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ORIGINAL RESEARCH

Epidemiological Characteristics and Outcomes Predictors for Intensive Care Unit COVID-19 Patients in Al-Madinah, Saudi Arabia. Retrospective Cohort Study

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Introduction: The global pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2, COVID-19) increased the demand for intensive care unit (ICU) services. Mortality and morbidity rates among ICU COVID-19 patients are affected by several factors, such as severity, comorbidities, and coinfections. In this study, we describe the demographic characteristics of COVID-19 patients admitted to an ICU in Saudi Arabia, and we determined the predictors for mortality and prolonged ICU length of stay. Additionally, we determined the prevalence of bacterial coinfection and its effect on the outcomes for ICU COVID-19 patients.

Methods: We retrospectively studied the medical records of 142 COVID-19 patients admitted to the ICU at a tertiary hospital in Madinah, Saudi Arabia. Data on demographics, medical history, mortality, length of stay, and presence of coinfection were collected for each patient.

Results: Neutrophil-to-Lymphocyte ratio (NLR) and intubation were reliable predictors of mortality and ICU length of stay among these ICU COVID-19 patients. Moreover, bacterial coinfections were detected in 23.2% of the patients and significantly ($p < 0.001$) prolonged their ICU length of stay, explaining the 10% increase in the length of stay for these patients. Furthermore, mortality reached 70% among the coinfected patients, and 60.8% of the isolated coinfecting pathogens were multidrug-resistant (MDR) strains of *Klebsiella pneumoniae, Acinetobacter baumannii*, and *Staphylococcus aureus*.

Conclusion: Increased NLR and intubation are predictors of mortality and prolonged length of stay in COVID-19 patients admitted to the ICU. Coinfection with MDR bacterial strains potentially results in complications and is a high-risk factor for prolonged ICU length of stay.

Keywords: COVID-19, mortality, neutrophil-to-lymphocyte ratio, ICU length of stay, coinfection, MDR bacteria, Al-Madinah, Saudi Arabia

Introduction

The COVID-19 pandemic is an ongoing challenge for health services worldwide. As of December 2022, there were more than 645 million confirmed cases with 6.6 million deaths.[1] COVID-19 is a highly transmissible virus that causes different illness severities, including asymptomatic, mild, moderate, and severe infection.[2] The virus may affect the respiratory system or develop into a systemic syndrome that affects different organs, such as the heart, liver, or kidneys.[3]

The proportion of asymptomatic and mild infections among COVID-19 cases is as high as 78%, and these patients recover without the need for medication, whereas others require medical care.[4] Serious illness develops in 14–30% of hospitalized COVID-19 patients, and the proportion of severe cases that require ICU admission ranges from 4% to 32%.[5,6]

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The mortality rate is as high as 67% among severely ill patients, particularly those who are admitted to the ICU. Advanced age and chronic diseases, such as diabetes, hypertension, and cardiovascular disease, are risk factors that have been associated with severe COVID-19 infection and ICU admission in several countries, such as China, Sweden, Italy, and the US.[5,7–9]

Several studies have reported predictors for mortality and a prolonged ICU length of stay among severely ill COVID-19 patients. For instance, an increased NLR, a systemic inflammation biomarker, is associated with COVID-19 prognosis and mortality.[10–12] Moreover, intubation has been reported to be associated with an increased mortality rate among ICU COVID-19 patients, and it is a predictor of a prolonged ICU length of stay.[13,14] Furthermore, hospital-acquired coinfection with MDR bacterial strains is an important factor that has had a significant effect on the mortality rate and on prolonging ICU length of stay in COVID-19 patients.[15,16]

There is a lack of data on the epidemiological and clinical characteristics and outcomes for ICU COVID-19 patients in Saudi Arabia. A better understanding of factors and predictors related to a prolonged ICU length of stay and mortality among ICU COVID-19 patients can improve the health service outcomes for patients in Saudi Arabia. In this study, we aimed to describe the demographic characteristics of ICU COVID-19 patients in Saudi Arabia and determine the predictors for mortality and a prolonged ICU length of stay. We also aimed to determine the prevalence of bacterial coinfection and its impact on ICU COVID-19 patient outcomes.

Materials and Methods

Study Design and Data Collection

In this retrospective cohort study, data were collected from 142 COVID-19 patients that were admitted to the ICU at Al-Madinah General Hospital in King Salman Medical City in Saudi Arabia, which was dedicated to COVID-19 patients from May 2020 until June 2021. We included COVID-19 patients who were admitted to the ICU during the study period, as confirmed via reverse transcription polymerase chain reaction (RT-PCR) from either nasopharyngeal or throat swabs. These were performed according to the guidelines from the Ministry of Health in Saudi Arabia, and none of the patients were vaccinated against COVID-19. We excluded unconfirmed ICU COVID-19 patients and COVID-19 patients who were admitted to other hospital wards. Bacterial coinfection was confirmed by positive culture results from the Microbiology Department at the hospital laboratory. Demographic and other data, including patient age, gender, comorbidities, microbiological culture results, mortality, intubation, and ICU length of stay, were extracted from the medical records, and personal information was removed. The minimum number of COVID-19 patients required for this study was 138 based on the expected coinfection prevalence of 10% among COVID-19 patients who were admitted to ICUs in Saudi Arabia (total width of 10% at a 95% confidence level).

