

## Research Article

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## Spontaneous Pneumothorax as a Rare Complication of Covid-19 Viral Pneumonia: A Single-Center Retrospective Descriptive Study

EL MAWLA Zeinab<sup>1,\*</sup>, Sfeir Pamela<sup>1</sup>, Masri Rim<sup>1</sup>, Koleilat Ziad<sup>2</sup>, Al- Musawi Ayad<sup>2</sup>, Salameh Pascale<sup>3</sup> and Hassoun Mahmoud<sup>4</sup>

<sup>1</sup>Faculty of Medicine, Lebanese University, Beirut, Lebanon

<sup>2</sup>Faculty of Medicine, Beirut Arab University, Beirut, Lebanon

<sup>3</sup>PharmD, MPH, PhD, HDR, Professor of Epidemiology, Lebanese University, Beirut, Lebanon

<sup>4</sup>Department of Pulmonary & Critical Care, Rafic Hariri University Hospital

### ABSTRACT

**Introduction:** A pneumothorax is the unusual presence of air in the pleural space; it can be spontaneous or iatrogenic with an incidence of 15% in critically ill patients. COVID-19 has a spectrum of disease ranging from mild to life threatening illness occurring in 1% of hospitalized patients. We herein describe the incidence of pneumothorax in Covid-19 hospitalized patients and present the clinical, laboratory and radiological characteristics of patients developing pneumothoraxes and its impact on total survival.

**Methods:** This single-center retrospective study was conducted in Rafic Hariri University Hospital in Beirut, in the COVID-19 center. From a total of 2726 patients who were diagnosed with COVID-19 pneumonia according to WHO guidelines and were hospitalized between February 2020 and August 2021, 28 patients developed at least one pneumothorax during their hospital stay and were enrolled in this study.

**Results:** From a total of 2726 patients, 28 were diagnosed to have pneumothorax and/or pneumomediastinum, with an overall incidence of 1.02% with a mortality rate of 89.3%. Twenty-one patients were males with a mean age of 54 years and 13 patients were smokers. All patients had at least one chronic disease and were found to have elevated inflammatory markers. The time from onset of symptoms to admission has a mean of 8.25 days and from admission to onset of pneumothorax 13.85 days. Fourteen patients (50%) had a large pneumothorax and 39.3% had a small pneumothorax on CT scan and 82% were found to have patchy ground glass opacities with 17.8% having mild (<40%) lung involvement, 35.7% having moderate (40-70%) lung involvement and 28.5% with severe (>70%) lung involvement. Oxygen requirement varied between HFNC (67.9%) and IMV (64.3%) and all patients were on steroid therapy. Chest tube was placed in 78.6%.

**Discussion:** The incidence of pneumothorax in COVID-19 patients was 1.02% slightly higher than other studies with a male predominance. Risk factors were variable: age, BMI, comorbidities, smoking history, use of mechanical ventilation, imaging findings, use of steroids, and increase in acute inflammatory markers. All contributed to the lung fragility and occurrence of air leak which was a bad prognostic factor leading to a mortality of 89.3% and higher morbidity and hospital stay. Pneumothorax in COVID-19 patients needs a high index of suspicion, a prompt diagnosis and a rapid treatment.

**Conclusion:** COVID-19 viral pneumonia caused very rarely spontaneous pneumothorax that can occur at any time during the course of the disease. Mechanical ventilation, imaging's characteristics mainly ground-glass opacities and crazy paving and use of steroids can all exacerbate the development of pneumothorax. High index of suspicion is needed for early diagnosis and appropriate treatment to decrease the length of hospital stay and the overall morbidity and mortality.

