Zagazig University Medical Journal
www.zumj.journals.ekb.eg
https://dx.doi.org/10.21608/zumj.2022.129209.2535 Volume 28, Issue 5, September 2022(1147-1155)
Manuscript ID ZUMJ-2203-2535 (R1)
DOI **10.21608/zumj.2022.129209.2535**

ORIGINAL ARTICLE

Bacterial Co-Infection Among Corona Virus Disease-19 Patients in Zagazig University Quarantine Intensive Care Units

***Saad Rabie Samra*[1], *Mohammed Fawzy Mohammed*[1], *Esam Albashir Ahmed*[2*], *Lamiaa Gaber Zake*[1]**
[1]Chest diseases Department, Faculty of Medicine, Zagazig University, Zagazig, Egypt
[2]Chest diseases Department, Faculty of Medicine, Tripoli University, Tripoli, Libya

***Corresponding Author:**
Esam Albashir Ahmed

Chest diseases Department, Faculty of Medicine, Tripoli University, Tripoli, Libya

E-mail: essambasher14@gmail.com

Submit Date	2022-03-24
Revise Date	2022-04-03
Accept Date	2022-04-03

ABSTRACT

Background: COVID-19 has affected millions of people worldwide. To date, efforts made to develop antiviral strategies for the treatment of COVID-19 remain underway. Respiratory viral infections predispose to co-infections which lead to increased disease severity and mortality. It is possible for some patients to die from bacterial co-infection rather than the virus itself. This study aimed to determine COVID-19 bacterial co-infection incidence and assess the severity and outcome among patients in Zagazig University quarantine ICUs.

Methods: This prospective cohort study was carried out on moderate and severe COVID-19 patients admitted to Zagazig University quarantine intensive care units. Full history was taken with complete physical examination, vital signs, laboratory investigations, bacterial co-infection assessment (within 48 hrs of admission) in form of persisting fever or leucocytosis (neutrophilia) and high procalcitonin with blood or sputum cultures and follow up the patients till discharge or death.

Results: Among 180 studied COVID-19 patients there was 21.1% of them had bacterial co-infection while 78.9 % were without bacterial co-infection. There were 8.9% positive blood cultures and 16.1% positive sputum cultures. There were significantly higher percentages of severity, CPAP need, and death rate among patients with bacterial co-infection. There was a statistically significant difference regarding the duration of ICU stay with a higher median in COVID-19 without bacterial co-infection.

Conclusions: The incidence of COVID-19 bacterial co-infection among patients in Zagazig University quarantine ICUs was 21.1% with Klebsiella organism the most causative organism and there were significantly higher percentages of severity and death rate among COVID-19 patients with bacterial co-infection.

Keywords: Bacterial co-infection; COVID-19; Intensive care units

INTRODUCTION

Coronaviruses which include a diverse group of viruses can cause mild to severe respiratory infections in humans. In 2002 and 2012, respectively, highly two pathogenic coronaviruses of zoonotic origin, Severe Acute Respiratory Syndrome Corona Virus (SARS-CoV) and Middle East Respiratory Syndrome Corona Virus (MERS- CoV) emerged in humans and caused fatal respiratory illness, making the emerging coronaviruses in the twenty-first century a new public health concern [1].

At the end of 2019, a novel coronavirus designated as SARS-CoV-2 emerged in the city of Wuhan in China and caused a pandemic of unusual viral pneumonia. Being highly transmissible, this novel coronavirus disease, also known as coronavirus disease 2019 (COVID-19), has spread fast all over the world [2].

Bacteria and viruses often occupy the same niches, however, interest in their potential collaboration in promoting wellness or disease development has only recently gained attention. The interaction of some bacteria and viruses are well characterized and researchers are typically now more interested in the location of the infection than the manner of cooperation [3]. So, this study aimed to determine COVID-19 bacterial co-infection incidence and assess the severity and outcome among patients in Zagazig University quarantine ICUs.

METHODS

This prospective cohort study was carried out at Zagazig University quarantine intensive care unit in the period from March 2021 to August 2021 for all COVID-19 patients who were admitted to those ICUs. Written consent of acceptance of sharing in the study was taken from

all patients. The study was approved by the research ethical committee of Faculty of Medicine, Zagazig University, and Police Hospital. The work has been carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion criteria were adult (>18 years) patients, moderate, severe, and critically ill cases, [4,5] confirmed COVID–19 patients admitted to quarantine ICU and confirmed by CT findings highly suspected CORAD 4, CORAD 5 and Positive PCR if possible [6], and patients either with or without comorbidities.

