# Bacterial Infection Among Covid-19-Infected Patients Admitted to the Intensive Care Unit at King Abdullah Hospital in Bisha: A Single-Centre Retrospective Observational Study

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**Abstract:** *Background*: The covid-19 pandemic has created significant challenges for healthcare systems worldwide, especially in intensive care units (ICU), which face unprecedented hardship. Despite the primary focus on viral infection, the precise influence of bacterial superinfections on the outcome of severe covid-19 cases, particularly in different hospital settings, remains uncertain.

*Objective*: to investigate the prevalence, characteristics, and outcomes of bacterial superinfections in covid-19 patients hospitalized in the ICU in Saudi Arabia during the second wave of the pandemic.

*Methods*: This study was conducted at King Abdullah Hospital in Bisha, Saudi Arabia, and involved retrospective observational analysis. This study examined 121 adult patients admitted to the ICU due to severe covid-19 between April and July 2021. Information regarding demographics, clinical characteristics, radiological findings, and microbiological data was also collected. This study examined the relationship between superinfections and mortality through rigorous statistical analyses, including chi-square testing and multivariable logistic regression.

*Results*: Most participants in the study were men (57.9%) and Saudi citizens (95.0%), with an average age of 63 ± 17 years. The incidence of superinfections among the patients was 43.8%, significantly higher than that reported in previous studies. Microbiological examinations revealed the presence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) organisms, particularly in respiratory samples. The most common isolates were KLEPNE-XDR (10.7%) and ACIBAU-XDR (8.3%). A statistically significant correlation was observed between superinfection and mortality (p=0.042). Patients with superinfections experienced a significantly higher mortality rate of 55.3% in comparison to those without superinfections, who had a mortality rate of 44.7%. Multivariable logistic regression identified age (aOR 1.040, 95% CI: 1.012-1.068, p=0.004) and non-Saudi nationality (aOR 12.320, 95% CI: 1.242-122.177, p=0.032) as significant predictors of mortality. Interestingly, a high percentage of the patients (89.3 %) were treated with carbapenems.

*Conclusion*: Our research revealed a notable prevalence of bacterial superinfections, including highly resistant strains, among severely ill covid-19 patients in the ICU. The significant link between superinfections and mortality underscores the pressing need for enhanced diagnostic tools, targeted antimicrobial therapies, and improved stewardship protocols in the ICU setting. The findings of this study have important implications for clinical care and public health policy in the ongoing battle against covid-19 and its consequences.

**Keywords:** Covid-19, bacterial Infection, multidrug resistance, ICU, MDR, XDR.

## INTRODUCTION

The covid-19 pandemic has significantly affected healthcare systems globally. As of 2022, SARS-CoV-2 had caused over 500 million confirmed cases and resulted in more than 6 million fatalities globally [1], indicating a significant impact. Considerable focus has been directed towards viral infection; however, the significance of secondary bacterial infections in the well-being and prognosis of covid-19 patients, particularly those requiring intensive care unit (ICU) therapy, is becoming increasingly evident [2].

It has long been recognized that superinfections, secondary bacterial illnesses, can exacerbate viral respiratory disorders. For instance, there have been previous outbreaks of coronaviruses, such as SARS and MERS [3, 4]. These infections can exacerbate respiratory difficulties in critically ill patients, leading to prolonged hospitalization in the ICU, increased reliance on potent medications, and potentially higher mortality rates [5]. Regarding covid-19, initial research has indicated that bacterial co-infections among patients admitted to the hospital varied from 3.5% to 14%. The incidence was elevated in locations such as the ICU [6]. In a study conducted by Langford *et al*. (2020), it was discovered that some covid-19 patients admitted to the hospital or ICU also had bacterial infections [7].

The etiology of the increased susceptibility of individuals with covid-19 to bacterial infections is multifaceted and intricate. When the body becomes infected with SARS-CoV-2, it can impair the immune system by inhibiting the correct functioning of Type I interferon responses and depleting T cells [8]. The

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E-ISSN: 1929-6029/24

virus can also damage the respiratory epithelium, impairing mucus clearance and alterations in lung microorganisms. These variables facilitate bacterial colonization and entry into the respiratory system [9]. In addition, immunomodulatory medications, such as corticosteroids and tocilizumab, and invasive procedures, such as mechanical ventilation in the ICU, might increase the susceptibility of patients to developing secondary infections [10, 11].

Despite extensive research on covid-19, our understanding of its prevalence, types of infection, and impact on severely ill individuals, particularly in diverse global regions and healthcare settings, remains incomplete. An extensive study has been conducted on bacterial infections upon patients' first admission to the hospital. However, there is little knowledge of the diseases that arise during their stay in the critical care unit [12]. Furthermore, the emergence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) bacteria in covid-19 is a distinct issue that requires further investigation [13].

The World Health Organization (WHO) has identified the global increase in antibiotic resistance as a significant public health concern. The covid-19 pandemic may have exacerbated this issue [14, 15]. At the onset of the pandemic, antibiotics were frequently administered without substantial evidence of bacterial illness, relying instead on experiential knowledge and observation [16]. Although this strategy intended to prevent bacterial superinfections, it may have inadvertently facilitated the emergence and dissemination of resistant species in hospitals [17]. Scientists have shown that individuals who have contracted covid-19 also have MDR microorganisms such as methicillin-resistant Staphylococcus aureus (MRSA), extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae, and carbapenem-resistant Acinetobacter baumannii [18]. However, the prevalence of antibiotic-resistant bacteria in secondary diseases associated with covid-19, particularly in ICU, remains uncertain in several locations.

This study aimed to address these information gaps by investigating the frequency, types, and impacts of microbial presence in covid-19 patients admitted to the critical care unit at King Abdullah Hospital in Bisha, Saudi Arabia. During the second wave of the pandemic, our primary objective was to meticulously examine a specific healthcare facility to identify all superinfection instances. This study aimed to investigate the frequency of the occurrence of MDR and XDR bacteria, patterns of antibiotic usage, and the impact of superinfections on patient outcomes.

The findings of this study have significant implications for doctors' provision of medical treatment and the establishment of safety regulations in hospitals. Analyzing the patterns of bacterial superinfections in very ill covid-19 patients might facilitate the development of more effective antibiotic therapies, the implementation of infection prevention measures, and the establishment of clinical care protocols.

## METHODS

### Study Design and Setting

This retrospective observational study was conducted at King Abdullah Hospital, a 600-bed tertiary care facility in Bisha, Saudi Arabia, which serves both urban and rural populations. The study focused on adult patients admitted to the ICU with severe covid-19 during the second wave of the pandemic, from April to July 2021. This timeframe and single-center focus allowed for a detailed examination of local healthcare practices and bacterial superinfection patterns.

### Patient Eligibility and Selection Criteria

**Inclusion criteria:** included adults (aged ≥18 years) who tested positive for SARS-CoV-2 infection using reverse transcription-polymerase chain reaction (RT-PCR) and were admitted to the ICU due to severe covid-19, defined according to World Health Organization (WHO) criteria.