### \*Corresponding author

EL MAWLA Zeinab, Faculty of Medicine, Lebanese University, Beirut, Lebanon. E-mail: Mawla.zeinab@hotmail.com

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### Introduction

A pneumothorax is the unusual presence of air in the pleural space; it can be spontaneous or iatrogenic. Any spontaneous pneumothorax can be primary (occurs without the presence of underlying lung disease), or secondary (occurs as a complication

of underlying lung diseases) [1]. It has an incidence of 15% in critically ill patients mainly those mechanically ventilated [2]. COVID-19, a newly diagnosed virus has a spectrum of disease ranging from mild to life threatening illness. Spontaneous pneumothorax has been reported in rare cases. Its incidence is not well known, although some retrospective studies mentions that spontaneous pneumothorax can occur in 1% of patients requiring hospitalization and 2% requiring ICU admission [3].

It has been linked to structural changes and alveolar damage caused by ARDS (acute respiratory distress syndrome), in addition to barotrauma and alveolar over-distension during mechanical ventilation, or can also be triggered by prolonged coughing which is a predominant symptom of COVID-19 virus [4]. Among patients who develop pneumothoraxes, and in the setting of mechanical ventilation, septic shock or evidence of tension physiology, the mortality and recovery rate are poor [5]. We herein describe the incidence of pneumothorax in Covid-19 hospitalized patients and present the clinical, laboratory and radiological characteristics of patients developing pneumothoraxes and its impact on total survival.

## Materials and Methods

### Study design and participants

This single-center retrospective descriptive study was conducted in Rafic Hariri University Hospital in Beirut, in the COVID-19 center. From a total of 2726 patients who were diagnosed with COVID-19 pneumonia according to WHO guidelines and were hospitalized between February 2020 and August 2021, 28 patients developed at least one pneumothorax during their hospital stay and were enrolled in this study. Their diagnosis was made based on polymerase chain reaction (PCR) testing of nasopharyngeal swab sampling. All patients had a computed tomography (CT) of the chest on admission, in addition to routine daily chest x-ray.

### Data Collection

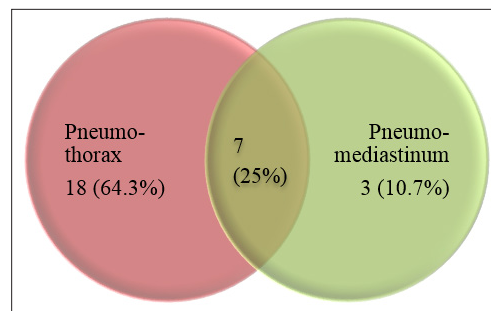
Data was collected after thorough review and analysis of patients' medical records. We collected data on age, sex, exposure history, chronic medical histories (chronic cardiac disease, chronic pulmonary disease, cerebrovascular disease, chronic neurological disorder, diabetes, malignancy, dementia, malnutrition, and smoking), vital signs at ICU admission (heart rate, respiratory rate, blood pressure, temperature), laboratory values on admission (hemoglobin concentration, lymphocyte count, platelet count, arterial blood gas analysis, FiO<sub>2</sub>, partial pressure of oxygen (PaO<sub>2</sub>), lactate concentration, troponin, D-dimer, I [1-6]. ferritin), coexisting infection, treatment (oxygen therapy, antiviral agents, antibacterial agents, corticosteroids, and convalescent plasma), as well as living status.

### Statistical Analysis

The data collected was analyzed using Statistical Package for the Social Sciences software (Version 19.0. Armonk, NY: IBM Corp) and was described using frequencies (N), percentages (%), means, and standard deviations. Absolute number and percentage reported categorical variables.

### Results

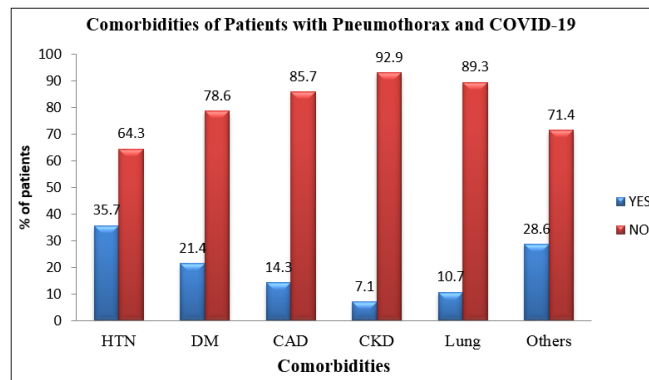
From February 2020 to August 2021, a total of 2726 patients were admitted to Rafic Hariri University Hospital with confirmed COVID-19 pneumonia, of which 28 were diagnosed to have pneumothorax and/or pneumomediastinum, with an overall incidence of 1.02%. Three (10.7%) of these patients had two distinct episodes or recurrent pneumothorax during the course of their admission. The distribution of patients is shown in Figure 1.