Ethical Approval

This study was approved by the King Salman Bin Abdulaziz Medical City Institutional Review Board in Al-Madinah Al Munwarah, IRB Log No: 064–22. The Ethics Committee waived the requirement for patient informed consent owing to the retrospective nature of the study. Patient privacy and data confidentiality were maintained according to the Helsinki Declaration.

Statistical Analysis

Descriptive statistics for categorical variables are presented as frequencies and percentages, while the data for continuous variables are presented as means ± standard deviation and medians [interquartile range]. Correlations between two categorical variables were assessed using Fisher's exact test. The chi-square test was used to determine whether there was a difference in coinfection status among the study population. The normality of distribution of all continuous variables (age, length of stay in ICU, and NLR) was assessed using the Shapiro–Wilk test ($p < 0.05$ for all). The Mann–Whitney *U*-test was used to compare the median between the two groups (bacterial coinfection vs no coinfection; discharged vs deceased). In the univariate analysis, a Bonferroni adjustment was used to correct for multiple testing. Simple linear regression analysis was performed to explore the predictors for the ICU length of stay. Additionally, logistic regression analysis was employed to investigate the odds ratio (OR) for mortality (outcome coded as died = 0 and discharged = 1) based on the presence of a bacterial coinfection (predictor coded as no = 0 vs yes = 1) and adjusting for the severity of the patient condition as expressed by the NLR. Analyses were performed using the IBM SPSS software platform (version 20.0. Armonk, NY: IBM Corp). Significance was assessed at the 95% confidence level.

Results

General Characteristics of the Study Sample

A total of 142 COVID-19 patients admitted to the ICU were included in this study: 89 males (62.7%) and 53 females (37.3%). The mean age for the studied population was 63.6 ± 16.6 years (median: 63.0 years [54.0–76.0]). In addition, 40% of the patients were <60 years old (n = 57, 38 male + 19 female) with a mean age of 63.3 years, and 60% were >60 years old (n = 85, 51 males + 34 females) with a mean age 63.6 of years; see Table 1. The overall mortality rate among these COVID-19 patients was 54.9% (n = 78). Overall, 18.3% of the patients required intubation (n = 26), and 73.9% (n = 105) had at least one chronic disease. Twenty-three percent (n = 33) of patients had a coinfection associated with COVID-19. Diabetes, hypertension, and cardiovascular disease were the most frequent chronic conditions reported in our sample (51.4%, 44.4%, and 21.1%, respectively). Detailed data on the patient's characteristics are provided in Table 1.

Table 1 Characteristics of Patients (N= 142)

	n	%
Age		
< 60 years	57	40.1
60–79 years	56	39.4
≥ 80 years	29	20.4
Sex		
Male	89	62.7
Female	53	37.3
Bacterial coinfection		
Yes	33	23.2
No	109	76.8
Mortality		
Dead	78	54.9
Discharged	64	45.1
Use of intubation		
Yes	26	18.3
No	116	81.7
Chronic diseases		
Yes	105	73.9
No	37	26.1
Coexistence of chronic diseases		
Yes	72	50.7
No	70	49.3

(*Continued*)

Table 1 (Continued).

	n	%
Type of chronic disease		
Diabetes	73	51.4
Hypertension	63	44.4
Cardiovascular disease	30	21.1
Chronic kidney disease	9	6.30
Hypothyroidism	9	6.30
Asthma	8	5.60
Other diseases	17	12.0

Mortality Risk Factors in Critically Ill COVID-19 Patients

In this study, the ICU COVID-19 patients were divided into two groups based on the outcome (deceased or discharged) to investigate the risk factors. No significant difference was observed between the median age of discharged and deceased patients (60.0 years [50.3–75.5] vs 65.0 years [58.0–77.5], respectively, $p = 0.046$) (Figure 1A). See additional risk factors listed in Table 2. However, a significant difference was found in the mean NLR between patients who were discharged (6.55 ± 6.31; median: 4.27 [1.81–9.62]) and patients who died (23.0 ± 17.7; median: 17.4 [11.0–32.8]). The median NLR of discharged patients was significantly lower than the median NLR of patients who died ($p < 0.001$) (Figure 1B). In addition, significantly more patients who underwent intubation died than patients who were intubated and discharged (96.2% vs 3.80%, respectively, $p < 0.001$) (Figure 1C). Moreover, the median ICU length of stay for discharged COVID-19 patients was significantly lower than that for patients who died (10.0 days [5.75–17.0] vs 18.0 days [10.0–32.0], respectively, $p < 0.001$) (Figure 1D). The logistic regression analysis for predictors of mortality among these ICU COVID-19 patients is presented in Table 3. The use of intubation significantly predicted mortality, as intubated patients had increased odds of dying (OR = 29.7 [95% CI: 3.90 to 227], $p = 0.001$). In addition, simple linear regression analysis revealed that a higher NLR significantly predicted higher mortality (OR: 0.84 [95% CI: 0.78–0.90], $p < 0.001$).