**Exclusion criteria:** individuals with insufficient medical data and those transferred from other facilities after being admitted to the ICU.

### Data Collection and Variables

Data were extracted from electronic medical records using a standardized data collection form designed to minimize variability and ensure consistency. Variables included in the statistical analysis were meticulously chosen based on their clinical relevance and potential association with outcomes.

The following variables were collected:

1. **Demographic Data:** Age, sex, nationality, and body mass index (BMI).

2. **Clinical Characteristics:** Comorbidities, vital signs (e.g., temperature, blood pressure, pulse

rate, and oxygen saturation) at admission, and length of ICU stay.

3. **Radiological Findings:** Results from chest radiography and computed tomography (CT) scans.

4. **Laboratory and Microbiological Data:** Complete blood counts, biochemical markers (e.g., D-dimer, ferritin, albumin), and culture results (blood, urine, and respiratory specimens). Cultures were processed in the hospital's licensed laboratory using Microscan Walk Away 96 Plus® equipment (Beckman Coulter, Switzerland) for identification and antimicrobial susceptibility testing.

5. **Treatment Data:** Use of mechanical ventilation, inotropic support, and antimicrobial therapies (antibiotics and antifungals).

6. **Outcomes:** Survival status (alive or deceased) and the occurrence of superinfections, defined as secondary bacterial or fungal infections diagnosed ≥48 hours after ICU admission.

### Microbiological Methods

Specimens (blood, urine, and respiratory) were collected for microbiological analysis upon clinical suspicion of superinfection. Antimicrobial susceptibility testing was performed using Microscan® AST cards (N1T1, N2T2, VP1, VP2, TDA, and PEP), following the Clinical and Laboratory Standards Institute (CLSI) guidelines for determining and interpreting Minimum Inhibitory Concentrations (MICs). Multidrug resistance (MDR) was defined as non-susceptibility to at least one agent in three or more antimicrobial categories, while extensively drug resistance (XDR) was defined as non-susceptibility to all but two or fewer antimicrobial categories.

### Statistical Analysis

Descriptive statistics were calculated for each variable. As applicable, continuous data were presented as mean and standard deviation (SD) or median and interquartile range (IQR). Categorical data were presented as frequencies and percentages. The chi-squared test was used to assess the correlation between superinfection and mortality. Multivariable binary logistic regression analysis was used to identify variables associated with mortality. These variables included superinfection status, age, sex, nationality, BMI, and length of ICU stay. Adjusted odds ratios (aOR) and 95% confidence intervals (CI) were calculated. For all studies, p-values less than 0.05 were considered statistically significant. Statistical analyses were performed using the IBM SPSS version 29.

### Ethical Considerations

The institutional review board of King Abdullah Hospital approved the study. Because the study was retrospectively completed, informed consent was waived. Strict patient confidentiality was maintained throughout the data collection and analysis methods.

## RESULTS

The study identified a range of multidrug-resistant (MDR) and extensively drug-resistant (XDR) bacterial strains. The most prevalent pathogens were Klebsiella pneumoniae XDR (KLEPNE-XDR, 10.7%) and Acinetobacter baumannii XDR (ACIBAU-XDR, 8.3%), predominantly found in respiratory specimens. Klebsiella pneumoniae MDR and Pseudomonas aeruginosa MDR were also significant contributors.

Table **1** shows the demographic features of the study sample, which included 121 ICU patients diagnosed with severe covid-19. Of the patients, 57.9% (n = 70) were male and 42.1% (n = 51) were female. Most patients (95.0%, n = 115) were Saudi citizens, with a small fraction (5.0%, n = 6) being non-Saudi citizens. The mean age of the patients was 63 ± 17 years. The patients' ages ranged from 24 to 103 years old. The average body mass index (BMI) was 28.0 ± 3.8 kg/m$^2$, ranging from 19.4 to 42.0.

**Table 1: Characteristics of ICU Patients with Severe COVID-19**

| Demographic characteristics | | N | % |
|---|---|---|---|
| Sex | Female | 51 | 42.1% |
| | Male | 70 | 57.9% |
| Nationality | Non-Saudi | 6 | 5.0% |
| | SAUDI | 115 | 95.0% |
| Age | Mean (SD), Range | 63 (17) | 24 -103 |
| BMI | Mean (SD), Range | 28.0 (3.8) | 19.4 - 42.0 |

Table **2** shows the clinical features of ICU patients with severe covid-19. The average ICU stay in the ICU was 18 ± 12 days. The length of stay varied greatly, from one to 64 days. The average temperature upon admission was 37.2 ± 0.7°C (range from 36.0°C to

**Table 2: Clinical Characteristics of Patients Admitted to the ICU with a Severe COVID-19 Infection**

| Clinical characteristics | Mean | SD | Minimum | Maximum |
|---|---|---|---|---|
| Duration of stay (days) | 18 | 12 | 1 | 64 |
| Temperature at admission | 37.2 | .7 | 36.0 | 39.5 |
| Systolic BP | 130 | 23 | 76 | 188 |
| Diastolic BP | 72 | 15 | 26 | 170 |
| O2 saturation | 84 | 8 | 55 | 100 |
| Pulse rate | 88 | 17 | 48 | 132 |

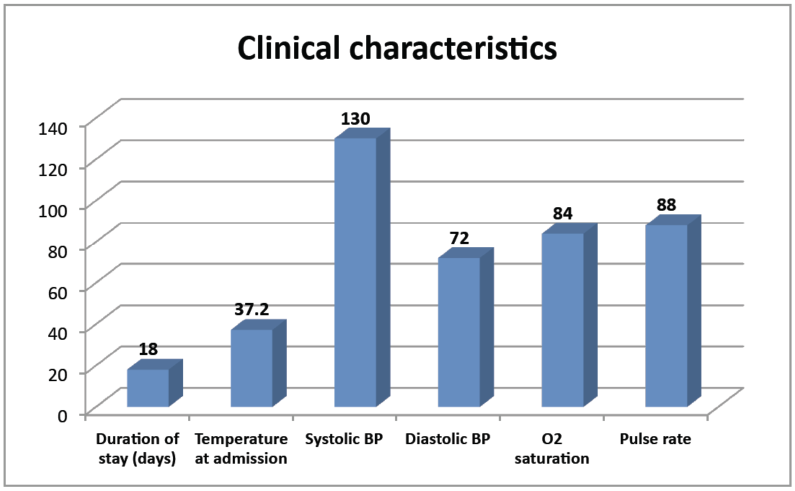


**Figure 1:** Clinical characteristics of patients admitted to the ICU with a severe covid-19 infection.

39.5°C). The average systolic blood pressure was 130 ± 23 mmHg, ranging from 76 mmHg to 188 mmHg. The average diastolic blood pressure was 72 ± 15 mmHg, ranging from 26 mmHg to 170 mmHg. The average oxygen saturation at admission was 84 ± 8%, with a 55–100% range. The mean pulse rate was 88 ± 17 beats/min. The range was 48–132 beats/min.

