PUBLICAÇÃO OFICIAL DO NÚCLEO HOSPITALAR DE EPIDEMIOLOGIA DO HOSPITAL SANTA CRUZ E PROGRAMA DE PÓS GRADUAÇÃO EM PROMOÇÃO DA SAÚDE - DEPARTAMENTO DE BIOLOGIA E FARMÁCIA DA UNISC

ISSN 2238-3360

Revista de Epidemiologia e Controle de Infecção

Original Article

Bacterial co-infections in patients with severe Covid-19 admitted to the intensive care unit in Brazil

Coinfecções bacterianas em pacientes com Covid-19 grave internados em unidade de terapia intensiva no Brasil
Coinfecciones bacterianas en pacientes con Covid-19 grave ingresados en la unidad de cuidados intensivos en Brasil

Site doi: https://doi.org/10.17058/reci.v16i.20522

Submitted: 07/06/2025
Accepted: 05/04/2026
Available online: 07/01/2026

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ABSTRACT

Background and Objectives: When associated with SARS-CoV-2, bacterial infections may significantly alter the host immune response and worsen the prognosis of Covid-19. This study aimed to determine the frequency of bacterial coinfection in patients with severe Covid-19, their antimicrobial resistance profiles, and the clinical and laboratory factors related to the presence of coinfection in patients admitted to the intensive care unit of a tertiary hospital in Northeastern Brazil. **Methods:** This was a retrospective cross-sectional study in which a data collection instrument was used based on medical records and laboratory results of patients admitted to the Intensive Care Unit of the Hospital das Clínicas of the Federal University of Pernambuco with severe Covid-19 between June and August 2020. An analytical statistical approach was used to compare differences between independent groups according to the presence of bacterial coinfection. **Results:** One hundred and one patients were evaluated, of whom forty-eight had death as the outcome. The frequency of bacterial coinfection was 32.7% (n = 33). The bacteria most associated with coinfection included Pseudomonas aeruginosa (39.4%), Acinetobacter baumannii (36.3%), Klebsiella pneumoniae (21.2%), and Staphylococcus aureus (21.2%). Resistance to carbapenems among Gram-negative bacteria and to macrolides among Gram-positive bacteria was particularly noteworthy. Laboratory analyses showed no significant differences between patients, except for elevated fibrinogen levels in coinfection cases, without an increase in mortality. **Conclusion:** A high frequency of bacterial coinfection and Covid-19 was observed, along with considerable antimicrobial resistance among the isolates studied. Despite the absence of relevant laboratory alterations or increased mortality rates, the importance of coinfection surveillance is emphasized for effective patient management and hospital resource allocation.

Keywords: *Covid-19. Coronavirus. Bacterial Infections. Infection Control. Hospital Infection.*

RESUMO

Justificativa e Objetivos: Quando associadas ao SARS-CoV-2, as infecções bacterianas podem alterar significativamente a resposta imunológica do hospedeiro e piorar o prognóstico da Covid-19. O estudo tem o objetivo de determinar a frequência de coinfecção bacteriana em pacientes com Covid-19 grave, seus perfis de resistência antimicrobiana e fatores clínicos e laboratoriais relacionados à presença da coinfecção, em pacientes na unidade de terapia intensiva de um hospital terciário da região Nordeste do Brasil. **Métodos:** Trata-se de um estudo de corte transversal retrospectivo no qual foi utilizado instrumento de coleta de dados com base nos prontuários e resultados laboratoriais de pacientes internados na Unidade de Terapia Intensiva do Hospital das Clínicas da Universidade Federal de Pernambuco com Covid-19 grave no período de junho a agosto de 2020. Utilizou-se abordagem estatística analítica para comparar as diferenças entre os grupos independentes relacionados à presença de coinfecção bacteriana. **Resultados:** Foram avaliados cento e um pacientes, dos quais quarenta e oito tiveram o óbito como desfecho. A frequência de coinfecção bacteriana foi de 32,7% (n=33). As bactérias mais associadas à coinfecção incluíram *Pseudomonas aeruginosa* (39,4%), *Acinetobacter baumannii* (36,3%), *Klebsiella pneumoniae* (21,2%) e *Staphylococcus aureus* (21,2%). Destaca-se a resistência aos carbapenêmicos nas bactérias gram-negativas e aos macrolídeos nas gram-positivas. As análises laboratoriais não mostraram diferenças significativas entre os pacientes, exceto por níveis elevados de fibrinogênio em casos de coinfecção, sem aumento na mortalidade. **Conclusão:** Observou-se uma alta frequência de coinfecção bacteriana e Covid-19, juntamente com considerável resistência antimicrobiana nos isolados estudados. Apesar da ausência de alterações laboratoriais relevantes ou aumento na taxa de mortalidade, enfatiza-se a importância da vigilância da coinfecção para o gerenciamento eficaz do paciente e alocação de recursos hospitalares.

