International Journal of General Medicine

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ORIGINAL RESEARCH

Pneumothorax in Critically Ill COVID-19 Patients: Prevalence, Analysis of Risk Factors and Clinical Outcomes

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Background: Previous studies have been conducted to assess pneumothorax. However, few studies were done to assess pneumothorax in COVID-19 patients in the intensive care unit (ICU).

Objective: Our aim is to describe and analyze the prevalence, clinical characteristics, risk factors, and outcomes of COVID-19 pneumothorax patients in the intensive care unit.

Methods: We performed a retrospective review of the medical records of 418 patients, who tested positive for COVID-19 by polymerase chain reaction test and required ICU admission in King Fahad Hospital of The University from 02/01/2020 to 01/09/2021. A total number of 36 pneumothorax patients were included in the study.

Results: Of 418 patients who were followed up in the intensive care unit as COVID-19 cases, 36 patients developed a pneumothorax (8.61%). The mean age of the patients was 55.6 ± 15.06 years, 23 patients were male, and 13 were female. Seventeen patients were obese, and only one patient was an active smoker. Twenty-four patients had at least one comorbidity; hypertension was the most common. Thirty-two patients were intubated, and the duration of intubation was 23.23 ±15.9 days. The time from intubation to pneumothorax development was 8.8 ± 9.3 days. Six patients were on bilevel positive airway pressure ventilation (BIPAP), 2 patients on continuous positive airway pressure ventilation (CPAP), 3 patients on High-Flow Nasal Cannula ventilation (HFNC), 9 patients on pressure-control ventilation (PC), and 16 patients on pressure regulated volume control ventilation (PRVC). Of 36 patients, 26 died, and the mortality rate was 72.2%.

Conclusion: Our study showed that risk factors of pneumothorax occurrence in COVID-19 critically ill patients include male patients, hypertension, diabetes mellitus, endotracheal intubation and mechanical ventilation. More efforts should be made to determine the risk factors and assess the outcomes of those patients to develop preventive measures and management guidelines.

Keywords: pneumothorax, COVID-19, intensive care unit, risk factors, outcomes

Introduction

COVID-19 (SARS-CoV-2) is a global pandemic that has been a concern for the health-care systems for the last two years. The World Health Organization (WHO) reports documented a total of 468 million confirmed cases and over 6 million deaths on the March 20, 2022, report.[1] Consequently, due to the high prevalence of the COVID-19 pandemic, diverse prognoses and complications might be developed, which in certain conditions might be life-threatening. Pneumothorax, per se, can result in severe complications that might change the patient's prognosis and overall mortality rate.[2] We reviewed the literature to identify the possible risk factors associated with the development of pneumothorax in COVID-19 patients who required admission to the intensive care unit (ICU).

Pneumothorax is defined as the "collection of air outside the lung but within the pleural cavity" which can result in a severe complication that might change the patient's prognosis and overall mortality rate.[3] In addition, the consequences

Received: 28 August 2022
Accepted: 15 November 2022
Published: 21 November 2022

are economically costly for the health-care systems, with a median cost of treatment of $6160 if conventional intercostal chest tube drainage was provided.[4]

Pneumothorax is either an unusual or under reported complication of COVID-19.[5] It was reported as a rare complication in COVID-19 patients occurs only in 1% or less of patients.[6,7] The prompt identification and management of pneumothorax in such patients are essential as it worsens the hypoxia and hence requires immediate intervention. Spontaneous pneumothorax caused by COVID-19 has been recorded on several occasions at the time of diagnosis or during therapy. However, late-onset spontaneous pneumothorax in individuals who recovered from COVID-19 is rare.[8] Nevertheless, we observed insufficient data regarding this condition among COVID-19 patients in the ICU. Therefore, this study analyzes COVID-19 patients who developed pneumothorax during their treatment course in the intensive care unit (ICU) in a university hospital in Saudi Arabia.

The aim is to identify the prevalence and risk factors for pneumothorax development and to analyze the clinical outcomes to facilitate a better understanding of such correlation, which can be of great value for interested scholars in the field to provide preventive measures and management guidelines for COVID-19 patients with pneumothorax in the ICU setting.

