Original paper • DOI: 10.2478/rjaic-2022-0002 • RJAIC 2022;29(1);8-15

Romanian Journal of Anesthaesia and Intensive Care

PNEUMOTHORAX IN CRITICALLY ILL COVID-19 PATIENTS IN THE INDIAN SUBCONTINENT

Anshul Singh

New Delhi, Delhi India

Abstract

Background and aims: *To explore the incidence and risk factors, as well as mortality, in critically ill COVID-19 patients who developed pneumothorax (PTX) and/or pneumomediastinum (PNM).*
Methods: *A retrospective cohort study was undertaken to analyse data of all patients with moderate to severe COVID-19 disease who were either RTPCR positive or had a clinico-radiological diagnosis. The exposure group consisted of COVID-19 patients who presented with PTX/PNM, whereas the non-exposure group consisted of patients who did not develop PTX and/or PNM during the stay.*
Results: *Incidence of PTX/PNM was observed to be 1.9% among critically ill COVID-19 patients. 94.4% (17/18) of patients in the PTX group received positive pressure ventilation (PPV); the majority of these patients were on non-invasive ventilation when they developed PTX/PNM; only one patient was receiving conventional oxygen therapy. COVID-19 patients who developed PTX/PNM had 2.7 times higher mortality. A mortality rate of 72.2% was observed in COVID-19 patients who developed PTX/PNM.*
Conclusion: *Development of PTX/PNM in critically ill COVID-19 patients is associated with more severe disease involvement, and institution of PPV is an additional risk factor. Significantly high mortality was observed following PTX/PNM in critically ill COVID-19 patients and is an independent marker of poor prognosis in COVID-19 disease.*

Keywords

COVID-19 • acute respiratory distress syndrome • pneumothorax • pneumomediastinum • positive pressure ventilation

Introduction

COVID-19 pneumonia resulting from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection [1] is a rapidly evolving condition that has become a challenge for the critical care physician owing to its highly infectious nature. Recent evidence suggests pneumothorax (PTX) and pneumomediastinum (PNM) commonly complicate the clinical course in COVID-19 patients in patients with moderate to severe COVID-19 disease.

Development of PTX/PNM is a known complication and is widely reported in ARDS patients receiving both invasive and non-invasive modes of ventilation [2]. The surge of the COVID-19 pandemic also witnessed the development of PTX/PNM in patients with SARS-CoV-2 pneumonia not only under invasive [3,4] or non-invasive [5] modes of ventilation but also in patients receiving conventional oxygen therapy [6–10]. There have also been reports of COVID patients presenting in the emergency department with PTX/PNM [5]. The occurrence of PTX/PNM even in spontaneously breathing COVID patients indicate that there must have been additional factors contributing to their development of PTX/PNM.

Till now four retrospective studies have evaluated patients' characteristics contributing to development of PTX/PNM in COVID-19 patients [4,5,11–12]. Both Wang et al. [4] and Enhakem et al. [11] concluded that pneumothorax is a frequent and fatal complication of critically ill patients with COVID-19. Wang et al. observed that the reduction of NMB, recruitment manoeuvres, severe cough, and changes in lung structure and function are factors responsible for development of PTX/PNM in COVID-19 patients [5]. Enakem et al. concluded that marked inflammatory response, fibrosis, and need for positive pressure ventilation in COVID-19 pneumonia are likely contributory to the development of pneumothorax in these patients. Martinelli et al. concluded that it was not an independent marker of poor prognosis, and that age >70 years and acidosis to be associated factors responsible for poor prognosis [6]. Two very recent studies concluded that baseline radiological findings of ground-glass opacities and consolidation and mechanical ventilation appeared to predict high risk of developing PTX/PNM [12,13]. The data from all these studies are from the first wave of COVID-19.

* Corresponding author e-mail: ansh.dadoc@gmail.com

However, in our literature search we could not retrieve any study exploring the risk factors predicting the development of PTX /PNM in COVID-19 patients, nor the incidence of PTX/PNM in the Indian subcontinent. Different strains of the COVID-19 virus are prevalent; therefore, it is desirable to have a study exploring their fatality and risk factors in different geographic regions.

