonia, with a significant association.

Descriptors: Ventilator-Associated Pneumonia; Healthcare-Associated Pneumonia; Cross Infection; Nursing; Risk Factors.

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INTRODUCTION

The Healthcare-Associated Infection (HAI) prevention measures were reviewed in 2017 by the Brazilian Health Regulatory Agency (ANVISA - *Agência Nacional de Vigilância Sanitária*), in order to keep the prevention measures protocols to reduce HAIs updated in the Brazilian scenario[1]. In 2019, the diagnostic criteria for infections went through changes, including Ventilator-Associated Pneumonia (VAP) and Hospital-Acquired Pneumonia (HAP)[2].

VAP are infections for more than two calendar days, with Day 1 (D1) being the day on which mechanical ventilation (MV) starts; on the date of infection, the patient was on MV or the mechanical respirator had been removed the day before[2-3].

VAP rates may vary depending on the affected patient population. According to a study conducted by Manfredini *et al*.[4], incidence increases with MV permanence and indicates rates of approximately 3% per day during the first five days of MV and then 2% for each day. Concerning mortality, 33% of those hospitalized with VAP died with a direct association with infection.

Among the main occurrences of HAIs, there is also HAP, which is acquired in the health service, but not associated with MV use[2]. At the moment, as there are virtually no requirements to monitor or report HAP cases, hospitals are less likely to monitor their own incidence and the associated damage[5].

The study carried out by Luyt *et al*.[6] indicates that HAP and VAP prevention remains a difficult and complex task. There was a relationship between the main microorganisms responsible, geographical areas, clinical and demographic conditions of patients in Intensive Care Units (ICUs), length of hospital stay, ICU stay, among other risk factors.

In a study conducted in 183 hospitals with 11,282 patients, of which 452 had one or more HAIs, researchers retrospectively reviewed medical records and estimated that there were 648,000 patients with 721,800 HAIs in US hospitals in 2011[7].

In 2020, Patty *et al*.[8] demonstrated that HAP incidence was 0.64 cases per 1,000 patients/day. The most prominent associated factors were advanced age and the presence of comorbidities. As a protective factor against the development of this infection, there was an emphasis on raising the head of the bed, with a 26% reduction in the chances

of developing the infection.

It is noteworthy that HAIs reach an average of 14% of hospitalizations nationwide and of the 234 million patients who are operated per year worldwide, on average, one million die[9].

According to Souza *et al*.[10], the high risk of HAI-related mortality is closely associated with the performance of invasive diagnostic and therapeutic procedures, the severity of the underlying disease that affects patients, the infection site, the adequacy of therapy and the sensitivity of microorganisms to antimicrobials.

Currently, there are several prevention strategies based on scientific evidence, which are proven effective when performed together[11]. In an integrative review, several studies on strategies for VAP prevention were analyzed. Of these, 95.6% indicated head elevation between 30º and 45º; 82.6% indicated oral hygiene; and 60.8% pointed to daily awakening of sedation weaning. Prophylaxis for gastric ulcers was mentioned in 47.8% of the articles. In a lower frequency, cuff maintenance was reported in 43.4%, and subglottic aspiration in 21.7%.

An observational study, conducted in 21 hospitals in an integrated health system, carried out interventions that included basic nursing care in order to prevent HAP, such as mobilization, vertical feeding, swallowing assessment, sedation restrictions, elevated headboard and oral care. Such measures resulted in a significant reduction in HAPs, from 5.92 to 1.79 per 1000 admissions[12].

Thus, a package of measures for VAP prevention, currently called bundles, was created, proposed by the Center for Disease Control and Prevention in the United States (CDC) (2003)[13], based on scientific evidence listed in the *5 million lives* campaign of the Institute for Healthcare Improvement (IHI)[14]. Considering the severity of the disease and based on risk factors for Healthcare-Associated Pneumonia, ANVISA(2017)[1] listed the main prevention measures divided between general measures, specific measures and other measures for the surveillance of each one pneumonia in hospitals.

