



Frequency of Multidrug-Resistant Microorganisms Associated with Bacterial Coinfections in Hospitalized Patient with Covid-19: A Literature Review

Maria Walcleanes Magalhães de Oliveira ^a,
Júlio César Sousa Prado ^a, Martinair Santana da Silva ^a,
Maria Gleiciane de Queiroz Martins ^b
and Francisco Cesar Barroso Barbosa ^{a*}

^a Federal University of Ceara (UFC), Sobral, CE, Brazil.

^b University Center INTA (UNINTA), Sobral, CE, Brazil.

Authors' contributions

This work was carried out in collaboration among all authors. Author MWMdO designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors JCSP and MSdS managed the analyses of the study. Author MSdS managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/ACRI/2024/v24i3640

Open Peer Review History:

This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: <https://www.sdiarticle5.com/review-history/113008>

Review Article

Received: 13/12/2023

Accepted: 16/02/2024

Published: 22/02/2024

ABSTRACT

Patients with a doença do coronavírus 2019 (COVID-19) may be at risk of associated bacterial co-infections, and the involvement of multidrug-resistant (MDR) microorganisms in these cases can lead to an increase in morbidity and mortality rates. The objective of this study was to describe the

*Corresponding author: Email: fcocesar@ufc.br;

frequency of the main MDR microorganisms associated with bacterial co-infections in patients hospitalized with COVID-19. To this end, we carried out a search in the PubMed and Regional Portal of the Virtual Health Library (VHL) databases, from December 2019 to September 2023, with the keywords COVID-19, co-infection and multidrug-resistant microorganism. Of the 535 articles initially found, only 14 were selected for analysis. Gram-negative bacteria were most frequently involved in bacterial co-infections in patients with COVID-19 (70%). Among these, *Klebsiella pneumoniae* and *Acinetobacter baumannii* predominated, with 85.71% and 78.57%, respectively. Among gram-positive bacteria, *Staphylococcus aureus* (71.42%) was the most common. Among MDR microorganisms, the prevalent species were carbapenem-resistant gram-negative bacilli (32%) and methicillin-resistant *S. aureus* (85.7%). Furthermore, a higher frequency of MDR microorganisms was observed in patients with COVID-19 in intensive care units (ICU). Thus, the findings of the present study indicate the need for attention to infections caused by multidrug-resistant microorganisms in critically ill patients with COVID-19.

Keywords: COVID-19; bacterial co-infections; multi-resistant microorganisms.

1. INTRODUCTION

The coronavirus disease 2019 (COVID-19) is a clinical condition caused by the novel coronavirus SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2), previously known as 2019-nCoV. Belonging to the Coronaviridae family, it is a zoonotic RNA virus that first emerged in late 2019 in Wuhan, China, with the hypothesis of bats and the Malayan pangolin as potential sources due to the genetic proximity between CoVs found in these animals and the current virus [1-3]. It primarily infects the respiratory system and is transmitted through respiratory droplets via close contact, leading to a spectrum of illness ranging from mild to critical conditions requiring specialized treatment in intensive care units [4].

Reports of secondary infections associated with COVID-19 have become increasingly common. The presence of other microorganisms, such as bacteria, fungi, and viruses, is a critical factor that can complicate the diagnosis, prognosis and treatment of the disease, as well as exacerbate and increase morbidity and mortality [5]. Coinfection is defined as the result of two or more infectious agents acting simultaneously [6,7]. For cases of patients diagnosed with COVID-19 who have coinfections with other respiratory pathogens, the immediate administration of antibiotics in accordance with antimicrobial susceptibility reports, as well as strict infection control strategies, are essential to reduce severity, complications, mortality, and the nosocomial transmission facilitated by these superbugs [8].

The emergence of infections caused by multidrug-resistant microorganisms (MDRs) has

become a health risk, since uncontrolled infections in the hospital setting can prolong patients' hospitalization period by complicating their clinical status and recovery [9].

The World Health Organization (WHO) defines healthcare-associated infection as "an infection occurring in a patient during the process of care in a hospital or other healthcare facility that was not present or incubating at the time of admission" [10]. Healthcare-associated infections can also encompass those that manifest within 72 hours of admission when associated with diagnostic and therapeutic procedures performed during this period [10].

Nosocomial infection is an event detected based on clinical and laboratory data, with the time frame varying depending on the patient's care unit. In intensive care units (ICUs), for example, the timeframe extends up to 48 hours after discharge [6].

Over the last decade, antibiotic resistance has become one of the major global public health concerns due to the emergence of pathogens with new resistance mechanisms. Antimicrobial resistance is a growing crisis that affects global health and demands urgent action [11]. Multidrug-resistant bacteria are microorganisms that are not susceptible to at least one antibiotic from three or more classes of antibiotics. They usually arise due to improper use of antimicrobials or their uncontrolled spread through contamination vectors, posing difficulties to clinical treatment [12].

Therefore, considering the relevance of multidrug-resistant bacteria in healthcare and aiming to highlight their role in the pandemic

scenario, we aimed to describe the frequency of the main MDR microorganisms associated with bacterial coinfection in hospitalized patients with COVID-19, based on the literature from December 2019 to September 2023.