There is very scant literature throwing light on mortality in patients who developed PT/PNM during COVID-19 and whether it is an independent marker of poor prognosis in COVID-19 patients, particularly those from the Indian subcontinent.

Therefore, with this background, we designed this retrospective cohort study to evaluate the incidence of mortality among COVID-19 patients with pneumothorax and/or pneumomediastinum and to determine the risk factors contributing to development of pneumothorax/pneumomediastinum in the Indian subcontinent during the second wave of COVID-19.

Methods

Study design

A retrospective cohort study with intragroup comparison was undertaken in a tertiary care hospital based in Delhi, India. All the patients with moderate to severe COVID-19 disease either RT PCR positive or had clinico-radiological diagnosis, who were admitted in the various intensive care units (ICUs) from 1st April 2021 till 30th June 2021 were included.

Patients who developed pneumothorax/pneumomediastinum (PTX/PNM) were selected for the exposure group. Amongst the patients who did not develop either, every 20th patient's case file was chosen, and these patients comprised the non-exposure group. The case files in our Medical Record Department (MRD) are arranged according to the date of discharge or death of patients and are stored according to month. Thus, the selection for either of the groups was independent of the outcome—i.e. discharge/death—and development of PTX/PNM was the main determining factor.

Participants

Exposure group consisted of COVID-19 patients who presented with PTX/PNM in the emergency room or developed it during the hospital stay. The non-exposure group was comprised of COVID-19 patients who were admitted in our ICUs but did not develop PTX and/or PNM during the stay. In all the patients who were diagnosed with PTX/PNM, the diagnosis was initially made clinically with sudden deterioration in oxygen saturation and haemodynamics; however, the diagnosis was finally confirmed radiologically. Therefore, only patients with radiologically confirmed diagnoses were included in the exposure group.

Procedure

After getting clearance from the institutional ethical committee—human research, the details regarding the patients were collected from the case files of COVID-19 patients admitted in our hospital from 1 April 2021 through 30 June 2021. The case files in our Medical Record block were retrieved according to the day of discharge or death. The case files were screened (AS and MS) to find patients who either presented in emergency with PTX/PNM or developed PTX/PNM during their hospital stay; this comprised an exposure group. From the rest of the files, every 20th patient file was analysed and included in the non-exposure group. The case files were first retrieved with the patients' names; however, they were later coded so as to maintain anonymity.

A patient proforma was filled from the information gathered after analysing the case files of patients retrieved from the MRD of the hospital. The information collected was demographic data, modes of ventilation, laboratory parameters, and outcomes. The data collected was kept confidential with the investigator.

Outcomes

Primary outcome was the incidence of mortality among COVID-19 patients with pneumothorax and/or pneumomediastinum in patients with COVID-19 pneumonia. Secondary outcome was incidence as well as the risk factors contributing to the development of pneumothorax or pneumomediastinum in patients with COVID-19 pneumonia.

Sample size

Based on the study conducted by Wang Xiao-Hui et al. the incidence of mortality among COVID-19 patients with pneumothorax was 80%. Based on the systematic review of mortality rates among COVID-19 patients in the intensive care unit, incidence of mortality was 41%.

$$N = \frac{\left\{ Z_{1-\frac{\alpha}{2}} \sqrt{2P\left(1-P\right)} + Z_{1-\beta} \sqrt{p1\left(1-p1\right) + p2\left(1-p2\right)} \right\}^2}{\left(p1-p2\right)^2}$$

$$\mathrm{P} = \frac{p1+p2}{2}$$

p1 = Incidence of mortality among exposed (pneumothorax) group = 80%

p2 = Incidence of mortality among unexposed group = 41%

$Z_{1-\frac{\alpha}{2}} = 1.96$ at 95% confidence interval

$Z_{1-\beta} = 0.84$ at 80% power

By using the above formula, minimum sample size was calculated as 17 for the exposure group and 34 for the non-exposure group with 1:2 as ratio.

Statistical analysis

Data was entered in MS Excel and analysis was done using SPSS 21.0 version. Data was presented as mean and standard deviation for continuous variables and as percentages for categorical variables. Independent t-test or Mann–Whitney *U* test, chi-square test or Fisher exact test was done to find the association between categorical variables. Relative risk was calculated to estimate the magnitude of risk. P-value of less than or equal to 0.05 was considered significant.