The Ministry of Health (MoH) implemented, through Ordinance 2,216 of 1998, the Hospital Infection Control Committee (HICC). HICC works to reduce the incidence and severity of the progression of

inpatients, reduce hospital costs by controlling and preventing HAIs by applying bundles. It is worth mentioning that nursing actions are essential for the development of services. Nursing actions routinely inspect all units and the development of the work of health professionals, develop and update standard operating procedures, carry out epidemiological surveillance of HAIs, strengthen the knowledge of professionals through permanent and continuing education, among other functions[14].

Based on herein arguments, this study aims to verify the association of sociodemographic and clinical characteristics with VAP and HAP.

METHOD

This is an analytical, cross-sectional and quantitative study, which used secondary data obtained from HAI notification forms as an information source. The study was carried out at the University Hospital of *Universidade Estadual de Londrina* (UH/UEL), located in the city of Londrina, state of Paraná, Brazil.

The studied population covered all reported cases of individuals who had HAP or PAV. Adult patients, aged 18 and over, admitted to emergency rooms (ER), inpatient units (IU), ICU, Burn Treatment Centers (BTC), or Burn Intensive Care Units (BICU), diagnosed with HAP or VAP from January 2017 to December 2018 have been included. HAP and VAP diagnoses were performed by a HICC physician, according to the International Disease Code (ICD-10) classification and ANVISA definition[3]. Notified cases where the records had incomplete data have been excluded.

Patient identification was performed by active search, considering patients with antimicrobial prescription. In the hospital where the study was conducted, antibiotic therapy is started only after HICC releases. In this regard, with the work of this committee, it is possible to identify all patients who have been prescribed antimicrobials. After identifying patients with some type of infection, a suspicion of HAI is opened; for confirmed cases, the HAI notification form will be used.

The HAI notification form was prepared by the HICC team according to the criteria established by ANVISA[3], containing the clinical, laboratory, and imaging items. Completion is carried out by undergraduate

volunteers/HICC interns, trained by a nurse, PhD in education and responsible for the sector, during the course of patient hospitalization, i.e., interns follow up and update the information, from notification to discharge or death.

All data from the HAI notification form were collected by typing in an Excel spreadsheet. It is worth mentioning that this form was already in use before the data collection period and proved to be complete, for the HICC team, regarding HAI-related data.

Data collection was carried out from March to December 2019 by two researchers trained by the researcher guiding this research, and it was performed in the HICC room, once a week in the afternoon.

The following demographic and clinical variables were collected: sex (male or female), age (in years), length of hospitalization stay, length of hospitalization stay until pneumonia diagnosis, admission unit and unit where pneumonia was diagnosed (ER, IU, ICU, BTC, or BICU), type of pneumonia (HAP or VAP), diagnostic cultures (aspirate of tracheal secretion and/or blood culture), type of microorganism, and death.

Diagnostic cultures were performed at the request of the physician responsible for the patient, considering clinical (hyperthermia, changes in tracheal secretion), laboratory (leukogram results), and imaging (x-ray) aspects.

Tracheal secretion collection was performed by aspiration of the airways using a catheter. Blood culture was performed from two peripheral vein or artery punctures and blood collection in aerobic and anaerobic blood culture bottles. After collection, the material was sent to the laboratory for clinical analysis at HU/UEL for tracheal secretion and blood culture analysis using the automated Bactec™ system.

The numerical variables were categorized into age (18 to 59 years old and 60 old and older), length of hospitalization stay (up to 30 days and 31 days or more) and length of hospitalization stay until diagnosis (up to 14 days and 15 days or more).

Data analysis was performed using the Statistical Package for the Social Sciences (SPSS®), version 20.0. HAP and VAP (independent variables) were associated with sex, age, length of stay, length of stay until

diagnosis, unit of stay, deaths and diagnostic cultures (dependent variables), using chi-square test. The level of significance adopted was 5%.

The study was approved by the Research Ethics Committee of *Universidade Estadual de Londrina* (REC/UEL) according to the Directives and Regulatory Norms for Research on Human Beings, Resolution 466/2012 of the Brazilian National Health Council (CNS – *Conselho Nacional de Saúde*), under CAAE (*Certificado de Apresentação para Apreciação Ética* - Certificate of Presentation for Ethical Consideration) 00745218.0.0000.5231, Opinion 2,978,943, issued on October 24, 2018.