ICU Length of Stay for Critically Ill COVID-19 Patients

The mean ICU length of stay for these 142 COVID-19 patients was 16.1 ± 11.8 days (median: 11.0 days [6.75–25.0]). No significant difference in ICU length of stay was found for patients with different ages, genders, or chronic diseases. However, bacterial coinfection, intubation, and increased NLR were correlated with a prolonged ICU length of stay. Intubation predicted the ICU length of stay (B = 6.40, SE = 2.46, [95% CI: 1.53–11.3], $p = 0.010$), and the use of intubation explained 5% of the change in the dependent variable (ICU length of stay). Furthermore, NLR predicted the ICU length of stay (B = 0.19, SE = 0.06, [95% CI: 0.07–0.31], $p = 0.002$), and NLR explained 7% of the change in the dependent variable (ICU length of stay). No other variables predicted the ICU length of stay (see Table 4).

Bacterial Coinfection in Critically Ill COVID-19 Patients

Distribution of Bacterial Coinfection in Critically Ill COVID-19 Patients

Of the 142 ICU COVID-19 patients, 33 (23.2%) had bacterial coinfections, and 109 (76.8%) did not have coinfections, according to the culture results shown in Figure 2A. Different bacterial species were identified, including *Klebsiella pneumoniae* (47%), *Staphylococcus haemolyticus* (15.6%), methicillin-resistant *Staphylococcus aureus* (MRSA) (12.5%), *Acinetobacter baumannii* (9.3%), *Staphylococcus hominis* (6.2%), *Corynebacterium diphtheriae* (3.1%), *Serratia marcescens* (3.1%), and *Staphylococcus epidermidis* (3.1%) (Figure 2B). They were isolated from different samples, including sputum, blood, urine, and nasal swabs. Most of the Gram-negative species (14/19) are multidrug-

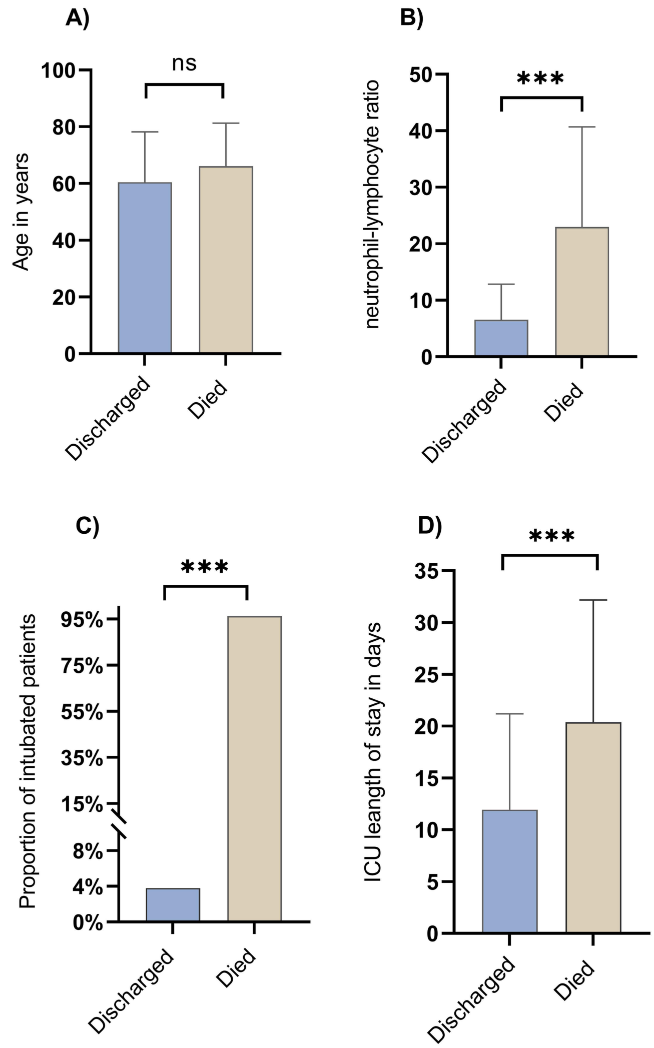

Figure 1 Comparisons between dead and discharged patients. (**A**) Difference of ages between dead and discharged patients. (**B**) Different NLR between died and discharged patients. (**C**) intubation proportion between dead and discharged patients. (**D**) ICU length of stay between died and discharged patients. ***p< 0.001.
Abbreviation: ns, not significant.

resistant strains (MDR), and 50% (7/14) have been reported as extended-spectrum beta-lactamase (ESBL)-producing strains, whereas only five of the 14 Gram-positive species have been reported as MDR (MRSA).

Comparisons Between Coinfected and Non-Coinfected Critically Ill COVID-19 Patients

The characteristics of patients with bacterial coinfection were compared to those without coinfection, and no significant difference was found regarding patient gender, age, mortality, chronic diseases, and other potential risk factors. For example, Fisher's exact test showed no significant difference in the distribution of bacterial coinfection between male and female patients ($p = 0.540$). Additional results are provided in Table 5. Moreover, the median age of patients with bacterial coinfection was similar to the median age of patients without coinfection (59.0 years [53.5–76.5] vs 63.0 years [54.5–76.0], respectively, $p = 0.662$). Furthermore, no significant difference in the median NLR was found between the COVID-19 patients with bacterial coinfection and those without coinfection ($p = 0.196$).

