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Pneumothorax and subcutaneous emphysema in post COVID-19 patients in intensive care settings in a tertiary centre of North India: A retrospective study

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ABSTRACT

Introduction: COVID-19 pandemic has been the major cause of mortality around the globe due to highly infectious nature of the virus and its tendency to cause serious manifestations like pneumonia, acute respiratory distress syndrome (ARDS) and ultimately respiratory failure. The incidence of patients developing pneumothorax and subcutaneous emphysema are also on the rise which has further increased the mortality. We conducted a retrospective analysis of COVID-19 patients who turned RT-PCR negative but still required intensive care, to see the incidence of pneumothorax and subcutaneous emphysema in ventilated as well as non-ventilated patients.

Materials and Methods: The data was collected from the hospital patient records between October 1, 2020 and May 31, 2021. The hospital medical records were used to furnish the various demographic, clinical and treatment details.

Results: Out of 102 patients received in intensive care unit (ICU) during the study period, 9 developed pneumothorax and 4 of them also developed subcutaneous emphysema. 7 patients were male and 2 were female with median age of 52 years. Right sided pneumothorax was found in 7 patients while left lung was involved in 2 patients. Lab investigations of all these patients revealed raised inflammatory markers. Diagnosis was confirmed by clinical findings and chest X-ray findings. 7 patients had associated comorbidities like diabetes, hypertension etc.

Conclusion: The occurrence of pneumothorax and subcutaneous emphysema in COVID-19 patients indicate the severity of the illness. Other factors like raised inflammatory markers, male gender, associated co-morbidities like diabetes, hypertension and old age have also been linked with increased incidence of pneumothorax and subcutaneous emphysema.

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1. Introduction

Coronavirus disease 2019 (COVID-19), pandemic has been the major cause of respiratory complications and deaths around the globe, increasing the burden on the healthcare system, with maximum occupancy of ICU by these patients. The severity of illness has been associated with comorbidities like diabetes, hypertension, COPD, congestive heart failure, chronic kidney disease and old

age.¹ The most common manifestations of COVID-19 are pneumonitis, which is often bilateral² and acute respiratory distress syndrome (ARDS), which may lead to respiratory failure.³ Pneumothorax and subcutaneous emphysema usually occur secondary to pneumonitis as a complication of mechanical ventilation due to barotrauma. Pulmonary barotrauma is characterized by presence of extra-alveolar air due to rupture of alveolar walls and air leakage to the perivascular sheath.⁴ The incidence of pneumothorax and subcutaneous emphysema has been reported to be as high as 15% in patients on mechanical

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ventilation.⁵ Spontaneous pneumothorax has also been reported as a complication of severe ARDS with an incidence of 1.7% in admitted patients.⁶ Hence, we conducted a retrospective analysis of patients of COVID-19 who turned reverse transcriptase-PCR (RT-PCR) negative but still required intensive care, to analyse the occurrence of pneumothorax and subcutaneous emphysema in ventilated as well as non-ventilated patients, and the factors responsible for this complication.

2. Materials and Methods

This was a retrospective study of the patients who turned COVID negative but still required ICU care at our tertiary hospital and subsequently developed pneumothorax. The data was collected from the hospital patient record system between October 1, 2020 and May 31, 2021. The diagnosis of COVID-19 diagnosis had been made using a real-time RT-PCR executed on a nasopharyngeal swab. A repeat RT-PCR test was performed on nasopharyngeal swabs of COVID-19 patients after 10th day of their initial sample. As per the protocol patients used to be shifted to general (non-COVID) ICU if still required intensive care, after their report turning negative. The medical records were used to furnish the various demographic, clinical and treatment details viz. age, sex, past or present medical history, laboratory investigations (including complete hemogram, random blood sugar, CRP, serum ferritin, Pro-BNP, pro-calcitonin, and d-dimer levels), chest X-ray, clinical management, patient progress and survival.

