

## Pleural and Primary Mediastinal Complications and Treatment of COVID-19 Patients

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### Abstract

The persistent disease 2019 (COVID-19) presents prodigious challenges for research and medical practice, mainly due to its specific epidemiological and clinical characteristics. Patients with COVID-19 pneumonia may have conditions ranging from asymptomatic to death due to respiratory failure. COVID-19 pneumonia may be associated with pleural complications such as pneumothorax (PT), pneumomediastinum (PM), pleural effusion, and empyema. This study investigates primary Pleural and Mediastinal Complications (PPMCs) and their treatment in patients with COVID-19. In this cross-sectional study, 10,000 patients with COVID-19 were investigated for the incidence of mediastinal and pleural effusions between the beginning of the second half of 2019 and the end of the first half of 2020. The average age of patients with PPMC was  $54.29 \pm 14.69$  years. 62% (124 patients) were male and 38% (76 patients) were female. Among 10,000 patients with COVID-19, 600 patients (6%) had pleural effusion, of which 456 (4.56%) had mild pleural effusion, and 144 (1.44%) had moderate to severe pleural effusion. The frequency of PPMC in COVID-19 patients was as follows: 0.53% (53 cases) PT, 0.09% (9 cases) hemothorax, 0.06% (6 cases) empyema, 0.96% (96 cases) PM, 0.12% (12 cases) pericardial effusion, 0.17% (17 cases) atelectasis, and 0.04% (4 cases) emphysema. The most frequent pleural complication was pleural effusion, with a frequency of 6%, and the second most common complication was PM, with a prevalence of 0.96%. Being elderly was strongly associated with the rate of intubation and mortality in the hospital ( $P < 0.05$ ). No significant relationship existed between patients' age and PPMC ( $p > 0.05$ ). There was no significant difference in PPMC between men and women ( $p > 0.05$ ). The results of our study show that PPMC in patients with COVID-19 have a low prevalence, and if they do occur, the most frequent are related to pleural effusion and PM.

**Keywords:** COVID-19, Complications, Pleural Effusion

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### Introduction

Coronavirus Disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was declared a pandemic by the World Health Organization on March 11, 2020. Reports indicate high rates of mortality and pulmonary complications after surgical procedures performed on COVID-19-positive patients [1, 2]. Several complications, such as secondary bacterial infections, cardiac arrhythmia, cardiomyopathy, acute kidney injury, and liver dysfunction, have been

shown to be associated with COVID-19. Moreover, pleural complications, including pneumothorax (PT) and pneumomediastinum (PM), were also reported. The severity of the clinical presentation ranges from a mild common cold-like illness to severe disseminated viral pneumonia leading to acute respiratory distress syndrome (ARDS) [3, 4]. Critical cases with significant hypoxia and organ failure may need admission to the intensive care unit (ICU) and mechanical ventilation support. Besides the symptomatic cases, asymptomatic cases have also been reported [5]. Numerous complications of COVID-19 include the risk of PM

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and pneumomediastinum, both spontaneous and associated with mechanical ventilation. PM is an infrequent complication with an incidence of 1.2–3.0/100,000 cases of COVID-19 in retrospective analyses [6]. Pleural abnormalities in COVID-19 are either less common or underappreciated. In early disease, localized pleural thickening adjacent to the parenchymal lesion and pleural retraction can occur. Pleural effusion occurs in a minority of patients. Potentially life-threatening complications, such as pneumothorax, are uncommon [7]. Pleural complications arising in COVID-19 pneumonia cases increase mortality, morbidity, interventional procedures, and patient costs [8].

In the pathophysiology of PM in COVID-19 pneumonia, the Macklin effect, in which alveolar ruptures form due to increased intrathoracic pressure caused by coughing, results in free alveolar air moving from the hilus to the mediastinum through the bronchovascular sheaths. PM can occur spontaneously due to pneumonia, or it can be barotraumatic with positive airway pressure in patients on mechanical ventilators [8].

Sometimes, a bilateral ground-glass appearance can be seen on a CT scan for asymptomatic cases of COVID-19. The most common features of the chest radiographic manifestations of COVID-19

are bilateral infiltration, bilateral ground-glass appearance, bilateral pneumonia (patches), and pleural effusion [5]. In this study, we aimed to evaluate the primary pleural and mediastinal complications (PPMC) post-COVID-19 infection.