Full history was taken including age, sex, symptoms (fever, cough, dyspnea, anosmia, ...) and medication history of drugs taken, associated comorbidities with complete physical examination, and the vital signs (Heart rate, Respiratory rate, Temperature, Blood pressure, and Oxygen saturation), and laboratory investigations in the form of (Complete blood count, C-reactive protein, Procalcitonin, Lactate dehydrogenase, D-dimer, and Ferritin). All the patients underwent a common protocol in the treatment and assessment of bacterial co-infection (within 48 hrs of admission) by the following clinical and laboratory evidence in the form of persistent fever or leucocytosis (neutrophilia) and high procalcitonin with blood or sputum cultures [7].

The outcome of the study included ICU length of stay and survival rate.

Statistical analysis:

All data were collected, tabulated, and statistically analyzed using IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp. Quantitative data were expressed as the mean ± SD & (range), and qualitative data were expressed as percentages. The t-test was used to compare two groups of normally distributed variables. Mann-Whitney U test was used to compare two groups of non-normally distributed variables. Percentages of categorical variables were compared using the Chi-square test or Fisher exact test when appropriate. All tests were two-sided. P-value < 0.05 was considered statistically significant (S), P-value < 0.001 was considered statistically highly significant (S) and P-value ≥ 0.05 was considered statistically insignificant (NS).

RESULTS

The studied COVID-19 patients were 88 females (48.9%) and 92 males (51.1%). The mean age of all patients was 61.3 ± 14.85 years and ranged from (18-95) years. 53.3% of patients were on reservoir, 32.2% of patients were on CPAP, 3.9% on a simple face mask and only 10.6% were on invasive mechanical ventilation (Table 1).

Among 180 studied COVID-19 patients there was 21.1% of them had bacterial co-infection while 78.9% were without bacterial co-infection. There were 8.9% positive blood cultures while 16.1% were positive sputum cultures, both positive blood and sputum culture mainly with Klebsiella organism (Table 2).

Table 3 showed that there was a statistically insignificant relation between patients' comorbidities among COVID-19 patients with bacterial co-infection and those without bacterial co-infection, except for cardiac comorbidity, there was a highly statistically significant difference in patients with bacterial co-infection, and all cardiac patient developed an infection.

Table 4 showed that WBCs, neutrophils, and CRP at admission were significantly higher among COVID-19 patients with bacterial co-infection. While there was no statistically significant difference between COVID-19 patients with bacterial co-infection and COVID-19 patients without co-infection regarding lymphocyte at admission, LDH, procalcitonin, D-dimer, Ferritin (p > 0.05).

Table 5 showed that 47.2% of patients died and only 52.8%of the patients were survived. There were significantly higher percentages of the severity of disease, CPAP need, and death rate among COVID-19 patients with bacterial co-infection (Table 6).

Table 7 showed that there was a statistically significant difference between COVID-19 patients with and without bacterial co-infection regarding the duration of ICU stay with a higher median in COVID-19 patients without bacterial co-infection group.

Table 1: Demographic data, oxygenation, and ventilation of studied patients (n.180).

Variables		
Age per years Mean ±SD Range	61.3 ± 14.85 18 - 95	
Sex	**n.**	**%**

Variables		
Females	88	48.9
Males	92	51.1
Oxygenation and ventilation		
CPAP(NIV)	58	32.2
Reservoir (BAG)	96	53.3
Invasive mechanical Ventilation	19	10.6
Simple Face mask	7	3.9

Table 2: Frequency distribution of co-bacterial infection and organism presentation in sample cultures among COVID-19 patients.

	n.	%
Bacterial co-infection		
YES	38	21.1
No	142	78.9
Blood culture		
Positive	16	8.9
No growth	164	91.1
Types of organism		
E-coli	4	2.2
Klebsiella	12	6.7
Sputum culture		
Positive	29	16.1
No growth	151	83.9
Types of organism		
E-coli	8	4.4
Enterococci	1	0.6
Klebsiella	20	11.1

Table 3: Relation between patients' characters and bacterial co-infection among COVID-19 patients.