Effect of Bacterial Coinfection on ICU Length of Stay

ICU COVID-19 patients with bacterial coinfection had a prolonged ICU length of stay. Specifically, the median ICU length of stay was significantly longer for patients with bacterial coinfection than for patients without coinfection (25.0 days [10.0–34.0] vs 11.0 days [6.00–21.0], respectively, $p < 0.001$) (Figure 3A). In addition, among the deceased

Table 2 Characteristics of COVID-19 Patients in Intensive Care Unit Stratified by Mortality Status (N= 142)

	Discharged (n= 64)	Dead (n= 78)	*p*-value
Age			
< 60 years	32 (56.1)	25 (43.9)	0.060
60–79 years	19 (33.9)	37 (66.1)	
≥ 80 years	13 (44.8)	16 (55.2)	
Sex			
Male	39 (43.8)	50 (56.2)	0.730
Female	25 (47.2)	28 (52.8)	
Use of intubation			
Yes	1 (3.80)	25 (96.2)	< 0.001*
No	63 (54.3)	53 (45.7)	
Chronic diseases			
Yes	47 (44.8)	58 (55.2)	1.00
No	17 (45.9)	20 (54.1)	
Coexistence of chronic diseases			
Yes	28 (38.9)	44 (61.1)	0.177
No	36 (51.4)	34 (48.6)	
Type of chronic disease			
Diabetes	32 (43.8)	41 (56.2)	0.866
Hypertension	28 (44.4)	35 (55.6)	1.00
Cardiovascular disease	13 (43.3)	17 (56.7)	1.00
Chronic kidney disease	3 (33.3)	6 (66.7)	0.514
Hypothyroidism	7 (77.8)	2 (22.2)	0.079
Asthma	4 (50.0)	4 (50.0)	1.00
Other diseases	5 (31.2)	11 (68.8)	0.293

Note: *Significant at the 95% confidence level.

patients, those who had a bacterial coinfection stayed longer in the ICU than those who did not have a bacterial coinfection (32.0 days [16.0–36.0] vs 17.0 days [9.00–25.0], respectively, p = 0.002) (Figure 3B). However, among the discharged patients, no significant difference in the ICU length of stay was found between the patients with bacterial coinfection and those without coinfection (Figure 3C). Moreover, among the patients with bacterial coinfection, there was a significant difference in ICU length of stay between those who died compared with discharged patients (32.0 days [16.0–36.0] vs 9.50 days [6.50–22.8], respectively, p = 0.013) (Figure 3D). Similarly, among the COVID-19 patients with no coinfection, the median ICU length of stay of those who were discharged was significantly lower than that of patients who died (10.0 days [5.00–15.5] vs 17.0 days [9.00–25.0], respectively, p = 0.002) (Figure 3E). Furthermore, simple linear regression analysis showed that the presence of coinfection predicted the ICU length of stay (B = 8.80, SE = 2.24, [95% CI: 4.37–13.2], p < 0.001), and coinfection explained 10% of this change in the dependent variable (ICU length of stay) (see Table 4).

Bacterial Coinfection and Mortality

Of the 142 ICU COVID-19 patients in this study, 55% (78/142) died. The mortality rate in the patients without bacterial coinfection was 50%, whereas it reached 70% in the patients with bacterial coinfection, as shown in Figure 4. No significant difference was observed in the mortality distribution between patients without bacterial coinfection and those with bacterial coinfection (p = 0.072), see Table 5. In addition, the presence of bacterial coinfection in the ICU COVID-19 patients did not predict mortality (B = 2.26 [95% CI: 0.98–5.19], p = 0.055), and none of the detected microorganisms were correlated with mortality (p > 0.05 for all). The risk of death correlated with the presence of bacterial coinfection in these ICU COVID-19 patients is presented in Table 6.

Table 3 Logistic Regression Analysis of Predictors of Mortality Among COVID-19 Patients in an Intensive Care Unit (N= 142)

	OR	95% Confidence Interval	*p*-value
Age			
< 60 years	1.58	0.64 to 3.87	0.322
60–79 years	0.63	0.25 to 1.58	0.327
≥ 80 years	*Reference Category*		
Sex			
Male	*Reference Category*		
Female	1.15	0.58 to 2.27	0.698
Have chronic disease			
Yes	*Reference Category*		
No	1.05	0.49 to 2.23	0.901
Coexistence of chronic disease			
Yes	*Reference Category*		
No	1.66	0.85 to 3.24	0.134
Use of intubation			
Yes	*Reference Category*		
No	29.7	3.90 to 227	0.001*

Note: *Significant at the 95% confidence level.

Table 4 Simple Linear Regression Analysis of Predictors of Duration of Stay in Intensive Care Unit

	B	SE	95% Confidence Interval	*p*-value	R-Square
Age, years	0.01	0.06	−0.12 to 0.13	0.905	0.00
NLR	0.19	0.06	0.07 to 0.31	0.002*	0.07
Sex (male= 1; female= 2)	−3.11	2.05	−7.16 to 0.94	0.131	0.02
Presence of coinfection (no=0; yes= 1)	8.80	2.24	4.37 to 13.2	< 0.001*	0.10
Have chronic disease (no=0; yes= 1)	−4.66	2.33	−9.27 to −0.06	0.047	0.03
Coexistence of chronic disease (no=0; yes= 1)	−1.08	1.98	−5.01 to 2.84	0.587	0.00
Use of intubation (no=0; yes= 1)	6.40	2.46	1.53 to 11.3	0.010*	0.05

Note: *Significant at the 95% confidence level.