Table **3** shows the radiological findings of the ICU patients who developed severe covid-19. All patients underwent chest radiography, and 88.4% (n = 107) showed infiltrates, whereas 11.6% (n = 14) did not. Additionally, CT scans were performed, and the findings were divided into five groups. Clear lungs were the most common finding in 47.1% (n = 57) of patients. Consolidation was discovered in 22.3% (n = 27) of patients, whereas pleural effusion was observed in 25.6% (n = 31). Only a tiny percentage of patients (1.7%, n = 2) had both consolidation and pleural effusion, whereas 3.4% (n = 4) had pneumothorax.

Table **4** shows the hematological parameters of patients in the ICU with severe covid-19. The average WBC count was 12.86 x 10^9 ± 10.70 cells/L, ranging

**Table 3: Radiographic Findings of ICU Patients with Severe COVID-19**

| Radiological findings | | N | % |
|---|---|---|---|
| Chest x-ray - infiltrate | No | 14 | 11.6% |
| | Yes | 107 | 88.4% |
| CT scan | Clear | 57 | 47.1% |
| | Consolidation | 27 | 22.3% |
| | Consolidation + pleural effusion | 2 | 1.7% |
| | Pleural effusion | 31 | 25.6% |
| | Pneumothorax | 4 | 3.4% |

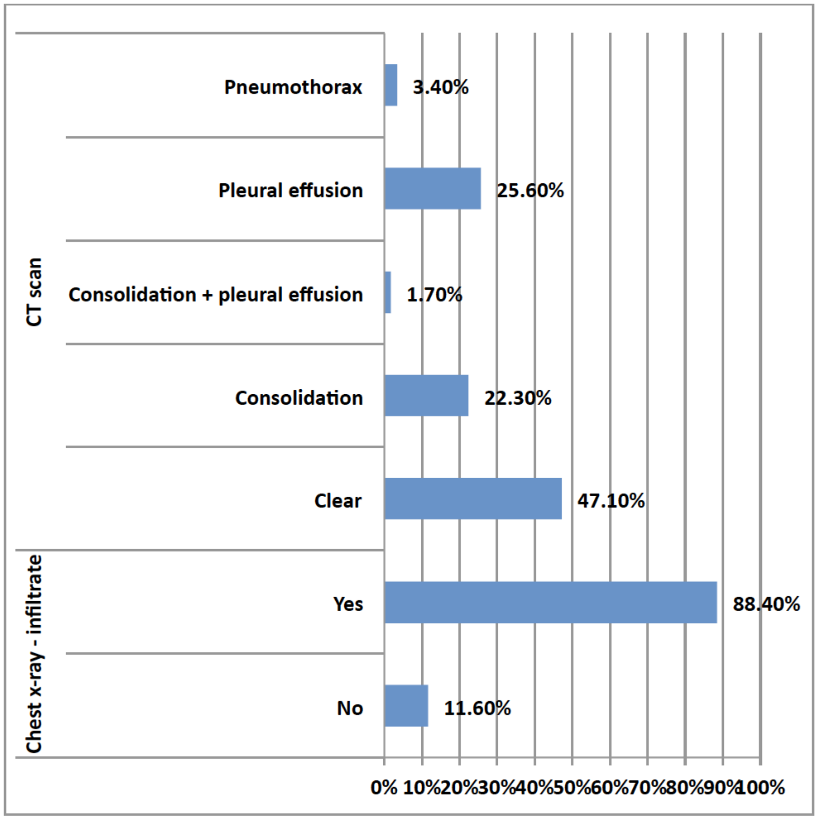


**Figure 2:** Radiographic findings of ICU patients with severe covid-19.

**Table 4: Hematological Parameters of ICU Patients with Severe COVID-19**

| Hematological parameters | Mean | SD | Minimum | Maximum |
|---|---|---|---|---|
| WBC Count (x10^9) | 12.86 | 10.70 | 2.57 | 103.00 |
| Haemoglobin (g/dl) | 12.37 | 1.94 | 7.80 | 17.40 |
| Platelets (x10^9 ) | 225.5 | 98.5 | 27.1 | 481.0 |
| Neutrophil count (x10^9) | 81.22 | 11.76 | 41.00 | 99.00 |
| Lymphocyte count (x10^9) | 13.71 | 8.85 | 2.10 | 46.40 |

from 2.57 to 103.00 x 10^9 cells/L. The mean hemoglobin level was 12.37 ± 1.94 g/dL and varied between 7.80 and 17.40 g/dL. The platelet counts averaged 225.5 x 10^9 ± 98.5 cells/L and ranged from 27.1–481.0 x 10^9 cells/L. The mean neutrophil count was 81.22 x 10^9 ±11.76 cells/L and varied from 41.00 to 99.00 x 10^9 cells/L. The average lymphocyte count was 13.71 x 10^9 ± 8.85 cells per liter, ranging from 2.10 to 46.40 x 10^9 cells per liter.

Table **5** shows the biochemical features of ICU patients hospitalized with severe covid-19 infection. The mean erythrocyte sedimentation rate (ESR) was 50.5 ± 34.3 mm/hr, and values varied between 2.6 and 121.0 mm/hr. The mean lactate dehydrogenase (LDH) level was 615.85 ± 339.8 u/L, and levels varied between 1.72 and 1917.00 u/L. The mean creatinine kinase (CK) level was 340.4 ± 767.1 u/L, and levels measured varied from 8.0 to 5803.0 u/L.

The average CKMB value was 37.00 ± 33.57 u/L, and levels varied between 8.10 and 202.00 u/L. The ferritin level averaged 1217.2 ± 567.0 μ/L and ranged from 9.0 to 2000.0 μ/L. The average D-dimer concentration was 3.41 ± 5.93 ng/mL, ranging from 0.17 to 35.56 ng/mL. The mean albumin level was 30.25 ± 4.95 g/L, and values varied between 18.70 and 45.80 g/L.

The mean alanine aminotransferase (ALT) level was 86.4 ± 163.7 u/L, which varied between 2.3 and 1332.0 u/L. The mean aspartate aminotransferase (AST) level was 90.1 ± 228.5 u/L, and values varied