Variables	Bacterial infection				n.	t/χ^2	P-value
	With infection n.38		Without infection n.142				
	No.	%	No.	%			
Age per years	62.94 ± 13.4		57.04 ± 17			1.96	0.051
Sex	.	.					
Females	23	26.1	65	73.9	88	2.61	0.106
Males	15	16.3	77	83.7	92		
Smokers	11	20.4	43	79.6	54	0.025	0.873
HTN	12	17.9	55	82.1	67	0.65	0.417
DM	19	16.7	55	83.3	74	1.236	0.266
Renal	2	13.3	13	86.7	15	f	0.74

Variables	Bacterial infection				n.	t/χ^2	P-value
	With infection n.38		Without infection n.142				
	No.	%	No.	%			
Hepatic	3	18.8	13	81.2	16	f	1.0
Cancer	1	12.5	7	87.5	8	f	1.0
Cardiac	13	100	0	0.0	13	f	<0.0001
Pulmonary	7	41%	10	58%	17	f	0.650

χ2 = Chi square test **f** = Fisher Exact test **P > 0.05** = non-significant

Table 4: Relation between laboratory parameters among bacterial co-infection and non-bacterial co-infection COVID-19 patients.

Variables	Studied COVID-19 patients		U	P
	With infection n. 38	Without infection n. 142		
WBCs at admission Median (range)	16 (1.3-35)	10.6 (1.1-35)	4.05	0.0001 (HS)
Neutrophil at admission Median (range)	14 (1-36)	9 (.7-36)	4.437	0.0001 (HS)
Lymphocyte at admission Median (range)	0.9 (0-3)	0.7 (0-3.4)	1.598	0.110
CRP at admission Median (range)	170 (30-400)	116 (1-144)	2.95	0.003 (S)
LDH Median (range)	494 (128-980)	498 (118-1650)	0.222	0.824
Procalcitonin Median (range)	0.6 (0.04-5.0)	0.3 (.02-4.8)	0.187	0.852
D dimer Median (range)	1.2 (0.2-6)	1.0 (0.1-6)	1.16	0.246
Ferritin Median (range)	1270 (190-1999)	1210 (67-8050)	0.829	0.407

U = Mann-Whitney U test of sig **P < 0.05** = significant
P < 0.001 = highly significant **P > 0.05** = non-significant

Table 5: The survival rate of studied COVID-19 patients (n.180).

Variable	Number	%
Died	85	47.2
Survived	95	52.8

Table 6: Outcome of COVID-19 patients with bacterial co-infection versus COVID-19 patients without bacterial co-infection.

Variables	Bacterial infection				χ^2	P-value
	With infection n.38		Without infection n.142			
	No.	%	No.	%		
Severity of disease						
Moderate	14	36.8	104	73.2	17.58	0.0001
Severe and critically ill	24	63.2	38	26.8		(HS)
Oxygenation and ventilation	.	.	.	.		
CPAP	19	50.0	39	27.5		
Reservoir (bag) Simple face mask	11 2	29 5.2	85 5	59.8 3.5	10.96	0.004
Invasive mechanical	6	15.8	13	9.2		**(S)**

Variables	Bacterial infection				χ^2	P-value
	With infection n.38		Without infection n.142			
	No.	%	No.	%		
Ventilation						
Survived	.	.	.	.		
Died	27	71.1	58	40.8	10.97	0.0009
Survival	11	28.9	84	59.2		(S)

χ^2 = Chi-square test **f** = Fisher Exact test
P < 0.05 = significant **P < 0.001** = highly significant
P > 0.05 = non-significant

Table 7: Duration of ICU stay of COVID-19 patients with bacterial co-infection versus without bacterial co-infection.

	With infection n.38	Without infection n.142	U	P
ICULOS Median (range)	8 (1-37)	12 (1-42)	2.97	0.003

U = Mann-Whitney U test of sig **P > 0.05** = non-significant

DISCUSSION

Coronavirus disease-19 pandemic raised the attention toward bacterial co-infection which affects the outcome of the disease, needs more investigations, and also accelerates the surge of COVID-19, therefore information on the actual extent of bacterial co-infection in COVID-19 patients is crucial to inform appropriate treatment [8].

So, the objectives of this study were to determine COVID-19 bacterial co-infection incidence and assess the severity and outcome among patients in Zagazig University quarantine ICUs.