Discussion

The medical records of the 142 ICU COVID-19 patients were reviewed to investigate possible predictors for their mortality, prolonged stay in the ICU, and the prevalence of bacterial coinfection among them. No significant correlation was observed between the patient characteristics, such as age, gender, and comorbidities, and their death rate or ICU length of stay. However, increased NLR and intubation were associated with mortality and prolonged ICU length of stay. In addition, bacterial coinfection was detected in 23% of the ICU COVID-19 patients and significantly correlated with a prolonged ICU length of stay ($p < 0.001$).

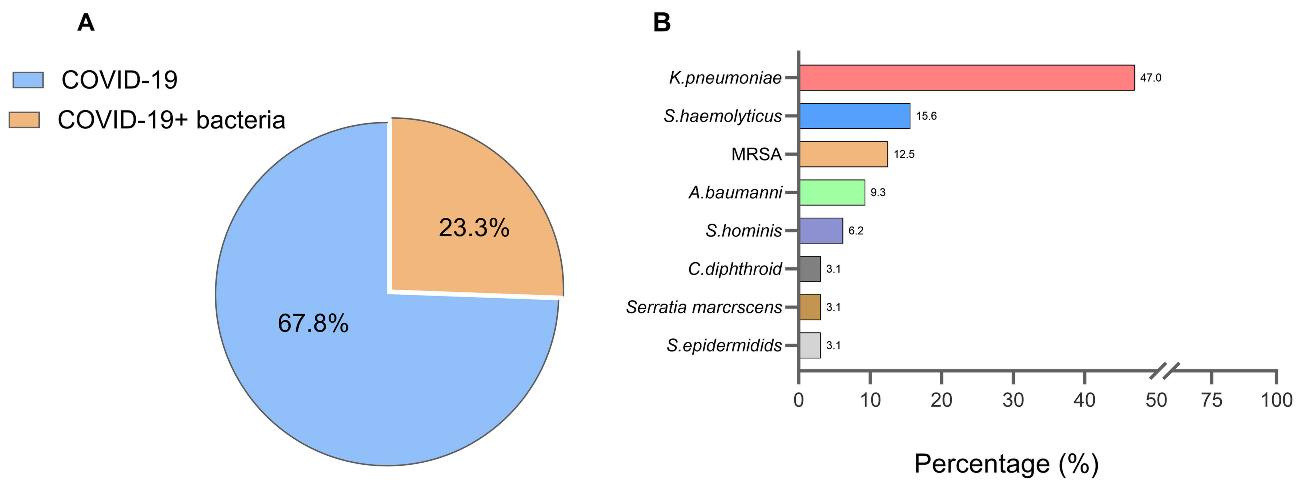

Figure 2 Bacterial coinfection among critical COVID-19 patients. (**A**) proportion of bacterial coinfections in the studied population. (**B**) frequency of the different bacterial coinfection causative species among critical COVID-19 patients.

Mortality reached 55% (78/142) in the studied population, and no significant correlations between death and patient characteristics, such as age, gender, and comorbidities, were observed, as shown in Table 2. However, the NLR significantly differed ($p < 0.001$) between the deceased and discharged ICU COVID-19 patients (Figure 1B), and simple linear regression analysis indicated that a higher NLR significantly predicted mortality ($p < 0.001$). This finding agrees with previous observations in Wuhan, China, where an increased NLR indicated a severe medical condition and was correlated with mortality among critically ill COVID-19 patients.[17,18] In addition, 96.2% of the ICU COVID-19 patients in this study who received intubation died, with a significant correlation ($p < 0.001$) between intubation and death among

Table 5 Characteristics of COVID-19 Patients in Intensive Care Unit Stratified by Presence of Bacterial Coinfection (N= 142)

	Coinfected, (n= 33)	Non-Coinfected (n= 109)	*p*-value
Age			
< 60 years	17 (29.8)	40 (70.2)	0.226
60–79 years	9 (16.1)	47 (83.9)	
≥ 80 years	7 (24.1)	22 (75.9)	
Sex			
Male	19 (21.3)	70 (78.7)	0.540
Female	14 (26.4)	39 (73.6)	
Mortality			
Dead	23 (29.5)	55 (70.5)	0.072
Discharged	10 (15.6)	54 (84.4)	
Use of intubation			
Yes	9 (34.6)	17 (65.4)	0.197
No	24 (20.7)	92 (79.3)	
Chronic diseases			
Yes	24 (22.9)	81 (77.1)	0.825
No	9 (24.3)	28 (75.7)	
Coexistence of chronic diseases			
Yes	17 (23.6)	55 (76.4)	1.00
No	16 (22.9)	54 (77.1)	

(*Continued*)

Table 5 (Continued).