Descritores: *Covid-19. Coronavírus. Infecções Bacterianas. Controle de Infecções. Infecção Hospitalar.*

RESUMEN

Justificación y Objetivos: Cuando se asocian al SARS-CoV-2, las infecciones bacterianas pueden alterar significativamente la respuesta inmunológica del huésped y empeorar el pronóstico de la Covid-19. Este estudio tuvo como objetivo determinar la frecuencia de coinfección bacteriana en pacientes con Covid-19 grave, sus perfiles de resistencia antimicrobiana y los factores clínicos y laboratoriales relacionados con la presencia de coinfección en pacientes ingresados en la unidad de cuidados intensivos de un hospital terciario de la región Nordeste de Brasil. **Métodos:** Se trata de un estudio transversal retrospectivo en el que se utilizó un instrumento de recolección de datos basado en historias clínicas y resultados laboratoriales de pacientes ingresados en la Unidad de Cuidados Intensivos del Hospital das Clínicas de la Universidad Federal de Pernambuco con Covid-19 grave, entre junio y agosto de 2020. Se utilizó un enfoque estadístico analítico para comparar las diferencias entre grupos independientes relacionadas con la presencia de coinfección bacteriana. **Resultados:** Se evaluaron ciento un pacientes, de los cuales cuarenta y ocho tuvieron la muerte como desenlace. La frecuencia de coinfección bacteriana fue del 32,7% (n = 33). Las bacterias más asociadas a la coinfección incluyeron Pseudomonas aeruginosa (39,4%), Acinetobacter baumannii (36,3%), Klebsiella pneumoniae (21,2%) y Staphylococcus aureus (21,2%). Se destacó la resistencia a los carbapenémicos en las bacterias Gram negativas y a los macrólidos en las Gram positivas. Los análisis laboratoriales no mostraron diferencias significativas entre los pacientes, excepto por niveles elevados de fibrinógeno en los casos con coinfección, sin aumento de la mortalidad. **Conclusión:** Se observó una alta frecuencia de coinfección bacteriana y Covid-19, junto con una considerable resistencia antimicrobiana en los aislamientos estudiados. A pesar de la ausencia de alteraciones laboratoriales relevantes o aumento en la tasa de mortalidad, se enfatiza la importancia de la vigilancia de la coinfección para el manejo eficaz del paciente y la asignación de recursos hospitalarios.

Palabras Clave: *Covid-19. Coronavirus. Infecciones bacterianas. Control de infecciones. Infección hospitalaria.*

INTRODUCTION

SARS-CoV-2, the causative agent of Covid-19, is a zoonotic RNA virus of the Coronaviridae family associated with respiratory infections.[1] The main signs and symptoms of Covid-19 are fever, dry cough, headache, fatigue, and runny nose. Some individuals may experience sore throat and diarrhea.[2] Additionally, some patients present with more severe respiratory symptoms and may progress to severe acute respiratory syndrome.[3,4] Furthermore, studies have shown that Healthcare-Associated Infections (HAIs), generally defined as infections acquired during hospitalization more than 48 hours after admission, are associated with a worsened prognosis for Covid-19 in patients hospitalized with severe forms of the disease, with bacterial infections being the most common. 5 This progression of the disease to more severe forms, over a relatively short period of time, led to a high demand for hospital beds, particularly in Intensive Care Units (ICUs), during periods of peak incidence of the SARS-CoV-2 pandemic.[5]