Results

A total of 934 patients were admitted in various ICUs during the designated period. Out of this, 788 patients reported positive reverse transcriptase polymerase chain reaction for COVID-19, and in the rest of the patients, a clinico-radiological diagnosis was made. Twenty-two patients left against medical advice and no data is available for them. Finally, 912 patients were included in the study. On screening the files of all these patients, it was observed that 18 patients developed PTX and/or PNM, an incidence of 1.9% (18/912). Thirty-four patients were included in the non-exposure group of COVID-19 patients, i.e. who did not develop PTX/PNM.

The clinical characteristics of COVID-19 patients with PTX/PNM.

The baseline characteristics of patients who developed PTX/PNM are shown in Tables 1, 2, and 3. Both groups were comparable with respect to age and gender distribution well as time of onset of the disease; therefore, both the groups were matched. Various comorbidities such as COPD, asthma, hypertension, and diabetes were comparable between the two groups.

Table 1: Demographic profile

Variables	Pneumothorax (N=18)	No Pneumothorax (N=34)	P-value
Gender (M/F)	15/3	21/13	0.109*
Age (Mean ± SD)	46.4 ± 13.5	53 ± 16.3	0.148¥
Diabetes	6 (33.3%)	10 (29.4%)	0.771*
Hypertension	6 (33.3%)	17 (50.0%)	0.250*
COPD	0 (0.0%)	1 (2.9%)	1.000¶
Asthma	0 (0.0%)	2 (5.9%)	0.539¶
Time of onset in days (Mean ± SD)	10.6 ± 11.0	5.2 ± 3.4	0.010#
CT severity score (Mean ± SD)	19.9 ± 3.5	19.0 ± 4.3	0.536¥
Invasive ventilation	4/18	2/34	0.166¶
PS	20.9 ± 2.8	18.3 ± 3.2	0.022¥
PEEP	9.7 ± 2.4	10.0 ± 2.1	0.623¥
FiO2	1.0 ± 0.1	1.0 ± 0.1	0.633¥
Duration of Ps support in days	16.4 ± 10.7	18.1 ± 10.5	0.648¥
Management: Chest pain/Conservative	9/9	1/33	<0.001¶

= Mann–Whitney *U* test , ¥ = Unpaired t-test, * = Chi-square test, ¶ = Fisher exact test.

Depicts the demographic profile of the COVID-19 patients in both PTX and non PTX groups: patients who developed PTX/PNM during the course of their illness and patients who did not, respectively.

Table 2: Number of patients being administered oxygen therapy through various routes in both the groups.

Route of oxygenation	Pneumothorax		No Pneumothorax		Chi-square test P-value
	Count	Column N %	Count	Column N %	
BiPAP	0	0.0%	9	26.5%	0.005
CPAP	13	72.2%	15	44.1%	
HFM	0	0.0%	7	20.6%	
MV	4	22.2%	1	2.9%	
NONE	1	5.6%	2	5.9%	
Total	18	100.0%	34	100.0%	

Depicts the number of patients in each of the PTX and non PTX groups who received various modes of oxygenation.

Table 3: Various laboratory variables in both the groups at designated time intervals.

