

# Pneumomediastinum: Radiological profile and associations of uncommon complication of COVID-19

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## ABSTRACT

**Introduction:** Spontaneous pneumomediastinum is an uncommon complication of Corona Virus Disease (COVID)-19 presenting mostly in moderate to severe cases. **Materials and Methods:** This is a retrospective observational imaging and hospital data-based study done on 15 confirmed patients of COVID-19 who underwent high resolution computed tomography (HRCT) thorax at the Department of Radio-Diagnosis of a tertiary medical center in the Himalayan foothills. The clinico-radiological profile of the study group was assessed and it was aimed at finding the association of pneumomediastinum with the severity of lung changes. **Results:** A strong association of pneumomediastinum was observed with severe lung changes on HRCT thorax ( $n = 13$ , 87%,  $P < 0.00001$ ). Dyspnea was the most common presenting factor. The mortality rate is high in mechanically intubated patients of pneumomediastinum with COVID-19 (75%). **Conclusion:** Pneumomediastinum is a complication of a severe COVID-19 disease spectrum. Along with severe lung parenchymal disease, systemic inflammation, systemic steroid therapy, comorbid state, and mechanical intubation, it is a part of the pool of poor prognostic factors. HRCT is essential for making a quick and comprehensive diagnosis, thereby, guiding the clinician for further management.

**Keywords:** COVID-19, pandemic, thoracic imaging

## Introduction

The global pandemic of COVID-19 is a new and devastating disease with significant mortality and morbidity. Various clinical and radiological presentations of the disease are still under evaluation. Since the disease is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV2), which is primarily a respiratory virus, pulmonary involvement is the major presentation in moderate to severe cases.<sup>[1-3]</sup> Imaging plays a pivotal role in both the diagnosis and prognostic evaluation with HRCT thorax being the cornerstone of imaging. While

assessing the pulmonary features of COVID-19 on HRCT, researchers observed an uncommon but potentially threatening complication of spontaneous pneumomediastinum in the COVID-19 patients.<sup>[4]</sup> This is a descriptive study examining the radiological and clinical profile of pneumomediastinum in the COVID-19 patients presenting for HRCT thorax.

## Materials and Methods

This was a retrospective descriptive study based on imaging and hospital data of COVID-19 patients in the Department of Radio-Diagnosis of a tertiary hospital in the Himalayan foothills.

The study aimed at evaluating the clinical and radiological profile and associations of all Reverse transcription–Polymerase chain reaction (RT-PCR)-positive COVID-19 patients who showed pneumomediastinum in HRCT thorax done at this department.

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The primary goal was to assess the association severity of the pneumonitis changes on HRCT with pneumo-mediastinum.

**Inclusion criteria**

1. All RT-PCR-positive COVID-19 patients showing pneumo-mediastinum on HRCT thorax.

**Exclusion criteria**

1. Patients with negative RT-PCR report.
2. Patients lost to follow-up after HRCT thorax.

**Study design**

After due clearance from the Institute’s Ethical Committee, this retrospective observational study was done on the imaging and hospital-based data. A consent waiver was obtained since the patients had already undergone the required investigations for clinical requirements.

“All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.”

Two radiologists with 9 and 10 years of experience in chest radiology, independently assessed and documented the HRCT findings of the study population. In case of conflict, the senior radiologist’s opinion presided.

The HRCT findings were documented as

1. The severity of pneumonitis: mild, moderate, and severe.
2. Presence and characters of pneumomediastinum along with its associations as in the pneumothorax and subcutaneous emphysema.
3. Other associated findings in HRCT thorax.

The clinical and demographic profiles of all the patients were obtained from the hospital database. The treatment protocols used and the current outcomes of the patients were also documented and descriptive statistics were analyzed.

**Statistical analysis**

Continuous variables were assessed as mean/median. Categorical variables were studied as percentages. Tests of associations were done by the Chi-square test and Fisher’s exact test. A *P* value of < 0.05 was considered significant. All statistical analysis was done using Graph Pad 9.1.2.

**Results**

The HRCT thorax features of all RT-PCR-positive patients of COVID-19 presenting to the Department of Radio-Diagnosis in April and May 2021, were retrospectively analyzed. Out of a total of 175 confirmed cases of COVID-19, 15 were found to have pneumomediastinum with an incidence of 8.57%.

These 15 patients comprised the study group. Clinical, demographical, and imaging features of the study group were further analyzed.