Materials and Methods

Methods

We performed a retrospective review of the medical records of 418 patients, who tested positive for COVID-19 by polymerase chain reaction test (PCR) and required ICU admission in King Fahad Hospital of The University from January 2020 to September 2021. A total number of 36 pneumothorax patients were included in the study. The diagnosis of pneumothorax was made based on daily clinical and radiological assessments, and 38 patients were found to have pneumothorax during their ICU management.

We excluded patients with the following criteria: patients with positive COVID-19 tests admitted to the regular ward, ICU patients with pneumothorax and negative COVID-19 PCR test, and positive COVID-19 patients admitted to the ICU without Pneumothorax and patients with traumatic pneumothorax and positive COVID-19 admitted to ICU care (Figure 1). Two patients were excluded from the study because of pneumothorax-related blunt chest trauma.

The data collection sheet includes the following variables: the patient's age, sex, BMI, patients' comorbidities [chronic obstructive pulmonary disease (COPD), asthma, hypertension (HTN), diabetes mellitus (DM), chronic kidney disease (CKD), coronary artery disease (CAD), cerebrovascular disease (CVD), active cancer and smoking status], laboratory investigations [hemoglobin level, leucocyte count, lymphocyte count, D-dimer level, creatinine, lactic dehydrogenase (LDH), aspartate aminotransferase (AST), C-reactive protein (CRP), and procalcitonin level], and radiological studies variables including pleural effusion, lung ground-glass opacity, pneumomediastinum, subcutaneous emphysema, and location of pneumothorax. Furthermore, we recorded the presenting patients' complaints at admission, the need for intubation, length of stay in ICU and the modes of oxygenation applied to the patient [bilevel positive airway pressure ventilation (BIPAP), continuous positive airway pressure ventilation (CPAP), High-Flow Nasal Cannula ventilation (HFNC), pressure-control ventilation (PC), pressure regulated volume control ventilation (PRVC)].

Data Analysis

All data were gathered retrospectively from the hospital's electronic medical system. Subsequently, to facilitate the analysis, we collected the data into an Excel sheet to preserve the patients' confidentiality by listing them randomly by medical record numbers without names.

The statistical package for the social sciences (IBM-SPSS®, version 25.0) was used for statistical analysis. Descriptive (frequency, percentage, mean, and standard deviation) was used in this study.

The study received approval from the institutional ethics committee of Imam Abdulrahman Bin Faisal University on October 31, 2021, with the number IRB-UGS-2021-01-389. The study was conducted in accordance with the Declaration of Helsinki.