When associated with SARS-CoV-2, bacterial infections can significantly alter the host's immune response; furthermore, bacterial colonization and proliferation cause tissue damage and worsen the prognosis of Covid-19.[5] The increased incidence of these bacterial co-infections during ICU admission for Covid-19 has been linked to prolonged antibiotic therapy and the development of healthcare-associated infections, particularly ventilator-associated pneumonia.[6] The reported rate significantly exceeds the pre-pandemic figures cited by the European Centers for Disease Control.[6]

Certain factors may pose a risk for bacterial coinfection in patients with Covid-19, such as advanced age, comorbidities, and abnormal laboratory parameters, with the presence of elevated inflammatory markers—including D-dimer, C-reactive protein, interleukin-6, and lactate dehydrogenase—being particularly significant.[7] The different outcomes of coinfection depend on complex interactions between viral replication, host conditions, and the infecting bacterial species.[8] The bacteria most commonly associated with bacterial coinfection and severe Covid-19 have been: *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Enterococcus faecalis*. *Mycoplasma pneumoniae, Pseudomonas aeruginosa*, and *Haemophilus influenzae*.[9,10] Pathogens commonly isolated from blood cultures were *E. faecalis* and *S. aureus*, and in respiratory tract infections, *P. aeruginosa*.[8]

Patients hospitalized for Covid-19 are vulnerable to colonization by multidrug-resistant bacteria.[11] Recent studies have shown that approximately 70% of ICU patients with suspected or confirmed Covid-19 received at least one antibiotic to treat or prevent bacterial infections.[12] Regarding Gram-positive bacteria, high resistance to beta-lactams and moderate resistance to amikacin and levofloxacin have been observed. On the other hand, most isolates have been susceptible to vancomycin, linezolid, and tigecycline. Gram-negative bacteria have mostly been producers of Extended-Spectrum Beta-Lactamases, leading to high resistance to penicillins and cephalosporins, including broad-spectrum ones (ceftazidime and ceftazidime); furthermore, carbapenemases have been detected, conferring resistance to carbapenems.[13,14]

In Brazil, it has been observed that deaths due to infections secondary to severe Covid-19 in the ICU were primarily related to bacterial infections.[14] Although there are strong correlations between the presence of these co-infections and adverse outcomes (e.g., death), there is a scarcity of studies on bacterial co-infections in severe Covid-19 and other respiratory viral infections that progress to severe acute respiratory syndrome in Northeast Brazil.[15] Thus, this study aims to determine the frequency of bacterial coinfection in patients with severe Covid-19, their antimicrobial resistance profiles, and clinical and laboratory factors related to the presence of coinfection in patients in the intensive care unit of a tertiary hospital in the Northeast region of Brazil.

METHODS

Design, context, and participants

This is a retrospective cross-sectional study conducted at the Hospital das Clínicas of the Federal University of Pernambuco, in the Northeast region of Brazil, which included 101 patients admitted to the ICU for Covid-19 between June and August 2020 and diagnosed with severe Covid-19. The inclusion criteria were as follows: diagnosis of SARS-CoV-2 infection by real-time polymerase chain reaction, dyspnea, respiratory distress, oxygen saturation <95%, or hypotension.[16] The follow-up period for patients spanned from admission to the ICU until discharge from this unit to hospital ward beds or death. This study adhered to the principles outlined in Resolutions 466/12 and 510/16 of the National Health Council (CNS) and followed the guidelines set forth by the Declaration of Helsinki, and was approved by the Research Ethics Committee of the Hospital das Clínicas of the Federal University of Pernambuco (HC-UFPE) under opinion no. 4,579,183.