	Coinfected, (n= 33)	Non-Coinfected (n= 109)	*p*-value
Type of chronic disease			
Diabetes	19 (26.0)	54 (74.0)	0.435
Hypertension	14 (22.2)	49 (77.8)	0.844
Cardiovascular disease	7 (23.3)	23 (76.7)	1.00
Chronic kidney disease	2 (22.2)	7 (77.8)	1.00
Hypothyroidism	2 (22.2)	7 (77.8)	1.00
Asthma	1 (12.5)	7 (87.5)	0.681
Other diseases	1 (6.20)	15 (93.8)	0.118

Notes: Numbers presented in the table are frequencies and percentages. Fisher's exact test was used to assess significance (alpha=0.05).

them (Figure 1C). Moreover, logistic regression analysis showed that intubation increased the OR, as shown in Table 3. Our results are in agreement with an early US study, which reported that 97.2% of elderly critical COVID-19 patients who received intubation died.[19] However, different mortality rates, ranging from 8% to 67%, have been recorded in intubated COVID-19 patients in different countries, such as China, Italy, Spain, Denmark, Germany, and the United Kingdom.[20] Quah et al suggested a predictive score for early mortality risk factors after intubation to assist clinicians with choosing effective therapy.[21]

Correlations between ICU length of stay and patient characteristics, such as age, gender, and comorbidities, were insignificant, and simple linear regression analysis revealed that these characteristics did not significantly predict the ICU length of stay in our study; see Table 4. However, deceased ICU COVID-19 patients (average age of >60 years) stayed longer in the ICU than surviving patients (average age of ≤60 years) (Figure 1D). The difference in ICU length of stay may be attributed to a poorer prognosis and the slight difference in average age. A previous study by Xia et al reported the effect of patient age on the ICU length of stay and mortality.[22] In addition, a recent nationwide retrospective study in Saudi Arabia[23] suggested that comorbidities, including diabetes and cardiovascular disease, are significant risk factors associated with prolonged ICU length of stay. This is in contrast to our findings; we found no significant correlation between ICU length of stay and comorbidities, which is attributed to the fact that the majority (73.9%) of our included patients had one or more comorbidities, as shown in Table 1. However, intubation was a significant predictor of ICU length of stay, which is in agreement with the results of the abovementioned study. Moreover, simple linear regression analysis revealed that increased NLR predicted and explained 7% of the change in the ICU length of stay among the ICU COVID-19 patients, as shown in Table 4. A previous multicenter study documented a higher NLR for ICU COVID-19 patients than that for non-ICU hospitalized COVID-19 patients.[24]

In this study, bacterial coinfection with different species was detected in 23% of the ICU COVID-19 patients (Figure 2A). Previous studies reported bacterial coinfection in 34.5% of ICU COVID-19 patients in China and in 28% and 11% of severely ill COVID-19 patients in Italy and France, respectively.[24–26] Bacterial coinfection can occur after respiratory infection for several reasons; for example, respiratory viral infection can result in pulmonary tissue injury, including severe damage to the ciliated cells, leading to the deterioration of mucociliary clearance, and this consequently enhances bacterial adherence and colonization of the airway.[27] Moreover, during COVID-19 infection, immune system impairment may occur, as the virus may cause lymphopenia, which causes patients to be more susceptible to coinfection.[28] Furthermore, ICU COVID-19 patients are more likely to receive invasive treatment, such as catheters, auto-ventilation, and central lines, which increase the possibility of acquiring infection with MDR bacterial strains.[29] The abovementioned reasons and risk factors for bacterial coinfection are summarized in Figure 5.

No significant differences were observed between coinfected and non-coinfected ICU COVID-19 patients in terms of gender, age, mortality, comorbidities, or NLR (Table 5). However, our results revealed a significant correlation between coinfection and prolonged ICU length of stay, and simple linear regression analysis showed that coinfection explained 10% of the change in ICU length of stay for ICU COVID-19 patients. There was a considerable difference in ICU length