In the current study, the mean age was 61.3 (± 14.85) years, and 51.1% of patients were male. Comorbidities found in the patients were that 37.2 % of patients were HTN, 41.1% were diabetic, 8.3% had renal problems, 8.9% of patients were hepatic, 7.2% of cardiac patients, 9.4% with pulmonary disorders, and 4.4 % of them had a history of cancer. Also, 30% of patients were smokers, 53.3 % of patients were on reservoir, 32.2 % of patients were on CPAP, 3.9% were on simple face masks and only 10.6 % were on invasive mechanical ventilation (Tables 1,3) and these were in agreement with many studies as:

Asmarawati et al. [5] demonstrated a total of 218 patients confirmed for SARS-CoV-2 infection from moderate to critically ill conditions. Patients' characteristic symptoms were defined according to their severity. The median age of the study subject was 52.45 (± 14.44) years, and 55.05% of patients were male. Diabetes and hypertension were the most common comorbidities of patients among all subjects. 7.3% of patients who were critically ill manifested respiratory failure, and 23% of them were on a ventilator.

Garcia-Vidal et al. [9] assessed 989 consecutive adults with COVID-19. Of these, 56% were male, and the median age was 62 years.

Elabbadi et al. [10] reported that 101 COVID-19 patients were referred to the ICU with severe pneumonia after 8 days of symptoms onset, they were (78%) men, aged 61 (53–69) years, and frequent comorbid conditions, mainly arterial hypertension, and diabetes.

Ramadan et al. [11] demonstrated that among the COVID-19 suspected cases, 260 patients were confirmed to have COVID-19 infection by RT-PCR. The majority of the included cases were males (56%), and the most common age range was between 51 and 70 years. Hypertension and diabetes mellitus were the most common reported comorbidities.

Bourgoin et al. [12] reported that a total of their patients, 51% of them were women and 49% were men, with a mean age of 60 (± 18) years and the most frequent comorbidities of COVID-19 were high blood pressure (41%), cardiovascular diseases (37%), organ failure (33%), obesity (24%), diabetes (21%), asthma (13%), and about 9% were smokers.

Wang et al. [13] found that of 339 patients identified, the mean age was 71 years, and 51% were female, 60.7% of the patients had comorbidities, while 23.9% had two or more comorbidities. Common comorbidities included hypertension (40.8%), diabetes (16.0%) and cardiovascular disease (14.2%).

In the current study, among 180 studied COVID-19 patients, there were 38 (21.1%) of them had bacterial co-infection. They were both positive blood culture and sputum culture mainly with Klebsiella organism. Also, some had E-coli and Enterococci. 8.9 % were positive blood cultures as following E-coli (2.2 %) and Klebsiella (6.7%) while 16.1 % were positive sputum cultures as following E-coli (4.4 %), Enterococci (0.6 %) and Klebsiella (11.1 %) (Table 2).

Contou et al. [14] showed that a total of 92 adult patients were admitted to this ICU for acute respiratory failure due to SARS-CoV-2 pneumonia, 28.2% of patients were considered co-infected with a pathogenic bacterium upon ICU admission while no co-infection with a virus was detected. Among the 26 co-infected patients, a total of 32 bacteria were isolated from blood culture and/or PCRs: Haemophilus influenzae (7.6%)), Streptococcus pneumoniae (6.5%), Enterobacteriaceae (5.4%), Pseudomonas aeruginosa (2.1%) and Acinetobacter (1%). Among the 67 cultures of respiratory tract secretion samples (sputum) 26% were sterile, 26% grew oropharyngeal flora and 20.6% isolated one (n=14) or two (n=5) pathogenic bacteria. The leading micro-organisms isolated from the culture of respiratory tract secretions samples were Haemophilus influenzae (6.5%), Streptococcus pneumoniae (5.4%), and Enterobacteriaceae (5.4%).

Asmarawati et al. [5] found that bacterial co-infection incidence in their study was 23 %, collected 110 culture samples from suspected bacterial infection patients, consisting of 40 % blood samples and 51% sputum samples. Among them, bacteria were detected in blood cultures (8%) and sputum cultures (42.7%). Bacteria found in the blood were Klebsiella pneumoniae (1.8%), Pseudomonas fluorescens (0.9%), Pseudomonas putida (0.9%). There were 47 isolates found in sputum cultures, in which 6 of them were fungi (Candida spp). The most frequent bacteria found were Acinetobacter (8.2%), followed by Klebsiella pneumoniae (4.5%), Pseudomonas aeruginosa (3.6%) Escherichia Coli (1.8%), Enterobacter (2.7%).

Also, Clancy and Nguyen, [15] and Lehmann et al. [16] found that the incidence of bacterial co-infection in COVID-19 ranges from 3–30%.