RESULTS

In the period analyzed, 573 cases of HAP and 146 of VAP were reported, totaling 719 cases, and all the notified cases constituted the sample of this study. Among the 719 reported cases, two patients had both notification of HAP and VAP.

Considering both types of pneumonia, most patients were male. Concerning age, there was a higher frequency of elderly people with HAP, while for VAP, individuals up to 59 years old were more frequent. The association between age and type of pneumonia was significant (p=0.003) (Table 1).

Concerning length of hospital stay, in both groups, the period up to 30 days was more frequent and, with regard to length of hospitalization stay until pneumonia diagnosis, it stood out up to 14 days. There was no significant association between type of pneumonia and total length of stay and for pneumonia diagnosis.

The admission unit with the highest number of cases was the ER. There was a significant association between admission unit and type of pneumonia (p <0.001), with a higher frequency of VAP in the ICU/BICU/BTC group. There was also a significant association between the unit where pneumonia was diagnosed and type of pneumonia (p <0.001), with a higher frequency of VAP in the ICU/BICU/BTC group.

In 48.9% of notified cases of HAP and 69.2% of cases of PAV, patients died, with a significant association between death and type of pneumonia (p <0.001).

In 574 cases (79.8%) diagnostic cultures were performed (tracheal secretion aspirate and/or blood culture).

Table 1 - Descriptive analysis of the demographic and clinical characteristics of the 719 cases of pneumonia according to type of pneumonia and probability values (p) associated with chi-square test. Londrina, PR, Brazil, 2019

Demographic and clinical variables	Hospital-acquired pneumonia (n=573) n	%	Ventilator-associated pneumonia* (n=146) n	%	P value†
Sex					
Male	355	62.0	89	61.0	0.825
Female	218	38.0	57	39.0	
Age (years)					
18 to 59	227	39.6	78	53.4	0.003
60 or older	346	60.4	68	46.6	
Length of hospitalization stay					
Up to 30	379	66.1	98	67.1	0.823
31 or more	194	33.9	48	32.9	
Length of hospitalization stay until pneumonia diagnosis					
Up to 14 days	480	83.8	126	86.3	0.453
15 or more	93	16.2	20	13.7	
Admission unit					
ER‡	451	78.8	101	69.2	<0.001
IU§	61	10.6	5	3.4	
ICU/BICU/BTC§	61	10.6	40	27.4	
Unit where pneumonia was diagnosed					
ER†	222	38.7	38	26.1	<0.001
IU‡	166	29.0	10	6.8	
ICU/BICU/BTC‖	185	32.3	98	67.1	
Death					
Yes	280	48.9	101	69.2	<0.001
No	293	51.1	45	30.8	

*Mechanical Ventilation; †chi-square test; ‡Emergency Room; §Inpatient unit; ‖Intensive Care Units, Burn Intensive Care Units, and Burn Treatment Centers.

In both groups, most cases had a positive culture (HAP=56.3% and VAP=76.0%), with a significant association between positive culture and type of pneumonia (p <0.001).

With regard to type of microorganism, the most frequent were *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Staphylococcus aureuse*, and *Pseudomonas aeruginosa*. The association between microorganism and type of pneumonia was significant only for *Staphylococcus aureus* (p <0.001), with the presence of the microorganism being more frequent in cases of VAP, when compared to HAP (Table 2).

Table 2 - Descriptive analysis of the diagnostic cultures of the 574 cases of pneumonia, according to type of pneumonia and probability values (p) associated with chi-square test. Londrina, PR, Brazil, 2019