2. MATERIALS AND METHODS

This is an integrative literature review that utilized scientific literature to analyze the prevalence of multidrug-resistant microorganisms in hospitalized patients with COVID-19 during the period from December 2019 to September 2023. Its methodological structure consists of six vital phases, following the procedures described by Souza et al. [13].

In the first phase, the guiding question used to steer the research was: "Which multidrug-resistant bacteria have been prevalent in hospitalized patients with COVID-19?"

Multiresistant bacteria, according to the World Health Organization (WHO) [5], are those that are resistant to one or more antimicrobials from three or more tested categories.

In the second methodological phase, we conducted searches in the PubMed and Regional Portal of the Virtual Health Library (BVS) databases for scientific articles published between December 2019 and September 2023. The keywords used were: COVID-19, Bacterial Coinfection, and Multidrug-Resistant Microorganism. Boolean operators "and" and "or" were used as search tools, combining Health Sciences Descriptors (DeCS) in the regional BVS portal, resulting in: ("COVID-19") and ("coinfection") and ("bacteria or multiresistant") along with language filter (English) and publication year (2019 or 2023). The same combinations were used for MeSH (Medical Subject Headings) in PubMed searches, resulting in: ("COVID-19") AND ("coinfection") AND ("bacteria" OR "multidrug resistance"). The articles were directly related to the years 2019 to 2023, so no additional filters were necessary.

Each of the retrieved articles was analyzed according to the inclusion and exclusion criteria. Inclusion criteria were: the period between December 2019 and September 2023, studies investigating bacterial coinfection in hospitalized patients with COVID-19, studies reporting coinfection with multidrug-resistant bacteria, articles in English, and articles that addressed

the guiding question. Exclusion criteria were: articles that did not address the research question, articles focused on coinfections with other specific microorganisms that were not bacteria, duplicates, literature reviews, and letters.

In the third phase, an adapted instrument from Souza et al. [13] was used for data extraction and recording of selected articles. This instrument was structured with the following topics: article title, authors, year of publication, country, gender, age, department, material analyzed, prevalent bacteria, and sample size/outcome. An Excel spreadsheet was created for data storage and organization.

The fourth phase involved analysis of the selected articles. Titles and abstracts were read, and inclusion and exclusion criteria were applied to select the articles that were read in full.

The fifth phase involved the description and discussion of the results. Subsequently, in the sixth phase, the review was written.

3. RESULTS

Initially, 535 articles were found as result of the search in the databases using the associated descriptors and keywords. After analyzing the inclusion and exclusion criteria, 14 articles were chosen: 10 were identified in PubMed and 4 in the BVS Regional Portal (Fig. 1). Of these, 37.71% (5/14) corresponded to the year 2023, and 37.71% (5/14) to 2022, with the remaining ones pertaining to 2021 and 2020. Additionally, 50% of the studies were conducted in Asia, followed by 29% in Europe, and the remainder in Africa.

Twelve studies had more male patients, while the majority were female in only one study [14], and in another study the gender of the patients was not identified [27]. The median age of the studied populations was similar, ranging from 50 to 70 years old. Regarding the ward where the patients were hospitalized, 71.42% were in intensive care units (ICUs) [14,16,17,19-24,27]. In all articles, the analyzed material was collected from electronic patient record management systems. Ten studies provided details about the types of clinical samples cultured, including sputum, blood and urine, while four study did not specify the source of the sample, indicating only "patient record analysis" [16,17,19,22].

Regarding the occurrence of multidrug-resistant microorganisms (MDRs) in coinfections, gram-negative bacteria accounted for 70%. Among them, *Klebsiella pneumoniae* and *Acinetobacter baumannii* predominated with 85.71% and 78.57%, respectively. Among gram-positive bacteria (30%), *Staphylococcus aureus* was the most frequent at 71.42% [15-26]. Among MDR microorganisms, the most frequently isolated species were carbapenem-resistant gram-negative bacilli (32%), followed by methicillin-resistant *S. aureus* (10%) among gram-positive bacteria.

The sample size varied from study to study, and the number of deaths was not reported in some articles. The most common comorbidities among the participants in the different studies were diabetes mellitus, systemic arterial hypertension, kidney disease, and respiratory diseases [14-27]. Most patients received empirical antibiotic therapy upon admission to the ICU.reference?

Table 1 presents a list of the selected articles from the databases, describing the article title, authors, year of publication, country, gender, age, hospital sector, material analyzed, prevalent bacteria, and sample size/outcome.