Variables	Time of Collection	Pneumothorax		No Pneumothorax		Unpaired t-test p-value	Paired t-test p-value	
		Mean	SD	Mean	SD		Change from day of admission p-value Pneumothorax group SD	Unpaired t-test p-value Change from day of admission p-value Non-Pneumothorax group
HB	Day of Admission	12.9	2.5	12.6	1.6	0.607	-	-
	7 – 10 days	13.0	1.6	12.5	1.9	0.385	0.042	<0.001
	15 – 20 days	12.5	2.8	12.5	1.8	0.946	0.152	<0.001
	Day of Discharge	12.0	2.5	11.8	1.9	0.837	0.044	<0.001
TLC	Day of Admission	10537.7	4412.4	10168.7	4402.5	0.801	-	-
	7 – 10 days	11724.7	5021.2	11889.7	4310.0	0.910	0.002	0.040
	15 – 20 days	13358.3	8943.1	13704.8	5429.1	0.890	0.943	0.578
	Day of Discharge	13642.9	6048.9	10803.6	4685.8	0.185	0.947	0.427
PLATELET COUNT	Day of Admission	2.27	0.84	2.55	0.92	0.342	-	-
	7 – 10 days	2.55	0.78	3.03	1.11	0.144	0.388	0.013
	15 – 20 days	2.49	1.33	2.64	1.10	0.721	0.928	0.508
	Day of Discharge	2.52	0.91	2.56	0.95	0.916	0.777	0.730
ALBUMIN	Day of Admission	3.4	0.3	3.4	0.4	0.789	-	-
	7 – 10 days	3.4	0.3	3.3	0.4	0.561	0.367	0.327
	15 – 20 days	2.9	0.7	3.3	0.4	0.130	0.064	0.267
	Day of Discharge	3.1	1.0	3.3	0.6	0.601	0.343	0.302
PH	Day of Admission	7.39	0.06	7.37	0.07	0.314	-	-
	7 – 10 days	7.40	0.12	7.40	0.05	0.913	0.864	0.050
	15 – 20 days	7.40	0.09	7.41	0.05	0.913	0.931	0.057
	Day of Discharge	7.40	0.11	7.39	0.06	0.655	0.820	0.013
PCO2	Day of Admission	32.5	7.5	33.9	9.9	0.651	-	-
	7 – 10 days	39.1	14.5	34.5	7.9	0.184	0.217	0.736
	15 – 20 days	43.1	14.8	36.4	11.7	0.157	0.081	0.950
	Day of Discharge	45.5	16.9	36.6	7.9	0.041	0.020	0.874
PO2	Day of Admission	79.7	37.3	74.3	27.5	0.610	-	-
	7 – 10 days	72.5	41.3	81.7	25.9	0.374	0.285	0.262
	15 – 20 days	90.8	30.5	92.3	39.7	0.911	0.851	0.201
	Day of Discharge	64.2	24.0	93.1	34.9	0.035	0.110	0.059
HCO3	Day of Admission	20.8	4.8	21.9	3.6	0.434	-	-
	7 – 10 days	22.6	3.9	23.3	2.9	0.514	0.107	0.130
	15 – 20 days	25.0	2.3	24.8	4.1	0.865	0.050	0.010
	Day of Discharge	28.3	7.6	24.3	4.4	0.073	0.009	0.052

Depicts the various laboratory parameters at different time intervals in patients of both PTX and non PTX groups.

Amongst the 18 COVID-19 patients who developed PTX/PNM, only one patient had more than one episode of pneumothorax. This patient had a contralateral pneumothorax as compared to the initial pneumothorax. In terms of the initial pneumothorax of each patient, the majority were right-sided (12/19, 63%), followed by left-sided (5/19, 26%) and bilateral (1/19,5%). pneumomediastinum, in addition to PTX, was observed in 10/19 (53%) of cases.

Out of 18, 13 patients were on non-invasive ventilation (CPAP/BiPAP), four patients were on IPPV, and one was not on oxygen therapy (Table 2). Almost half, 9/19 (47%), of the pneumothoraces received tube thoracostomy for the

Table 4: Laboratory values of inflammatory markers in both the groups at designated time intervals.