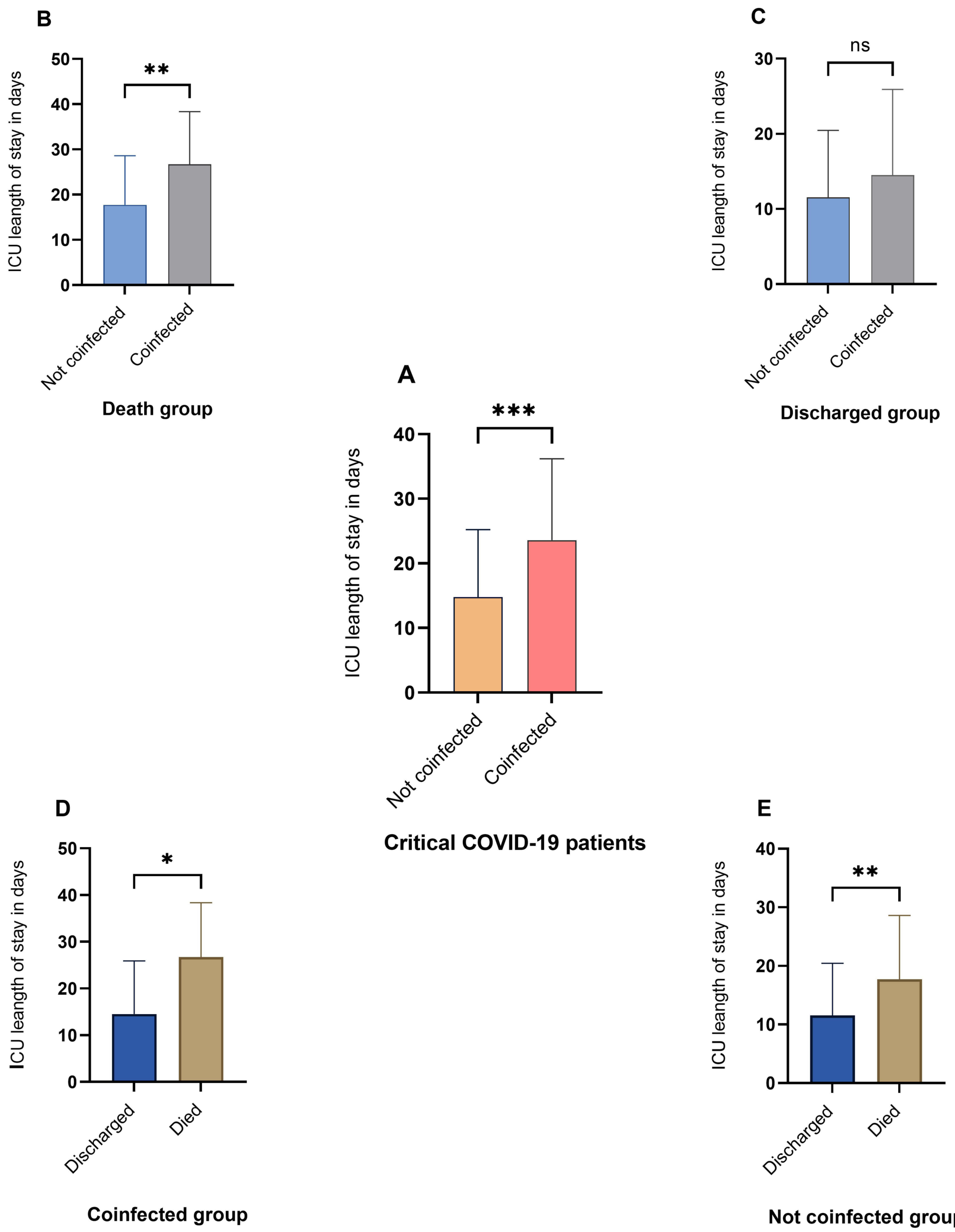

Figure 3 Association between bacterial coinfection and duration of stay in the intensive care unit. (**A**) Different ICU lengths of stay between coinfected and non-confected patients. (**B**) Different ICU lengths of stay among death cases between coinfected and not coinfected patients. (**C**) Different ICU length of stay among discharged cases between coinfected and not coinfected patients, (**D**) Different ICU length of stay among coinfected patients between died and discharged patients. (**E**) Different ICU lengths of stay among uninfected patients between died and discharged patients. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.
Abbreviation: ns, not significant.

of stay between the two groups, with patients with bacterial infections staying many more days than patients without coinfection (Figure 3A), which is consistent with prior results.[30]

In addition, as shown in Figure 3B, among the deceased patients, the coinfected patients had a more prolonged ICU length of stay than patients without coinfection; however, among the discharged patients, the ICU length of stay was similar for coinfected and non-coinfected patients (Figure 3C). Two potential explanations for this similarity are as follows: 1) samples from coinfected discharged patients were non-respiratory specimens, and 2) the isolated bacterial species in these patients were commensal non-virulent strains, such as *S. hominis, S. epidermidis*, and *S. marcescens.*

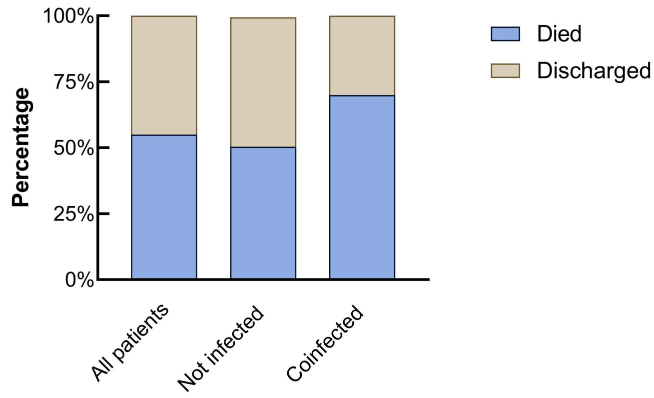

Figure 4 Mortality percentages for critical COVID-19 patients.

Coinfected patients who subsequently died stayed longer in the ICU than coinfected patients who were subsequently discharged (Figure 3D); this was also the case for those not coinfected (Figure 3E), which agrees with the results of other studies.[16,31,32]

No significant difference in mortality was observed between the coinfected patients and those without bacterial coinfection (p = 0.072) (Table 5). However, the mortality rate was higher in the coinfected patients than in those without coinfection patients (70% vs 50%, respectively) (Figure 4). MDR strains from different species, such as *K. pneumoniae, A. baumannii*, and *S. aureus* (MRSA), were commonly detected in the deceased patients, which is consistent with other studies that reported MDR bacterial strains in non-surviving ICU COVID-19 patients.[16,33,34] Despite the increased mortality rate among coinfected patients, logistic regression analysis showed that the presence of bacterial coinfection did not predict mortality among these ICU COVID-19 patients, as shown in Table 6.