Data source

The following epidemiological and laboratory data were evaluated through a review of medical records: sex, age, length of hospital stay, hemoglobin levels, total white blood cell count, absolute neutrophil count, absolute lymphocyte count, platelet count, International

Normalized Ratio (INR), fibrinogen levels, and D-dimer levels. In addition, the results of antimicrobial susceptibility testing for cultures with microbial growth were evaluated. Only the last period of hospitalization for each patient was considered in order to better assess disease outcome and subsequent survival analysis. Hematological analyses (complete blood count) were performed using the YUMIZEN – H2500 automated analyzer (Horiba, Japan), while assessments of biological analytes related to coagulation (International Normalized Ratio, fibrinogen, and D-dimer) were performed using the STA COMPACT MAX (Stago, France). Biochemical tests were performed using the Architect c8000 Chemistry Analyzer automated system (Abbott, United States). Real-time polymerase chain reaction followed the protocol of the Food and Drug Administration (United States) recommended in the CDC 2019-novel Coronavirus Real-Time RT-PCR Diagnostic Panel (https://www.fda.gov/media/134922/download).
Microbial identification and corresponding susceptibility testing were performed using the VITEK2 system (BioMérieux, France). It should be noted that all automated laboratory analysis systems were subject to both internal and external laboratory analytical quality control.

Statistical analyses

Epidemiological and laboratory data were presented using descriptive statistics, with continuous variables shown as medians and interquartile ranges and categorical variables as frequencies and percentages. The normality of the data was assessed using the Shapiro–Wilk test. Next, the Mann–Whitney test was used to compare differences between independent groups regarding the presence of bacterial coinfection. The collected data were exported to the Statistical Package for the Social Sciences, version 20.0. Initially, medians were calculated for the laboratory test variables collected over time during the patient's hospitalization. To verify differences between patients with and without bacterial coinfection regarding the variables of interest, the Chi-Square test of independence was used for qualitative/categorical variables, and the Mann-Whitney test was used for quantitative/numerical variables. Finally, it should be noted that all conclusions were drawn at a 5% significance level.

RESULTS

During the study period, 101 patients admitted to the ICU with severe Covid-19 were evaluated for the occurrence of bacterial co-infections. A high rate of bacterial coinfection was observed (n = 33; 32.7%). There was no statistically significant difference when relating sex and age to the presence of bacterial coinfections. Forty-eight patients died, with no significant difference between those with or without bacterial coinfection (p = 0.325). Regarding the laboratory variables analyzed, fibrinogen and D-dimer levels were higher in patients with bacterial co-infections (p-value = 0.022 and p-value = 0.050, respectively) (Table 1).

Table 1. Comparative analysis of sociodemographic and laboratory variables among patients admitted to the intensive care unit for severe Covid-19, with or without bacterial coinfection, 2020.

Variables	Total	Coinfection		p-value[a]
	N (%)	Yes N (%)	No N (%)	
Death	48 (50)	18 (54.5)	30 (44.1)	0.325[b]
Sex				
Male	48 (47.5)	18 (54.5)	30 (44.1)	0.325[b]
Female	53 (53.5)	15 (45.5)	38 (55.9)	
Age (years)[c]	56.5 (44.0–66.8)	53.5 (41.0–62.8)	59.0 (45.3–67.8)	0.196
Hemoglobin (g/dL)[c]	9.6 (8.5–11.8)	9.3 (8.4–12.1)	9.9 (8.8–11.8)	0.397
Total white blood cells (cel/mm³)[c]	11.310 (7.735–14.987.5)	11.790 (9.585–15.992.5)	11.010 (7.197.5–14.882.5)	0.266
Absolute neutrophil count (cel/mm³)[c]	8.110 (5.750–11.282.5)	9.360 (7.127.5–11.765.0)	7.730 (5.238.8–11.178.8)	0.203
Total lymphocytes (cel/mm³)[c]	1.000 (640–1.487.5)	1.000 (640–1.550)	957.5 (632.5–1.400)	0.584
Platelets (mm³)[c]	249.500 (150.250–340.000)	264.500 (233.250–347.750)	237.750 (144.000–315.375)	0.082
Glucose (mg/dL)[c]	150.8 (97.1–216.3)	154.9 (97.1–291.8)	150.2 (93.1–212.9)	0.648
INR[c]	1.1 (1.1–1.2)	1.1 (1.1–1.2)	1.1 (1.1–1.3)	0.688
Fibrinogen (mg/dL)[c]	663.0 (536.8–751.0)	710.0 (585.8–785.5)	619.8 (519.4–720.8)	0.022
D-dimer (ng/dL)[c]	2.390 (1.730–3.610)	3.072.5 (1.852.5–4.045.0)	2.124 (959–3.360)	0.050