Variables	Hospital-acquired pneumonia (n=428)		Ventilator-associated pneumonia* (n=146)		P value†
	n	%	n	%	
Positive diagnostic culture					
Yes	241	56.3	111	76.0	<0.001
No	187	43.7	35	24.0	
Acinetobacterbaumannii					
Yes	109	25.5	39	26.7	0.766
No	319	74.5	107	73.3	
Klebsiellapneumoniae					
Yes	63	14.7	24	16.4	0.617
No	365	85.3	122	83.6	
Staphylococcus aureus					
Yes	52	12.1	34	23.3	<0.001
No	376	87.9	112	76.7	
Pseudomonasaeruginosa					
Yes	50	11.7	17	11.6	0.990
No	378	88.3	129	88.4	
Cândida spp					
Yes	42	9.8	12	8.2	0.569
No	386	90.2	134	91.8	
Coagulase-negative staphylococci					
Yes	25	5.8	11	7.5	0.466
No	403	94.2	135	92.5	
Gram-positive cocci					
Yes	21	4.9	4	2.7	0.268
No	407	95.1	142	97.3	
Enterobacterclocae					
Yes	14	3.3	8	5.5	0.230
No	414	96.7	138	94.5	
Escherichia coli					
Yes	14	3.3	5	3.4	0.929
No	414	96.7	141	96.6	
Serratiamarcescens					
Yes	11	2.6	8	5.5	0.900
No	417	97.4	138	94.5	

*Mechanical Ventilation; †chi-square test.

DISCUSSION

The results show a sample made up of male patients aged over 60 years for cases of HAP and up to 59 years for cases of VAP. The study by Baker and Quinn[15] confirms that younger patients are also at risk and acquire pneumonia while in hospital.

Due to the high rate of comorbidities faced by the elderly population in Brazil, this age group has a high prevalence of hospitalizations[16]. The hospital setting of the research also suffers from this reality; in addition to being a reference for critically ill patients, it serves a high number of elderly people with chronic diseases and their physiological complications.

One justification is that they develop comorbidities throughout their lives that make them more susceptible to diseases, with a decrease in their activities, quality of life and, consequently, increasing the frequency of hospitalization[10]. In the study that assessed the risk factors for HAP, it was described that patients in all types of hospital units are at some risk for developing HAP, also highlights, increased risk for those undergoing surgery[15].

There was a significant association between age and type of pneumonia; in patients aged 18 to 59 years, VAP was more frequent. This is justified by the fact that young people are more intubated than elderly people. Often in hospital services, including the institution of the present study, patients with an unfavorable prognosis and advanced age are treated with non-invasive measures with the acceptance of patients' relatives. These measures that aim to provide comfort, relieve symptoms that cause suffering to patients, in addition to recognizing death as a natural process, are characterized by palliative care[16-18].

In our study, most patients were diagnosed with pneumonia within 14 days of hospitalization. In a study on VAP in ICUs, there was a positive association between pneumonia occurrence and length of hospital stay> 15 days and MV time> 10 days[19]. On the other hand, there is a strong discussion by researchers in defense that ICUs, despite presenting a greater risk for acquiring pneumonia, work in a systematic way, complying with the protocols for VAP prevention[11,17-18].

In relation to the unit where pneumonia was diagnosed, more than a third of the cases occurred in the ER. Despite

being considered a gateway unit, in the service analyzed, patients remain hospitalized and are often intubated. According to the study conducted by Di Pasquale *et al*.[20] seventy-three percent of HAP cases originated outside ICUs.

Supporting this discussion, a study carried out in the urgency and emergency service emphasized some factors that contribute to this scenario. They are spontaneous demand, overcrowding, long stay of patients in these units, lack of materials/beds/human resources. Therefore, it is necessary to reorganize the work processes, in order to reduce these modifiable risk factors for acquiring HAP[21].

It is important to note that the profile of patients seen in ER ranges from low complexity to the most severe. In an exploratory study carried out in an ER, in the city of Boa Vista, state of Roraima, at a hospital similar to our study, as it is an institution linked to teaching and of high complexity, it pointed out that 69.28% of the patients were classified as in intensive care, 13.86% in semi-intensive care and 11.45% in highly dependent care for the nursing service[22]. This demonstrates that the conditions are also inadequate for the nursing team, resulting in work overload and decreased quality of care.

We have found an association between unit and type of pneumonia, and in the ICU/BICU/BTC group, the frequency of VAP was 34.6%. ICUs have highly pathogenic microorganisms that often colonize patients leading to infections that are difficult to treat. It is known that the risk factors are divided into modifiable ones that can be associated with the environment, and not modifiable, related to individuals, such as age, severity score and comorbidities[23].