**Figure 1:** Frequency (Percentage) of Pneumothorax and Pneumomediastinum in Covid-19 Patients

Concerning sociodemographic characteristics, all patients were residents in Lebanon, but only 23 (82%) of them were Lebanese, others were from Nepal, Philippines or Syria. Twenty-one patients (75%) were males versus 7 (25%) patients who were females. A percentage of 46.4% (13 patients) were smokers. The mean age of patients with COVID-19 pneumonia who developed pneumothorax and/or pneumomediastinum was 54.53 ( $\pm$  17.97) years ranging between 19 and 84 years; and their BMI ranged between 17 and 40 with a mean of 28.6  $\pm$  7.83.

Almost all patients suffered from at least one chronic disease such as hypertension, diabetes mellitus, coronary artery disease, chronic kidney disease, lung disease, and others comorbidities such as cancer, heart failure, systemic lupus erythematosus... (Figure 2)



**Figure 2:** Distribution of Comorbidities of Covid-19 Patients with Pneumothorax/Pneumomediastinum

The time from onset of symptoms to admission to hospital ranged from 3 to 20 days with a mean duration of 8.25 ( $\pm$  4.28) days; While the mean duration from admission to onset of pneumothorax was 13.85 ( $\pm$  19.36) days.

The vital signs, shown in Table 1, varied between patients, with a mean near normal range. PO<sub>2</sub>/FiO<sub>2</sub> on admission varied between 40 and 490, with a mean of 102.98  $\pm$  (98.29).

**Table 1: Vitals Signs of patients with COVID-19 and Pneumothorax/Pneumomediastinum**

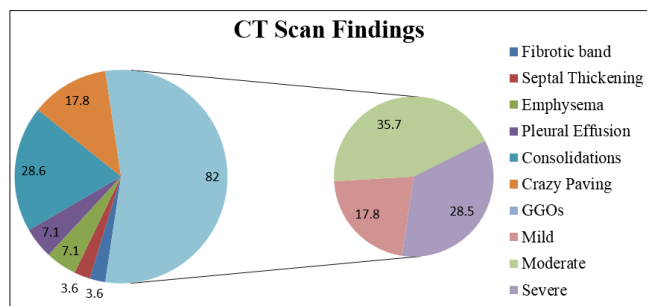
	Mean	Range
T (°C)	36.78 ± 0.65	36 – 39
SpO <sub>2</sub> (%)	85.86 ± 9.97	54 - 98
HR (bpm)	100.64 ± 19.05	68 – 134
RR (Bpm)	24.43 ± 4.94	17 – 39
SBP (mmHg)	117± 19.71	66- 152
DBP (mmHg)	74.32 ± 14.95	41 – 115

The different laboratory abnormalities are shown in Table2. The most common laboratory abnormality was leukocytosis. Most patients had end-organ damage such as acute kidney injury. The acute inflammatory markers (D-dimer, ferritin, interleukin-6 (IL-6), procalcitonin, LDH, pro-BNP and CRP) were significantly elevated.