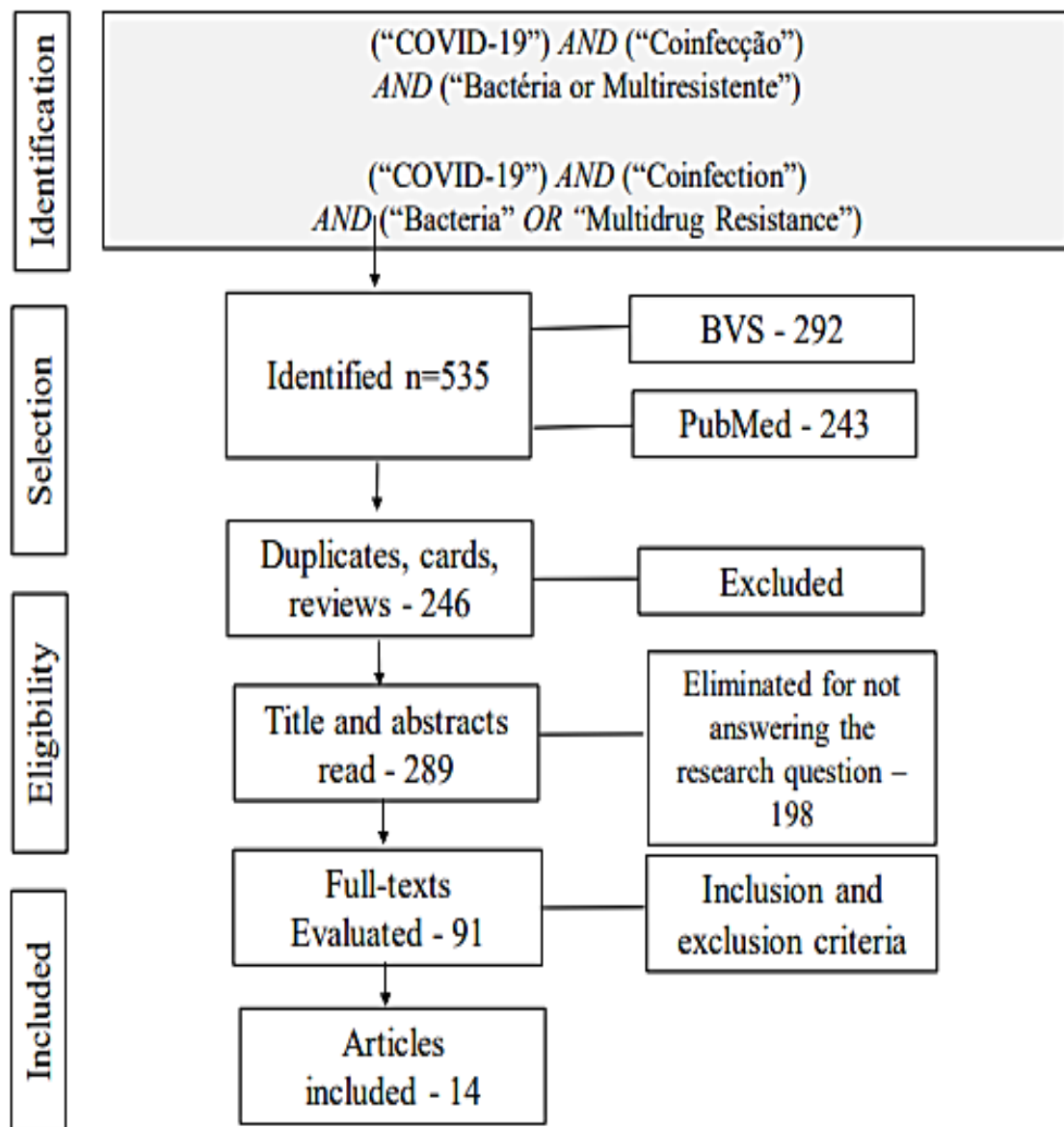


Fig. 1. Flowchart of the search and selection procedure of the articles included in the sample

Table 1. Highlighted results by study for the investigation of bacterial coinfections by MDR microorganisms in patients diagnosed with COVID-19 hospitalized in healthcare units