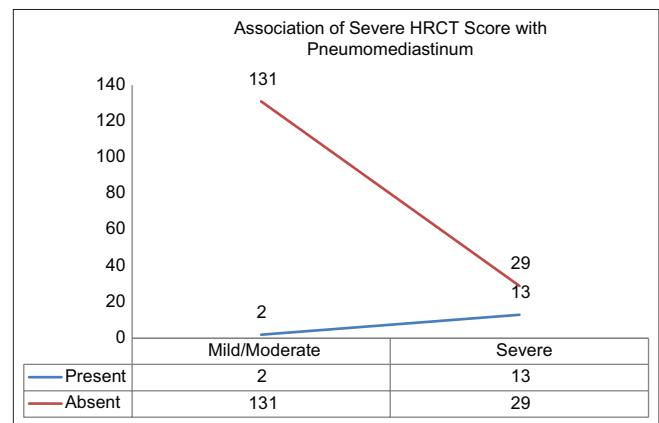
The study group comprised patients from 28 to 73 years of age with the mean age being 44.73 years. The males predominated the study population with 3/4<sup>th</sup> prevalence. Diabetes was the most common comorbidity with a 40% prevalence. The demographic details of the study group are presented in Table 1.

On analysis of the clinical details of the present illness, it was observed that all 15 (100%) patients presented with dyspnea which was the most common presenting complaint in patients of pneumomediastinum. This was followed by fever (*n* = 13, 86.6%) and cough (*n* = 12, 80%), which were also present in a majority of the patients.

Inflammatory marker C-reactive protein values were studied across the study group and were found to be raised beyond normal values in 87% of the subjects (*n* = 13). The clinical and management details are described in Table 2.

The major observations of this study were made in the HRCT findings of the study group. While assessing the HRCT score for the severity of lung involvement, it was observed that 13 out of 15 patients (86.67%) had severe lung involvement (score >18). While the remaining two patients had a moderate HRCT severity score (9–18). No patients in the study group had mild or absent lung involvement. This association of pneumomediastinum with severe lung involvement by COVID pneumonitis [Figure 1] was found to be extremely statistically significant (*P* < 0.00001) while the association with moderate cases was not statistically significant (*P* = 0.5408).

While studying other associations of pneumomediastinum on HRCT, it was observed that subcutaneous emphysema (*n* = 8, 53.33%) was a more common presentation than the worrisome pneumothorax (*n* = 6, 40%). Other associations included cardiomegaly in one-fourth of the study group. Pulmonary



**Figure 1:** Statistical analysis by Fisher’s exact test showing an extremely significant association between severe lung disease and pneumomediastinum on HRCT thorax (*P* < 0.00001)

thromboembolism, pericardial effusion, and cavitary lung changes were seen in one patient each ( $n = 1$ , 6.67%). The radiological findings are depicted in Table 3. A few representative cases are shown in Figures 2 and 3.

The treatment profile including medication and ventilation history were assessed from hospital-based records and it was observed that two-thirds of the study group was treated with

**Table 1: Demographic profile of the study group**

Variables	No. of Patients	Percentage
Age (in yrs)		
10-30	03	20
31-50	07	46.66
51-70	03	20
>70	02	13.33
Gender		
Male	12	80
Female	3	20
Comorbidities		
Diabetes	6	40
Hypertension	4	26.6
Tuberculosis	1	6.7

**Table 2: Clinical and management profile of the study group**

Variables	No. of patients	Percentage
Presenting Complaints		
Dyspnea	13	86.66
Fever	12	80
Cough	15	100
Others	1	6.7
Inflammatory Markers (CRP)		
<10	2	13.3
10-20	2	13.3
20-100	6	40
>100	5	33.33
Medication History		
Systemic steroids	10	66.6
Remdesivir	6	40
Antibiotics (azithromycin/doxycycline)	12	80

**Table 3: HRCT profile of COVID-19 patients with pneumomediastinum**

Variables	No. of Patients	Percentage
HRCT Score		
0-8	0	0
9-18	2	13.3
19-25	13	87.7
HRCT Associations		
Pneumothorax	6	40
Subcutaneous Emphysema	8	53.3
Pulmonary thromboembolism	1	6.7
Cardiomegaly	4	26.6
Pericardial effusion	1	6.7
Cavitary changes	1	6.7

systemic steroids ( $n = 10$ , 66.67%). Also, only one patient was maintaining oxygen saturation at room air (6.67%). Ten patients had to be given supplemental oxygen or non-invasive ventilation (NIV). Four (26.67%) patients had to be intubated and had to be put on mechanical ventilation.