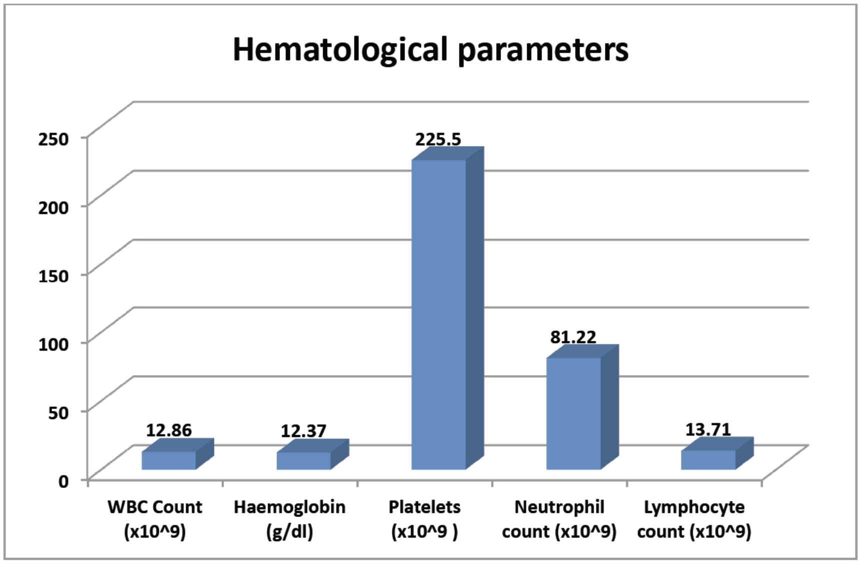


**Figure 3:** Hematological parameters of ICU patients with severe COVID-19.

**Table 5: Biochemical Parameters of ICU Patients with Severe COVID-19 Infection at Admission**

| Lab values at ICU admission | Mean | SD | Minimum | Maximum |
|---|---|---|---|---|
| Erythrocyte sedimentation rate (ESR) (mm/hr) | 50.5 | 34.3 | 2.6 | 121.0 |
| Lactate dehydrogenase (u/l) | 615.85 | 339.38 | 1.72 | 1917.00 |
| Creatinine kinase (u/l) | 340.4 | 767.1 | 8.0 | 5803.0 |
| CKMB (u/l) | 37.00 | 33.57 | 8.10 | 202.00 |
| Ferritin (µ/l) | 1217.2 | 567.0 | 9.0 | 2000.0 |
| D-dimer (ng/ml) | 3.41 | 5.93 | .17 | 35.56 |
| Albumin (g/l) | 30.25 | 4.95 | 18.70 | 45.80 |
| ALT | 86.4 | 163.7 | 2.3 | 1332.0 |
| Aspartate amino transferase (u/l) | 90.1 | 228.5 | 7.5 | 2147.0 |
| Creatinine (umol/l) | 122.20 | 112.17 | 19.50 | 721.00 |
| Urea (mmol/l) | 13.0 | 10.3 | 1.5 | 74.0 |

between 7.5 and 2147.0 u/L. The mean creatinine level was 122.20 ± 112.17 µmol/L, and values ranged from 19.50 to 721.00 µmol/L. The mean urea content was 13.0 ± 10.03 mmol/L, and levels varied between 1.5 and 74.0 mmol/L.

Table **6** shows the microbiological features of ICU patients with severe covid-19, including the results of blood, urine, and breathing specimen cultures. The most common isolate in blood cultures was KLEPNE-MDR, which accounted for 3.3% (n = 4) of the cases. Candida SPP had a prevalence of 1.7% (n = 2). Several bacteria were resistant to a variety of medications, including both MDR and XDR strains. Nevertheless, most blood cultures (86.8%, n = 105) showed no microbial growth.

Candida SPP was the most frequently identified organism in urine cultures, accounting for 6.6% (n = 8) of the cases. A few MDR bacteria were also present, such as ECOLI-MDR, Enterobacter-MDR, KLEPNE-MDR, P. aeruginosa-MDR, and Proteus mirabilis. Of the 108 urine cultures, the great majority (89.3%) did not grow.

The number of bacterial and fungal isolates in respiratory specimen cultures was higher than in the blood and urine cultures. The most common isolates were KLEPNE-XDR (10.7%, n = 13), followed by ACIBAU-XDR (8.3%, n = 10), KLEPNE-MDR (5.0%, n = 6), and P. aeruginosa-MDR (3.4%, n = 4). Additional isolates included MDR and XDR bacteria as well as Candida SPP. Nonetheless, many respiratory

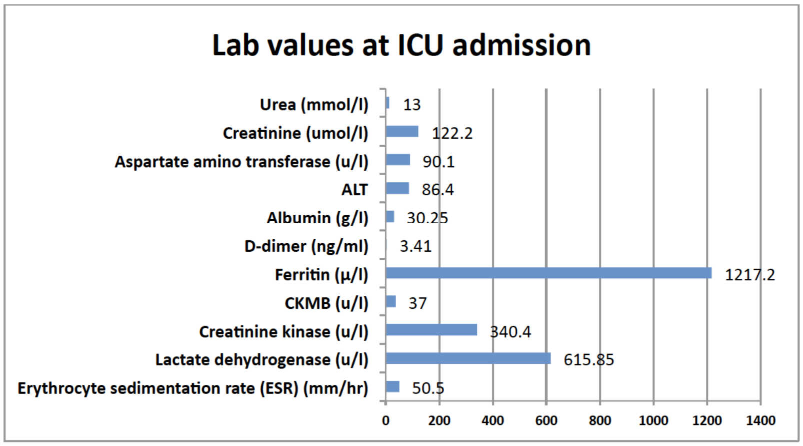


**Figure 4:** Biochemical parameters of ICU patients with severe COVID-19 infection at admission.

**Table 6: Microbiological Characterization of ICU Patients Afflicted with Severe COVID-19 Infection**

| Microbiological characterization | | N | % |
|---|---|---|---|
| Blood culture | ACIBAU-MDR | 1 | 0.8% |
| | Acinetobacter-MDR | 1 | 0.8% |
| | Candida SPP | 2 | 1.7% |
| | E-Coli MDR | 1 | 0.8% |
| | klebsiella -MDR | 2 | 1.6% |
| | klebsiella sp-XDR | 1 | 0.8% |
| | KLEPNE -MDR | 4 | 3.3% |
| | KLEPNE -XDR | 1 | 0.8% |
| | MRSA | 1 | 0.8% |
| | STAEPI-SENSITIVE | 1 | 0.8% |
| | Stenotrophomonas-XDR | 1 | 0.8% |
| | None | 105 | 86.8% |
| Urine culture | Candida SPP | 8 | 6.6% |
| | ECOLI-MDR | 1 | 0.8% |
| | Enterobacter-MDR | 1 | 0.8% |
| | KLEPNE-MDR | 1 | 0.8% |
| | P. Aeruginosa-MDR | 1 | 0.8% |
| | proteus mirabalis-MDR | 1 | 0.8% |
| | None | 108 | 89.3% |
| Respiratory specimen | ACIBAU-XDR | 10 | 8.3% |
| | Aeromonas caviae-MDR | 1 | 0.8% |
| | B.cepacia-MDR | 2 | 1.7% |
| | Candida SPP | 2 | 1.6% |
| | E.coli-MDR | 1 | 0.8% |
| | E.feacalis -SENSITIVE | 1 | 0.8% |
| | E.feacium-VRE | 1 | 0.8% |
| | KLEPNE-MDR | 6 | 5.0% |
| | KLEPNE-XDR | 13 | 10.7% |
| | NURF | 1 | 0.8% |
| | P. aeruginosa-MDR | 4 | 3.4% |
| | Stenotrophomonas-XDR | 1 | 0.8% |
| | No | 78 | 64.5% |