3. Results

There were 102 COVID-19 patients received in the general ICU after their RT-PCR reports turned negative during the study period. 9 out of 102 patients (8.9%) had developed pneumothorax with 7 developing right sided pneumothorax and 2 had left sided pneumothorax. (Table 1) Clinical findings along with chest X-ray confirmed the diagnosis of pneumothorax. 7 were male and 2 patients were female (M: F = 3.5:1) with median age of 52 years. Patients developed pneumothorax at different time duration of their illness ranging from 2 to 14 days (median duration of 8 days). 7 of 9 patients had associated comorbidities like diabetes mellitus, hypertension, and one of the patient had earlier underwent renal transplant. Four Patients in the study developed subcutaneous emphysema on the same day when they developed pneumothorax. Lab investigations of all patients showed increased levels with raised WBC counts, RBS, Ferritin, Pro-BNP, D-dimer, CRP and Pro-calcitonin. All nine patients required supportive oxygen therapy via High flow nasal cannulation (HFNC) initially and 7 patients were on ventilator support at the time of pneumothorax. Mode of ventilation in all these patients was pressure assist-control mode as per lung protective ventilation strategy,

with tidal volume of 4-6ml/kg, respiratory rate of 22-35/min, PEEP of 10-18 and keeping P-plateau of <28. Treatment was given as per standard protocols for COVID-19 patients along with supportive therapy, which included remdesivir, tocilizumab and dexamethasone. Pneumothorax of all patients was managed by chest tube insertion and subcutaneous emphysema was managed conservatively. All 9 patients who developed pneumothorax succumbed to the complications in the ICU after the median duration of 18 days (ranging from 10 to 24 days).

4. Discussion

The period between October 1, 2020 and May 31, 2021 saw a significant number of COVID-19 patients in India with a peak in the months of April and May 2021. Patients even after turning negative on RT-PCR had severe pulmonary complications in the form of pneumothorax and subcutaneous emphysema. The resultant respiratory failure was a major cause of concern as most of such patients usually succumbed to the illness.

The incidence of pneumothorax in the data analysed from our institution during the mentioned period turned out to be 8.9%. Spontaneous pneumothorax has been reported by researchers earlier with incidence varying from 1% to 15%.^{4,6–8} The occurrence of spontaneous pneumothorax in our study can be co-related to the severity of the COVID-19 illness as 7 patients were on mechanical ventilator support at the time of diagnosis and all 9 of our patients eventually succumbed to the illness. Similar findings were observed by many other studies; therefore, pneumothorax can be linked to poor prognosis in COVID-19 patients.^{5,6,9}

Many studies have tried to explain the mechanism behind pneumothorax and subcutaneous emphysema in COVID-19 patients, suggesting the role of direct viral induced lung damage, formation of micro-thrombi and exaggerated immune response as the factors.^{10,11} The diffuse and extensive alveolar damage adversely affects both alveolar ventilation and perfusion by occluding the micro-vasculature, leading to pulmonary tissue infarction and ultimately increasing the air leakage and interstitial emphysema.^{4,11–13} Post mortem findings of sixty three COVID-19 patients have further demonstrated the diffuse alveolar damage as the commonest histological finding.¹⁴ COVID-19 has also been found to directly damage pulmonary vascular endothelial cells leading to a hyper-coagulable state.¹⁵ Therefore, d-dimer is considered as a crucial biomarker for predicting thrombotic complications and prognosis of the illness in COVID-19 patients.¹⁶ In our study, all 9 patients had raised d-dimer levels, along with other inflammatory markers like CRP, ferritin, pro-BNP and leucocyte count further indicating the severity of the disease process. Raised inflammatory markers like CRP and ferritin, pro-BNP, raised TLC have also been suggested as predictors for COVID-19 severity in earlier studies.^{17–19}

