


Profile and antimicrobial sensitivity of bacteria in culture of patients with mechanical ventilation-associated pneumonia during the COVID-19 pandemic: An integrative review

 <https://doi.org/10.56238/sevned2024.001-014>

Hiago José Chaves Rodrigues¹, Sueli de Souza Costa², Felipe Ruda Silva Santos³, Jose Carlos Aragão Silva Júnior⁴, Denise Francisca dos Santos⁵ and Expedito Duarte de Lima⁶

ABSTRACT

Respiratory failure caused by the COVID-19 virus in severe cases requires the use of mechanical ventilation. In this context, ventilator-associated pneumonia (VAP) is a nosocomial infection that develops frequently and is related to a worse prognosis. Gram-negative bacteria are commonly isolated in cultures of tracheal secretion. However, the abusive use of antibiotics during the pandemic may have contributed to the selection of resistant bacteria. **OBJECTIVE:** To identify the main bacterial etiologies and antimicrobial susceptibility profile in patients with VAP during the COVID-19 pandemic. **METHODOLOGY:** This is a descriptive research, with a qualitative approach, in the form of an integrative literature review. Between March 2020 and May 2022, we searched for publications on bacterial etiologies and antimicrobial susceptibility profile in cultures of patients with VAP in the Scopus, Cochrane Library, US National Library of Medicine (PubMed), and International Health Sciences Literature (Medline) databases. The results of the selected articles were shown in a table. **RESULTS:** In 14 studies, Gram-negative bacteria were more prevalent. *Pseudomonas aeruginosa* was identified in 12 studies; *Klebsiella pneumoniae* in 10 studies; *Acinetobacter baumannii* in eight; *Staphylococcus aureus* was isolated in six studies. There was an increase in antimicrobial resistance, especially to carbapenems. *Pseudomonas aeruginosa* strains were resistant to amikacin, colistin, cefepime, ceftazidime, piperacillin/tazobactam (PIP/TAZ); *Klebsiella pneumoniae* has demonstrated extensive resistance to extended-spectrum cephalosporins, fluoroquinolones, and aminoglycosides. **CONCLUSION:** Knowledge of the profile of the main bacterial etiologies, as well as antimicrobial resistance, is essential for the adoption of prophylactic measures and treatment for VAP.

Keywords: Ventilator-Associated Pneumonia, Etiology, Bacteria, Antibiogram.

¹ Undergraduate student in Medicine - Federal University of Maranhão

² Doctor in Dental Sciences - Federal University of Maranhão

³ Anesthesiology Resident - Hospital Universitário João de Barros Barreto - UFPA

⁴ Physician - Federal University of Maranhão

⁵ Medical Doctor - Ceuma University

⁶ Undergraduate student in Medicine - Federal University of Maranhão



INTRODUCTION

COVID-19 is an infectious disease caused by severe acute respiratory syndrome-associated coronavirus 2 (SARS-CoV-2) (WANG et al., 2020). The pandemic unleashed by this new coronavirus has become the most significant in the recent history of humanity, with major impacts on the economy, public health, and the mental health of society as a whole (ALEXANDRINO, 2020). In this context, COVID-19 was classified as a pandemic by the WHO on March 11, 2020 (PAHO, 2020). In Brazil, the first cases were confirmed in February, leading to the implementation of a series of measures aimed at slowing the progression of infection cases (DIÁRIO OFICIAL DA UNIÃO, 2020).

SARS-CoV-2 is spread mainly by droplets, respiratory secretions, and direct contact with the infected patient (FAN et al., 2020). It is commonly a curable disease, but it can also be fatal, especially in high-risk groups, such as the elderly and those with chronic and/or pre-existing diseases (ARRUDA et al., 2020). In severe cases, it causes progressive respiratory failure (CAMPOS et al., 2020). In these clinical conditions, patients are referred to an Intensive Care Unit (ICU) for treatment with non-invasive or invasive ventilation. These intensive care procedures are recommended when there is deterioration in respiratory function, resulting in a decrease in the level of consciousness, increased respiratory rate, and the use of accessory muscles, which requires the use of supplemental oxygen (LIN et al., 2020).

In this scenario, ventilator-associated pneumonia (VAP) is one of the most prevalent infections, frequently developing in patients intubated for more than 48 hours (TEIXEIRA, 2021). This nosocomial infection is directly linked to the retention and aspiration of contaminated upper airway secretions, as well as the presence of resistant microorganisms on ICU surfaces and materials (NATIONAL HEALTH SURVEILLANCE AGENCY, 2017). Due to the severity of VAP, empirical treatment with broad-spectrum antibiotics is quickly initiated (LEAL et al., 2019).

According to studies, Gram-negative bacteria such as *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa*, and Gram-positive bacteria such as *Staphylococcus aureus*, are the most commonly isolated microorganisms from tracheal cultures (CANZI et al., 2016; COAST; MOTTA; ALFRADIQUE, 2018; CAVALCANTE et al., 2020). However, due to the abusive use of antibiotics during the COVID-19 pandemic, species such as *Mycoplasma pneumoniae*, *Haemophilus influenzae*, *beta-lactamase-resistant Klebsiella pneumoniae*, *Enterobacter sp.*, *Chlamydia sp.*, *Enterococcus faecium*, and *Serratia marscecens* they are also found in tracheal secretion culture (SILVA et al., 2021). Therefore, an adequate antimicrobial management program, as well as protocols for early detection of infections, based on the hospital bacterial profile, is essential to overcome this problem (MELO et al., 2019).



The indiscriminate use of antibiotics is considered the main factor for the development of bacterial resistance, often caused by the lack of knowledge of those who use them or by the difficulty of accessing health services, which leads the individual to self-medication (CANTÓN et al., 2020; HELLYER et al., 2020; LEAL et al., 2021). This situation is even more evident in the current scenario of the COVID-19 pandemic and, therefore, studies focusing on bacterial etiologies that presented microbial resistance to antibiotics are necessary.

The aim of this study is to conduct an integrative review in order to identify the main bacterial etiologies, as well as antibiotic sensitivity, of patients with ventilator-associated pneumonia (VAP) during the COVID-19 pandemic.

METHODOLOGY

This is a descriptive research, with a qualitative approach, in the form of an integrative literature review, whose objective is to synthesize knowledge from data from the theoretical and empirical literature, allowing a consistent construction of knowledge (PEREIRA et al., 2018; SOUZA et al., 2010).