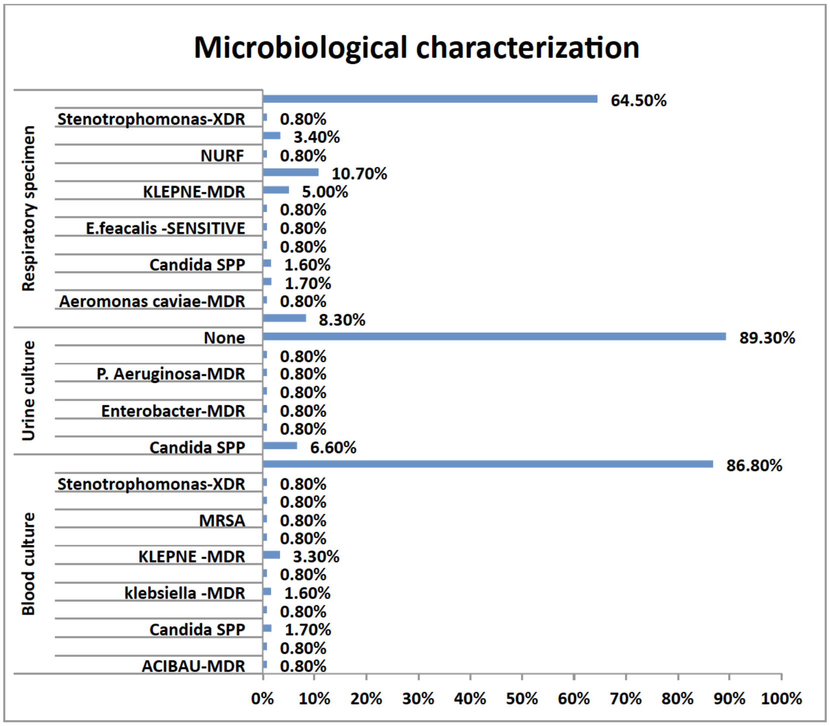


**Figure 5:** Microbiological characterization of ICU patients afflicted with severe COVID-19 infection.

specimen cultures (64.5%; n = 78) showed no bacterial or fungal growth.

Table **7** shows the medication and management techniques used for ICU patients with severe covid-19. Most patients (53.7%, n = 65) required intubation, indicating severe respiratory distress. Inotropic support was necessary for 39.7% (n = 48) of patients, indicating severe hemodynamic instability or shock.

A substantial percentage of the patients received carbapenem medication (89.3%, n = 108). These antibiotics are effective against many bacteria and are frequently used to treat severe bacterial infections, particularly those caused by MDR pathogens. Tigecycline, an antibiotic effective against various bacteria, was administered to 20.7% (n = 25) of the patients. Colistin, an antibiotic used to treat infections caused by XDR bacteria, was administered to 32.2% of patients (n = 39).

Linezolid and vancomycin, two drugs used to treat infections caused by gram-positive bacteria such as MRSA, were administered to 33.9% (n = 41) and 1.7% (n = 2) of patients, respectively. A total of 41.3% (n = 50) of the patients received antifungal therapy, suggesting that they had suspected or confirmed fungal infections. Tocilizumab, an immunomodulatory drug used to treat severe covid-19, was administered to only a small number of patients (7.4%, n = 9).

**Table 7: Management and Treatment of Patients with Severe COVID-19 Infection in the ICU**

| Management and treatment | | N | % |
|---|---|---|---|
| Intubated | No | 56 | 46.3% |
| | Yes | 65 | 53.7% |
| Inotropes | No | 73 | 60.3% |
| | Yes | 48 | 39.7% |
| Carbapenems | No | 13 | 10.7% |
| | Yes | 108 | 89.3% |
| Tigecycline | No | 96 | 79.3% |
| | Yes | 25 | 20.7% |
| Colistin | No | 82 | 67.8% |
| | Yes | 39 | 32.2% |
| Linezolid | No | 80 | 66.1% |
| | Yes | 41 | 33.9% |
| Vancomycin | Yes | 41 | 33.9% |
| | No | 80 | 66.1% |
| Antifungal drugs | Yes | 50 | 41.3% |
| | No | 71 | 58.7% |
| Tocilizumab | Yes | 112 | 92.6% |
| | No | 9 | 7.4% |

Table **8** displays the results and superinfection status of ICU patients with severe covid-19. Of the total

**Table 8: Outcomes and Superinfection Prevalence among ICU Patients with Severe COVID-19**

| Outcomes and superinfection | | N | % |
|---|---|---|---|
| Outcome | Survived | 74 | 61.2% |
| | Died | 47 | 38.8% |
| Superinfection | No | 68 | 56.2% |
| | Yes | 53 | 43.8% |

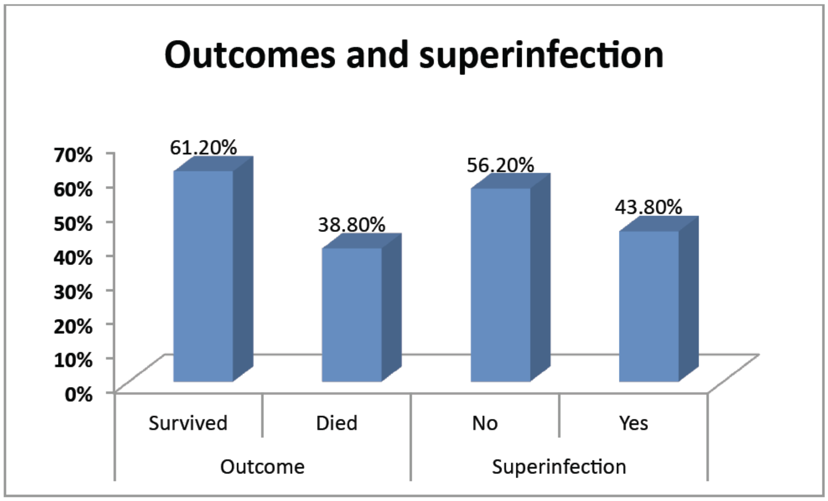


**Figure 6:** Outcomes and superinfection prevalence among ICU patients with severe covid-19.

number of patients, 61.2% (n = 74) survived, whereas 38.8% (n = 47) did not. Superinfections, defined as additional bacterial or fungal infections that develop during the initial viral infection, were detected in 43.8% (n = 53) of the patients. This finding is consistent with the bacterial features and widespread use of broad-spectrum antibiotics and antifungal drugs in this group of patients.

Table **9** shows the association between superinfection and mortality in ICU patients with severe covid-19. Among the patients who survived, 36.5% (n = 27) had superinfections, whereas 63.5% (n = 47) did not. In contrast, 55.3% (n = 26) had superinfections among patients who died, whereas 44.7% (n = 21) did not. A p-value of 0.042 demonstrates a statistically significant link between superinfection and death in this group. Superinfections are associated with a higher mortality rate than non-superinfections.

Table **10** displays the results of a multivariable logistic regression study that examined the variables associated with death in ICU patients with severe covid-19. The investigation investigated the possible causes of death, such as superinfection status, age, sex, nationality, BMI, and length of ICU stay.