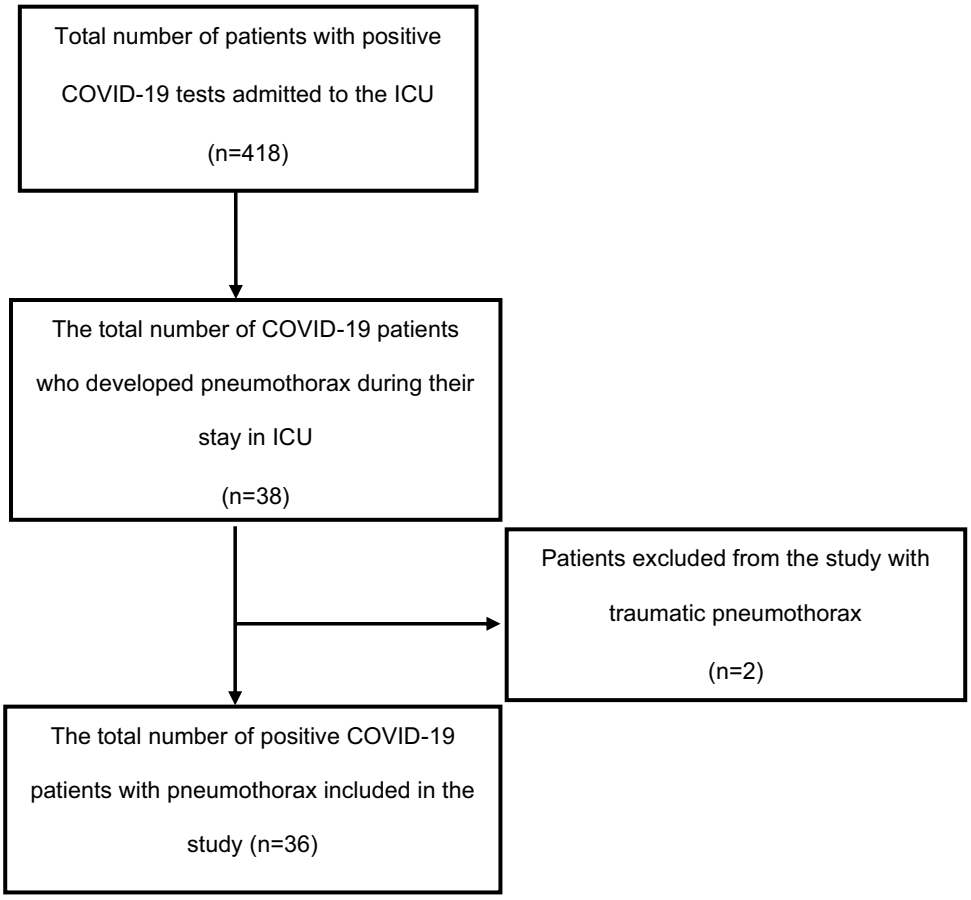

Figure 1 Patient selection flowchart.

Results

Of 418 patients who were followed up in the intensive care unit as COVID-19 cases, 36 developed pneumothorax. The prevalence of pneumothorax was 8.61%. The mean age of the patients was 55.6 ± 15.06 years, twenty-one patients (58.3%) aged between thirty to sixty, fourteen patients (38.9%) aged more than sixty years, and one patient (2.8%) was younger than thirty years. Twenty-three patients (63.9%) were male, and thirteen (36.1%) were female. Seventeen patients (47.2%) were obese, eleven patients (30.6%) were overweight, six patients (16.7%) were within normal weight, and one patient (2.8%) was underweight. However, only one patient (2.8%) was an active smoker (Table 1).

Twenty-four patients (66.67%) had at least one comorbidity, as shown in the most common comorbidity was HTN, with a total of seventeen patients (47.2%), followed by diabetes mellitus with eleven patients (30.6%). Two patients (5.6%) had bronchial asthma, and six patients (16.7%) were previously diagnosed with CAD. One patient (2.8%) had active cancer. Four patients (11.1%) had CKD, and four patients (11.1%) had a previous diagnosis of CVD (Table 2).

Out of 36 patients who developed pneumothorax, the most common complaint was dyspnea in 31 patients (86.1%), followed by cough in 28 patients (77.8%). The average length of stay in the critical care unit was 35.9 ± 26.2 days. Thirty-two patients (88.9%) were intubated, and the duration of intubation was 23.23 ±15.9 days. The average time from intubation to pneumothorax development was 8.8 ± 9.3 days. Thirty-five patients (97.2%) were treated by a chest tube. The duration of chest tube placement was as follows patients (58.3%) between one to thirteen days, 7 patients (19.4%) between fourteen to twenty-four days, and seven patients (19.4%) more than twenty-four days. Only one patient (2.8%) was treated conservatively. Regarding the mode of oxygenations, six patients (16.7%) on BIBAB, two patients (5.6%) on CPAP, three patients (8.3%) on HFNC, nine patients (25%) on pressure-control ventilation (PC), and sixteen patients (44.4%) on PRVC (Table 3).

Table 1 Demographics Data and Background of the Patients' Characteristics (n = 36)

Selected Characteristics	Frequency	Percent
Age (years)	55.6 ± 15.06	
Younger than 30	1	2.8
30–60	21	58.3
60+	14	38.9
Sex		
Male	23	63.9
Female	13	36.1
BMI (Grades)		
Under weight (<18.5)	1	2.8
Normal weight (18.5–24.9)	6	16.7
Overweight (25–29.9)	11	30.6
Obesity (>30)	17	47.2
Unknown	1	2.8
Active smoker	1	2.8

Table 2 Demographics Data and Background of the Patient's Characteristics (n = 36)

Diseases	Yes		No	
	F	%	F	%
COPD	–	–	36	100.0
Asthma	2	5.6	34	94.4
DM	11	30.6	22	61.1
HTN	17	47.2	19	52.8
CAD	6	16.7	30	83.3
Active cancer	1	2.8	35	97.2
CKD	4	11.1	32	88.9
CVD	4	11.1	32	88.9

Abbreviations: COPD: chronic obstructive pulmonary disease, DM: diabetes mellitus, HTN: hypertension, CAD: coronary artery disease, CVD: cerebrovascular diseases, and CKD: chronic kidney disease.