## Materials and Methods

### Study design and patient selection

This research was designed as a cross-sectional study, and the COVID-19 patients were referred to Baqiyatallah Hospital, Tehran, Iran. Between September 2020 and September 2021, they were screened for the primary inclusion criteria. All the patients who had clinical symptoms of ARDS (chills, sore throat, shortness of breath, cough, with or without fever), signs of ground-glass appearance or PPMCs in CT scan reports, and severe forms of pleural effusion (it is worth mentioning that each patient with a severe form of the disease was referred for a CT scan), were included in this study. The exclusion criteria for this study were defined as any sign of secondary pleural and mediastinal complications and any complication resulting from the treatment procedures. Figure 1 visualizes the study design.

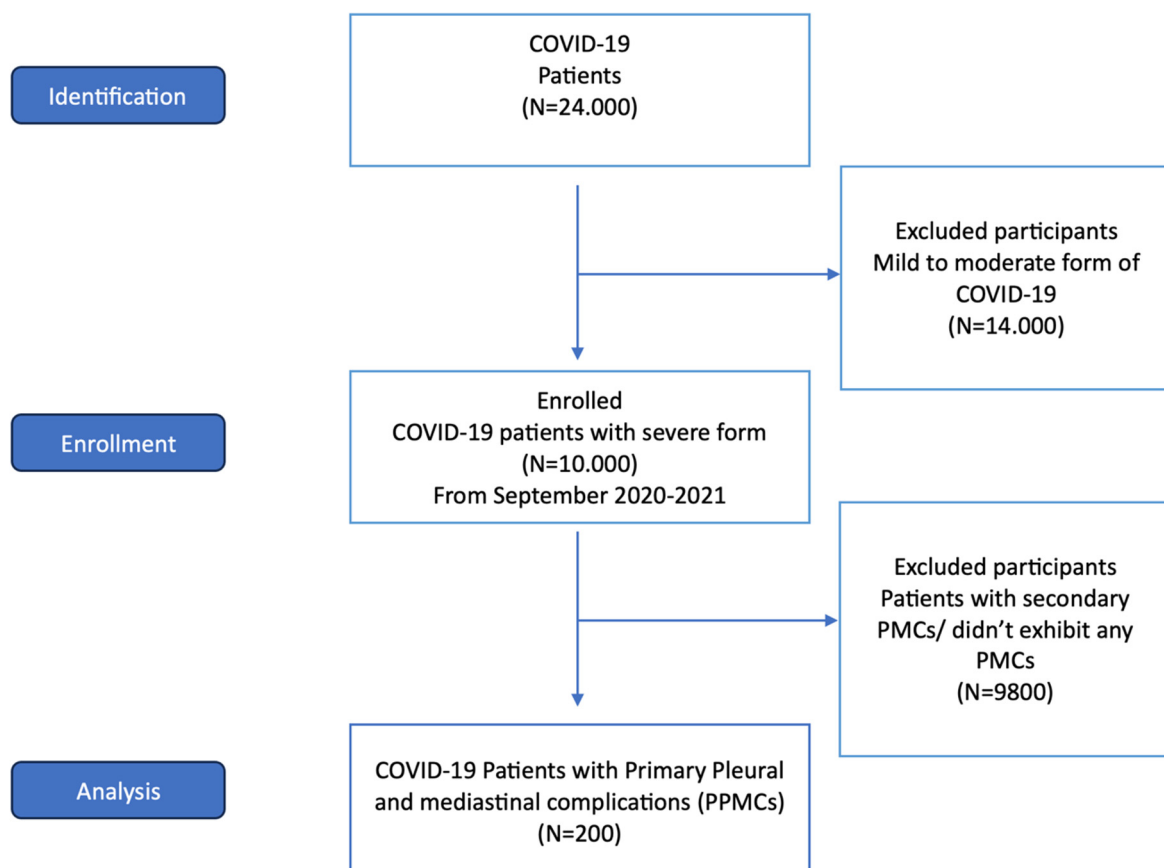


Fig. 1: Study design flowchart.