The adjusted odds ratio (aOR) for superinfection was 1.696 (95% CI: 0.725-3.967, p=0.223), indicating that superinfection was associated with a higher mortality risk than the absence of superinfection. However, this association remained statistically insignificant after controlling for the other variables.

**Table 9: Correlation between Superinfection and Death in ICU Patients with Severe COVID-19 Infection**

| Superinfection | Outcome | | | | p-Value |
|---|---|---|---|---|---|
| | Survived | | Died | | |
| | N | % | N | % | |
| No | 47 | 63.5% | 21 | 44.7% | 0.042 |
| Yes | 27 | 36.5% | 26 | 55.3% | |

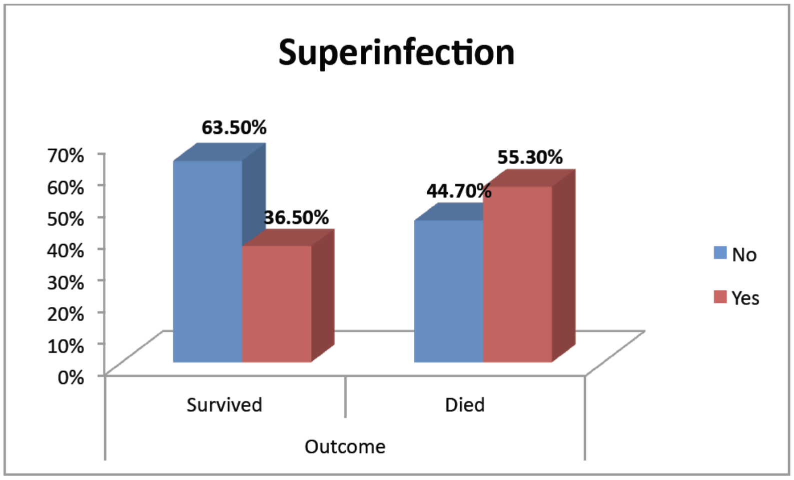


**Figure 7:** Correlation between superinfection and death in ICU patients with severe COVID-19 infection.

**Table 10: Multivariable Logistic Regression Analysis of Factors Associated with Mortality in ICU Patients with Severe COVID-19 Infection**

| Factors | B | p-Value | aOR | 95% C.I.for aOR | |
|---|---|---|---|---|---|
| | | | | Lower | Upper |
| Mortality, yes | | | | | |
| Superinfection, yes | .528 | .223 | 1.696 | .725 | 3.967 |
| Age (years) | .039 | .004 | 1.040 | 1.012 | 1.068 |
| Sex, Male | -.613 | .191 | .541 | .216 | 1.358 |
| Nationality, non-Saudi | 2.511 | .032 | 12.320 | 1.242 | 122.177 |
| BMI (kg /m2) | -.112 | .079 | .894 | .789 | 1.013 |
| Duration of stay (days) | .012 | .473 | 1.012 | .979 | 1.047 |

The study discovered a strong relationship between age and mortality, with an aOR of 1.040 (95% CI: 1.012-1.068, p=0.004). This finding suggests that the likelihood of death increased by 4% with each additional year of age, even when other factors were considered.

This study found a significant link between nationality and death. Non-Saudi patients had a significantly higher aOR of 12.320 (95% CI: 1.242–122.177, P =0.032) than Saudi patients. These findings indicate that non-Saudi patients had a significantly higher risk of death than Saudi patients, even after controlling for other variables. Multivariable analysis revealed no significant association between mortality and sex, BMI, or length of ICU stay.

## DISCUSSION

This study was conducted at a single site and involved a retrospective observational analysis. This study sheds light on the incidence, features, and effects of bacterial superinfections in covid-19 patients admitted to the ICU during the second wave of the pandemic. Our analysis demonstrated a high incidence of superinfections and underscored the difficulties in treating severely unwell covid-19 patients.

The study demonstrated that COVID-19 significantly exacerbates the risk of bacterial superinfections, with a prevalence of 43.8%, surpassing rates observed in other respiratory diseases like influenza and SARS. During the SARS pandemic, bacterial co-infections were reported in up to 30% of ICU patients, while influenza often sees co-infection rates between 11% and 35%. The higher incidence in COVID-19 patients may be attributable to factors unique to SARS-CoV-2, including prolonged ICU stays, extensive use of immunomodulatory therapies (e.g., corticosteroids and tocilizumab), and the virus's impact on the immune system. SARS-CoV-2 impairs Type I interferon responses, depletes T cells, and damages the respiratory epithelium, creating an environment conducive to bacterial colonization and superinfections [6].

Moreover, the severity of bacterial superinfections appears to be amplified in COVID-19 patients due to the extensive reliance on invasive procedures like mechanical ventilation. These interventions increase the risk of MDR and XDR pathogens, as reflected by the high prevalence of KLEPNE-XDR and ACIBAU-XDR in respiratory specimens. Comparing the outcomes of superinfections in COVID-19 with those in influenza or SARS suggests that COVID-19 patients face greater mortality risks, partly due to the compounded effects of viral pathology and antimicrobial resistance [7].

In our investigation, we identified a considerable increase in the incidence of superinfections compared with earlier data. Langford *et al*. (2020) made a remarkable discovery on patients in the critical care unit (ICU). It was discovered that 14% of these individuals had bacterial co-infection [7]. Musuuza *et al*. (2021) investigated the prevalence of bacterial coinfection among covid-19 patients admitted to the hospital. Their conclusions were based on rigorous meta-analysis. According to research findings, most patients had bacterial coinfections [19]. This fluctuation might be due to various variables, including the ever-changing nature of the pandemic, variability in viral strains, and variations in patient demographics and healthcare settings. Garcia-Vidal *et al*. (2021) presented a study in a famous publication that revealed the high frequency of superinfections among covid-19 patients in the hospital. This is consistent with our research, which showed a higher rate of such incidents [6]. The extensive range of reported rates underscores the difficulty of recognizing and classifying superinfections in connection with covid-19, as emphasized by Rawson *et al*. (2020) [20].

Our study revealed a troubling microbial profile. Respiratory specimens contained a significant number of MDR and XDR pathogens. The most prevalent isolates were KLEPNE-XDR (10.7%) and ACIBAU-XDR (8.3%). This finding is consistent with recent reports of antibiotic-resistant illnesses in individuals who have developed covid-19. Sharifipour *et al*. (2020) published their findings on the incidence of MDR bacteria among covid-19 patients in ICU [13]. In a recent study published in a respected publication, researchers discovered that MDR microorganisms were responsible for many infections acquired by covid-19 patients in the ICU [18]. The prevalence of these persistent bacteria creates considerable therapeutic hurdles, emphasizing the significance of appropriate antibiotic use and effective infection control.