**Table 2: Laboratory Findings of patients with Covid-19 and Pneumothorax/Pneumomediastinum**

Laboratory Tests	Mean	Range
Hemoglobin (g/dl)	13.47 ± 2.626	9.20 – 19.0
WBC (10 <sup>9</sup> /L)	17.45 ± 9.81	5.46 – 44.3
Neutrophils (%)	82.94 ± 15.68	21.6 – 97.0
Lymphocytes (%)	11.03 ± 14.91	1.35 – 77.5
Platelets (10 <sup>9</sup> /L)	281.64 ± 157.30	99.0 – 771.0
Creatinine (mg/dl)	1.35 ± 1.25	0.45 – 6.14
D-dimer /FEU (mcg/ml)	6.06 ± 5.87	0 – 19
Ferritin (ng/ml)	2340.60 ± 6444.55	39 – 30291
IL6 (ng/ml)	183.13 ± 330.01	3 – 1491
LDH (IU/L)	631.43 ± 380.03	196 – 1710
Procalcitonin (ng/ml)	3.25 ± 3.978	0 – 17
CRP (mg/L)	99.78 ± 86.37	1.4 - 348.0
Pro-BNP (pg/ml)	2812.98 ± 3828.058	75 – 13 117
troponin (ng/ml)	0.09 ± 0.18	0.003 – 0.73

Size of the pneumothorax was evaluated by chest CT scan; small pneumothorax was seen in 14 (50%) patients while large pneumothorax was detected in 11 (39.3%) patients. These findings are illustrated in Figure 3. A predominance of patchy grass-ground opacities (82%) was documented, divided into 3 groups according to the extent of lung involvement: 17.8% of patients had mild (<40 %) lung involvement, 35.7% had moderate (40- 70%) lung involvement and 28.5% had severe (>70%) lung involvement.



**Figure 3: CT Chest Findings of patients with Covid-19 and Pneumothorax/Pneumomediastinum** Nineteen (67.9%) patients were treated with high-flow nasal cannula (HFNC), four

(14.3%) with non-invasive mechanical ventilation (NIV), and eighteen patients (64.3%) needed the use of invasive mechanical ventilation (IMV). All patients were treated with glucocorticoids and anticoagulant drugs, and many other medical treatments were used in some patients such as ivermectin, remdesivir, tocilizumab.. (Figure 3, Table 3).

**Table 3: Treatments of patients with COVID-19 and Pneumothorax/Pneumomediastinum**

Treatment	Yes	No
<b>Oxygen requirement</b>		
< 15L	23 (82.1%)	5 (17.9%)
HFNC	19 (67.9%)	9 (32.1%)
BiPAP	4 (14.3%)	24 (85.7%)
MV	18 (64.3%)	10 (35.7%)
<b>Medical treatments</b>		
Remdesivir	2 (7.1%)	26 (92.9%)
Tocilizumab	7 (25%)	21 (75%)
Convalescent plasma	2 (7.1%)	26 (92.9%)
Ivermectin	2 (7.1%)	26 (92.9%)
Antibiotics	27 (96.4%)	1 (3.6%)
Prone	4 (14.3%)	24 (85.7%)

Chest tube was placed in 22 (78.6%) patients; fourteen patients (50%) had complete resolution of their pneumothorax and 6 (21.4%) patients had complete resolution of their pneumomediastinum. Three (10.7%) of these patients had recurrent pneumothorax and chest tube (chest tube2) was placed with complete resolution in two patients. None of the three patients with pneumomediastinum alone required specific intervention for pneumomediastinum.

Among these 28 patients with COVID-19 infection complicated by pneumothorax/ pneumomediastinum, 25 patients died during hospitalization with mortality rate was reaching 89.3%, within a mean of 9.75 ± 7.40 days after the occurrence of pneumothorax. The mean duration of ICU stay was 21.10 ± 21.67 days (0 -96), and the mean duration of total hospital stay was 23.60 ± 21.30 days (1-96).

### Discussion

COVID-19 virus caused a pandemic and was associated to an important morbidity and mortality worldwide. One of the rare complications of this virus encountered in hospitalized patients is spontaneous pneumothorax. In our study, we identified 28 out of 2726 patients with COVID-19 pneumonia who developed spontaneous pneumothorax, with an incidence of 1.02%. This was slightly higher than the known literature where the incidence of pneumothorax was 0.91% in a study by Martinelli et al [6]. And 0.56 % in a study by Miro et al [7].