Garcia-Vidal et al. [9] found that a total of 74 bacterial infections were diagnosed in 69% of patients (3 infections in one patient, 2 in 12 individual patients, and 1 in every remaining patient). The most common bacteria isolated were S. pneumoniae (13.6%), Pseudomonas aeruginosa (11.3%); Escherichia coli (7.9%), and Klebsiella pneumonia (6.8%). Nori et al. [17] demonstrated that the respiratory co-infections among a total of 152 patients were 59% with positive respiratory cultures. The most commonly identified organisms in sputum cultures were Klebsiella spp (10%), Enterobacter spp (8%), and E. coli (4%). Most patients were admitted to ICUs (93%) and were intubated (95%). In Bloodstream co-infections, the most frequently isolated organisms were Streptococcus spp (10%), Enterococcus spp(7%), Escherichia coli (7%), Pseudomonas aeruginosa (6%), Candida spp (5%), Klebsiella spp (3%), and Enterobacter spp (3%).

In a systematic review of these 17 studies on bacterial co-infection in COVID-19 patients, specific co-infecting pathogens were identified. The most frequently detected bacterial pathogens were Mycoplasma pneumoniae, followed by Pseudomonas aeruginosa and Haemophilus influenzae, and Klebsiella pneumoniae. Other bacteria detected were Enterobacter species, Acinetobacter, and Chlamydia [18].

Langford et al. [19] reported prevalence of co-infections was 3.5%.

Wang and colleagues [13] reported that 29 of 69 patients undergoing sputum culture on admission to the hospital to identify respiratory bacterial co-infection. Of these, 5 of 69 (7%) had positive microbiology. The overall low rate of bacterial infections in these studies was due to over 70% of patients received antibiotics, with the majority constituting broad-spectrum agents such as fluoroquinolones and third-generation cephalosporins. Also, they included patients in ICU and inpatient settings while our study included ICU patients only [16].

The result of this study showed a statistically insignificant relation between patients' characters and bacterial co-infection among COVID-19 patients, except for cardiac comorbidity. There was a highly statistically significant difference with a higher percentage in patients with bacterial co-infection Table (3).

In agreement with our study, Elabbadi et al. [9] said that there was no difference in comorbidities between patients with or without early bacterial co-infection.

Asmarawati et al. [5] found that there were no sex differences between bacterial infection and no bacterial infection patients. Patients with a bacterial infection have an older mean age than no bacterial infection, although, among elderly patients, there were no differences in bacterial infection rate, other comorbidities such as diabetes, hypertension, and chronic kidney disease did not differ between the two categories.

Cheng et al. [20] found that in a comparison of patients with COVID-19 with and without bacterial co-infections, bacterial co-infections occurred more commonly in men and older patients; however, the difference was not statistically significant.

In this study, the white blood cells, neutrophil, and C-reactive protein at admission were significantly higher among COVID-19 patients with bacterial co-infection: P-values were 0.0001(HS), 0.0001(HS), and 0.003(S) respectively while there was no significant difference regarding procalcitonin, LDH, D-dimer, and Ferritin > 0.05. (NS)

This came in agreement with Nasir et al. [21] who did not find procalcitonin to be a reliable marker of distinguishing patients who had bacterial infections and those who did not have bacterial infections,

In addition, Vanhomwegen et al. [22] found that PCT is not reliable to diagnose bacterial co-infection within 48 h of admission. Also, Heer et al. [23] found that there was no significant difference was found between procalcitonin concentrations of patients with positive and negative bacterial co-infection. Müller et al. [24] found that the lack of a procalcitonin rise in viral infections may be due to virus-stimulated production of interferon-γ by macrophages, which inhibits TNF-α in the immune response.

In disagreement with our study, Han et al. [25] suggested that raised procalcitonin observed in COVID-19 could be due either to bacterial co-infection, which was itself causing increased severity and driving systemic sepsis or as a direct marker of a more severe or widespread viral infection.

Variance in procalcitonin levels has previously been proposed to differentiate systemic inflammation of a bacterial origin from a viral origin in pneumonia and sepsis, with a significant rise indicating bacterial co-infection. However, it has its diagnostic and prognostic role in bacterial infection and sepsis [24].

In disagreement with our study, Cheng et al. [20] found that co-infected patients had comparable absolute neutrophil and lymphocyte counts. Among all the inflammatory biomarkers evaluated in the study, LDH (p = 0.033) levels were significantly higher in patients with bacterial co-infections.