Our findings demonstrated a significant relationship between superinfection and mortality (p = 0.042). Patients with superinfections had a significantly higher death rate (55.3%) than those without (44.7%). Zhou *et al*. (2020) discovered a worrying pattern among those who died of covid-19. It was revealed that these individuals had a higher risk of secondary infections [2]. Karami *et al*. (2021) published their findings in shining light on a strong correlation between bacterial coinfections and increased mortality risk in covid-19 patients. These findings suggest a significant effect on patient outcomes [21].

Our data revealed a significant association between superinfection and higher mortality rates. The adjusted odds ratio was 1.696, with a 95% confidence range of 0.725-3.967. Unfortunately, the relationship remained statistically insignificant even after controlling for other factors. This shows that age and country may have influenced mortality in our group. The substantial connection between age and mortality (adjusted odds ratio [aOR] 1.040, 95% [CI]: 1.012-1.068, p=0.004) corresponds to worldwide trends in covid-19 outcomes [22]. More studies are needed to acquire a thorough understanding of the significant increase in death rates among individuals of Saudi nationality. The odds ratio 12.320 (95% CI: 1.242-122.177, p = 0.032) emphasizes the need for additional inquiry. Various variables, including inequities in healthcare access and variances in underlying health problems, can influence differences in death rates between demographic groups. Similar trends have been observed in other nations [23].

We have been using a variety of potent antibiotics, including carbapenems, tigecycline, and colistin. This underscores the difficulties in treating critically ill covid-19 patients, who may also be battling bacterial superinfections. Although this approach may be helpful for acute therapy, concerns about its long-term influence on antibiotic resistance exist. Huttner *et al*. (2020) stressed the need to adhere to antimicrobial stewardship techniques during the covid-19 pandemic [17]. The high level of carbapenem usage in our study is a reason for concern because it exceeded the rates found in prior studies. According to a survey by Vaughn *et al*. (2021), carbapenem was administered to 45.5% of covid-19 patients in the ICU [24].

Notably, many patients (41.3%) were found to be using antifungal drugs, indicating a high incidence of fungal infections. This rate exceeded those reported in numerous earlier studies. A recent study in a respected publication revealed an alarming finding: many ICU patients with covid-19 acquired invasive fungal infections [25]. A worrying finding was discovered in pioneering research by White *et al*. (2020). Many covid-19 patients who require mechanical breathing develop invasive fungal infections [26]. The higher frequency observed in our analysis might be attributed to variations in patient demographics, diagnostic criteria, or protocols for starting antifungal therapy. Furthermore, there are concerns regarding the abuse of antifungal drugs and the need for improved diagnostic tools to detect fungal infections in patients with covid-19.

Our research found a significant prevalence of infiltrates on chest X-rays (88.4%) and a variety of abnormalities on CT scans, as indicated by radiological findings. These findings are consistent with the well-known respiratory symptoms associated with severe covid-19. These findings are consistent with those of Shi *et al*. (2020), who comprehensively described CT scan alterations identified in covid-19 patients [27]. The radiological abnormalities seen in indigent covid-19 patients and the increased frequency of superinfections highlight the intricate link between viral pathology and subsequent bacterial infections in the lungs.

## CLINICAL IMPLICATIONS FOR PRACTICE

The findings have profound implications for clinical practice. The high prevalence of MDR and XDR pathogens necessitates the urgent adoption of enhanced diagnostic and therapeutic strategies in ICU settings. Rapid microbiological testing and antimicrobial susceptibility profiling should become standard to ensure timely and targeted treatment. Furthermore, the association of superinfections with increased mortality rates highlights the importance of rigorous infection prevention and control measures, such as stringent hygiene protocols and judicious use of antibiotics. The study also emphasizes the need for antimicrobial stewardship programs to curb the overuse of broad-spectrum antibiotics, thereby mitigating the long-term impact of antimicrobial resistance. Clinicians should remain vigilant about the potential for superinfections in covid-19 patients, particularly those undergoing invasive procedures or receiving immunomodulatory therapies, and tailor interventions to improve outcomes while safeguarding public health.

## STRENGTHS OF THE STUDY

This study provides critical insights into the prevalence, characteristics, and outcomes of bacterial superinfections among ICU patients with severe covid-19 during the pandemic's second wave. A key strength lies in its focus on multidrug-resistant (MDR) and extensively drug-resistant (XDR) pathogens, which adds to the limited literature on antimicrobial resistance trends during the covid-19 pandemic. By employing robust microbiological and statistical analyses, the study elucidates important correlations between superinfections, mortality, and demographic factors, offering actionable data for clinical and public health interventions. Furthermore, the detailed examination of antimicrobial use provides valuable information about therapeutic practices in a resource-constrained setting, contributing to global efforts in antimicrobial stewardship.

## LIMITATIONS OF THE STUDY

Despite its strengths, the study has several limitations. Being a single-center retrospective analysis, its findings may not be generalizable to other regions or healthcare systems with differing patient populations, resources, and care protocols. The absence of a control group of non- covid-19 ICU patients limits the ability to ascertain whether the observed patterns of superinfection are unique to covid-19 or reflective of broader trends in critically ill populations. Additionally, the retrospective design constrains the ability to establish causal relationships between variables, such as superinfection status and mortality. Finally, the reliance on available electronic medical records may have introduced bias due to incomplete or inconsistent data collection.

Future research should focus on improving the efficiency and precision of the instruments used to detect bacterial and fungal superinfections in covid-19 patients. Furthermore, this article should investigate the most effective techniques for handling antibiotics during a pandemic. More studies are needed to verify our findings and examine the potential long-term effects of superinfections. Using immunomodulatory methods and developing specific antimicrobial medicines can improve the outcomes of critically ill covid-19 patients with superinfections. Intensivists, infectious disease experts, microbiologists, and public health professionals must collaborate to treat covid-19 superinfections. We can improve patient outcomes while ensuring antibiotic efficacy for future generations by gaining a more thorough understanding of these complicated illnesses.

## CONCLUSION

This study presents findings that indicate a significant prevalence of bacterial superinfections

(43.8%) among covid-19 patients in the ICU, which surpasses previous research. The prevalence of drug-resistant bacteria and viruses, including highly resistant strains, highlights the increasing concern regarding antimicrobial resistance to covid-19. While the occurrence of superinfections was linked to higher mortality rates, age and nationality were found to have a more significant impact on determining unfavourable outcomes. Although essential for treating severely ill individuals, the extensive use of broad-spectrum antibiotics gives rise to apprehensions regarding the emergence of long-term antimicrobial resistance. These findings highlight the need for enhanced diagnostic tools, focused antimicrobial strategies, and efficient stewardship practices. This study provides significant insights into the clinical procedures and public health policies addressing covid-19 and its associated complications. This highlights the necessity for further research to tackle the multifaceted issues brought about by the epidemic.

## FUNDING STATEMENT

No external funding.

## CONFLICT OF INTEREST

The authors declare that they have NO affiliations with or involvement in any organization or entity with any financial interest in the subject matter or materials discussed in this manuscript.

## AUTHOR CONTRIBUTIONS

All authors contributed equally.