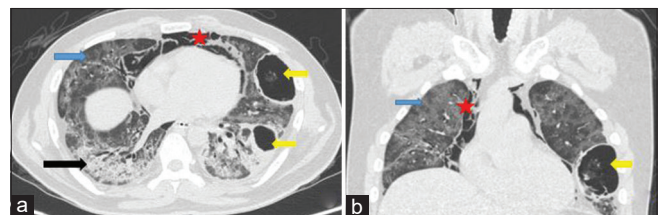
All the patients were followed up for the final outcome post this phase of illness. It was noted that at the time of writing this study, seven patients (46.67%) of the study group were discharged from the hospital on room air. Four patients (26.67%) were deceased. Out of the rest of the three patients, one (6.67%) was still on mechanical ventilation while three were on oxygen supplementation (20.0%).

We re-evaluated the profile of the deceased patients to recognize any specific associations. Patient one was a 73-year-old diabetic and hypertensive female with an HRCT score of 25/25. She had extensive pneumomediastinum with accompanying pneumothorax and subcutaneous emphysema. She had a C Reactive Protein (CRP) of 235 mg/L. She was being given systemic steroids and NIV. Patient two was a 35-year-old male with an HRCT picture of pulmonary tuberculosis with cavitary changes. He had a CRP of 142 mg/L and an HRCT score of 25/25. The patient was put on mechanical ventilation. There was no associated pneumothorax or subcutaneous emphysema. Patient three was a 50-year-old diabetic and hypertensive female with an HRCT score of 25/25. The CRP was 50 mg/L. The treatment profile included systemic steroids and mechanical ventilation. Patient four was a 53-year-old diabetic and hypertensive male with a CRP of 18 mg/L. The HRCT score was 17/25 and associated subcutaneous emphysema was noted. The patient had complained of generalized body swelling and had ascites. He was given systemic steroids and remdesivir along with mechanical ventilation.

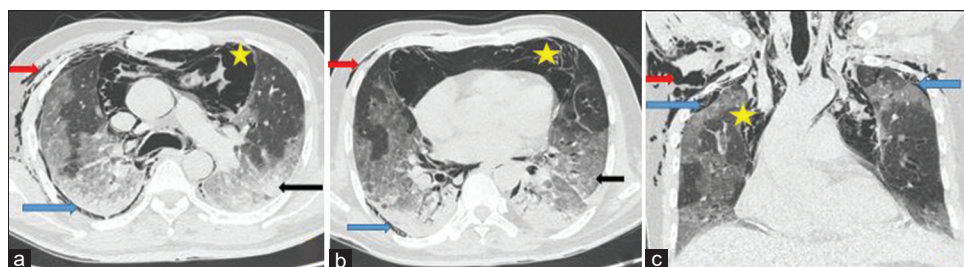
The death rate in the study cohort was 26.66%, while it was 33.33% in the patients with an HRCT score of more than 20. However, this difference was not statistically significant. In the patients who had to be mechanically ventilated, the death rate was 75%.

## Discussion

The global pandemic of COVID-19 caused by SARS-CoV-2 has varied pulmonary and systemic manifestations in humans. Since



**Figure 2:** HRCT scan of Chest : Axial and coronal lung windows show pneumomediastinum (red star) with diffuse ground-glass opacification in both the lungs (blue arrow) with basal consolidation (black arrow) and two cavities in the left lung (yellow arrows)



**Figure 3:** HRCT CHEST: Axial (a and b) and coronal (c) lung window show gross pneumomediastinum (Yellow Star) with bilateral pneumothorax (blue arrows) and subcutaneous emphysema in bilateral chest wall and neck (red arrow) diffuse ground-glass opacification is seen in both the lungs (black arrow)

it is a respiratory virus with primary involvement of the lungs, the HRCT thorax forms the cornerstone of the diagnosis and prognostic evaluation.<sup>[1,4,5]</sup>

The disease involves both the lung alveoli and interstitium with the predominant radiographic presentation being the peripheral and basal predominant ground-glass opacities along with reticular interstitial thickening.<sup>[3,6]</sup> Lymphadenopathy and pleural effusion are rare presentations.<sup>[1]</sup> The uncommon extra-pulmonary thoracic manifestations include pneumomediastinum and associated pneumothorax.<sup>[1,3]</sup>

Since pneumomediastinum is a rare complication, its clinico-radiological profile and associations are essential to be assessed in the COVID-19 patients. In the study cohort, the males were the predominant group (80%) with a mean age of 44.73 years. This is similar to the observations of Lemmers *et al.*<sup>[7]</sup> and Kangas-Dick *et al.*<sup>[2]</sup> The most common clinical presentation was dyspnea, followed by cough and fever, which are non-specific to both pneumomediastinum and COVID-19 pneumonitis.<sup>[1,4]</sup>