Variables	Time of Collection	Pneumothorax			No Pneumothorax			Mann–Whitney U test p-value	Wilcoxon signed rank test p-value	
		Median	Q1	Q3	Median	Q1	Q3		Change from day of admission p-value Pneumotho-rax group	Change from day of admission p-value Non-Pneumo-thorax group
IL 6	Day of Admission	41.1	27.8	63.3	12.6	3.7	59.6	0.147	-	-
	7 – 10 days	64.30	28.40	230.20	14.90	3.27	33.90	0.078	0.593	0.959
	15 – 20 days	15.8	2.5	80.0	10.6	6.5	12.8	0.475	0.593	0.484
	Day of Discharge	15.0	13.8	30.4	9.7	3.6	85.7	0.898	0.655	0.889
FERRITIN	Day of Admission	1425.0	805.9	1650.0	916.5	462.0	1480.0	0.263	-	-
	7 – 10 days	1101.8	1101.8	1101.8	482.0	243.0	1141.0	0.800	0.317	0.109
	15 – 20 days	1650.0	815.0	1650.0	1002.9	430.0	1321.0	0.202	0.317	0.285
	Day of Discharge	579.0	181.9	1226.5	416.5	144.6	1121.0	0.886	0.180	0.317
D DIMER	Day of Admission	897.0	131.0	1012.0	310.0	143.0	488.0	0.319	-	-
	7 – 10 days	543.0	368.0	5000.0	321.5	152.9	359.0	0.114	0.655	0.144
	15 – 20 days	374.5	299.0	808.0	354.5	217.0	1285.0	1.000	0.180	0.866
	Day of Discharge	87.9	48.9	282.0	565.0	414.2	904.5	0.114	0.109	0.593
CRP	Day of Admission	79.0	18.0	101.0	40.0	11.0	61.8	0.062	-	-
	7 – 10 days	55.5	31.6	66.8	60.4	32.6	126.1	0.596	0.273	0.064
	15 – 20 days	13.0	8.2	14.0	19.0	5.0	24.4	0.661	0.655	0.508
	Day of Discharge	35.7	12.3	60.7	20.2	1.5	68.1	0.951	1.000	0.445
PCT	Day of Admission	0.1	0.0	0.5	0.0	0.0	0.1	0.237	-	-
	7 – 10 days	0.1	0.0	0.3	0.1	0.0	0.1	0.727	0.180	0.893
	15 – 20 days	7.2	0.0	13.0	0.0	0.0	0.3	0.381	0.317	0.786
	Day of Discharge	0.0	0.0	0.0	0.1	0.0	0.2	0.154	1.000	1.000

Depicts serum levels of various inflammatory markers at different time intervals in both PTX and non PTX groups.

management of their pneumothorax, whereas the remainder, 10/19 (53%), did not need any intervention.

COVID-19 patients who developed pneumothorax and/or pneumomediastinum demonstrated mortality of 72.2%; among the patients who did not develop PTX/ PNM mortality was observed to be 26.5% (Table 5). COVID patients who developed PTX/PNM had 2.7 times higher risk of mortality as compared to the patients who did not develop PTX/PNM. P-value was observed to be 0.001 (<0.05) which signifies that the difference in mortality between the two groups was statistically significant. The 95% C.I. was observed to be 1.45–5.12 (Table 5). Median survival time in non-survivors who developed PTX/PNM was observed to be 5.61–8.38 days (Table 6).

Table 5: Comparison of mortality between the groups.

Mortality	Pneumothorax		No Pneumothorax		Chi-square test P-value
	Count	Column N %	Count	Column N %	
Dead	13	72.2%	9	26.5%	0.001 RELATIVE RISK = 2.73 (95% C.I. 1.45–5.12)
Alive	5	27.8%	25	73.5%	
Total	18	100.0%	34	100.0%	

Depicts the mortality of patients in both PTX and non PTX groups.

With respect to age and sex distribution, no statistically significant difference was observed between the two groups (Table 1). Incidence of systemic comorbidities, diabetes mellitus, hypertension, previous lung disease such as

Table 6: Kaplan Meier survival analysis reflecting the median survival time among pneumothorax/pneumomediastinum patients.

Median survival time among Pneumothorax patients			
Estimate	Standard Error	95% Confidence Interval	
		Lower Bound	Upper Bound
7.0 days	0.707	5.614	8.386

Depicts median survival of patients in both PTX and non PTX groups.

bronchial asthma, and chronic obstructive lung disease was observed to be comparable between the two groups (Table 1). CT severity scores were found to be higher in the group which developed PTX/PNM (19.9 ± 3.5) as compared to the non-exposure group (19.0 ± 4.3); however, the difference was observed to be statistically non-significant (p>0.05) (Table 1). With respect to modes of ventilation, 17 (94.4%) patients received positive pressure ventilation in the exposure group, out of which 13 (72.2%) of patients were administered non-invasive mechanical ventilation in the form of CPAP and 4 patients (22.2%) received invasive mechanical ventilation. This is in contrast to the non-exposure group, where 25 patients (63.5 %) received positive pressure ventilation, with 24 patients administered non-invasive mechanical ventilation whereas only one patient (2.9%) was administered invasive mechanical ventilation.