Table 1: Clinical profile of COVID-19 patients with pneumothorax in our study

S.No.	1	2	3	4	5	6	7	8	9
Age (years)	48	60	40	78	22	52	40	65	74
Sex	M	M	M	F	M	M	M	M	F
Medical History (DM, HTN, CAD, COPD, CA)	DM	DM, HTN, COPD	HTN	DM, HTN		DM, HTN	Post renal transplant patient	Nil	DM
HFNC/NRM/ Face Mask/ Intubation	HFNC, Intubated RR-20-28 /min, VT-4-6ml/kg, PEEP 8-18	HFNC, Intubated RR-28-35, PEEP-10-14	HFNC, Intubated RR-28-35, PEEP-10-14	HFNC	HFNC, Intubated RR-22-35, PEEP-12-18	NRM, HFNC	HFNC, Intubated RR-24-35, PEEP-12-18	HFNC, Intubated, RR-22-32, PEEP-8-12	HFNC
ICU day at pneumothorax	14	9	9	6	8	3	2	7	12
ICU day at subcutaneous emphysema	14	-	-	6	-	-	2	-	12
CXR (pneumo-thorax)	left lung	right lung	Right lung	Right lung	Left lung	Right lung	Right lung	Right lung	Right lung
WBC count(/ul)	14000	9500	26000	14000	18000	17000	27000	23000	6000
RBS (mg/ml)	256	210	122	210	156	286	280	267	196
Ferritin (ng/ml)(20-250ng/ml)	766	1137	780	446	1095	970	1563	2684	88
BNP (pg/ml) (n<125pg)	424	1250	1260	424	815	2408	2367	3868	699
d-DIMER (ug/ml) (n<0.50)	0.8	1.05	.62	0.61	6.74	5.76	1.83	3.35	0.44
Procal. (n<0.1ng/ml)	0.13	0.848	0.53	0.16	1.59	18.5	8.64	0.8	1.59
CRP (mg/dl)	1.42	<6	24	<6	8.30	>48	>24	>12	8.30
Treatment	Rem+ Tocil+ Dexa	Rem+ Dexa	Rem+ Dexa	Dexa	Rem+ Dexa+ Tocil	Rem+ Dexa	Rem+ Dexa+ Tocil	Dexa	Rem+ Dexa
Progress and survival	Died at 24 th day	Died at 10 th day	Died at 12 th day	Died at 18 th day	Died at 18 th day	Died at 12 th day	Died at 12 th day	Died at 19 th day	Died at 24 th day

M- male, F- female, DM- diabetes mellitus, HTN- hypertension, CAD- coronary artery disease, COPD- chronic obstructive pulmonary disease, CA- cancer, HFNC- high flow nasal cannula, NRM- non rebreathable mask, CRP- c reactive protein, CXR- chest X ray, Procal- Procalcitonin, Rem- Remdesivir, Dexa- Dexamethasone, Tocil- Tocilizumab

The median duration of occurrence of pneumothorax was 8 days (varied from 2–14 days) of ICU stay and 18 days of their total illness. This can be explained by the fact that, there is progression of worsening of lung condition as a secondary response to infection due to cytokine storm.

Out of 9 patients, 7 were male who developed pneumothorax, other studies have also found its predominance in men.^{2,20} Most of our patients developed right sided pneumothorax which could be attributed to anatomical feature of right bronchus being more vertical and shorter than the left. Co-morbidities like hypertension and diabetes mellitus were observed in most of the patients who developed pneumothorax in our study; similar observations have been made by earlier researchers too.⁷

5. Conclusion

Pneumothorax and subcutaneous emphysema are a known complication in COVID-19 patients correlating with severity of illness characterizes by persistent hypoxemia and increased mortality. Elderly patients, patients with comorbidities, male gender have been found to have more chances of developing these complications.

6. Limitation of the Study

The study has been conducted only on those COVID-19 patients which were admitted in the ICU after turning RT-PCR negative after 10th day of their illness, so the data cannot be generalized to all COVID-19 positive patients which were treated in the COVID-19 ICU and wards.

7. Source of Funding

None.

8. Conflict of Interest

None.

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