Elabbadi et al. [10] said that there was no difference in laboratory characteristics between patients with or without early bacterial co-infection, except for a trend towards a more pronounced lymphopenia.

In this study, 47.2 % of patients died and only 52.8 % of the patients survived (Table 5) as all patients in this study were ICU admitted with moderate, severe, and critically ill, old aged patients with frequent comorbidities.

This came in agreement with Nori et al. [17] who found that in total, 99 patients (65%) were admitted to intensive care units (ICUs) and 74% of patients received mechanical ventilation (in the ICU or ward). Overall, 57% of patients died and 16% of patients were discharged.

Also, Nasir et al. [21] found that the overall mortality was 30%.

This is also consistent with data of Goncalves et al. which was reported from Europe and parts of Asia 30% [26].

Langford et al. [19] found that in patients infected with SARS-CoV-2, co-infection of viruses, bacteria, and fungi was an important factor that cannot be ignored. Co-infection of SARS-CoV-2 with viruses, bacteria, and fungi will increase the difficulty of diagnosis, treatment, and prognosis of COVID-19 and even increase the symptoms and mortality of the disease. At the same time, co-infected microorganisms may also become a new strategy for the development of new treatments for SARS-CoV-2 infection.

Garazzino et al. [27], Bengoechea and Bamford, [28] reported that the infection rate of bacterial co-infection with SARS-CoV-2 was proportional to the severity of the disease, and the co-infection can increase mortality.

In the current study, there was a significantly higher percentage of the severity of disease (HS)=0.0001, CPAP need (S)=0.004, and death rate (HS) =0.0009 among COVID-19 patients with bacterial co-infection. 71.1% of patients with bacterial co-infection died while only 40.8% of patients without bacterial co-infection died and 63.2 % of patients with bacterial co-infection were severe cases while 26.8 % of patients without co-infection were severe (Table 6).

Also, Zhou et al. [29] showed that in the current coronavirus disease 2019 (COVID-19) pandemic, 50% of patients who died had bacterial infections, while another study showed the presence of both bacterial and fungal infections [30].

Asmarawati et al. (5) found higher proportions of respiratory failure, ICU admission, and invasive mechanical ventilation use in the bacterial co-infection group. Mortality occurred in 16.28 % of COVID-19 patients with bacterial infections, which was higher than those without bacterial infection (8%).

In addition, Qin et al. [31] reported that the mortality was more significant in severe cases

compared with the non-severe group due to the higher co-infection rate in severe patients.

In disagreement with our study, Cheng et al. [20] found that the need for oxygen therapy and ventilatory support during hospitalization did not significantly differ between patients with and without bacterial co-infections.

Also, in this systematic review of 17 studies on bacterial co-infection in COVID-19 patients, a pooled analysis of crude odds ratios for death indicated that COVID-19 patients with a co-infection were more likely to die than patients who did not have a co-infection [18].

In the current study, there was a statistically significant difference (P =0.003) between COVID-19 patients with and without bacterial co-infection regarding the duration of ICU stay with the median higher in the without bacterial infection group (12 days) than with infection group (8 days) (Table 7) due to frequent complications of bacterial co-infection which leads early death. This came in agreement with Yang et al. [32] who found that bacterial co-infection was a major inducer of death with a shorter length of stay as it could eventually lead to many organs and system failures, including severe bacterial pneumonia, sepsis, and bacterial meningitis.

However, Asmarawati et al. [5] found that COVID-19 patients with bacterial infections had a longer hospital length of stay.

Alqahtani et al. [33] showed that the length of stay in the ICUs for patients infected with both SARS-CoV-2 and bacterial infection was 35.2 days, compared to 16.2 days for patients infected with only SARS-CoV-2 (p = 0.0001).

Nori et al. [17] reported that for patients admitted to intensive care units, the median length of hospitalization was 13 days with a range of (6–21) days.

Baskaran et al. [34] found that the proportion of pathogens detected increased with the duration of ICU stay, consisting largely of Gram-negative bacteria, particularly Klebsiella pneumoniae and Escherichia coli.

This difference in length of stay can be explained by the high death rate in our patients with bacterial co-infection in the early days of admission.

CONCLUSION

We concluded that the incidence of COVID-19 bacterial co-infection among patients in Zagazig University quarantine ICUs was 21.1% with Klebsiella organism the most causative organism and there were significantly higher percentages of the severity of disease and death rate among COVID-19 patients with bacterial co-infection. Rapid characterization of co-infection is essential in the treatment of most COVID-19 patients, and could help to save lives, and will improve antimicrobial stewardship during the pandemic.