Title	Author/Year of Publication/Country	Gender/age	Sector	Material Analyzed	Prevalent Bacteria	Total Patients/Outcome
Characteristics and Risk Factors of Secondary Bacterial Infections in Patients with COVID-19[14]	Wu et al.; 2023; China.	51.2% were female; average age of 68 years.	ICU; others.	Blood, urine, and sputum cultures; data extracted from the electronic patient record management system.	<i>Acinetobacter baumannii</i> ; <i>Klebsiella pneumoniae</i> ; <i>Escherichia coli</i> ; <i>Enterococcus faecium</i> ; <i>Staphylococcus aureus</i> (MRSA)	43; not specified.
Bacterial Coinfection at Hospital Admission in Patients with COVID-19 [15]	Moreno-García et al.; 2022; Spain.	64.5% were male; average age of 54 years.	Not specified.	Blood cultures; urinary antigen test (pneumococcal); sputum culture; patient record data.	<i>Streptococcus pneumoniae</i> ; <i>Pseudomonas aeruginosa</i> ; <i>Staphylococcus aureus</i> ; <i>K. pneumoniae</i> ; <i>E. coli</i>	122; not specified
Coinfection and Superinfection in Critically Ill ICU Patients with Severe Pneumonia due to COVID-19 and Influenza Pneumonia: Are the Profiles Different? [16]	Chen et al.; 2023; China.	80.5% were male; average age of 69 years.	ICU	Electronic patient record management system.	<i>P. aeruginosa</i> ; <i>A. baumannii</i> ; <i>K. pneumoniae</i> ; <i>S. aureus</i> ; <i>Enterococcus faecium</i>	27; not specified
Epidemiology of Bacterial Coinfections and Risk Factors in Patients Hospitalized for COVID-19 in Spain: A National Study [17]	López et al.; 2020; Spain.	66.55% were male; average age of 67 years.	ICU	Patient records.	<i>Pseudomonas</i> spp.; <i>S. pneumoniae</i> ; <i>Staphylococcus</i> spp.; <i>S. aureus</i> ; <i>Streptococcus</i> spp.; <i>Enterococcus</i> spp.	4,754; 1,590 deaths.
Incidence of Coinfections and Superinfections in Hospitalized Patients with COVID-19: A Retrospective Cohort Study [18]	García-Vidal et al.; 2020; Spain.	55.8% were male; average age of 62 years.	Not specified.	Clinical samples of sputum, blood cultures, urine cultures, urinary antigen tests; data extracted from patient records.	<i>P. aeruginosa</i> ; <i>E. coli</i> ; <i>K. pneumoniae</i> ; <i>S. aureus</i> ; <i>S. pneumoniae</i>	61; 13 deaths.
Multidrug-Resistant Infections by <i>Acinetobacter baumannii</i> in COVID-19 Patients Hospitalized in ICU [19]	Russo et al.; 2022; Italy.	66% were male; average age of 62 years.	ICU	Patient records and in hospital computerized databases.	<i>Acinetobacter baumannii</i> multidroga resistente (MDR-AB).	32; 26 deaths.
Bacterial Infections Associated with COVID-19 in the Intensive Care Unit: A Case-Control Study [20]	Kaçmaz et al.; 2023; Turkey.	60% were male; average age of 71 years.	ICU	Clinical samples detected by cultures and/or molecular tests in the first episode; data extracted from patient records.	<i>Staphylococcus</i> spp.; <i>Acinetobacter</i> spp.; <i>Klebsiella</i> spp.; <i>P. aeruginosa</i>	67; 18 deaths.

Title	Author/Year of Publication/Country	Gender/age	Sector	Material Analyzed	Prevalent Bacteria	Total Patients/Outcome
Secondary Infections in Critically Ill Patients with COVID-19-Associated ARDS in the ICU: Frequency, Microbiological Characteristics, and Risk Factors [21]	Taysi et al.; 2023; Turkey	50.8% were male; average age of 70 years.	ICU	Clinical samples of sputum and tracheal aspirate; blood culture and urine culture; data extracted from patient records.	<i>Klebsiella spp.</i> ; <i>A. baumannii</i> ; <i>E. coli</i> ; <i>P. aeruginosa</i> ; <i>S. aureus</i> ; <i>Enterobacter aerogenes</i>	61; not specified.
The Impact of the COVID-19 Pandemic on Healthcare-Associated Infections: A University Hospital Experience [22]	Obeidat et al.; 2023; Jordan.	82% were male, average age of 72 years.	ICU; others.	Patient records.	<i>A. baumannii</i> ; <i>E. coli</i> ; <i>K. pneumoniae</i> ; <i>P. aeruginosa</i> ; <i>S. aureus</i>	17; 15 deaths.
Profile of Coinfections and Secondary Infections in COVID-19 Patients at a COVID-19 Dedicated Facility in an Indian Tertiary Care Hospital: Implications for Antimicrobial Resistance [23]	Khurana et al.; 2021; India.	62.5% were male (ICU); 63% were male (Wards); average age of 50 years.	ICU (n= 56); Wards (n= 95).	Clinical samples of blood, urine, respiratory samples, pus; patient records.	<i>K. pneumoniae</i> ; <i>A. baumannii</i> ; <i>E. coli</i> ; <i>P. aeruginosa</i> .	151; 51 deaths.
Profiles of Bacterial Coinfection and Antibiotic Resistance among Hospitalized Patients with COVID-19 [24]	Bazaid et al.; 2022; Saudi Arabia.	55% were male; average age 60 years.	ICU (n= 49); Wards (n= 24).	Clinical samples of blood, urine, sputum, and wound smears; patient records.	<i>K. pneumoniae</i> ; <i>A. baumannii</i> ; <i>P. aeruginosa</i>	73; not specified.
Preditores de gravidade e perfil de resistência à coinfeção em pacientes com COVID-19: primeiro relatório do Alto Egito [25]	Radaman et al.; 2020; Egypt.	55.4% were male; the most common age range was 51 to 70.	Not specified.	Blood samples, sputum, endotracheal aspirates; culture, genetic tests, antibiogram, and statistical analysis.	<i>K. pneumoniae</i> ; <i>A. baumannii</i> ; <i>P. aeruginosa</i> ; <i>S. aureus</i> ; <i>S. pneumoniae</i> ; <i>E. faecalis</i>	260; 24 deaths.
Prevalence and Clinical Impact of Coinfection in Patients with Coronavirus Disease 2019 in Korea [26]	Jeong et al.; 2022; South Korea.	51.4% were male; average age 70 years.	Not specified.	Clinical samples of sputum, nasal swab, and tracheal aspiration; patient records.	<i>A. baumannii</i> (CRAB); <i>P. aeruginosa</i> (CRPA); <i>S. aureus</i> (MRSA), <i>K. pneumoniae</i> ; <i>E. coli</i> . (produtoras de ESBL)	30; not specified.
A Comparative Study on Bacterial Coinfections and the Prevalence of Multidrug-Resistant Organisms among Patients in COVID and Non-COVID Intensive Care Units [27]	Sathyakamala et al; 2022; India.	Not specified.	ICU.	Clinical samples of blood, urine, and sputum; patient records.	<i>E. coli</i> , <i>Klebsiella spp.</i> ; <i>Pseudomonas spp.</i> ; <i>Acinetobacter spp.</i> ; <i>Citrobacter spp.</i> ; <i>Proteus spp.</i>	203; not specified.