### Data Collection

This study was conducted over a period of one year (2020-2021) in Baqiyatallah Hospital, Tehran. All the inpatient files and CT scan images belonging to the included participants were investigated, and an expert radiologist re-assessed them. The severity criteria of COVID-19, comprising clinical signs, SaO<sub>2</sub> drop rate, multiple organ failure, need for mechanical ventilation, shock, and the percentage of pulmonary involvement, were extracted from the patient's CT scans, according to the latest guidelines of the National Health Ministry of Iran and the World Health Organization (WHO). Patients' demographic data, such as sex, age, smoking status, and comorbidities, were collected prior to study initiation. Moreover, COVID-19-related complications, including disease severity, mortality, needs for CCU and ICU admission, PPMCs, and requirements for interventions like surgery (chest tube and tracheostomy), were evaluated during the study in all the included patients.

### Ethical Approval

This study was approved by the research and ethical committee of Baqiyatallah University of Medical Sciences (BMSU). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee(s) and with the Helsinki Declaration of 1975 (as revised in

2013). Written informed consent was obtained from the patient for the publication of this manuscript.

### Statistical Analysis

All the analyses were performed using SPSS (Ver 20.) software. Descriptive analyses were performed by number and percentage of frequency, mean, and standard deviation. Analytical analyses were performed using t-test, chi-square, variance analysis, and logistic regression. A p-value of <0.05 was considered statistically significant.

### Results

In this survey, primarily 10,000 COVID-19-infected patients were included; however, only 200 patients presented both primary pleural and mediastinal complications. Among them, the average age was  $54.29 \pm 14.69$  years, with the youngest and oldest being 18 and 89 years old, respectively. 62% (124) of the patients were male and 38% (76) were female. In terms of comorbidities, cardiovascular diseases and hypertension (HTN) were more prevalent (17.5%) among the studied patients. Additionally, we recorded 99 mortality cases among patients with PPMCs. 132 and 18 patients needed to be admitted to the ICU and CCU, respectively (Table 1).

None of the comorbidities were relevant to mortality and incidence of the PPMCs (p-value > 0.05) (Table 2).

Among the 10,000 COVID-19 patients, the most

**Table 1:** Demographic data of the patients who exhibit PPMCs.

Variables	F (%) or Mean $\pm$ SD	
Age	54.29 $\pm$ 14.69	
sex	Male	124 (62)
	Female	76 (38)
comorbidity	Diabetes	31 (15.5)
	HTN*	35 (17.5)
	Dyslipidemia	12 (6)
	Pulmonary Disease	35 (17.5)
	Cardiovascular Disease	7 (3.5)
Smoke status	Cancer	
	Yes	22.5%
Mortality	No	77.5%
		99 (49.5)
ICU & CCU admission	CCU	18
	ICU	132

\*Hypertension

**Table 2:** Correlation of the comorbidities with mortality and complications occurrence.

Comorbidity	Mortality (P-value)	PPMC occurrence (P-value)
Diabetes	0.09	0.85
HTN	0.61	0.15
Cardiovascular diseases	0.78	0.08
Hyperlipidemia	0.16	0.07

frequent pleural complication was pleural effusion (6%), affecting 600 patients; more specifically, 4.56% had mild effusion, while 1.44% had moderate to severe pleural effusion. The second most prevalent complication was PM, which affected 0.96% of the patients (Figure 2). Furthermore, 77.5% of the patients who had PPMCs were non-smokers (Table 1).

In 130 (65%) of the studied patients with PPMCs, surgical intervention was performed, and 99 (49.5%) were intubated (Figure 3). Our findings showed that intubation and mortality were significantly correlated with age ( $p$ -value  $< 0.05$ ). However, age and PPMCs did not display any correlation ( $p$ -value  $> 0.05$ ). Moreover, gender was an influential factor in the incidence of PPMCs ( $p$ -value  $< 0.05$ ). Mortality of the patients with moderate to severe pleural effusion was reported as 1.02%.

In correlation with intubation and different types of PPMCs, the prevalence of PM was significantly related to intubation ( $p$ -value = 0.014).