The research was composed of five guiding stages: 1) Elaboration of the main guiding question of the research: "What is in the literature on bacterial etiologies and the profile of antimicrobial susceptibility in cultures of patients with VAP during the COVID-19 pandemic?"; 2) Search for studies related to the theme published in the years 2020 to 2022, in accordance with the inclusion and exclusion criteria; 3) Data collection; 4) Critical analysis of the selected articles and 5) Presentation and discussion of results.

The search for articles was carried out in a round of research in the following databases: Scopus, Cochrane Library, US National Library of Medicine (PubMed) and International Health Sciences Literature (Medline). Based on the guiding question of the research, the following descriptors were associated, according to the Health Sciences Descriptors (DeCS): "ventilator-associated pneumonia and bacteria and etiology or ventilator-associated pneumonia and antibiogram"

The search for publications related to the theme took place in the time interval between March 2020 and May 2022, and this period of publication of articles was established in view of the time elapsed between the beginning of the COVID-19 pandemic and the completion of this research.

Inclusion criteria were primary and original articles that addressed at least one of the specific objectives of the study, published in English or Portuguese during March 2020 to May 2022. Exclusion criteria were studies that were not available in full text, free of charge and that were duplicates.

The results of the selected articles were arranged in a systematic analysis instrument, made in the Microsoft Word 2019 program, containing year of publication, authors, objectives, and main results.

As this is a literature review and does not directly involve research with humans, this study did not require approval from the Research Ethics Committee. This work is based on the guidelines and regulatory standards established in resolutions No. 466/2012 and 580/2018 of the National Health Council of the Ministry of Health.

RESULTS

The descriptors and the association between them and the databases used can be seen in Table 1.

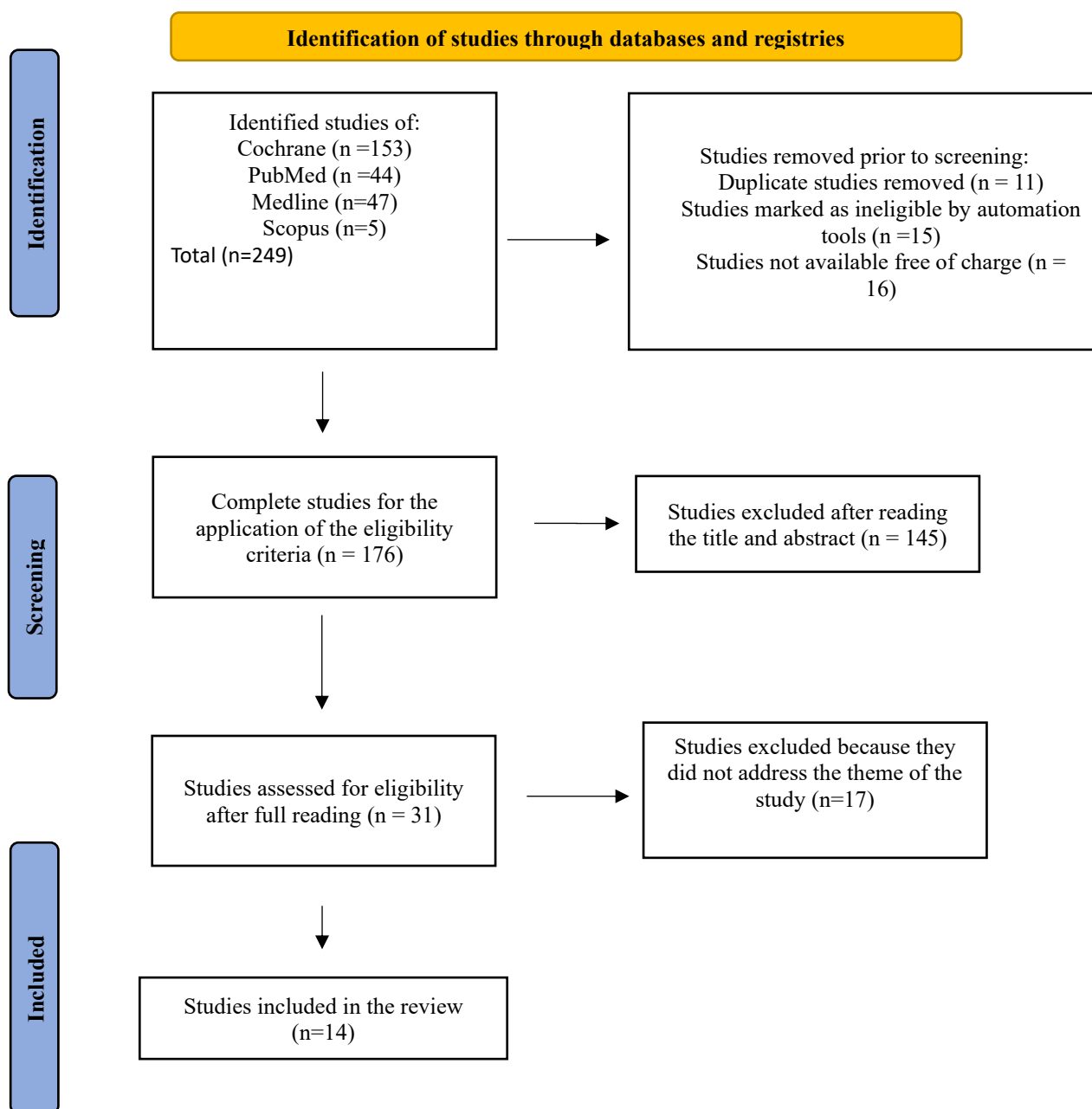
Table 1: Disposition of the number of articles according to the arrangements of the descriptors used in the database search.

Association of descriptors:	Cochrane Library	SCOPUS	MEDLINE	PUBMED
"Ventilator-Associated Pneumonia AND Bacteria AND Etiology OR Ventilator-Associated Pneumonia AND Antibioqram"	153	5	47	44
Total:	153	5	47	44

Source: Authors. Data were obtained from the COCHRANE LYBRARY, SCOPUS, MEDLINE and PUBMED databases.

The first stage of the research process resulted in a total of 249 articles. Of these, 11 duplicate articles were removed and 15 were not available due to an error in the online source of the study and 16 articles were not freely available. After reading the title and abstract, 145 articles were excluded because they did not address the theme of the study, then, after reading the full study, 17 articles were discarded because they did not meet the inclusion criteria. Figure 1 illustrates the schematization of the research process employed.

Figure 1 – Flow Diagram



FONTE: PAGE et al. (2021).