Source: Authors, 2023

4. DISCUSSION

Microbial coinfection plays a significant role in the occurrence and development of SARS-CoV-2 infection, increasing the challenges in diagnosing, treating, and predicting COVID-19, and even exacerbating the disease's symptoms and mortality [28].

In this study, the rate of bacterial coinfection ranged from 9.6% to 29.8%. Ripa et al. [29] found a coinfection rate of 9.3% in hospitalized COVID-19 patients. Yu et al. [30] investigated the rate of secondary infection in 226 critically ill COVID-19 patients, and found a coinfection rate of 21.7%. A meta-analysis conducted in 2020 concluded that 7% of patients had bacterial coinfection, a rate that increased to 14% for patients admitted to the ICU [31]. Huang et al. [31] reported that four cases (9.8%) had secondary bacterial infections among 41 hospitalized COVID-19 patients. In the case of COVID-19 coinfections, the mechanisms leading to a low incidence are not well understood [32]. Several hypotheses have been raised, including prophylactic antibiotic therapy upon hospital admission and the presence of an immune factor such as macrophage hyperactivation [33].

The results of this study showed that bacterial coinfections can affect the progression of COVID-19 and mortality, especially in patients in intensive care units (ICUs) [14,16,17,19-24,27]. Other studies have reported similar results, with only 7% of hospitalized patients presenting bacterial coinfections and a high degree of heterogeneity, increasing to 14% in ICU patients [34,35].

According to Sharifipour et al. [36], the observed prevalence of bacterial coinfection among COVID-19 patients in ICUs can be attributed to various factors, including compromised immunity, low adherence to self-protection measures by healthcare professionals and patients, weak infection control in wards, high workload, and staff shortages.

Additionally, we observed that the majority of COVID-19 patients with coinfections were male, reaching up to 80% in some studies [16,22]. Studies suggest that most coinfections involve male patients, which is an additional independent risk factor in the more severe cases of this condition, in addition to the major comorbidities and the use of immunosuppressive medications that favor this outcome [37-39].

In addition to male sex, risk factors such as comorbidities: diabetes, hypertension, obesity and advanced age have been associated with co-infection [14,16,17,21,22,24-26].

Regarding the prevalent microorganisms found in hospitalized COVID-19 patients in our study, gram-negative bacteria stood out (70%), among which *Klebsiella pneumoniae* (85.71%) and *Acinetobacter baumannii* (78.57%) predominated [14,16,18-27]. Among gram-positive bacteria, *Staphylococcus aureus* had the highest frequency at 71.42% [14-17,18,20-22,25,26], followed by *Streptococcus pneumoniae* (35.71%) [15,17,18,25,]. In line with these findings, Obeidat et al. [22] reported, in a study involving the distribution of reported microorganisms, that gram-negative and gram-positive bacteria were isolated in 72% and 8.5% of cases, respectively. This finding differed from a Chinese study, where gram-negative bacteria accounted for 87.5%, and gram-positive isolates were identified in 12.0% of cases [40].

A study conducted in Bahrain demonstrated the prevalence of gram-negative isolates in over 1,380 COVID-19 patients, distributed as follows: *Klebsiella pneumoniae* (23.8%), *Pseudomonas aeruginosa* (23.2%), *Acinetobacter baumannii* (22.0%), and *Escherichia coli* (17.1%) [41]. Furthermore, among 1,495 COVID-19 patients hospitalized in Wuhan with secondary bacterial infections, the most commonly isolated bacteria were *Acinetobacter baumannii* (35.8%) and *Klebsiella pneumoniae* (30.8%) [42]. Conversely, an international retrospective study showed that gram-positive bacteria were the most commonly isolated microorganisms in COVID-19 patients, with *Streptococcus pneumoniae* and *Staphylococcus aureus* each occurring in 16.2% of patients. These studies suggest that drug resistance and the distribution of these pathogenic microorganisms vary among countries [22].

In this integrative review, multidrug-resistant microorganisms were reported in 85.7% of cases. The most frequently isolated species were carbapenem-resistant gram-negative bacteria and methicillin-resistant *Staphylococcus aureus* (MRSA). The most prevalent resistant microorganisms in the analyzed studies were methicillin-resistant *Staphylococcus aureus* (MRSA; 64.00%), followed by carbapenem-resistant *Acinetobacter baumannii* (CRAB; 57.14%) and extended-spectrum beta-lactamase-producing *Klebsiella pneumoniae*

(ESBL+; 42.85%). However, in the study by Mahmoudi [43] and the one conducted by Khurana et al. [44], there were higher occurrences of multidrug-resistant species of *Klebsiella*, followed by *Acinetobacter* spp. On the other hand, the study by Rezasoltani et al. [45] observed a higher prevalence of *Staphylococcus aureus* (MRSA).