Abbreviation: [a]Mann-Whitney test. [b]Chi-square test of independence. [c]Variables presented as median (Q1;Q3).

An analysis of the frequency of bacteria most commonly associated with co-infections in ICU patients with severe Covid-19 revealed, primarily, *Pseudomonas aeruginosa* (39.4%; n=13/33), *Acinetobacter baumannii* (36.3%; n=12/33), *Klebsiella pneumoniae* (21.2%; n=7/33), and *Staphylococcus aureus* (21.2%; n=7/33) (Table 2). The antibiograms and antimicrobial resistance profiles of these four most common bacterial species were analyzed. P. aeruginosa demonstrated high resistance to carbapenems (imipenem = 63.6%; meropenem = 46.1%) and third- and fourth-generation cephalosporins (ceftazidime and cefepime, both with an approximate frequency of 40%) (Figure 1.A). All *A. baumannii* isolates tested for piperacillin-tazobactam were resistant, and high rates of resistance to carbapenems were detected (imipenem = 75% and meropenem = 83%) (Figure 1.B).

More than half of the *K. pneumoniae* isolates exhibited resistance to second-, third-, and fourth-generation cephalosporins; and although resistance to carbapenems was lower than for *P. aeruginosa* and *A. baumannii*, it was still considered high (28.6%) (Figure 1.C). S. aureus exhibited high resistance to benzylpenicillin (85.7%) and clindamycin (100%). Additionally, all strains were classified as methicillin-resistant S. aureus. No antimicrobial resistance was detected to vancomycin, tigecycline, teicoplanin, or linezolid (Figure 1.D).

Table 2. Prevalence of bacteria isolated from patients admitted to the intensive care unit for severe Covid-19 with bacterial coinfection, 2020.

Isolated bacteria	N (%)
Gram-positive cocci N (%)	
Enterococcus faecium	02 (6.0)
Staphylococcus aureus	07 (21.2)
Gram-negative bacilli N (%)	
Enterobacteria	
Escherichia coli	02 (6.0)
Enterobacter cloacae	03(9.0)
Klebsiella pneumoniae	07 (21.2)
Proteus mirabilis	01 (3.0)
Non-fermenting	
Acinetobacter baumannii	12 (36.3)
Pseudomonas aeruginosa	13 (39.4)