Table 3 Symptoms and Clinical Features of Pneumothorax Patients (n = 36)

Symptoms and Clinical Features	Yes		No	
	F	%	F	%
Symptoms				
Chest pain	3	8.3	31	86.1
Cough	28	77.8	6	16.7
Fever	21	58.3	13	36.1
Fatigue	8	22.2	26	72.2
Headache	5	13.9	29	80.6
Dyspnea	31	86.1	3	8.3
Sore throat	2	5.6	32	88.9
Vomiting	9	25.0	25	69.4
Diarrhea	6	16.7	28	77.8

(*Continued*)

Table 3 (Continued).

Symptoms and Clinical Features	Yes		No	
	F	%	F	%
ICU DAYS	35.9 ± 26.2			
Intubation	32	88.9	4	11.1
Duration of Intubation	23.23 ±15.9			
Time from intubation to pneumothorax development	8.8 ± 9.3			
Treatment (Chest tube, Conservative)	35	97.2	1	2.8
Chest tube duration				
1–13 days	21	58.3	–	–
14–24 days	7	19.4	–	–
More than 24 days	7	19.4	–	–
Mode of oxygenation				
BIPAP	6	16.7	–	–
CPAP	2	5.6	–	–
HFNC	3	8.3	–	–
PC	9	25.0	–	–
PRVC	16	44.4	–	–

Abbreviations: ICU: intensive care unit, BIBAB: Bilevel positive airway pressure ventilation, CPAP: continuous positive airway pressure ventilation, HFNC: high-frequency nasal canula ventilation, PC: pressure-control ventilation, PRVC: pressure regulated volume control ventilation.

All pneumothoraxes patients underwent chest X-ray as part of the daily clinical and radiological assessments for ICU patients. As Table 4 shows, twelve patients (33.3%) had right-sided pneumothorax, sixteen patients (44.4%) had left-sided pneumothorax, and eight patients (22.2%) had a bilateral pneumothorax. Four patients (11.1%) developed pleural

Table 4 Laboratory Parameters and Radiological Findings (n = 36)

	Yes		No	
	F	%	F	%
Laboratory parameters				
Hemoglobin (g/L)	12.7 ± 2.06			
Leukocyte count (cells/mL)	8.0 ± 5.5			
Lymphocyte count (cells/mL)	2.4 ± 5.4			
D-dimer (ng/mL)	2.3 ± 4.04			
Creatinine (mg/dL)	1.3 ± 1.2			
Aspartate aminotransferase (IU/L)	61.7 ± 51.3			
LDH (IU/L)	571.5 ± 51.3			
C-reactive protein (mg/dL)	12.8 ± 8.7			
Procalcitonin (ng/mL)	1.5 ± 4.4			
Radiological findings				
Plural effusion	4	11.1	32	88.9
Lung Ground glass opacity	36.0	100.0	-	-
Pneumothorax location				
Right	12	33.3	-	-
Left	16	44.4	-	-
Bilateral	8	22.2	-	-
Pneumomediastinum	8	22.2	28	77.8
Subcutaneous emphysema	17	47.2	19	52.8

effusion. All patients' chest X-rays showed lung ground opacity. Eight patients (22.2%) developed pneumomediastinum, and seventeen (47.2%) their chest X-rays showed subcutaneous emphysema.

Out of thirty-six patients, twenty-six patients died (72.2%), two patients (5.6%) developed bleeding during ICU stay, and nine patients (25%) had recurrent pneumothorax.