### Discussion

In late 2019, the world was overwhelmed by

the emergence of a new respiratory infection called SARS-CoV-2, which spread rapidly worldwide [9]. Patients with COVID-19 pneumonia may experience a wide range of clinical conditions, from being asymptomatic to death due to respiratory failure. COVID-19 pneumonia may be accompanied by some pleural complications such as PT, PM, pleural effusion, and empyema [10-13]. In the pathophysiology of PM in COVID-19 pneumonia, the McLean effect, in which alveolar rupture occurs due to increased intrathoracic pressure caused by coughing and leads to the movement of free alveolar air from the hilus to the mediastinum through the bronchial sheaths, leads to the development of PM [14]. PT can occur spontaneously due to pneumonia, or it can be barotrauma with positive airway pressure in patients on mechanical ventilators [15, 16].

In our study, 10,000 COVID-19 patients were included to study the PPMCs and how to treat these complications; the most frequently reported complication was pleural effusion, which arose in 600 patients (6%) (456 showed the mild type of pleural effusion (4.56%), and 144 had moderate to severe pleural effusion (1.44%). The second most prevalent

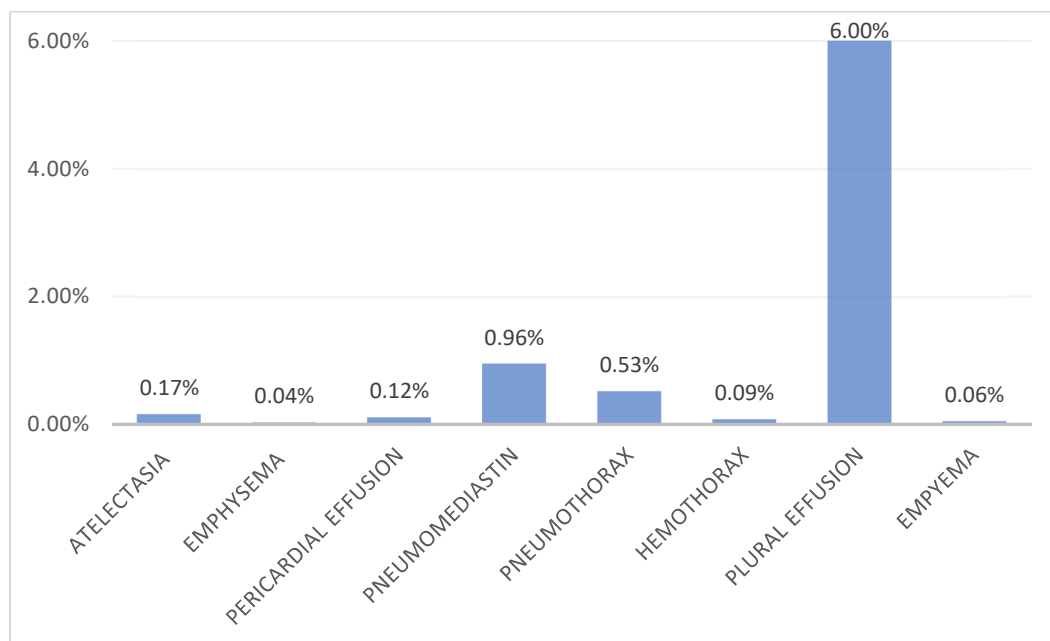
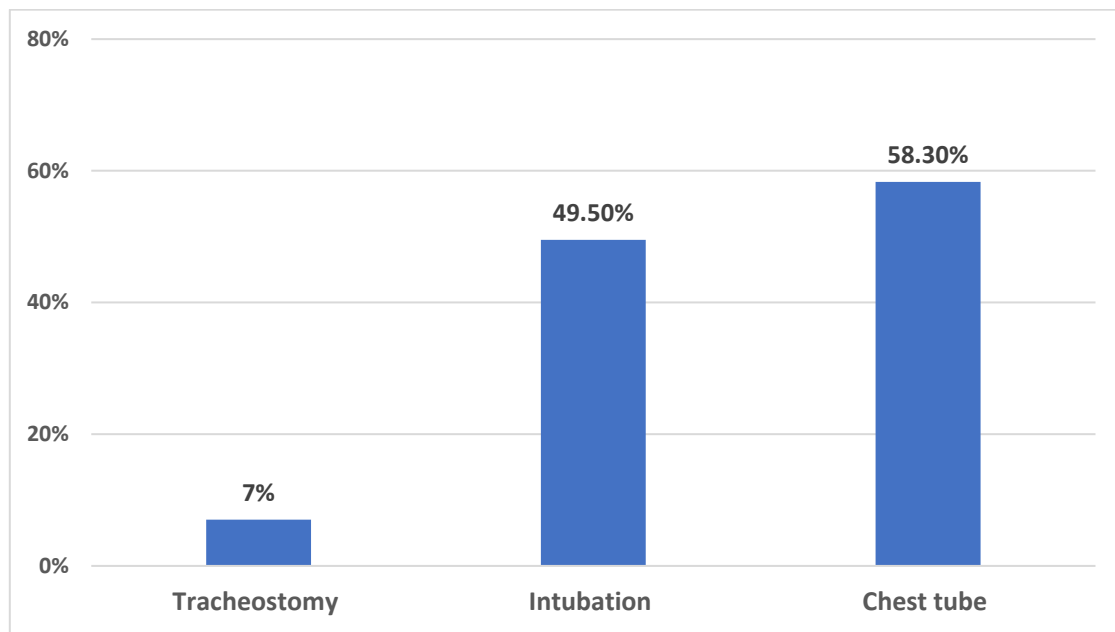