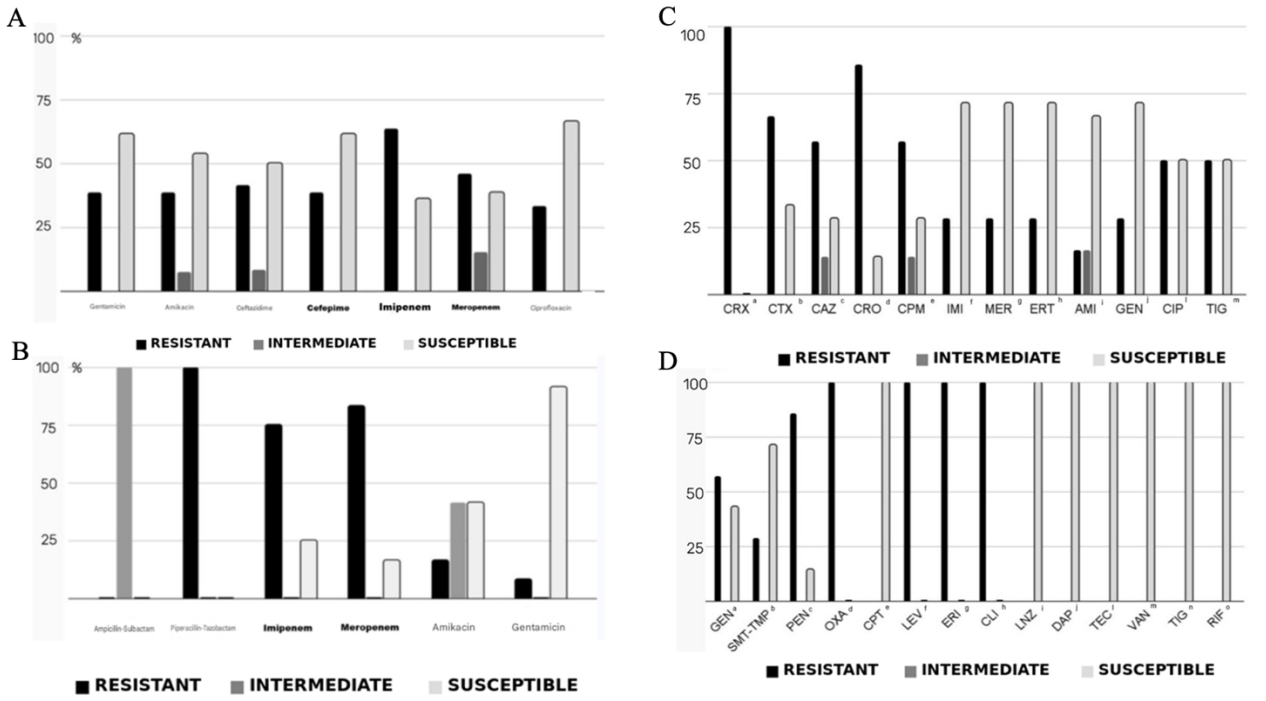

Figure 1. Antimicrobial resistance profile of bacteria isolated from patients admitted to the ICU with severe Covid-19 and bacterial coinfection, 2020.

Abbreviation: A. Antimicrobial resistance profile of *Pseudomonas aeruginosa* isolates (n=13). B. Antimicrobial resistance profile of *Acinetobacter baumannii* isolates (n=12). C. Antimicrobial resistance profile of *Klebsiella pneumoniae* isolates (n=7). Note: [a]CRX: cefuroxime; [b]CTX: cefoxitin; [c]CAZ: ceftazidime; [d]CRO: ceftriaxone; [e]CPM: cefepime; [f]IMI: imipenem; [g]MER: meropenem; [h]ERT: ertapenem; [i]AMI: amikacin; [j]GEN: gentamicin; [l]CIP: ciprofloxacin; [m]TIG: tigecycline. D. Antimicrobial resistance profile of Staphylococcus aureus isolates (n=07). Note: [a]GEN: gentamicin; [b]SMT-TMP: sulfamethoxazole-trimethoprim; [c]PEN: benzylpenicillin; [d]OXA: oxacillin; [e]CPT: ceftaroline; [f]LEV: levofloxacin; [g]ERI: erythromycin; [h]CLI: clindamycin; [i]LNZ: linezolid; [j]DAP: daptomycin; [l]TEC: teicoplanin; [m]VAN: vancomycin; [n]TIG: tigecycline; [o]RIF: rifampicin.