## REFERENCES

[1] WHO. WHO Coronavirus (COVID-19) Dashboard | WHO Coronavirus (COVID-19) Dashboard With Vaccination Data. Accessed May 15, 2022. Available at: https://covid19.who.int/

[2] Zhou F, Yu T, Du R, *et al.* Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. The Lancet 2020; 395: 1054-1062. https://doi.org/10.1016/S0140-6736(20)30566-3

[3] Lai CC, Shih TP, Ko WC, Tang HJ, Hsueh PR. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. International Journal of Antimicrobial Agents 2020; 55: 105924. https://doi.org/10.1016/j.ijantimicag.2020.105924

[4] Yin MZ, Zhang LJ, Deng GT, *et al.* Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during pregnancy in China: A retrospective cohort study. medRxiv 2020. https://doi.org/10.1101/2020.04.07.20053744

[5] Rouzé A, Martin-Loeches I, Povoa P, *et al.* Relationship between SARS-CoV-2 infection and the incidence of ventilator-associated lower respiratory tract infections: A European multicenter cohort study. Intensive Care Medicine 2021; 47: 188-198. https://doi.org/10.1007/s00134-020-06323-9

[6] Garcia-Vidal C, Sanjuan G, Moreno-García E, *et al.* Incidence of co-infections and superinfections in hospitalized patients with COVID-19: A retrospective cohort study. Clinical Microbiology and Infection 2021; 27: 83-88. https://doi.org/10.1016/j.cmi.2020.07.041

[7] Langford BJ, So M, Raybardhan S, *et al.* Bacterial co-infection and secondary infection in patients with COVID-19: A living rapid review and meta-analysis. Clinical Microbiology and Infection 2020; 26: 1622-1629. https://doi.org/10.1016/j.cmi.2020.07.016

[8] Blanco-Melo D, Nilsson-Payant BE, Liu WC, *et al.* Imbalanced host response to SARS-CoV-2 drives development of COVID-19. Cell 2020; 181: 1036-1045.e9. https://doi.org/10.1016/j.cell.2020.04.026

[9] Mason RJ. Pathogenesis of COVID-19 from a cell biology perspective. European Respiratory Journal 2020; 55: 2000607. https://doi.org/10.1183/13993003.00607-2020

[10] RECOVERY Collaborative Group. Dexamethasone in hospitalized patients with Covid-19. New England Journal of Medicine 2021; 384(8): 693-704. https://doi.org/10.1056/nejmoa2021436

[11] Beer A, Hudler H, Hader M, *et al.* Tocilizumab for treatment of mechanically ventilated patients with COVID-19. Clinical Infectious Diseases 2019; 54: 1-54.

[12] Contou D, Claudinon A, Pajot O, *et al.* Bacterial and viral co-infections in patients with severe SARS-CoV-2 pneumonia admitted to a French ICU. Annals of Intensive Care 2020; 10: 119. https://doi.org/10.1186/s13613-020-00736-x

[13] Sharifipour E, Shams S, Esmkhani M, *et al.* Evaluation of bacterial co-infections of the respiratory tract in COVID-19 patients admitted to ICU. BMC Infectious Diseases 2020; 20: 1-7. https://doi.org/10.1186/s12879-020-05374-z

[14] Getahun H. Antimicrobial resistance. Sustainable Development Goals Series 2023; 143-147. https://doi.org/10.1007/978-3-031-33851-9_22

[15] Zyoud SH. The state of current research on COVID-19 and antibiotic use: Global implications for antimicrobial resistance. Journal of Health, Population and Nutrition 2023; 42: 42. https://doi.org/10.1186/s41043-023-00386-2

[16] Rawson TM, Moore LSP, Zhu N, *et al.* Bacterial and fungal co-infection in individuals with coronavirus: A rapid review to support COVID-19 antimicrobial prescribing. Clinical Infectious Diseases 2020; 71: 2459-2468. https://doi.org/10.1093/cid/ciaa530

[17] Huttner BD, Catho G, Pano-Pardo JR, Pulcini C, Schouten J. COVID-19: Don't neglect antimicrobial stewardship principles!. Clinical Microbiology and Infection 2020; 26: 808-810. https://doi.org/10.1016/j.cmi.2020.04.024

[18] Suarez-de-la-Rica A, *et al.* Microbiological profile and antibiotic resistance in intensive care unit-acquired infections during COVID-19 pandemic. Antibiotics 2021; 10: 401.

[19] Musuuza JS, Watson L, Parmasad V, *et al.* Prevalence and outcomes of co-infection and superinfection with SARS-CoV-2 and other pathogens: A systematic review and meta-analysis. PLoS One 2021; 16: e0251170. https://doi.org/10.1371/journal.pone.0251170

[20] Rawson TM, Moore LSP, Zhu N, *et al.*: Bacterial and Fungal Coinfection in Individuals with Coronavirus: A Rapid Review to Support COVID-19 Antimicrobial Prescribing. Clin Infect Dis 2020, 71: 2459-68.

https://doi.org/10.1093/cid/ciaa530

[21] Karami Z, Knoop BT, Dofferhoff ASM, *et al.* Mortality of hospitalized patients with bacterial infections and COVID-19: A systematic review and meta-analysis. Microbial Pathogenesis 2021; 157: 104931. https://doi.org/10.1016/j.micpath.2021.104931

[22] O'Driscoll M, Ribeiro Dos Santos G, Wang L, *et al.* Age-specific mortality and immunity patterns of SARS-CoV-2. Nature 2021; 590: 140-145. https://doi.org/10.1038/s41586-020-2918-0

[23] Mackey K, Ayers CK, Kondo KK, *et al.* Racial and ethnic disparities in COVID-19-related infections, hospitalizations, and deaths: A systematic review. Annals of Internal Medicine 2021; 174: 362-373. https://doi.org/10.7326/M20-6306

[24] Vaughn VM, Gandhi TN, Petty LA, *et al.* Empiric antibacterial therapy and community-onset bacterial coinfection in patients hospitalized with coronavirus disease 2019 (COVID-19): A multi-hospital cohort study. Clinical Infectious Diseases 2021; 72: E533-E541. https://doi.org/10.1093/cid/ciaa1239

[25] Bartoletti M, Pascale R, Cricca M, *et al.* Epidemiology of invasive pulmonary aspergillosis among intubated patients with COVID-19: A prospective study. Clinical Infectious Diseases 2021; 73: E3606-E3614. https://doi.org/10.1093/cid/ciaa1065

[26] White PL, Dhillon R, Cordey A, *et al.* A national strategy to diagnose coronavirus disease 2019-associated invasive fungal disease in the intensive care unit. Clinical Infectious Diseases 2021; 73: E1634-E1644. https://doi.org/10.1093/cid/ciaa1298

[27] Shi H, Han X, Jiang N, *et al.* Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: A descriptive study. The Lancet Infectious Diseases 2020; 20: 425-434. https://doi.org/10.1016/S1473-3099(20)30086-4

Received on 30-10-2024 Accepted on 29-11-2024 Published on 31-12-2024

https://doi.org/10.6000/1929-6029.2024.13.41