It was most common in male population with 75% concordant with the findings in other studies [3]. Occurrence of pneumothorax in COVID-19 pneumonia patient was also reported to be more common in young patients due to relatively high incidence of barotrauma in a young age group [8]. In our study, the mean age group for development of pneumothorax is 58 years concordant with the literature. Concerning the presence of comorbidities, 57% of the patients had at least one chronic disease (lung disease, cardiac disease, kidney dysfunction) and 43% did not have any underlying disease to increase their risk of becoming

critically ill and developing complications. In addition, 78% of our patients were overweight/ obese, contrasting with the fact that pneumothorax is usually associated with thin and tall morphology [9].

As mentioned, occurrence of air leak in a patient with pneumonia is considered to be an adverse prognostic factor and is associated with significant increase in mortality. In our study, the mortality rate was 89.1% versus 74 % in a study by Udawadia et al [10]. However, the survival rate was important in other studies reaching 63% in the Martinelli et al. study. It has also influenced the length of hospital stay with 19 days as a mean in our study compared to 25 days in McGuinness et al. study [6].

The risk factors for the development of pneumothorax were numerous [11]. First, smoking was thought to be a factor increasing the risk of pneumothorax because of the underlying lung disease, but in our study 50% of the patients were non-smokers and though developed severe pneumothorax; so smoking is not alone a risk factor for the development of air leak. Besides, the use of invasive mechanical ventilation is considered to be a predominant risk factor specially with the presence of concomitant ARDS and the use of high PEEP, high tidal volumes and high minute ventilation needed to reach the oxygenation target in the presence of severely decreased lung compliance [12]. A study by Aiodfi and colleagues mentioned two cases of patients with persistent pneumothorax while on mechanical ventilation for COVID-19 pneumonia [13]. Whereas Wang et al. reported a case of pneumothorax and pneumomediastinum in a patient who was not on invasive mechanical ventilation [14]. In our study, 64% of patients who developed pneumothorax were on mechanical ventilation, but 36% of patients developed pneumothorax without being exposed to mechanical ventilation, and thus it is not the sole risk factor for development of air leak. Other factors can also contribute [15].

Baseline imaging findings can also predict the development of pneumothorax. Development of cystic lung lesions and bulla due to COVID-19 virus that can rupture is a major risk factor [16,17]. Our patients developed ground glass opacities, crazy paving, consolidations, fibrotic bands, emphysema and effusions; bullas and emphysema can rupture especially if positive pressure is applied; this was consistent with the study of Zantah et al [4].

All our patients were placed on steroids since the time of admission and several studies suggested that steroid exposure is a contributing risk factor to lung fragility, impaired healing in the same mechanism found in interstitial inflammatory lung diseases and can contribute to air leak in lungs [18]. Laboratory findings were significant for elevated inflammatory markers (D-dimer, ferritin, IL-6, LDH) which are thought to play an important role in the disease pathogenesis as the cytokine storm dysregulates the immune system, cause a hyper inflammatory response and contribute to the development of ARDS and so to the formation of pneumothorax [19].

The diagnosis of pneumothorax requires a high index of suspicion with daily CXR follow-ups. The mean time from admission to onset of air leak was 8 days versus 6 days in a study by Udawadia et al [10]. Besides, 10.7% of our patients developed only pneumomediastinum which is very difficult to diagnose. Prompt treatment is important in the early stages of air leak to decrease morbidity related to this complication. 78% of our patients had a chest tube inserted, 50% had complete resolution of pneumothorax and only 10% had recurrent pneumothorax

treated with insertion of a second chest tube. Our study has potential limitations. It is a retrospective study with a small sample size. A control group was not taken. Also there is not enough data about guidelines.

### Conclusion

In conclusion, COVID-19 viral pneumonia caused very rarely spontaneous pneumothorax that can occur at any time during the course of the disease. Mechanical ventilation, imaging's characteristics mainly ground-glass opacities and crazy paving and use of steroids can all exacerbate the development of pneumothorax. High index of suspicion is needed for early diagnosis and appropriate treatment to decrease the length of hospital stay and the overall morbidity and mortality.

### Conflict of Interest

The authors have no conflicts of interest to declare.

### Financial Disclosure

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