DISCUSSION

The study provides an overview of the incidence of bacterial co-infections in patients admitted to the ICU with a diagnosis of severe Covid-19 during the first wave of the SARS-CoV-2 pandemic in 2020. The frequency of bacterial coinfection in these patients was 32.7% (33/101). Mortality corresponded to a frequency of 50% (48/96). However, no statistical association was observed between deaths and the presence of bacterial infections in patients with severe Covid-19. The most prevalent bacteria, in descending order, were Pseudomonas aeruginosa, Acinetobacter baumannii, and, with equal frequency, Staphylococcus aureus and Klebsiella pneumoniae. The observed data corroborate a

study conducted on critically ill ICU patients in the state of Rio de Janeiro (Brazil), which reported 29.8% of secondary bacterial infections. The most frequently isolated bacteria were also: *Acinetobacter baumannii* (28.9%), *Pseudomonas aeruginosa* (22.7%), and *Klebsiella pneumoniae* (14.4%).[14] International studies have also shown high frequencies of *A. baumannii*, *K. pneumoniae*, and *P. aeruginosa*, confirming the importance of these bacterial species in morbidity among patients hospitalized for Covid-19.[17,18]

Non-fermenting Gram-negative bacilli exhibited higher frequencies of resistance to carbapenems (meropenem, imipenem). Acinetobacter baumannii demonstrated resistance in all strains tested to piperacillin-tazobactam. Meanwhile, low levels of resistance were found for aminoglycosides (gentamicin – 8.4% and amikacin – 16.6%). A Brazilian study also reported a similar resistance profile to piperacillin-tazobactam.[19] However, it showed higher rates of resistance to carbapenems and aminoglycosides when compared to the results of this study.

Of particular concern is the high antimicrobial resistance exhibited by Acinetobacter baumannii in this study, particularly to some of the antibiotic classes used to treat its infection, such as beta-lactams and carbapenems.[20] In Pseudomonas aeruginosa isolates, higher resistance to carbapenems was observed (meropenem = 46%; imipenem = 63%) compared to ceftazidime (41.7%), cefepime (38.5%), and aminoglycosides (38.5%). The findings of this study regarding high levels of resistance to carbapenems and third- and fourth-generation cephalosporins are concerning, given that these have been the drugs of choice for treating multidrug-resistant Pseudomonas aeruginosa, particularly when combined with beta-lactamase inhibitors.[21]

K. pneumoniae showed high resistance to second-, third-, and fourth-generation cephalosporins, as all tested strains were resistant to cefuroxime (a second-generation cephalosporin) and more than half were resistant to cefepime (a fourth-generation cephalosporin). However, it is worth noting that *K. pneumoniae* demonstrated lower resistance to carbapenems (~25%) when compared to *A. baumanni* and *P. aeruginosa*. Although the patterns of resistance to cephalosporins were similar, resistance rates to carbapenems were lower when compared to ICUs in tertiary hospitals in the southern region of the country.[19]

Among the Gram-positive microorganisms, *S. aureus* was the most common (n=7; 21.2%). All isolates were resistant to oxacillin and were identified as methicillin-resistant S. aureus. In addition, they exhibited high resistance to benzylpenicillin (85.7%), clindamycin, and erythromycin (both 100%). All isolates were susceptible to linezolid, teicoplanin, vancomycin, and tigecycline. In a five-year longitudinal study (2014–2019) conducted in southern Brazil, high resistance to macrolides (erythromycin and clindamycin) was also observed, at 74.2% and 46.1%, respectively; however, this indicates lower macrolide resistance than that observed in our study. At the same time, no resistance to linezolid and vancomycin was observed, corroborating our data.[22] Results from an antimicrobial resistance surveillance study in Brazil, conducted with community and hospital bacterial isolates, showed that S. aureus was the most frequent Gram-positive microorganism (15.2%), with 24% of the strains classified as MRSA and a high level of macrolide resistance (erythromycin: 60% and clindamycin: 56%).[23]