Fig. 2: pleural and mediastinal complications of the studied COVID-19 patients.

Table 3: Correlation of intubation and chest tube with different types of PPMCs.

Surgery procedure		PPMCs			
		PM	PT	Hemothorax	Moderate to severe Pleural Effusion
Intubation		54(52.9%)	28 (27.4%)	-	-
Chest Tube	Applicated	-	-	41(77.3%)	84(58.3%)
	N/A	-	-	12 (22.6%)	60 (41.7%)



**Fig. 3:** Prevalence of patients with PPMCSs who need intubation, chest tube, and tracheostomy.

complication was PM, which affected 0.96% of the patients.

The imperative reasons to perform surgical intervention were PT resolve failure, pneumatocele accompanied by continued air leakage, empyema, and hemothorax. It was reported that the survival rate of the patients who had undergone surgery was 77%, whereas we found a mortality rate of 1.02% in the case of moderate to severe pleural effusion, and the total survival rate was more than 90%. Furthermore, patients who died had risk factors (more than 70 years old and comorbidity such as pulmonary diseases). While our findings suggested that PPMCs and age didn't show any significant correlation ( $p$ -value > 0.05), Chang et al. [17] described that being elderly is related to intubation and the extubation period. In our study, comorbidities and mortality didn't show any correlation ( $p$ -value > 0.05). However, our investigation showed a correlation between PPMCs and cardiovascular diseases ( $p$ -value = 0.08). Likewise, other studies confirmed that elders, males, specific races (African, Spanish, and South Asian), and comorbidities (including hypertension, diabetes, cardiovascular, chronic pulmonary, chronic renal, chronic hepatic diseases, and cancer) had a worse prognosis [17-22].

The intubation rate in patients with PPMCs was reported as 49.50%, which was much higher than similar previous studies that reported the intubation rate within the range of 12.2-33.1% [18, 23-25]. PM incidence had a significant relation with intubation in patients ( $p$ -value = 0.014), which could explain

that PM could occur due to the positive pressure of intubation. PM is mostly accompanied by barotrauma, and although it is a rare complication, viral pneumonia, such as H1N1, was reported [26]. Hameed et al. [27], in a case series study containing 3 COVID-19 patients, performed tracheostomy for 2 of them and explained that empyema is an infrequent complication in the case of COVID-19. Correspondingly, our outcomes disclosed only 0.06% empyema in COVID-19 patients. In another retrospective study, which investigated COVID-19 patients with pleural pneumonia complications, 65% displayed PT [8]. A study [17] reported that only 0.7% of the hospitalized patients needed a chest tube (out of 1954 studied patients), while in our study, 1.5% of them required a chest tube. Spontaneous PT and PM have been described as complications in previous coronaviruses, such as SARS-CoV-1 and Middle East respiratory syndrome-associated coronavirus (MERS) infections [28].

### Conclusion

Our study outcomes expressed that pleural complications and effusion in patients with COVID-19 had a low prevalence, and if they occur, pleural effusion and PM are the most common. In our study, old age was strongly related to the intubation rate and hospital mortality ( $p$  < 0.05). No significant relationship existed between patients' age and PPMCs ( $p$  > 0.05). Additionally, there was no significant difference between PPMCs in men and women ( $p$  > 0.05).

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## Founds

None.

## Declaration of interest

None.

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