Obeidat et al. [22] reported several resistance mechanisms among microorganisms. However, extended-spectrum beta-lactamase (ESBL) production was the leading cause of antimicrobial resistance among *Klebsiella* spp. and *E. coli*, reaching 67% and 52%, respectively. Moreover, a high occurrence of carbapenem-resistant gram-negative bacteria was observed, with 97% for *A. baumannii* (CRAB) and 44% for *P. aeruginosa*. This fact certainly is important and can lead to severe complications in cases of coinfection in COVID-19 patients. Although these data are higher than those reported in a Chinese study, where the rates of occurrence of coinfections by *E. coli* (ESBL), *K. pneumoniae* (ESBL), *A. baumannii* (CRAB), and *P. aeruginosa* (CRO) were 30.5%, 16.1%, 19.5%, and 10.0%, respectively [46].

The extensive use of broad-spectrum antimicrobial drugs during the COVID-19 outbreak in hospitalized patients, especially in ICUs, may have contributed to the selection of pathogens with different resistance profiles. Additionally, microorganisms such as *S. aureus*, *Enterococcus* spp., Enterobacteriaceae, *P. aeruginosa*, and *Acinetobacter* spp. are often responsible for healthcare-associated infections and are prone to developing multidrug resistance.

5. CONCLUSION

[This integrative literature review found that patients hospitalized in ICUs with COVID-19 who presented bacterial coinfection were more frequently infected by multidrug-resistant microorganisms in comparison with patients admitted to other hospital wards/sectors. The microorganisms most frequently isolated in these individuals with a multidrug resistance profile were *A. baumannii* (CRAB), *K. pneumoniae*, *E. coli* (ESBL), and *P. aeruginosa* (CRO). Additionally, among gram-positive bacteria, *S. aureus* (MRSA) stood out. Therefore, it is important to emphasize that bacterial coinfections in critically ill patients should not be underestimated. These results indicate the need

to pay attention to infections caused by multidrug-resistant microorganisms, and reinforce the need for ethical and rational use of antibiotics.

ACKNOWLEDGEMENTS

A brief acknowledgement section may be given after the conclusion section just before the references. The acknowledgments of people who provided assistance in manuscript preparation, funding for research, etc. should be listed in this section. All sources of funding should be declared as an acknowledgement. Authors should declare the role of funding agency, if any, in the study design, collection, analysis and interpretation of data; in the writing of the manuscript. If the study sponsors had no such involvement, the authors should so state.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Khalil OAK, da Silva Khalil S. SARS- CoV-2: Taxonomy, origin and constitution. *Revista de Medicina*. 2020; 99(5):473-479.
2. Vieira MCS, Sardinha DM, Silva MJA, Lima LNGC, Lima KVB. SARS-CoV-2 infection. In: Rodrigues YC, Lima KVB. Infectious and parasitic agents of importance in the Brazilian Amazon: Updates on clinical, epidemiological and molecular aspects. Bauru: Gradus Editora. 2021:285-304.
3. Manzini S, Rodrigues NJL, Bertozzo TV, Aires IN, Lucheis SB. SARS-COV-2: Its relationship with animals and potential zoonotic disease. *Veterinaria e Zootecnia*; 2021.
4. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Tan W. A novel coronavirus from patients with pneumonia in China, 2019. *New England journal of medicine*. 2020;382(8):727-733.
5. WHO, World Health Organization. Report on the burden of endemic health care associated infection worldwide: A systematic review of the literature. Geneva: The critical role of infection prevention and control; 2017. Accessed March 8, 2023.
6. Hinrichsen SL, Gallindo M, Galvão BHA, Costa IC, Hinrichsen BL. Healthcare-