Although our study provides useful findings about the epidemiological characteristics of ICU COVID-19 patients, it has some limitations. First, the study was conducted in a single center, and we analyzed medical records for 142 ICU patients; thus, we cannot generalize our findings to all ICU COVID-19 patients. Second, we were unable to collect and analyze some clinical information, such as medications administered and the COVID-19 mutant type. These may affect mortality, ICU length of stay, and bacterial coinfections. Third, the determination of the presence of bacterial coinfection depended on the specific culturing method, which could falsely indicate a low coinfection rate, particularly if antibiotics

Table 6 Risk of Death Associated with Presence of Bacterial Coinfection Among COVID-19 Patients in Intensive Care Unit (N= 33)

	OR	**95% Confidence Interval**	***p*-value**
Presence of bacterial coinfection			
Yes	*Reference Category*		
No	2.26	0.98 to 5.19	0.055
Detected organisms among patients with coinfection			
Klebsiella pneumoniae	*Reference Category*		
Acinetobacter baumannii	0.00	0.00	0.999
Staphylococcus aureus (MRSA)	2.67	0.30 to 23.9	0.380
Staphylococcus epidermidis; Staphylococcus hominis; Staphylococcus haemolyticus	2.40	0.36 to 16.2	0.369
Others (*C. diphtheriae; Serratia marcescens*)	Undefined[a]	Undefined[a]	0.999

Note: [a]Odd ratio cannot be calculated with zero cell.

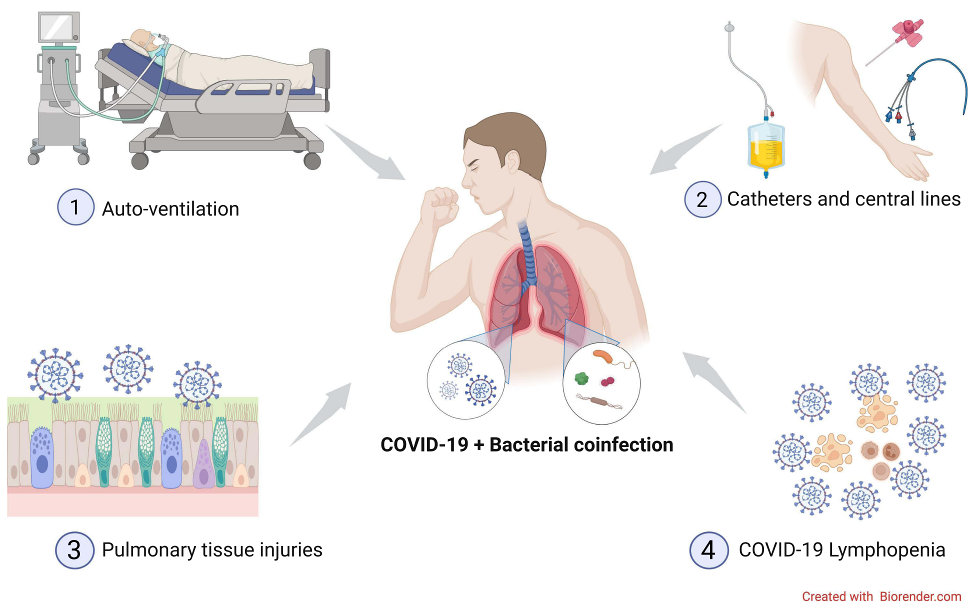

Figure 5 Enhancing factors for acquired bacterial coinfection among ICU COVID-19 patients.

were given before sampling. Finally, the bacterial species detected may reflect a site-specific microbiological profile because this was a single-center study.

Future Directions and Concluding Remarks

This retrospective single-center study revealed that increased NLR and intubation use were associated with prolonged ICU length of stay and mortality in this cohort of 142 ICU COVID-19 patients in Saudi Arabia. Bacterial coinfection was significantly associated with prolonged ICU length of stay for these patients. The mortality rate among the ICU COVID-19 patients with MDR bacterial coinfection was higher than among the patients without bacterial coinfection. Considering that these parameters ma clinicians manage and predict outcomes in ICU COVID-19 patients, multi-center studies are needed that include larger cohorts to expand our understanding of the risk factors affecting these patients and to explore additional patient outcome predictors, particularly after the emergence of new COVID-19 strains and vaccination implementation.

Institutional Review Board Statement

Ethical approval for this study was obtained from King Salman Bin Abdulaziz Medical City Institutional Review Board in Al-Madinah Al Munwarah, IRB log No: 064-22; patients' informed consents were waived by the Ethics Committee due to the retrospective nature of the study. Patient privacy and data confidentiality were maintained according to the Helsinki declaration.

Informed Consent Statement

The Patient's informed consent was waived by the IRB due to the study's retrospective nature.

Data Sharing Statement

All data and materials generated during the current study are available from the corresponding author upon reasonable request.

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Author Contributions

All authors contributed to data analysis, drafting or revising the article, have agreed on the journal to which the article will be submitted, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

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