Moreover, care in ICUs is aimed at users with systemic instability who have greater complexity in care and who suffer from excessive manipulation and invasive procedures, which increases the risk of infections[18].

VAP is one of the most frequent complications in patients affected by burns, and is frequently found in BICU. Intense sedation and mechanical ventilation support are often used as treatment, which may be related to the higher frequency of VAP[24]. Bundle implementation stands out as an institutional protocol can reduce VAP rates, in order to ensure patient safety[25].

There was a significant association

between death and type of pneumonia, and of the 146 cases of VAP, 101 died. According to Weyland *et al*.[26], mortality associated with MV varies between 20% and 60% and this can be a result of several factors such as severity of underlying diseases, organ failure ,and virulent etiological agent involved. There is evidence that the risk of death in cases of pneumonia caused by gram-negative microorganisms can reach 68%[27].

In the present study, the presence of types of microorganisms by culture was also identified. According to the São Paulo Association of Epidemiology and HAI Control (*Associação Paulista de Epidemiologia e Controle de IRAS*)[28], etiological agents vary according to MV time and microbiota of each health institution; however, in general they are divided into two groups: early-onset VAP (when it occurs within the first four days of MV), with a predominance of multi-sensitive agents *Streptococcuspneumoniae*, *Haemophilusinfluenzae*, *Staphylococcus aureus* oxacillin-sensitive and the enterobacteria *Escherichia coli, Klebsiellapneumoniae, Enterobacter spp, Proteus spp*, and *Serratiamarcescens*.

In late VAP, resistant *Staphylococcus aureusoxacillin* predominates, non-fermenting gram-negative bacteria (GNB): *Pseudomonasaeruginosa*, *Acinetobacter spp* and other GNB with resistance pattern compatible with extended spectrum beta-lactamase (ESBL) and carbapenemase producers (blaKPC gene, NDM, etc.)[28]. According to the study "SENTRY Antimicrobial Surveillance Program", the six main pathogens accountable for 80% of pneumonia related to Healthcare-Associated Pneumonia were *Staphylococcus aureus* (30%), *Pseudomonasaeruginosa* (24%), *Klebsiella spp* (11%), *Escherichia coli* (8%), *Acinetobacter spp*, and *Enterobacter spp* (7%)[29].

Therefore, it is justified to perform cultures routinely as well as the sensitivity test to antimicrobials. The main etiologic agents of VAP and sensitivity to antimicrobials differ between services, which is why epidemiological surveillance is necessary in an attempt to contribute to adequate therapy institution. These data show the importance of the HICC work. Care and strategies must be determined for each team, respecting local uniqueness[28].

Concerning VAP, there was an association with *Staphylococcus aureus*,

which are gram-positive cocci with morphological and physiological characteristics that contribute to their virulence. They are sensitive to high temperatures, disinfectants, and antiseptic solutions. They survive dry surfaces for a long time and are part of an individual's microbiota, in the epidermis and nasopharynx in 15% of healthy individuals. They are responsible for many of the HAIs due to these characteristics[30].

As a limitation of the study, we pointed out care non-assessment, described in medical records, which could result in the analysis of other variables associated with Healthcare-Associated Pneumonia.

For practice and research, it is necessary that future studies take place, especially longitudinal studies that follow up patients with pneumonia from diagnosis to discharge from hospital or death, in addition to the need to implement bundles, thus ensuring that new standards are incorporated into care practice, reducing the risk of adverse events such as HAI.

CONCLUSION

There was a statistically significant association between type and pneumonia and age, with VAP being more frequent in young people. There was also a significant association between type of pneumonia and unit, with more frequent VAP in ICUs, BICUs, and BTCs.

The association between type of pneumonia and death was also statistically significant, and of the 146 cases of VAP, 101 died. The association with the microorganism and the most frequent pneumonia was VAP only for *Staphylococcus aureus*. Among the two types of pneumonia (VAP and HAP), the most frequent microorganisms were *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*.

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