Interestingly, the proportion of patients who received oxygen therapy via simple face masks was found to be comparable between the two groups (5.6% vs. 5.9%) (Table 2).

Driving pressures in patients of the exposure group who were administered invasive mechanical ventilation were found to be higher (20.9 ±) as compared to the non-exposure group (18.3 ±); the difference was observed to be statistically significant (p=0.02) (Table 2). This denotes poorer respiratory mechanics in COVID-19 patients who developed PTX/PNM.

With respect to lab parameters, in both the groups haemoglobin concentration was observed to decline with time. The decline was statistically significant in both the groups at day 7, day 15, and day 28, as compared to the baseline (Table 3).

No statistically significant difference was observed with respect to total leukocyte count and platelet count levels. However, the fall in serum albumin levels in the PTX group was found to be closely significant (p=0.06) at 15–20 days of illness (Table 3). Baseline values of S. interleukin-6 levels in PTX vs. non-PTX group (41.1 vs. 12.6), S. ferritin values (1425.0 vs. 916.5), and C-reactive protein levels (79.0 vs. 40.0) in PTX group were found to be higher as compared to the non-PTX group (Table 4). The difference between the CRP values of the two groups was observed to be closely significant (p=0.06).

Discussion

Incidence of pneumothorax/pneumomediastinum was observed to be 1.9% among the critically ill COVID-19 patients admitted in the ICUs of our tertiary care hospital (18/934). COVID-19 patients who developed PTX/PNM had 2.7 times higher risk of mortality as compared to the patients who did not develop PTX/PNM (p=0.001), reflecting significantly higher mortality in PTX/PNM group than in the non-PTX/PNM group. A mortality rate of 72.2% was observed in COVID-19 patients who developed pneumothorax and /or pneumomediastinum. Median survival time in COVID-19 patients who developed PTX/PNM was observed to be between 5.61–8.38 days.

In a retrospective study conducted by Wang et al. evaluating the outcomes in COVID-19 patients who developed PTX/PNM, mortality of 80% was observed [3]. The sample size taken in this study was smaller [5]. The results of our study are in concordance with Wang et al., as we observed a mortality of 72.2%. McGuiness et al. identified 89 patients with barotrauma and reported an overall incidence of 15% in mechanically ventilated COVID-19 patients and concluded that barotrauma was associated with increased risk of death [14]. Perhaps the high mortality observed in our study was due to the fact that 17 out of 18 patients were administered positive pressure ventilation, 13 patients were on non-invasive ventilation, and 4 were on invasive mechanical ventilation. Associated barotrauma as a result of PPV in COVID-19 patients might have contributed to the high mortality of 72% in our study cohort.

Miro et al. in a recent study compared the outcome of non-intubated patients with COVID-19 infection who presented to the Emergency Department with a pneumothorax to those without a pneumothorax and observed that patients who developed pneumothorax had four times higher risk of death as compared to patients who did not [15]. The findings of our study are concordant with the results of Miro et al., as we observed 2.7 times higher risk of death in critically ill COVID-19 patients who developed PTX/PNM as compared to patients who did not develop PTX/PNM. Therefore, we believe that PTX/PNM is an independent marker of poor prognosis in COVID-19 patients and is associated with significantly high mortality.

In a systematic review conducted by Chong et al., the authors concluded that age, pre-existing lung diseases, and active smoking status are not shown to be risk factors. There is perhaps an additional mechanism specific to COVID-19 disease that precipitated the development of PTX and PNM in these patients. In this context, various authors have observed that this disease is characterised radiographically by ground glass opacities, evolving into consolidative changes and in late stages of the disease, fibrotic changes, bullous formation as well as diffuse cyst formation [16–19]. Similar changes in the form of diffuse alveolar damage have also been observed in patients infected with SARS-CoV2 who developed spontaneous pneumothorax; none of the patients received positive pressure ventilation [20]. Of patients who

developed PTX/PNM in our study, 94.4% received positive pressure ventilation (PPV) in the exposure group, as compared to COVID-19 patients who did not develop PTX/PNM, where a lower proportion of patients (63.5%) received positive pressure ventilation. We also observed significantly high inspiratory airway pressures in the patient population that developed PTX/PNM. We believe that instituting positive pressure ventilation with less than optimum ventilator management in the COVID-19 patients who have developed the aforementioned pathological changes might have precipitated the development of PTX and PNM.