Discussion

In this study, we analyzed 36 patients found to have developed pneumothorax among 418 patients treated for Covid-19 in the ICU. Pneumothorax is a clinical pathology that develops secondary to the accumulation of free air in the pleural cavity for various reasons and results in lung collapse. It can be spontaneous or can be seen due to secondary causes.[9] The exact mechanism of pneumothorax development secondary to COVID-19 disease is not fully understood. However, the most probable pathophysiology underlying such a condition is that SARS-CoV-2 infection leads to necrotic and fibrotic changes in the parenchyma of the lungs. In addition, radiological studies found that COVID-19 infection is associated with architectural distortion and cyst formation of lungs parenchyma, which may be an additional cause leading to pneumothorax. Despite the previously suggested mechanisms, barotrauma, secondary to the management of acute respiratory distress syndrome (ARDS), is a known mechanism leading to pneumothorax.[10–13]

Previous studies were conducted to assess the incidence of pneumothorax among patients infected with SARS-CoV-2. In a Chinese study, the incidence of pneumothorax was around 1% in all COVID-19 patients.[14] Likewise, a large multicenter study involving 71,904 patients infected with SARS-CoV-2 and evaluated by emergency departments (EDs) in Spain found that 0.56% of patients had a pneumothorax at the time of presentation.[15] In our study, we found that the total number of patients who developed a pneumothorax is 36 patients (8.61%) out of 418 COVID-19 critically ill patients who were admitted to the Intensive Care Unit (ICU), which is considered to be an increased incidence compared to the studies reviewed in the literature.

Demographically, COVID-19 pneumothorax patients had an average age of 66 years, and (73%) were men.[16] However, our data showed that the mean age of our patients was 55.6 years. There were 21 patients (58.3%) aged between (30–60), while 14 patients (38.9%) aged more than 60 years, and one patient (2.8%) Younger than 30 years. Concerning gender, as previous studies illustrated, being male is a risk factor for pneumothorax.[17] Our analysis has shown a higher incidence in males compared to females, 63.9% and 36.1%, respectively.

Evaluating the relation of the comorbidities to pneumothorax development in the literatures, the Spanish multicenter showed that 20% had asthma, 10% had COPD, and 10% were current smokers.[15] Asthma as a risk factor for poor prognosis and outcome in COVID-19 patient is still controversial. Bhattarai et al conducted a systematic review and meta-analysis of the studies that reported the medical prognosis and outcomes of COVID-19 in patients with asthma. They concluded that asthma was not associated with a higher risk of ICU admission and the need for mechanical ventilation. However, stronger evidence is still needed before overlooking the effect of SARS-CoV-2 on individuals with asthma.[18]

A study by Özdemir et al found CAD was present in 2 (25.0%) patients, HTN in 1 patient (12.5%), and cerebrovascular disease and epilepsy in 1 patient (12.5%) patient.[19] We believe that pre-existing respiratory diseases and smoking do not have a solid relation to developing pneumothorax as only two patients came with asthma. None of our patients was known to have COPD, and only one patient was an active smoker, according to our data. On the other hand, the most common comorbidity was HTN (%47.2), followed by diabetes mellitus (30.6%) in which they are cumulatively accounting for more than half of our patients, thus we believe that there might be a relation between those two diseases with incidence of pneumothorax and efforts should be made from scholars to determine whether the presence of HTN and DM represent risk factors to develop pneumothorax in COVID-19 critically ill patients or not. The rate of CAD, CKD, and CVD were lower as follows: 6 patients (16.7%) had CAD, 4 patients (11.1%) had CKD, and 4 patients (11.1%) Cerebrovascular diseases. Nevertheless, some studies showed that COVID-19 patients can have spontaneous pneumothorax without any clear risk factors (smoking, lung pathology, previous history of pneumothorax, or family history) and were not on mechanical ventilation.[20,21]

Regarding symptoms and their frequency, Miro et al stated that the most frequently occurring symptoms were dyspnea (88%) followed by cough (53%), chest pain (40%), and fever (38%).[15] In comparison, our analysis yielded

similar results to this previous study, as dyspnea comes the highest among symptoms of pneumothorax patients (86.1%), followed by cough (77.8%), and fever comes third (58.3%).