Conflict of Interest: None.

Financial Disclosures: None.

REFERENCES

1. Cui J, Li F, Shi ZL. Origin and evolution of pathogenic coronaviruses. Nat. Rev. Microbiol. 2019; 17 (3): 181–92.
2. Wu F, Wang A, Liu M, Wang Q, Chen J, Xia S, et al. Neutralizing antibody responses to SARS-CoV-2 in a COVID-19 recovered patient cohort and their implications. medRxiv. 2020; 1-12.
3. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A Novel Coronavirus from Patients with Pneumonia in China, N Engl J Med. 2020; 382 (8): 727–33.
4. World Health Organization. (2020). Clinical management of severe acute respiratory infection when novel coronavirus (nCoV-2019) infection is suspected: interim guidance. 28 January 2020. Available at: https://apps.who.int/iris/handle/10665/330893
5. Asmarawati TP, Rosyid AN, Suryantoro SD, Mahdi BA, Windradi C, Wulaningrum PA, et al. The clinical impact of bacterial co-infection among moderate, severe and critically ill COVID-19 patients in the second referral hospital in Surabaya. F1000Research. 2021; 10.
6. Gietema HA, Zelis N, Nobel JM, Lambriks LJ, van Alphen LB, Oude Lashof AM, et al. CT in relation to RT-PCR in diagnosing COVID-19 in The Netherlands: A prospective study. PloS one, 2020; 5 (7): e0235844.
7. Sharifipour E, Shams S, Esmkhani M, Khodadadi J, Fotouhi-Ardakani R, Koohpaei A, et al. Evaluation of bacterial co-infections of the respiratory tract in COVID-19 patients admitted to ICU. BMC Infect. Dis. 2020; 20 (1): 1-7.
8. Prasetyoputri A. Detection of Bacterial Coinfection in COVID-19 Patients Is a Missing Piece of the Puzzle in the COVID-19 Management in Indonesia. ACS Infect. Dis. 2021; 7 (2): 203-5.
9. Garcia-Vidal C. Sanjuan G, Moreno-García E, Puerta-Alcalde P, Garcia-Pouton N, Chumbita M, et al. Incidence of co-infections and superinfections in hospitalized patients with COVID-19: a retrospective cohort study. Clin. Microbiol. Infect. 2021; 27 (1): 83–8.
10. Elabbadi A, Turpin M, Gerotziafas GT, Teulier M, Voiriot G, Fartoukh M. Bacterial coinfection in critically ill COVID-19 patients with severe pneumonia. Infection. 2021; 49 (3): 559-62.
11. Ramadan HK, Mahmoud MA, Aburahma MZ, Elkhawaga AA, El-Mokhtar MA, Sayed IM, et al. Predictors of severity and co-infection resistance profile in COVID-19 patients: First report from upper Egypt. Infect. Drug Resist. 2020; 13: 3409.
12. Bourgoin P, Soliveres T, Barbaresi A, Loundou A, Belkacem IA, Arnoux I, et al. CD169 and CD64 could help differentiate bacterial from CoVID-19 or