It is now known that an excessive host immune response can be triggered in COVID-19, leading to extensive alveolar damage. Interleukin-6 (IL-6) is considered a main trigger of such an immune response. Higher values of CRP levels as well as IL-6 levels at different time intervals in the PTX group as compared to non-PTX denote higher magnitudes of systemic inflammation and more severe disease involvement leading to more extensive alveolar damage; however, the difference was statistically non-significant ($p>0.05$). High levels of serum CRP and IL-6 are strongly associated with venous thromboembolism, acute kidney injury, critical illness, and mortality in COVID-19 disease [21]. This also additionally explains the poorer prognosis and significantly higher mortality (2.7 times) in COVID-19 patients who developed PTX/PNM.

Initial studies from China reported an incidence of pneumothorax of approximately 1% in all patients infected with COVID-19 [22,23]. A large multicentre study was conducted across 61 emergency departments (ED) in Spain, involving 71,904 COVID-19 patients, which observed the pneumothorax incidence to be 0.56% [15]. In the systematic review by Chong et al., the incidence was observed to 0.3% among hospitalised COVID patients in different centres in the United States. However, in our literature search we could not retrieve any study assessing the incidence of PTX/PNM in critically ill COVID-19 patients in the Indian subcontinent. We observed the incidence of PTX/PNM in COVID-19 patients to be higher in the Indian population (1.9%). The higher incidence can also be attributed to the high virulence of the Delta strain of SARS-CoV-2 virus, which was the prevalent strain in the second wave of COVID-19 pandemic in our nation.

There were several limitations of our study. As it was a retrospective analysis, we could not record the ventilatory parameters in real time. Second, it is a single-centre study. Third, the available therapy and outcomes of the COVID-19 disease have been changing drastically over time [13]. So, a possibility that our results, including mortality as well as risk factors, could not be extrapolated to future critically ill COVID-19 infected patients, cannot be ruled out.

Nonetheless, our study is the first valid attempt at the evaluation of incidence, risk factors, as well as mortality in the subset of Indian patients who developed PTX/PNM during the COVID-19 disease.

Conclusions

To summarise, 1.9% of critically ill COVID-19 patients were admitted in the intensive care units, in the subset of the Indian population. COVID-19 patients who developed PTX/PNM had 2.7 times higher risk of mortality as compared to the patients who did not develop PTX/PNM. A mortality rate of 72.2% was observed in COVID-19 patients who developed pneumothorax and/or pneumomediastinum. A higher proportion of patients requiring PPV signifies more severe disease involvement; patients who developed PTX/PNM had more severe disease. Taking into account the associated pathological changes in lung parenchyma, stricter implementation of lung protective ventilation strategy in COVID-19 patients will reduce the incidence of PTX/PNM.

References

[1] Hu B, Guo H, Zhou P, Shi ZL. Characteristics of SARS-CoV-2 and COVID-19. Nat Rev Microbiol 2021; 19(3): 141–154.

[2] Writing Group for the Alveolar Recruitment for Acute Respiratory Distress Syndrome Trial (ART) Investigators, Cavalcanti AB, Suzumura ÉA, Laranjeira LN, Paisani DM, Damiani LP, et al. Effect of lung recruitment and titrated positive end-expiratory pressure (PEEP) vs. low PEEP on mortality in patients with acute respiratory distress syndrome: A randomized clinical trial. JAMA 2017; 318(14): 1335–1345.

[3] Chopra A, Al-Tarbsheh AH, Shah NJ, Yaqoob H, Hu K, Feustel PJ, et al. Pneumothorax in critically ill patients with COVID-19 infection: Incidence, clinical characteristics and outcomes in a case control multicenter study. Respir Med 2021; 184: 106464. doi:.

[4] Wang XH, Duan J, Han X, Liu X, Zhou J, Wang X, et al. High incidence and mortality of pneumothorax in critically ill patients with COVID-19. Heart Lung 2021; 50(1): 37–43.