Through the methodology used in this research, 14 articles published between the years 2020 (n=3; 21%), 2021 (n=7; 50%) and 2022 (n=4; 28%) were selected. Of these, six (42%) are multicenter studies, while eight (57%) are monocenter. The data shown in Chart 1 allow the visualization of the main bacterial etiologies, as well as the antimicrobial susceptibility profile.

Table 1: Summary of articles published in this integrative review.

Author and year	Type of production	Objectives	Main results
MARJANO VIC et al., 2021	Randomized, multicenter, controlled, and open-label.	To identify whether continuous regulation of the tracheal cuff using a pneumatic device is preferable to intermittent regulation using a portable manometer in reducing the incidence of VAP in patients with severe trauma.	Greater colonization by <i>Staphylococcus aureus</i> (n=48 [44%]), <i>Haemophilus influenzae</i> (n=23 [21%]) and <i>Escherichia coli</i> (n=19 [17%]) was identified in early VAP and <i>Staphylococcus aureus</i> (n=15 [28%]), <i>Pseudomonas aeruginosa</i> (n=10 [19%]) and <i>Escherichia coli</i> (n=9 [17%]) in late VAP.
YOSHIMURA et al., 2022	Multicenter, open-label, randomized non-inferiority clinical trial.	To compare the clinical response to Gram stain-guided restricted antibacterial therapy to broad-spectrum antibacterial therapy for patients with VAP.	<i>Staphylococcus aureus</i> (n = 103 [50.0%]) was the most frequently isolated bacterium from endotracheal aspirate, followed by <i>Klebsiella sp.</i> (34 [16.5%]) and <i>Haemophilus influenzae</i> (20 [9.7%]).
TITOV et al., 2020	Randomized, controlled, double-blind phase 3 study	To evaluate the efficacy and safety of imipenem/cilastatin/relebactam in the treatment of hospital-acquired/ventilator-associated bacterial pneumonia (HABP/VABP).	The most frequent pathogens were <i>Klebsiella pneumoniae</i> , <i>Pseudomonas aeruginosa</i> , <i>Acinetobacter calcoaceticus-baumannii complex</i> and <i>Escherichia coli</i> . Regarding antimicrobial susceptibility, 79.7% of patients in the imipenem/cilastatin with relebactam (IMI/REL) group and 65.8% in the piperacillin/tazobactam (PIP/TAZ) group had all of these baseline pathogens susceptible to the respective drugs.
DAMAS et al., 2022	This is a prospective, multicenter, randomized, controlled, double-blind study.	To evaluate the potential benefit of the noble metal coating of endotracheal tubes for the prevention of VAP.	<i>Pseudomonas aeruginosa</i> , <i>Staphylococcus aureus</i> , <i>Klebsiella pneumoniae</i> and <i>Enterobacter cloacae</i> were the microorganisms most associated with VAP.
HABIB et al., 2020	Monocentric randomized clinical study.	To evaluate the role of probiotics in VAP prophylaxis in patients critically injured.	The bacterial species <i>Pseudomonas sp.</i> , <i>Klebsiella sp.</i> , <i>Acinetobacter sp.</i> and <i>Streptococci sp.</i> There were more incidents.
AKBIYIK et al., 2021	Randomized controlled experimental study.	To investigate the effect of oropharyngeal aspiration on the incidence of VAP-associated pneumonia immediately prior to the patient's change of position.	<i>Acinetobacter baumannii</i> and <i>Pseudomonas aeruginosa</i> MDR (Multidrug-Resistant) were detected in 33.4% and 16.8%, respectively, of the cultures.
LI et al., 2021	This is a single-center, prospective, randomized, controlled study.	To explore the efficacy and safety of the rapid flow expulsion maneuver in the prevention of VAP compared to standard subglottic secretion drainage.	<i>Acinetobacter baumannii</i> (n=15 [62%]) and <i>Pseudomonas aeruginosa</i> (n=6 [25%]) were the most commonly detected pathogens.
KUMAR et al., 2021	Prospective, hospital-based cross-sectional study	To investigate the clinical-microbiological profile, antibiogram and production of metallo- β -lactamases (MBLs) in VAP infections with their subsequent outcome.	A higher frequency of <i>Acinetobacter baumannii</i> , <i>Pseudomonas aeruginosa</i> , <i>Klebsiella pneumoniae</i> and <i>Staphylococcus aureus</i> was observed in bacterial cultures. Among the Gram-negative bacteria, 144 (85%) were multidrug-resistant, 58% resistant to carbapenems. Regarding Gram-positive

			patients, 92% were <i>methicillin-resistant Staphylococcus aureus</i> (MRSA).
MAEBED et al., 2021	Observational and prospective incidence study	To identify the main pathogens causing VAP at the Beni-Suef University Hospital (BSU)	The most prevalent isolates were <i>Klebsiella pneumoniae</i> , <i>Acinetobacter baumannii</i> and <i>Moraxella sp.</i> Most of the <i>K. pneumoniae</i> isolates showed resistance to multiple drugs, while the <i>Acinetobacter</i> isolates showed pan-resistance patterns, including carbapenems, extended-spectrum cephalosporins, fluoroquinolones, and aminoglycosides.
BAIDYA et al., 2021	Laboratory-based cross-sectional study	To determine the biofilm produced by VAP-causing pathogens and their relationship to drug resistance.	Among the bacterial isolates, <i>Pseudomonas aeruginosa</i> (31%) was the most prevalent microorganism, followed by the <i>Acinetobacter calcoaceticus baumannii</i> complex (ACBC) totaling 16%. All cultures were susceptible to vancomycin, teicoplanin (gram-positive) and colistin (gram-negative). Finally, less than 50% of gram-negative isolates were sensitive to carbapenem.
GARDEN et al., 2022	This is a descriptive, retrospective and monocentric study.	To determine the bacterial agents isolated in tracheal aspirate cultures of patients in general Covid-19 intensive care, in addition to evaluating the bacterial resistance profiles to common antibiotics, comparing with the pre-pandemic period.	Pre-pandemic samples detected <i>Acinetobacter baumannii</i> , <i>Klebsiella pneumoniae</i> , <i>Pseudomonas aeruginosa</i> , <i>Staphylococcus aureus</i> , and <i>Escherichia coli</i> more frequently. During the pandemic, they were <i>A. baumannii</i> , <i>K. pneumoniae</i> , <i>P. aeruginosa</i> , and <i>E. faecium</i> . In addition, <i>A. baumannii</i> , <i>K. pneumoniae</i> , and <i>P. aeruginosa</i> showed increased resistance to amikacin, meropenem, and colistin during the pandemic.
MOTSCH et al., 2020	Randomized, multicenter, controlled, double-blind, phase 3 trial.	To compare imipenem/cilastatin/relebactam (IMI/REL) with colistin-based therapy for severe gram-negative bacterial infections, not susceptible to imipenem.	The most frequent baseline pathogens were <i>Pseudomonas aeruginosa</i> , <i>Klebsiella pneumoniae</i> , and other <i>Enterobacteriaceae</i> .
DATA et al., 2022	This is a multicenter, open-label, randomized, controlled study.	To assess whether continuous cuff pressure control (CPC) is associated with reduced incidence of ventilator-associated respiratory infection compared to intermittent CPC.	The main etiologies isolated were <i>Pseudomonas aeruginosa</i> , <i>Klebsiella pneumoniae</i> and <i>Staphylococcus aureus</i> .
GYSIN et al., 2021	Single-center, prospective observational study.	To analyze the bacterial spectrum and antimicrobial susceptibility patterns of Gram-negative bacilli isolated from ICU-ventilated patients during the first wave of COVID-19 in Switzerland.	The Gram-negative pathogens isolated were <i>Pseudomonas aeruginosa</i> , <i>Enterobacter cloacae</i> and <i>Klebsiella pneumoniae</i> . A high proportion of <i>P. aeruginosa</i> isolates were resistant to the antibiotics cefepime, ceftazidime, meropenem and, especially, piperacillin/tazobactam. <i>Enterobacter cloacae</i> and <i>Klebsiella pneumoniae</i> were resistant to piperacillin/tazobactam, ceftriaxone and ceftazidime.