other viral infections in the Emergency Department. Cytometry Part A. 2021; 99 (5): 435-45.
13. Wang Z, Yang B, Li Q, Wen L, Zhang R. Clinical features of 69 Cases with Coronavirus Disease 2019 in Wuhan, China. Clin. Infect. Dis.. 2020; 71 (15): 769-77.
14. Contou D, Claudinon A, Pajot O, Micaëlo M, Longuet Flandre P, Dubert M, et al. Bacterial and viral co-infections in patients with severe SARS-CoV-2 pneumonia admitted to a French ICU. Ann Intensive Care. 2020; 10 (1): 1-9.
15. Clancy CJ, Nguyen MH. Coronavirus Disease 2019, Superinfections, and Antimicrobial Development: What Can We Expect? Clin Infect Dis. 2020; 71 (10): 2736-43.
16. Lehmann CJ, Pho MT, Pitrak D, Ridgway JP, Pettit NN. Community-acquired coinfection in coronavirus disease 2019: a retrospective observational experience. Clin Infect Dis. 2021; 72 (8): 1450-2.
17. Nori P, Cowman K, Chen V, Bartash R, Szymczak W, Madaline T, et al. Bacterial and fungal coinfections in COVID-19 patients hospitalized during the New York City pandemic surge. Infect. Control Hosp. Epidemiol. 2021; 42 (1): 84-8.
18. Lansbury L, Lim B, Baskaran V, Lim WS. Co-infections in people with COVID-19: a systematic review and meta-analysis. J Infect. 2020; 81 (2): 266-75.
19. Langford BJ, So M, Raybardhan S, Leung V. Westwood D, MacFadden DR, et al. Bacterial co-infection and secondary infection in patients with COVID-19: a living rapid review and meta-analysis. Clin Microbiol Infect. 2020; 26 (12): 1622-9.
20. Cheng LS, Chau SK, Tso EY, Tsang SW, Li IY, Wong BK, et al. Bacterial co-infections and antibiotic prescribing practice in adults with COVID-19: experience from a single hospital cluster. Ther Adv Infect Dis. 2020; 7: 2049936120978095.
21. Nasir N, Rehman F, Omair SF. Risk factors for bacterial infections in patients with moderate to severe COVID-19: A case-control study. J Med Virol. 2021; 93 (7): 4564-9.
22. Vanhomwegen C, Veliziotis I, Malinverni S, Konopnicki D, Dechamps P, Claus M, et al. Procalcitonin accurately predicts mortality but not bacterial infection in COVID-19 patients admitted to intensive care unit. Ir J Med Sci. 2021; 190 (4): 1649-52.
23. Heer RS, Mandal AK, Kho J, Szawarski P, Csabi P, Grenshaw D, et al. Elevated procalcitonin concentrations in severe Covid-19 may not reflect bacterial co-infection. Ann Clin Biochem. 2021; 58 (5): 520-7.
24. Müller B, Becker KL, Schächinger H, Rickenbacher PR, Huber PR, Zimmerli W, et al. Calcitonin precursors are reliable markers of sepsis in a medical intensive care unit. Crit Care Med. 2000; 28 (4): 977-83.
25. Han J, Gatheral T, Williams C. Procalcitonin for patient stratification and identification of bacterial co-infection in COVID-19. Clini Med (Lond). 2020; 20 (3): e47-e7.
26. Goncalves Mendes Neto A, Lo KB, Wattoo A, Salacup G, Pelayo J, DeJoy III R, et al. Bacterial infections and patterns of antibiotic use in patients with COVID-19. J Med Virol. 2020; 93 (3): 1489-95.
27. Garazzino S, Montagnani C, Donà D. Meini A, Felici E, Vergine G, et al. Multicentre Italian study of SARS-CoV-2 infection in children and adolescents, preliminary data. Euro Surveill. 2020; 25 (18): 2000600.
28. Bengoechea JA, Bamford CG. SARS-CoV-2, bacterial co-infections, and AMR: the deadly trio in COVID-19? EMBO Mol Med. 2020; 12 (7): e12560.
29. Zhou F, Yu T, Du R, Fan G. Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020; 395 (10229): 1054-62.
30. Rawson TM, Moore LS, Zhu N, Ranganathan N, Skolimowska K, Gilchrist M, et al. Bacterial and Fungal Coinfection in Individuals With Coronavirus: A Rapid Review To Support COVID-19 Antimicrobial Prescribing. Clin Infect Dis. 2020; 71 (9): 2459-68.
31. Qin C, Zhou L, Hu Z. Zhang S, Yang S, Tao Y, et al. Dysregulation of Immune Response in Patients With COVID-19 in Wuhan. China. Clin Infect Dis. 2020; 71 (15): 762–8.
32. Yang X, Yu Y, Xu J, Shu H, Liu H, Wu Y, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med. 2020; 8 (5): 475–81.
33. Alqahtani A, Alamer E, Mir M, Alasmari A, Alshahrani MM, Asiri M, et al. Bacterial Coinfections Increase Mortality of Severely Ill COVID-19 Patients in Saudi Arabia. Int J Environ Res Public Health. 2022; 19 (4): 2424.
34. Baskaran V, Lawrence H, Lansbury LE, Webb K, Safavi S, Zainuddin NI, et al. Co-infection in critically ill patients with COVID-19: an observational cohort study from England. J Med Microbiol. 2021; 70 (4): 001350.

To cite:
Ahmed, E., Samra, S., Mohammed, M., Zake, L. Bacterial Co-Infection Among Corona Virus Disease-19 Patients in Zagazig University Quarantine Intensive Care Units. *Zagazig University Medical Journal*, 2022; (1147-1155): -. doi: 10.21608/zumj.2022.129209.2535