- associated infection: Importance and control. In: Hinrichsen SL. Biosafety and infection control: Hospital health risk. 3rd ed. Rio de Janeiro: Guanabara Koogan. 2018;273-81.
7. Da Silva, RA, Freitas, DKP de, Souza RV. Impact of covid-19 on patients with leprosy. *Multidisciplinary Health Journal*. 2021;2(4):122-122.
 8. Rawson TM, Moore LS, Zhu N, Ranganathan N, Skolimowska K, Gilchrist M, Holmes A. Bacterial and fungal coinfection in individuals with coronavirus: a rapid review to support COVID-19 antimicrobial prescribing. *Clinical Infectious Diseases*. 2020;71(9):2459-2468.
 9. Brazil. National Health Surveillance Agency. Prevention of infections by multidrug-resistant Microorganisms in healthcare services: Patient safety and quality in healthcare services series. Brasília: Anvisa. 2021;103. [cited 2021 Jul 20]. Available at: <https://pncq.org.br/wp-content/uploads/2021/03/manual-prevencaode-multirresistencias7.pdf>.
 10. WHO, World Health Organization. Report on surveillance of antibiotic consumption; 2018. Accessed January 10, 2022. Available: <https://www.who.int/antimicrobial-resistance/publications/surveillance-system-manual/en/>.
 11. Brazil. Ministry of Health. Ordinance no. 2616, Official Gazette of the Union, Brasília; 1998, May 12. Available at: http://bvsmis.saude.gov.br/bvs/saudelegis/gm/1998/prt2616_12_05_1998.html Accessed in March. 2023.
 12. Bradford PA, Bratu S, Urban C, Visalli M, Mariano N, Landman D, Quale J. Emergence of carbapenem-resistant *Klebsiella* species possessing the class A carbapenem-hydrolyzing KPC-2 and inhibitor-resistant TEM-30 β -lactamases in New York City. *Clinical Infectious Diseases*. 2004;39(1):55-60.
 13. Souza MTD, Silva MDD, Carvalho RD. Integrative review: What is it? How to do it? *Einstein (São Paulo)*. 2010;8:102-106.
 14. Wu G, Lu J, Liu D, He Y. Characteristics and risk factors of secondary bacterial infections in COVID-19 patients. *Antimicrobial Stewardship & Healthcare Epidemiology*. 2023;3(1):e156.
 15. Moreno-García E, Puerta-Alcalde P, Letona L, Meira F, Dueñas G, Chumbita M, Garcia-Vidal C. Bacterial co-infection at hospital admission in patients with COVID-19. *International Journal of Infectious Diseases*. 2022;118:197-202.
 16. Chen Z, Zhan Q, Huang L, Wang C. Coinfection and superinfection in ICU critically ill patients with severe COVID-19 pneumonia and influenza pneumonia: Are the pictures different? *Frontiers in Public Health*. 2023;11.
 17. López-Herrero R, Sánchez-de Prada L, Tamayo-Velasco A, Lorenzo-López M, Gómez-Pesquera E, Sánchez-Quirós B, Álvaro-Meca A. Epidemiology of bacterial co-infections and risk factors in COVID-19-hospitalized patients in Spain: a nationwide study. *European Journal of Public Health*. 2023;ckad060.
 18. Garcia-Vidal C, Sanjuan G, Moreno-García E, Puerta-Alcalde P, Garcia-Pouton N, Chumbita M, Torres A. Incidence of co-infections and superinfections in hospitalized patients with COVID-19: A retrospective cohort study. *Clinical Microbiology and Infection*. 2021;27(1):83-88.
 19. Russo A, Gavaruzzi F, Ceccarelli G, Borrazzo C, Oliva A, Alessandri F, Venditti M. Multidrug-resistant *Acinetobacter baumannii* infections in COVID-19 patients hospitalized in intensive care unit. *Infection*. 2022;1-10.
 20. Kaçmaz B, Keske Ş, Şişman U, Ateş ST, Güldan M, Beşli Y, Ergönül Ö. COVID-19 associated bacterial infections in intensive care unit: a case control study. *Scientific Reports*. 2023;13(1):13345.
 21. Taysi MR, Yildirim F, Simsek M, Dural HI, Sencan I. Secondary infections in critical patients with COVID-19 Associated ARDS in the ICU: Frequency, Microbiologic Characteristics and Risk Factors. *J. Coll. Physicians Surg. Pak*. 2023;33:181-187.
 22. Obeidat H, El-Nasser Z, Amarin Z., Qablan A, Gharaibeh F. The impact of COVID-19 pandemic on healthcare associated infections: A teaching hospital experience. *Medicine*. 2023;102(15).
 23. Khurana S, Singh P, Sharad N, Kiro VV, Rastogi N, Lathwal A, Mathur P. Profile of co-infections & secondary infections in COVID-19 patients at a dedicated COVID-19 facility of a tertiary care Indian hospital: Implication on antimicrobial resistance. *Indian journal of medical microbiology*. 2021;39(2):147-153.