Source: Authors.

According to Chart 1, the most frequently detected microorganism was the Gram-negative bacterium *Pseudomonas aeruginosa*, with an incidence ranging from 16% to 31%. The presence of this pathogen was identified in 12 studies (85%), in addition, *Pseudomonas aeruginosa* was the main etiological agent of the samples collected from patients diagnosed with VAP (BAIDYA et al., 2021; DATA et al., 2022; GYSIN et al., 2021; HABIB et al., 2020; MOTSCH et al., 2020).

Ademais, outras bactérias Gram-negativas foram isoladas em culturas de secreção traqueal, como *Klebsiella pneumoniae*, identificada em 10 estudos (BAHÇE et al., 2022; DAMAS et al., 2022; DATA et al., 2022; GYSIN et al., 2021; HABIB et al., 2020; KUMAR et al., 2021; MAEBED et al., 2021; MOTSCH et al., 2020; TITOV et al., 2020; YOSHIMURA et al., 2022), *Acinetobacter baumannii* em oito (AKBIYIK et al., 2021; BAHÇE et al., 2022; BAIDYA et al., 2021; HABIB et al., 2020; KUMAR et al., 2021; LI et al., 2021; MAEBED et al., 2021; TITOV et al., 2020) e *Escherichia coli* em três (BAHÇE et al., 2022; MARJANOVIC et al., 2021; TITOV et al., 2020).

In four (28%) of the 14 scientific productions selected, *Acinetobacter baumannii* was the predominantly isolated organism (AKBIYIK et al., 2021; BAHÇE et al., 2022; KUMAR et al., 2021; LI et al., 2021).

Among the Gram-positive bacteria, *Staphylococcus aureus* was the most isolated. Six (42%) studies have identified this bacterium in tracheal secretion samples from patients with VAP and its incidence frequency ranged from 9% to 50% (BAHÇE et al., 2022; DAMAS et al., 2022; DATA et al., 2022; KUMAR et al., 2021; MARJANOVIC et al., 2021; YOSHIMURA et al., 2022). Other bacteria such as *Haemophilus influenzae*, *Enterobacter cloacae* and *Moraxella sp* were isolated less frequently than the others.

Regarding antimicrobial sensitivity, cultures of *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *Acinetobacter baumannii* have demonstrated resistance to carbapenems such as meropenem above 50% (BAIDYA et al., 2021; GYSIN et al., 2021; KUMAR et al., 2021). Furthermore, in two studies, isolated Gram-negative individuals were considered Multidrug Resistant (MDR) (KUMAR et al., 2021; MAEBED et al., 2021). Also, according to Gysin et al. 2021, the analysis of the antibiogram of *Pseudomonas aeruginosa* isolates found resistance to amikacin, colistin, cefepime, ceftazidime, piperacillin/tazobactam (PIP/TAZ), while those of *Klebsiella pneumoniae* showed patterns of extensive resistance to drugs, such as extended-spectrum cephalosporins, fluoroquinolones, and aminoglycosides. Among *Staphylococcus aureus* cultures, 92% were *Methicillin-Resistant Staphylococcus Aureus (MRSA)* (KUMAR et al., 2021).

On the other hand, in the study by TITOV et al. (2020), 79% of the samples of *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and *Escherichia coli* were susceptible to imipenem/colistin, and 65% to piperacillin/tazobactam. The antimicrobial colistin

was effective against *Pseudomonas aeruginosa* and *Acinetobacter baumannii* (BAIDYA et al., 2021).

DISCUSSION

The ICU environment is seen as an important source of outbreaks of multidrug-resistant microorganisms, with the excessive use of antibiotics as a risk factor, as well as the vulnerability of the hospitalized population, which increases the risk of infection (LONDE et al., 2017). In addition, the higher mortality rates in the case of ventilator-associated pneumonia (VAP) are linked to the presence of high-risk pathogens or situations in which initial antibiotic therapy is not adequate for the etiologic agent (COSTA et al., 2016).

In the present study, there was a predominance of colonization by Gram-negative bacteria. The main etiology associated with VAP was *Pseudomonas aeruginosa*, followed by *Klebsiella pneumoniae*, *Acinetobacter baumannii* and *Escherichia coli*, as well as the Gram-positive bacterium *Staphylococcus aureus*. In an investigational study on secondary bacterial infections in patients with COVID-19 on mechanical ventilation, the most isolated bacteria were *A. baumannii*, *P. aeruginosa*, *E. coli*, and *K. pneumoniae* (ZANCO, 2021). Another study conducted in a tertiary hospital in southern Brazil detected a higher incidence of *Acinetobacter baumannii* and *Klebsiella pneumoniae* (TEJO et al., 2021). *Acinetobacter sp.* presents the highest risk of contamination in hospital environments, as it can often be found in valves and mechanical ventilation circuits, as well as in the oral cavity of ICU patients (ARAÚJO et al., 2018; EUGÊNIO et al., 2018). High-risk patients are more vulnerable to infection, especially those who use mechanical ventilation (MV), which is a probable explanation for its high prevalence in the samples of so many multicenter studies, such as those evaluated here (SÁ et al., 2021).