The pathophysiology of pneumomediastinum is known to be alveolar damage caused by increased airway pressure which may be secondary to trauma, iatrogenic causes, mechanical ventilation, or spontaneous. However, spontaneous pneumomediastinum in the absence of mechanical ventilation or other lung diseases in the COVID-19 patients is explained by the Macklin Effect which ascertains that the alveolar damage caused by infiltration of both Types I and II pneumocytes leads to the leak of air along the vascular sheaths in the interstitium which further circulates into the mediastinum.<sup>[8-11]</sup> In patients with COVID-19-associated pneumonitis, spontaneous pneumomediastinum is seen in around 10% of the hospitalized patients in various studies similar to our observation of an incidence of 8.75%.<sup>[4,10,12]</sup>

COVID-19 has been known to manifest stronger in patients with comorbidities. On assessing the risk profile of patients, we observed that 40% ( $n = 6$ ) of the study cohort was diabetic while 1/4<sup>th</sup> ( $n = 4$ ) was hypertensive. This was similar to the observations of Loffi *et al.*<sup>[4]</sup> and Kangas-Dick *et al.*<sup>[2]</sup>

It has been also postulated that not only the viral load, but cytokine storm-related alveolar damage in severe COVID cases is also responsible for pneumomediastinum.<sup>[4,13]</sup> We also made

a similar observation that 87% of the study cohort had raised inflammatory markers (CRP).

The role of a radiologist in suspected cases of pneumomediastinum is to assess the severity of pneumonitis, pneumomediastinum, and its complications such as pneumothorax and mediastinal changes.<sup>[14]</sup> A definite association of severe COVID pneumonitis changes (87%,  $n = 13$ ) was observed with pneumomediastinum. The statistical association with severe HRCT scores was extremely significant in this study ( $P < 0.00001$ ) while no significant association of pneumomediastinum could be made with moderate HRCT scores. This is in concordance with the previous literature which observes that the severity of alveolar damage is proportional to the risk of pneumomediastinum.<sup>[4,7,9,12]</sup> While studying other radiological associations, it was observed that subcutaneous emphysema was more common than a pneumothorax. Other sporadic findings included pulmonary thromboembolism and cardiomegaly.

The treatment profile of patients before the diagnosis of pneumomediastinum was observed and it was observed that 66% of the patients had received systemic steroids. This may be correlated with the higher inflammatory responses and more prevalence of severe disease in this cohort which caused the need for steroidal support.<sup>[13,15]</sup> A majority of the patients were treated with antibiotics ( $n = 12$ , 80%) and other supportive medications.

At the time of the diagnosis of pneumomediastinum, 1/4<sup>th</sup> of the study cohort had been put under mechanical ventilation ( $n = 4$ , 26.6%). Supplemental oxygen support and non-invasive ventilator support were the most common respiratory supportive modules used in this study group ( $n = 10$ , 66.67%) while only one patient was maintaining saturation at room air at the time of diagnosis.

Pneumomediastinum may further proceed to cause pneumothorax and other complications which may lead to poor prognosis in the presence of an already compromised pulmonary state. With the addition of mechanical ventilation, the chances of increased severity of pneumomediastinum and its complications become a severe threat. We also observed that the death rate among the mechanically ventilated patients was as high as 75% in the study group in comparison to 26.66% in the study group as a whole, similar to the observations of Machiuraju *et al.*<sup>[9]</sup> and Kangas-Dick *et al.*<sup>[2]</sup>



The common factors observed in the patients of pneumomediastinum who died were comorbid state, most commonly with diabetes, very high HRCT scores (>20 in three out of four deceased), along with consistently raised inflammatory markers, previous treatment with systemic steroids, and a need for mechanical ventilation.

Thus, in a combination of a multitude of factors, spontaneous pneumomediastinum is both an indicator of severe disease and poor prognosis in patients of COVID-19.

### Limitations

Even though this study cohort is among the largest reported for pneumomediastinum in COVID-19 patients, it is a retrospective imaging-based study. A larger prospective study group with detailed clinical input may be more beneficial in depicting the utility of pneumomediastinum alone as a prognostic factor in the absence of other confounding factors. Still, the authors felt it was necessary to present a radiologist's perspective to this uncommon complication of COVID-19.

### Conclusion

Pneumomediastinum is a complication of the severe COVID-19 disease spectrum. Along with lung parenchymal disease and other clinical presentations, it is a part of the pool of poor prognostic factors. HRCT is essential for making a quick and comprehensive diagnosis, thereby, guiding the clinician for further management.

### Key message

Pneumomediastinum is an uncommon complication often associated with severe disease in COVID-19 patients.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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