24. Bazaid AS, Barnawi H, Qanash H, Alsaif G, Aldarhami A, Gattan H, Alfouzan F. Bacterial coinfection and antibiotic resistance profiles among hospitalised COVID-19 patients. *Microorganisms*. 2022;10(3):495.
25. Ramadan HKA, Mahmoud MA, Aburahma MZ, Elkhawaga AA, El-Mokhtar MA, Sayed IM, Medhat MA. Predictors of severity and co-infection resistance profile in COVID-19 patients: First report from upper Egypt. *Infection and Drug Resistance*. 2020;3409-3422.
26. Jeong S, Lee N, Park Y, Kim J, Jeon K, Park MJ, Song W. Prevalence and clinical impact of coinfection in patients with coronavirus disease 2019 in Korea. *Viruses*. 2022;14(2):446.
27. Sathyakamala R, Peace AR, Shanmugam P. A comparative study on bacterial co-infections and prevalence of multidrug resistant organisms among patients in COVID and non-COVID intensive care units. *Journal of Preventive Medicine and Hygiene*. 2022;63(1):E19.
28. Chen X, Liao B, Cheng L, Peng X, Xu X, Li Y, Ren B. The microbial coinfection in COVID-19. *Applied Microbiology and Biotechnology*. 2020;104:7777-7785.
29. Ripa M, Galli L, Poli A, Oltolini C, Spagnuolo V, Mastrangelo A, Vinci C. Secondary infections in patients hospitalized with COVID-19: Incidence and predictive factors. *Clinical Microbiology and Infection*. 2021;27(3):451-457.
30. Yu Y, Xu D, Fu S, Zhang J, Yang X, Xu L, Shang Y. Patients with COVID-19 in 19 ICUs in Wuhan, China: A cross-sectional study. *Critical Care*. 2020;24:1-10.
31. Lansbury L, Lim B, Baskaran V, Lim WS. Co-infections in people with COVID-19: A systematic review and meta-analysis. *Journal of Infection*. 2020;81(2): 266-275.
32. Cao M, Zhang D, Wang Y, Lu Y, Zhu X, Li Y, Lu H. Clinical features of patients infected with the 2019 novel coronavirus (COVID-19) in Shanghai, China. *MedRxiv*. 2020;03.
33. Garcia-Vidal C, Sanjuan G, Moreno-García E, Puerta-Alcalde P, Garcia-Pouton N, Chumbita M, Torres A. Incidence of co-infections and superinfections in hospitalized patients with COVID-19: A retrospective cohort study. *Clinical Microbiology and Infection*. 2021;27(1):83-88.
34. Fu Y, Yang Q, Xu M, Kong H, Chen H, Fu Y, Zhou J. (2020, June). Secondary bacterial infections in critical ill patients with coronavirus disease 2019. In *Open forum infectious diseases*. US: Oxford University Press. 2021;7(6):ofaa220.
35. Lansbury L, Lim B, Baskaran V, Lim WS. Co-infections in people with COVID-19: A systematic review and meta-analysis. *Journal of Infection*. 2020;81(2):266-275.
36. Sharifipour E, Shams S, Esmkhani M, Khodadadi J, Fotouhi-Ardakani R, Koohpaei A, Ej Golzari S. Evaluation of bacterial co-infections of the respiratory tract in COVID-19 patients admitted to ICU. *BMC Infectious Diseases*. 2020; 20(1):1-7.
37. Da Silva Sousa AH, Martins SB, Cortez ACL. Influence of comorbidities on the health of the elderly in the face of the Covid-19 pandemic: An integrative review. *Research, Society and Development*. 2021;10(17):e199101724678-e199101724678.
38. Pereira Filho AR, Navarini A, Mimica LMJ. Association of COVID-19 to multidrug-resistant bacterial superinfections and coinfections: an integrative review. *Medical Archives of the Hospitals and Faculty of Medical Sciences of Santa Casa de São Paulo*, 1-of; 2022.
39. Machado ABS, Alves AF, Araújo HR, Barros JF, Teixeira LSF, de Moura RS. Immunosuppressive therapies in the treatment of COVID-19: An integrative literature review. *Brazilian Journal of Health Review*. 2021;4(2):5115-5130.
40. Wei XL, Zeng QL, Xie M, Bao Y. Pathogen distribution, drug resistance risk factors, and construction of risk prediction model for drug-resistant bacterial infection in hospitalized patients at the respiratory department during the COVID-19 pandemic. *Infection and Drug Resistance*. 2023;1107-1121.
41. Saeed NK, Al-Khawaja S, Alsalman J, Almusawi S, Albaloooshi NA, Al-Biltagi M. Bacterial co-infection in patients with SARS-CoV-2 in the Kingdom of Bahrain. *World Journal of Virology*. 2021; 10(4):168.
42. Li J, Wang J, Yang Y, Cai P, Cao J, Cai X, Zhang Y. Etiology and antimicrobial resistance of secondary bacterial infections in patients hospitalized with COVID-19 in Wuhan, China: A retrospective analysis. *Antimicrobial Resistance & Infection Control*. 2020;9(1):1-7

43. Mahmoudi H. Bacterial co-infections and antibiotic resistance in patients with COVID-19. *GMS Hygiene and Infection Control*. 2020;15.
44. Khurana S, Singh P, Sharad N, Kiro VV, Rastogi N, Lathwal A, Mathur P. Profile of co-infections & secondary infections in COVID-19 patients at a dedicated COVID-19 facility of a tertiary care Indian hospital: Implication on antimicrobial resistance. *Indian Journal of Medical Microbiology*. 2021;39(2):147-153.
45. Rezasoltani S, Yadegar A, Hatami B, Asadzadeh Aghdai H, Zali MR. Antimicrobial resistance as a hidden menace lurking behind the COVID-19 outbreak: The global impacts of too much hygiene on AMR. *Frontiers in Microbiology*. 2020;11:590683.
46. Nasir N, Rehman F, Omair SF. Risk factors for bacterial infections in patients with moderate to severe COVID-19: A case-control study. *Journal of Medical Virology*. 2021;93(7):4564-4569.

© Copyright (2024): Author(s). The licensee is the journal publisher. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:

The peer review history for this paper can be accessed here:
<https://www.sdiarticle5.com/review-history/113008>