The distribution of etiologic agents varies among ICUs, depending on demographic variables, such as the patient population and the ICU model (DIAS et al., 2021). However, Gram-negative bacteria are often related to VAP (BATISTA et al., 2014). A cross-sectional study conducted at the Hospital de Clínicas of the Federal University of Uberlândia reported an increase in the prevalence of *Acinetobacter baumannii* and *Pseudomonas aeruginosa*, in addition to a decrease in Gram-positive bacteria, such as *Staphylococcus aureus* (MOREIRA et al., 2013). In another study conducted in 2017, the predominant bacterium was *Acinetobacter baumannii*, followed by *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* (PHU; NADJM; DUY, 2017).

Furthermore, data from a study conducted in the Pediatric Intensive Care Unit of a tertiary hospital in northern India corroborate the bacterial profile identified in other studies. Among bacterial etiologies, *Acinetobacter baumannii* (47%) was the most common, followed by *Pseudomonas aeruginosa* (28%) and *Klebsiella* (14%) (VIJAY et al., 2018). The most isolated

agent, in a retrospective observational study conducted between January 2010 and June 2015, was *Acinetobacter baumannii* susceptible to colistin, the other causative agents of VAP were *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* (DJORDJEVIC et al., 2017).

Regarding the sensitivity of bacterial isolates to antimicrobials, colistin also demonstrates effectiveness against *Acinetobacter baumannii* strains. A study conducted at two coronavirus referral hospitals in Qom, Iran, showed that strains of *A. baumannii* were resistant to different classes of antibiotics except colistin (SHARIFIPOUR et al., 2020). However, seven studies, out of the 14 analysed here, identified Multidrug-Resistant (MDR) bacteria (AKBIYIK et al., 2021; BAIDYA et al., 2021; BAHÇE et al., 2022; GYSIN et al., 2021; KUMAR et al., 2021; MAEBED et al., 2021; TITOV et al., 2020).

Carbapenemic resistance was higher in the strains of *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Acinetobacter baumannii*, being above 50%. According to Castilho et al. (2017), in a study that evaluated 1,333 patients in five ICUs, most of the *A. baumannii* found were resistant to beta-lactam antimicrobials, specifically, cephalosporins and 3rd and 4th generation carbapenems, and 91.1% of the isolates were multidrug-resistant (MDR).

In addition, this study also identified resistance of *Pseudomonas aeruginosa* to amikacin, colistin, cefepime, ceftazidime, piperacillin/tazobactam (PIP/TAZ). This result is similar to that of a study carried out in the ICU of a teaching hospital, in which *P. aeruginosa* isolates showed greater resistance to beta-lactams: ceftriaxone (85%), piperacillin-tazobactam (55%), imipenem (40%) and meropenem (30%) (ALVARES et al., 2021). *P. aeruginosa* has a wide range of antibacterial drug resistance mechanisms at its disposal, such as multi-drug efflux pumps, changes in its outer membrane porins, and the expression of β -lactamases (HORCAJADA et al., 2019). The repercussion of inadequate therapy in these infections is significant, the World Health Organization reported in 2017 that carbapenem-resistant *P. aeruginosa* was listed in the "critical" group, requiring the urgent need for new antibiotics (TACCONELLI et al., 2018).

Based on the data, the cause of this scenario of widespread bacterial resistance is assumed to be the increased demand and use of antibiotics, especially during the COVID-19 pandemic (BATISTA et al., 2022). Despite the fact that only 15% of COVID-19 patients had a secondary bacterial infection, a study conducted at two hospitals in China found that 95% of these patients were using antimicrobial drugs (ZHOU et al., 2020).

It is noteworthy that some limitations of the study should be explained, such as the use of only four databases, in addition to the fact that the results of research comparing the clinical evolution or mortality caused by the strains in patients with VAP are not integrated into the study. In addition, not all of the analyzed diseases had etiological analysis as the main objective of the study. Therefore, based on the literature, Gram-negative microorganisms are the main etiologies associated



with VAP, both before and during the COVID-19 pandemic. However, resistance to antibiotics has grown, especially carbapenems. The results of the study justify further exploration, since the time frame of this study is recent.

CONCLUSION

The COVID-19 pandemic still poses a challenge to physicians and the scientific community. Secondary bacterial infections can arise during or after COVID-19, which makes them inevitable. In this context, this study found greater bacterial colonization of patients with VAP by Gram-negative strains, especially *P. aeruginosa*, *Klebsiella pneumoniae* and *Acinetobacter baumannii*. *Staphylococcus aureus* representing Gram-positive microorganisms was present in smaller quantities.

No significant change in the microbiota involved in VAP cases was detected, however antimicrobial resistance increased considerably, especially to beta-lactam antimicrobials, such as carbapenems. Colistin showed good results in the fight against *A. baumannii* and *P. aeruginosa*.