Another point to consider is the increase in fibrinogen and D-dimer levels among patients with bacterial coinfection and severe Covid-19. However, it should be emphasized that, regarding D-dimer, this association should be interpreted with caution, as the statistical association was borderline. On the other hand, it should be noted that higher levels of cardiovascular disease markers (D-dimer, GDF-15, and sICAM-1) have been shown to be associated with disease severity.[24] It is worth noting that, as with our sample, these data were evaluated in patients selected from a period of the pandemic when vaccination campaigns for the general population had not yet been fully implemented. Other studies have shown that the progression to unfavorable outcomes in severe Covid-19 has been linked to a variety of molecular pathways related to chemotaxis, innate immune response, the complement system, cell adhesion, angiogenesis, and hemostasis.[25]

It is important to acknowledge the limitations of this study, including the sample size and the retrospective nature of the analysis. However, even though it was conducted at a single hospital, the study managed to include approximately one hundred patients. Furthermore, given the ongoing evolution of the pandemic and the geographical and hospital-specific variations in the types of pathogens associated with healthcare-associated infections, further research is needed to better understand bacterial co-infections in patients with severe Covid-19 or other respiratory viral infections that progress to severe acute respiratory syndrome and their clinical implications. For the plasma glucose and D-dimer variables, only a fraction of the total sample could be analyzed (47/101 and 51/101, respectively), which may have introduced selection bias in the comparison analysis between groups with or without coinfection.

Despite advances in hospital protocols for the prevention and treatment of healthcare-associated infections, infectious complications in hospitalized patients remain a public health problem, associated with longer hospital stays as well as increased consumption of medications and supplies. Despite the importance of monitoring these secondary infections during hospital

stays, there are few studies on the subject, especially in the Northeast region of Brazil. In the post-Covid-19 pandemic period, a significant increase was observed in the incidence of multidrug-resistant bacterial isolates, particularly in Gram-negative pathogens such as Klebsiella pneumoniae and Acinetobacter baumannii, with the latter being associated with in-hospital mortality in critically ill patients and the intensive use of carbapenems during hospitalization.[26, 27]

In light of the above, a high frequency of bacterial co-infections and severe Covid-19 is confirmed, involving Gram-negative (Pseudomonas aeruginosa and Acinetobacter baumannii) and Gram-positive (Staphylococcus aureus) bacteria with high antimicrobial resistance to carbapenems and methicillin, respectively. Additionally, elevated levels of D-dimer and fibrinogen were noted in patients with coinfection, possibly associated with disorders of coagulation mechanisms.

Data availability:

The database and analysis codes used in the study are not publicly available, as they involve analyses of health indicators derived from the medical records of patients admitted to the intensive care unit of a tertiary care hospital.

Use of generative artificial intelligence:

Please note that no generative artificial intelligence was used in the preparation of this article.

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AUTHORS' CONTRIBUTIONS

Júlia Pereira Câmra contributed to data analysis and interpretation, drafting the article, literature review, proofreading, and statistics. **Amanda Palmeira Marques Santos** contributed to data analysis and interpretation, drafting the article, literature review, proofreading, and statistics. **Ana Carolina Mattos Uchôa de Moraes** contributed to data analysis and interpretation, article writing, literature review, proofreading, and statistics. **Madi Veiga Diniz** contributed to project management, literature review, and proofreading. **Alexandro Pedro da Silva** contributed to project management, literature review, and proofreading. **Wagner Roberto Cirilo da Silva** contributed to project management, literature review, and proofreading. **Kledoaldo Lima** contributed to project management, data analysis and interpretation, literature review, article writing, proofreading, and statistics.

All authors approved the final version to be published and are responsible for all aspects of the work, including ensuring its accuracy and integrity.

Please cite this article as: Câmara JP, Santos APM, Moraes ACMU, Diniz MV, Silva AP, Silva WRC, Lima K. Bacterial co-infections in patients with severe Covid-19 admitted to the intensive care unit in Brazil. Rev Epidemiol Control Infect [Internet]. 2026 Jul. 1; 16. Available from: https://seer.unisc.br/index.php/epidemiologia/article/view/20522