In addition, less frequent symptoms appeared in patients including vomiting (25.0%), fatigue (22.2%), diarrhea (16.7%), headache (13.9%), and chest pain (8.3%). The least frequent symptom was sore throat (5.6%).

In term of management, Martinelli et al reported that ventilatory support which is not uncommon in COVID-19 critically ill patients should be performed to protect the lung and prevent hypoxia, nevertheless, using ventilatory support by itself carry a risk of having pneumothorax. Sixty patients out of 71 developed pneumothoraxes, 38 of pneumothoraxes patients received invasive ventilatory support, 26 of them pneumothorax occurred during invasive ventilation. At the same time, 12 of them required additional ECMO.[22] Furthermore, Capaccione et al study reported that 18 patients out of 132 that developed pneumothorax.[10] Pneumothoraces that ranged from moderate to large were treated by inserting a chest tube, while the small pneumothoraces were observed with serial radiography. In 16 out of 18 patients (89%), pneumothorax had occurred after endotracheal intubation.

Regarding the time from intubation to the development of pneumothorax, of these 16 patients, three cases developed pneumothorax on the day of intubation, and the average time of development of pneumothorax after intubation in the remaining 13 was 14.9 ± 10.0 days.[10] In contrast, our results showed that, out of a total of 36 patients, 32 patients were intubated (88.9%). The mean duration of intubation was 23.23 days, and the time from intubation to pneumothorax development was 8.8 days. Only one patient was treated conservatively, while the rest of our patients were treated with chest tube insertion. Regarding the duration of the chest tube, most of our patients (58.3%) were kept on a chest tube between 1 and 13 days, whereas an equal number of patients were kept on a chest tube between 14 and 24 as well as more than 24 days which account (19.4%) for each period.

In addition, we analyzed the radiological findings and observed that most pneumothoraces were ipsilateral (right-sided in 33.3%, left-sided in 44.4%). The incidence of bilateral pneumothorax was least frequent and observed in 22.2%.

Regarding the mode of oxygenation, there were 16 patients (44.4%) on PRVC, 9 patients (25.0%) on PC, and 6 patients (16.7%) on BIPAP. In addition, 3 patients (8.3%) kept on HFNC and 2 (5.6%) on CPAP. We analyzed the oxygenation mode among our patients to assess its relation to the survival rate. We divided the patients into two groups (spontaneous and barotrauma) based on their oxygenation mode. However, the p-value for the mode of oxygenation and survival among critical COVID-19 patients with pneumothorax was (0.841), which is not statistically significant; nonetheless, the initial results suggest that the mode of oxygenation did not affect survival among critical COVID-19 patients with pneumothorax.

According to Chong et al, COVID-19-related pneumothoraxes are associated with increased length of stay in the hospital, increased risk of admission to the ICU, and mortality rate reaching up to 100%, especially among the elderly.[20] Consequently, we assessed the duration of intubation and ICU stay with survival, there was no statistical correlation between duration of intubations and ICU stay with the survival among critical COVID-19 patients with pneumothorax, the p values were (0.221–0.447) respectively, which implying that duration of intubations and duration of ICU stay did not affect survival among critical COVID-19 patients with pneumothorax.

Furthermore, we studied the relationship between bleeding and recurrent pneumothorax to the survival rates. There was no statistical correlation between bleeding and recurrence of pneumothorax with survival among critical COVID-19 patients who had pneumothorax, the p values were (0.470–0.197), respectively. Thus, we propose that bleeding and recurrent pneumothorax do not negatively impact the survival in critically COVID-19 pneumothorax patients.

This study has two main limitations. First, the retrospective nature of the study makes it liable to bias in data collection as well as missing some data. Second, the number of patients is relatively small that might compromise the conclusion withdrawn from our study.

Conclusion

Pneumothorax is an uncommon complication of COVID-19; nevertheless, it is serious and has a high mortality rate reaching 72.2% in our study. The risk of development of pneumothorax in critically ill patients was not related to preexisting respiratory diseases, as well as different mode of oxygenations. Gender, hypertension and DM were common

findings in our group of patients. More efforts to conduct well-structured studies to develop evidence-based prevention measures and management guidelines are required.

Disclosure

The authors report no conflicts of interest in this work.

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