REFERENCES

1. Agência Nacional de Vigilância Sanitária. (2017). Medidas de Prevenção de Infecção Relacionadas à Assistência à Saúde. Recuperado de <http://www.riocomsaude.rj.gov.br/Publico/MostrarArquivo.aspx?C=pCiWUy84%2BR0%3D>
2. Akbiyik, A., et al. (2021). O efeito da aspiração orofaríngea antes da mudança de posição na redução da incidência de pneumonia associada à ventilação mecânica. *Eur J Clin Microbiol Infect Dis, 40*, 615–622. DOI: <https://doi.org/10.1007/s10096-019-03789-4>
3. Alexandrino, S. M. (2020). Desafios para o enfrentamento da pandemia covid-19 em hospitais universitários. *Revista Paulista de Pediatria, 38*. Recuperado de <https://www.scielo.br/j/rpp/a/p4KZzTP9sMKPfVC9fqrwnys/?lang=pt>
4. Alvares, F. A., et al. (2021). Pneumonia associada à ventilação mecânica: incidência, etiologia microbiana e perfil de resistência aos antimicrobianos. *Revista De Epidemiologia E Controle De Infecção, 11*(4). DOI: <https://doi.org/10.17058/reci.v11i4.16781>
5. Araújo, P. L., et al. (2018). Prevalência de infecção relacionada à assistência à saúde em pacientes internados em unidade de terapia intensiva. *Enfermagem Mundial, 17*(4), 278-315. DOI: <https://doi.org/10.6018/eglobal.17.4.289311>
6. Arruda, D. É. G., et al. (2020). Prognóstico de pacientes com COVID-19 e doenças crônicas. *Comunicação em Ciências da Saúde, 31*(3), 79–88. DOI: <https://doi.org/10.51723/ccs.v31i03.748>
7. Bahçe, Y. G., et al. (2022). Avaliação de agentes bacterianos isolados de culturas de aspirado endotraqueal de pacientes de terapia intensiva geral Covid-19 e seus perfis de resistência a antibióticos em comparação com condições pré-pandemia. *Microbial Pathogenesis, 164*. DOI: <https://doi.org/10.1016/j.micpath.2022.105409>
8. Baidya, S., et al. (2021). Formação de Biofilme por Patógenos Causando Pneumonia Associada à Ventilação em Unidades de Terapia Intensiva em um Hospital Terciário: Uma Armadura para Refúgio. *BioMed Research Internacional, 2021*. DOI: <https://doi.org/10.1155/2021/8817700>
9. Batista, F. S., et al. (2022). Impactos na resistência antimicrobiana para além da pandemia de COVID-19: uma revisão descritiva da literatura. Trabalho de Conclusão de Curso, Universidade Federal Do Rio Grande Do Sul. Recuperado de <https://www.lume.ufrgs.br/handle/10183/249355>
10. Batista, O. M. A., et al. (2014). Sensibilidade de germes relacionados à pneumonia associada à ventilação mecânica. *R. pesq. cuid. fundam. online, 5*(6), 224-233. DOI: <https://doi.org/10.9789/2175-5361.2013.v5i6.224-233>.
11. Campos, N. G., et al. (2020). Pulmonary repercussions caused by the new Coronavírus (COVID-19) and the use of invasive mechanical ventilation. *Health Biol Sci, 8*(1), 1-3. DOI: <http://dx.doi.org/10.12662/2317-3076jhbs.v8i1.3185.p1-3.2020>. Recuperado de <https://periodicos.unichristus.edu.br/jhbs/article/view/3185>
12. Cantón, R., et al. (2020). Antimicrobial resistance in ICUs: an update in the light of the COVID-19 pandemic. *Current Opinion in Critical Care, 5*, 433-441. DOI: [10.1097/MCC.0000000000000755](https://doi.org/10.1097/MCC.0000000000000755). Recuperado de https://journals.lww.com/criticalcare/Fulltext/2020/10000/Antimicrobial_resistance_in_ICUs__an_update_in_the.2.aspx

13. Canzi, K. R., & Colacite, J. (2016). Frequência de pneumonia associada à ventilação mecânica com base em resultados de culturas quantitativas de secreções traqueais. *Revista Brasileira de Análises Clínicas, 48*(2). Recuperado de <http://www.rbac.org.br/artigos/frequencia-de-pneumonia-associada-a-ventilacao-mecanica-com-base-em-resultados-de-culturas-quantitativas-de-secrecoes-traqueais-48n-2/>
14. Castilho, S. R. A., et al. (2017). Acinetobacter baumannii strains isolated from patients in intensive care units in Goiânia, Brazil: Molecular and drug susceptibility profiles. *PLoS One, 12*(5). DOI: <https://doi.org/10.1371/journal.pone.0176790>. Recuperado de <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5419545/>
15. Cavalcante, A. B. L., et al. (2020). Pneumonia associated with mechanical ventilation: consequences and mortality in an intensive therapy unit. *Electronic Journal Collection Health, ed. 44*, 2385. DOI: <https://doi.org/10.25248/reas.e2385.2020>. Recuperado de <https://acervomais.com.br/index.php/saude/article/view/2385>
16. Costa, R. S., Motta, L. C. S., & Alfradique, M. D. (2018). O perfil epidemiológico do paciente com pneumonia associada à ventilação mecânica. *Revista da Faculdade de Medicina de Teresópolis, 2*(2). Recuperado de <https://revista.unifeso.edu.br/index.php/faculadadedemedicinadeteresopolis/article/view/1020/0>
17. Costa, J. B., et al. (2016). Os principais fatores de risco da pneumonia associada à ventilação mecânica em uti adulta. *Revista Científica da Faculdade de Educação e Meio Ambiente, 7*(1), 80–92. DOI: <https://doi.org/10.31072/rcf.v7i1.361>. Recuperado de <https://revista.faema.edu.br/index.php/Revista-FAEMA/article/view/361>
18. Damas, P., et al. (2022). Prevenção de pneumonia associada à ventilação mecânica por revestimento de metal nobre de tubos endotraqueais: um estudo multicêntrico, randomizado e duplo-cego. *Annals of Intensive Care, 12*(1). DOI: <https://doi.org/10.1186/s13613-021-00961-y>. Recuperado de <https://annalsofintensivecare.springeropen.com/articles/10.1186/s13613-021-00961-y#article-info>
19. Data, V. Q., et al. (2022). Eficácia do Controle Contínuo da Pressão do Manguito Endotraqueal para a Prevenção de Infecções Respiratórias Associadas à Ventilação: Um Ensaio Aberto, Randomizado e Controlado. *Clinical Infectious Diseases, 74*(10), 1795–1803. DOI: <https://doi.org/10.1093/cid/ciab724>. Recuperado de <https://academic.oup.com/cid/article/74/10/1795/6356213#356920821>
20. Diário Oficial da União. (2020). Portaria nº 188, de 3 de fevereiro de 2020. Declara Emergência em Saúde Pública de importância Nacional (ESPIN) em decorrência da Infecção Humana pelo novo Coronavírus (2019-nCoV). Recuperado de <https://www.in.gov.br/web/dou/-/portaria-n-188-de-3-de-fevereiro-de-2020>
21. Dias, A. T. P., et al. (2021). Perfil das infecções hospitalares em um Hospital Universitário do Submédio do Vale do São Francisco – Brasil. *Revista de Ensino, Ciência e Inovação em Saúde, 2*(1), 101-110. DOI: <https://doi.org/10.51909/recis.v2i1.117>. Recuperado de <http://recis.huunivasf.esbserh.gov.br/index.php/recis/article/view/117>
22. Djordjevic, Z. M., et al. (2017). Distribution and antibiotic susceptibility of pathogens isolated from adults with hospital-acquired and ventilator-associated pneumonia in intensive care unit. *Journal of Infection and Public Health, 10*(6), 740-744. DOI:

23. Eugênio, F., et al. (2018). Colonização bacteriana na cavidade bucal por patógenos causadores da pneumonia associada à ventilação (Dissertação de mestrado, Universidade Federal do Tocantins). Recuperado de <http://repositorio.uft.edu.br/handle/11612/1049>
24. Fan, C., et al. (2020). Prediction of Epidemic Spread of the 2019 Novel Coronavirus Driven by Spring Festival Transportation in China: A Population-Based Study. *Int. J. Environ. Res. Public Health, 17*(5). DOI: <https://doi.org/10.3390/ijerph17051679>. Recuperado de <https://www.mdpi.com/1660-4601/17/5/1679>
25. Gysin, M., et al. (2021). Padrões de suscetibilidade antimicrobiana de isolados bacterianos Gram-negativos respiratórios de pacientes com COVID-19 na Suíça. *Ann Clin Microbiol Antimicrob, 20*(64). DOI: <https://doi.org/10.1186/s12941-021-00468-1>. Recuperado de <https://ann-clinmicrob.biomedcentral.com/articles/10.1186/s12941-021-00468-1#article-info>
26. Habib, D., et al. (2020). Probióticos antecipados na prevenção de pneumonia associada ao ventilador após trauma múltiplo. *Asian J Pharm Clin Res, 13*(10), 83-85. DOI: <https://doi.org/10.22159/ajpcr.2020.v13i10.38114>. Recuperado de <https://innovareacademics.in/journals/index.php/ajpcr/article/view/38114>
27. Hellyer, T. P., et al. (2019). Biomarker-guided antibiotic stewardship in suspected ventilator-associated pneumonia (VAPrapid2): a randomised controlled trial and process evaluation. *The Lancet Respiratory Medicine, 8*, 182-191. DOI: [https://doi.org/10.1016/S2213-2600\(19\)30367-4](https://doi.org/10.1016/S2213-2600(19)30367-4). Recuperado de [https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(19\)30367-4/fulltext#seccestitle10](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(19)30367-4/fulltext#seccestitle10)
28. Horcajada, J. P., et al. (2019). Epidemiology and Treatment of Multidrug-Resistant and Extensively Drug-Resistant Pseudomonas aeruginosa Infections. *Clin Microbiol Rev., 32*(4). DOI: <https://doi.org/10.1128/cmr.00031-19>. Recuperado de <https://pubmed.ncbi.nlm.nih.gov/31462403/>
29. Kumar, M., et al. (2021). Emergência de bacilos Gram-negativos produtores de blaNDM-1 e blaVIM em pneumonia associada ao ventilador no Laboratório de Referência Regional de Vigilância AMR na Índia. *PLoS ONE, 16*(9). DOI: <https://doi.org/10.1371/journal.pone.0256308>. Recuperado de <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0256308#abstract0>
30. Leal, R. S., et al. (2019). Pneumonia associated with mechanical ventilation in injured patients in intensive therapy units. *Revista de Medicina de Família e Saúde Mental, 1*(1), 141-151. Recuperado de <https://www.unifeso.edu.br/revista/index.php/medicinafamiliasaudemental/article/view/1587/624>
31. Leal, W. S., et al. (2021). Análise da automedicação durante a pandemia do novo coronavírus: um olhar sobre a azitromicina. *Revista Ibero-Americana De Humanidades, Ciências E Educação, 7*(8), 580–592. DOI: <https://doi.org/10.51891/rease.v7i8.1984>. Recuperado de <https://periodicorease.pro.br/rease/article/view/1984>
32. Li, Y., et al. (2021). Manobra de expulsão de fluxo rápido na depuração de secreção subglótica para prevenir pneumonia associada à ventilação mecânica: um estudo controlado randomizado. *Ana Cuidados Intensivos, 11*(98). DOI: <https://doi.org/10.1186/s13613-021-00887-5>.

Recuperado de <https://annalsofintensivecare.springeropen.com/articles/10.1186/s13613-021-00887-5#Abs1>

33. Lin, L., et al. (2020). Hypothesis for potential pathogenesis of SARS-CoV-2 infection—a review of immune changes in patients with viral pneumonia. *Emerging Microbes & Infections, 9*(1), 727-732. DOI: <https://doi.org/10.1080/22221751.2020.1746199>. Recuperado de <https://www.tandfonline.com/doi/full/10.1080/22221751.2020.1746199>
34. Londe, L. P., et al. (2017). Pneumonia Nosocomial e sua relação com a saúde bucal. *Revista Ciências e Odontologia, 1*(1), 24-28. Recuperado de <http://revistas.icesp.br/index.php/RCO/article/view/141>
35. Maebad, A. Z. M., et al. (2021). Etiologias microbianas da pneumonia associada à ventilação mecânica (PAV) na unidade de terapia intensiva do Hospital Universitário de Beni-Suef. *Beni-Suef Univ J Basic Appl Sci, 10*(41). DOI: <https://doi.org/10.1186/s43088-021-00130-x>. Recuperado de <https://bjbas.springeropen.com/articles/10.1186/s43088-021-00130-x#article-info>
36. Marjanovic, N., et al. (2021). Regulação pneumática contínua da pressão do manguito traqueal para diminuir a pneumonia associada à ventilação em pacientes com trauma que foram ventilados mecanicamente. *Critical Care Original Research, 160*(2), 499-508. DOI: <https://doi.org/10.1016/j.chest.2021.03.007>. Recuperado de [https://journal.chestnet.org/article/S0012-3692\(21\)00481-5/fulltext#secsectitle0031](https://journal.chestnet.org/article/S0012-3692(21)00481-5/fulltext#secsectitle0031)
37. Melo, M. M., et al. (2019). Pneumonia Associada à Ventilação Mecânica: Conhecimento dos Profissionais de Saúde Acerca da Prevenção e Medidas Educativas. *Rev Fund Care Online, 11*(2), 377–382. DOI: <http://dx.doi.org/10.9789/2175-5361.2019.v11i2.377-382>. Recuperado de http://www.seer.unirio.br/index.php/cuidadofundamental/article/view/6575/pdf_1
38. Moreira, M. R., et al. (2013). Antimicrobial use, incidence, etiology and resistance patterns in bacteria causing ventilator-associated pneumonia in a clinical-surgical intensive care unit. *Rev. Soc. Bras. Med. Trop, 46*, 39-44. DOI: <https://doi.org/10.1590/0037-868216722013>. Recuperado de <https://doi.org/10.1590/0037-868216722013>
39. Motsch, J., et al. (2020). RESTORE-IMI 1: Um estudo multicêntrico, randomizado e duplo-cego comparando a eficácia e a segurança de imipenem/relebactam versus colistina mais imipenem em pacientes com infecções bacterianas não suscetíveis ao imipenem. *Clinical Infectious Diseases, 70*(9), 1799–1808. DOI: <https://doi.org/10.1093/cid/ciz530>. Recuperado de <https://academic.oup.com/cid/article/70/9/1799/5546004#204028695>
40. OPAS. (2020). Organização Pan-Americana da Saúde: Folha informativa sobre COVID-19. In: Histórico da pandemia de COVID-19. Recuperado de <https://www.paho.org/pt/covid19/historico-da-pandemia-covid-19>
41. Page, M. J., et al. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ, 372*, n71. DOI: <https://doi.org/10.1136/bmj.n71>. Recuperado de <http://www.prisma-statement.org/>
42. Pereira, A. S., et al. (2018). Metodologia da pesquisa científica. Recuperado de <http://repositorio.ufsm.br/handle/1/15824>
43. Phu, V. D., et al. (2017). Ventilator-associated respiratory infection in a resource-restricted setting: impact and etiology. *J intensive care, 5*(69). DOI: <https://doi.org/10.1186/s40560-017-0266->