[5] Martinelli AW, Ingle T, Newman J, Nadeem I, Jackson K, Lane ND, et al. COVID-19 and pneumothorax: a multicentre retrospective case series. Eur Respir J 2020; 56(5): 2002697.

[6] Elhakim TS, Abdul HS, Pelaez Romero C, Rodriguez-Fuentes Y. Spontaneous pneumomediastinum, pneumothorax and subcutaneous emphysema in COVID-19 pneumonia: a rare case and literature review. BMJ Case Rep 2020; 13(12): e239489.

[7] Kolani S, Houari N, Haloua M, Lamrani YA, Boubbou M, Serraj M, et al. Spontaneous pneumomediastinum occurring in the SARS-COV-2 infection. ID Cases 2020; 21: e00806.

[8] Zhou C, Gao C, Xie Y, Xu M. COVID-19 with spontaneous pneumomediastinum. 510Lancet Infect Dis 2020; 20 [PMC free article] [PubMed] [Google Scholar].

[9] Mohan V, Tauseen RA. Spontaneous pneumomediastinum in COVID-19. BMJ Case Rep 2020; 13: e236519.

[10] Wang J, Su X, Zhang T, Zheng C. Spontaneous pneumomediastinum: a probable unusual complication of Coronavirus disease 2019 (COVID-19) pneumonia. Korean J Radiol 2020; 21: 627–628.

[11] Ekanem E, Podder S, Donthi N. Spontaneous pneumothorax: an emerging complication of COVID-19 pneumonia. Heart Lung 2021 doi: 10.1016/j.hrtlng.2021.01.020.

[12] Zantah M, Dominguez Castillo E, Townsend R, Dikengil F, Criner GJ. Pneumothorax in COVID-19 disease: Incidence and clinical characteristics. Respir Res 2020; 21(1): 236.

[13] Chong WH, Saha BK, Hu K, Chopra A. The incidence, clinical characteristics, and outcomes of pneumothorax in hospitalized COVID-19 patients: A systematic review. Heart Lung. 2021; 50(5): 599–608.

[14] McGuinness G, Zhan C, Rosenberg N. Increased incidence of barotrauma in patients with COVID-19 on invasive mechanical ventilation. Radiol 2020; 297(2): E252–E262.x.

[15] Miró Ò, Llorens P, Jiménez S, Piñera P, Burillo-Putze G, Martín A, et al. Frequency, risk factors, clinical characteristics, and outcomes of spontaneous pneumothorax in patients with coronavirus disease 2019: A case-control, emergency medicine-based multicenter study. Chest 2021 Mar; 159(3): 1241–1255.

[16] Hosseiny M, Kooraki S, Gholamrezanezhad A, Reddy S, Myers L. Radiology perspective of coronavirus disease 2019 (COVID-19): Lessons from severe acute respiratory syndrome and Middle East respiratory syndrome. AJR Am J Roentgenol. 2020 May; 214(5): 1078–1082.

[17] Yang F, et al. Analysis of 92 deceased patients with COVID-19. J Med Virol 2020; 10.1002/jmv.25891.

[18] Kong M, Yang H, Li X, Shen J, Xu X, Lv D. Evolution of chest CT manifestations of COVID-19: a longitudinal study. J Thorac Dis 2020; 12(9): 4892–4907.

[19] Liu K, Zeng Y, Xie P. COVID-19 with cystic features on computed tomography: a case report. Medicine. 2020; 99(18).

[20] Chu CM, Leung YY, Hui JYH, Hung IFN, Chan VL, Leung WS, et al. Spontaneous pneumomediastinum in patients with severe acute respiratory syndrome. Eur Respir J 2004; 23: 802–4.

[21] Smilowitz NR, Kunichoff D, Garshick M, Shah B, Pillinger M, Hochman JS, et al. C-reactive protein and clinical outcomes in patients with COVID-19. Eur Heart J 2021 Jun 14; 42(23): 2270-2279.

[22] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020; 395(10223): 507–513.

[23] Yang F, Shi S, Zhu J, Shi J, Dai K, Chen X. Analysis of 92 deceased patients with COVID-19. J Med Virol 2020; 92(11): 2511–2515.