4. Recuperado de <https://jintensivecare.biomedcentral.com/articles/10.1186/s40560-017-0266-4#citeas>
44. Sá, P. K. O., et al. (2021). Pneumonia associada à ventilação mecânica em pacientes com COVID-19: Avaliação das culturas de aspirados traqueais. *BRAZ J INFECT DIS, 25*(S1). DOI: <https://doi.org/10.1016/j.bjid.2020.101088>. Recuperado de <https://www.bjid.org.br/en-pneumonia-associada-a-ventilacao-mecanica-articulo-S1413867020302166>
45. Sharifipour, E., et al. (2020). Evaluation of bacterial co-infections of the respiratory tract in COVID-19 patients admitted to ICU. *BMC Infect Dis., 20*(646). DOI: <https://doi.org/10.1186%2Fs12879-020-05374-z>. Recuperado de <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7461753/#CR26>
46. Silva, K. M. R., et al. (2021). Implicações do uso de antibióticos durante a pandemia de COVID-19. *Pesquisa, Sociedade e Desenvolvimento, 10*(7). DOI: <http://dx.doi.org/10.33448/rsd-v10i7.15684>. Recuperado de <https://rsdjournal.org/index.php/rsd/article/view/15684/14690>
47. Souza, M. T., et al. (2010). Revisão integrativa: o que é e como fazer. *Einstein, São Paulo, 8*(1). DOI: <https://doi.org/10.1590/S1679-45082010RW1134>. Recuperado de <https://www.scielo.br/j/eins/a/ZQTBkVJZqcWrTT34cXLjtBx/?lang=pt>
48. Tacconelli, E., et al. (2018). Discovery, research, and development of new antibiotics: the WHO priority list of antibiotic-resistant bacteria and tuberculosis. *Lancet Infect Dis., 18*(3), 318-327. DOI: [10.1016/S1473-3099\(17\)30753-3](https://doi.org/10.1016/S1473-3099(17)30753-3). Recuperado de <https://pubmed.ncbi.nlm.nih.gov/29276051/>
49. Teixeira, L. K. T. S. (2021). Atuação interprofissional na prevenção da pneumonia associada à ventilação mecânica em Unidade de Terapia Intensiva. (Dissertação de mestrado, Universidade Federal do Rio Grande do Norte). Recuperado de <https://repositorio.ufrn.br/handle/123456789/46587>
50. Tejo, A. M., et al. (2021). Caracterização microbiológica das pneumonias bacterianas em pacientes internados por COVID-19. *BRAZ J INFECT DIS, 25*(S1). DOI: <https://doi.org/10.1016/j.bjid.2020.101079>. Recuperado de <https://www.bjid.org.br/en-caracterizacao-microbiologica-das-pneumonias-bacterianas-articulo-S1413867020302075>
51. Titov, I., et al. (2020). Um estudo randomizado, duplo-cego e multicêntrico comparando a eficácia e a segurança de imipenem/cilastatina/relebactam versus piperacilina/tazobactam em adultos com pneumonia bacteriana adquirida no hospital ou associada à ventilação mecânica (estudo RESTORE-IMI 2). *Clinical Infectious Diseases, 73*(11), 4539-4548. DOI: <https://doi.org/10.1093/cid/ciaa803>. Recuperado de <https://academic.oup.com/cid/article/73/11/e4539/5891450>
52. Vijay, G. V., et al. (2018). Ventilator Associated Pneumonia in Pediatric Intensive Care Unit: Incidence, Risk Factors and Etiological Agents. *Indian J Pediatr, 85*(10), 861-866. DOI: <https://doi.org/10.1007/s12098-018-2662-8>. Recuperado de <https://link.springer.com/article/10.1007/s12098-018-2662-8#article-info>
53. Wang, C., et al. (2020). A novel coronavirus outbreak of global health concern. *Lancet, 395*(10223), 470-473. DOI: [https://doi.org/10.1016/S0140-6736\(20\)30185-9](https://doi.org/10.1016/S0140-6736(20)30185-9). Recuperado de [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)30185-9/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30185-9/fulltext)



54. Yoshimura, J., et al. (2022). Efeito da terapia antibiótica inicial guiada por coloração de Gram na resposta clínica em pacientes com pneumonia associada à ventilação mecânica. *JAMA Network Open, 5*(4). DOI: 10.1001/jamannetworkopen.2022.6136. Recuperado de <https://jamanetwork.com/journals/jamannetworkopen/fullarticle/2790906>
55. Zanco, T. G. (2021). Infecções bacterianas secundárias em pacientes com covid-19 em uso de ventilação mecânica. (Trabalho de Conclusão de Curso, Universidade Federal Do Rio Grande Do Sul). Recuperado de <https://lume.ufrgs.br/bitstream/handle/10183/239995/001141581.pdf?sequence=1&isAllowed=y>
56. Zhou, F., et al. (2020). Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The Lancet, 395*(10299), 1054-1062. DOI: [https://doi.org/10.1016/S0140-6736\(20\)30566-3](https://doi.org/10.1016/S0140-6736(20)30566-3). Recuperado de [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)30566-3/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30566-3/fulltext)