ORIGINAL ARTICLE

Clinical Profile of Patients with Severe Acute Respiratory Syndrome Coronavirus 2 Infection Developing Pulmonary Barotrauma on Mechanical Ventilation

Ketan V Kargirwar[1], Darshana Rathod[2], Vivek Kumar[3], Mayur Patel[4], Mehul Shah[5], Himanshu Choudhury[6], Kavita Shalia[7]

Abstract

Background: There is limited information on clinical profile and outcomes of patients on mechanical ventilation (MV) who developed pulmonary barotrauma (PBT) in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.

Patients and methods: In a retrospective observational study, all SARS-CoV-2 pneumonia patients admitted from March 28, 2020, to August 31, 2020, at Sir HN Reliance Foundation Hospital and Research Center and Seven Hills Hospital (Reliance Facility), Mumbai, India, of 18 years and above on MV and developed PBT, were included.

Results: A total of 14 SARS-CoV-2 patients of 45 on MV (31.0%) developed PBT of 1,029 hospitalized. All patients were male and divided as per admission into PaO_2/FiO_2 (P/F) ≤100 (median 80) and P/F >100 (median 222) group. Pneumothorax developed in seven and six cases of P/F ≤100 and P/F >100 groups, respectively. Three patients in each group developed subcutaneous emphysema, while four developed pneumomediastinum in P/F >100 group. Twelve patients (7, P/F ≤100, and 5, P/F >100) were on invasive, while two (P/F >100) were on noninvasive MV. The mean P/F on the day of PBT was reduced by 27.5 and 65.3%, while peak inspiratory pressure was elevated with a median of 36 and 28 cm H_2O in P/F ≤100 and P/F >100 groups, respectively. The median highest tidal volume (420 mL), positive-end expiratory pressure (8 vs 6 cm H_2O) on the day of PBT, and length of hospital stay (11 vs 25 days) did not differ between two groups. Survival was 28.6% (4/14).

Conclusion: SARS-CoV-2 patients requiring MV with PBT had poor outcomes. Clinicians should be vigilant about the diagnosis of PBT.

Keywords: Barotrauma, ICU, Mechanical ventilation, Severe acute respiratory syndrome coronavirus 2.

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Highlight of Study

In retrospective analysis of SARS-CoV-2 pneumonia patients with very low PaO_2/FiO_2, elevated inflammatory markers, radiological evidence of diffuse ground-glass opacities, and consolidations as well as on MV appear to be at high risk of developing PBT despite lung protective ventilation strategy.

Introduction

In the ongoing coronavirus disease-2019 (COVID-19) pandemic, an overwhelming number of patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection producing pneumonia and acute respiratory failure were admitted to intensive care units (ICUs). The cause of acute respiratory failure varied between primary viral pneumonia and acute respiratory distress syndrome (ARDS). These patients required support for acute hypoxemic respiratory failure; modality used varied from noninvasive ventilation (NIV) to invasive mechanical ventilation (IMV). Mechanical ventilation (MV) is an important strategy to treat such patients, and lung mechanics have both prognostic and therapeutic implications. The mortality rate of SARS-CoV-2-related ARDS can be as high as 40%.[1] It is established that patients with ARDS are particularly prone to the development of pulmonary barotrauma (PBT) in the presence of high airway pressures as during ventilation. The overall incidence of PBT among non-SARS-CoV-2 ARDS patients in the ICU is 15–32%.[2,3]

PBT is one of the potential causes of morbidity and mortality, and it can prolong ICU and length of hospital stay.[4] It manifests as complications, such as pneumothorax, pneumomediastinum, and subcutaneous emphysema, and is associated with IMV well as NIV in patients with ARDS, chronic obstructive pulmonary disease (COPD), and interstitial lung disease (ILD). Use of a lung-protective ventilation (LPV) strategy has been shown to reduce the risk of lung injury and improve outcomes in patients with the ARDS.[5] A relationship of SARS-CoV-2 pneumonia and increased susceptibility to PBT has not yet been established.

[1–5]Department of Critical Care Medicine, Sir HN Reliance Foundation Hospital and Research Centre, Mumbai, Maharashtra, India

[6]Department of Radiology, Sir HN Reliance Foundation Hospital and Research Centre, Mumbai, Maharashtra, India

[7]Sir HN Medical Research Society, Sir HN Reliance Foundation Hospital and Research Centre, Mumbai, Maharashtra, India

Corresponding Author: Ketan V Kargirwar, Department of Critical Care Medicine, Sir HN Reliance Foundation Hospital and Research Centre, Mumbai, Maharashtra, India, Phone: +91 8454888103, e-mail: ketankargirwar00@gmail.com

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However, barotrauma as one of the pulmonary complications in SARS-CoV-2 patients has been recently published, especially amongst patients requiring MV.[6]

We present a retrospective observational study of PBT occurring in patients with SARS-CoV-2 pneumonia who required IMV or NIV. Our study aims to describe the clinical characteristics, demographic features, and outcomes of these patients and dwells upon the prognostic value of PBT in patients with SARS-CoV-2 pneumonia.

Methods

We conducted a retrospective observational study at Sir HN Reliance Foundation Hospital (Sir HNRFH) and Research Center, Mumbai, and Seven Hills Hospital (Reliance facility) Mumbai, India. Patients admitted between March 28, 2020, and August 31, 2020, of age 18 years and above with RT-PCR confirmed SARS-CoV-2 pneumonia, receiving IMV or NIV who developed pneumothorax, pneumomediastinum, and subcutaneous emphysema; pathological characteristics described under PBT were included in the study. Patients with PaO_2/FiO_2 (P/F) >300, not on NIV or IMV, were excluded from the study.

Patients were divided into two groups on the basis of P/F calculated at admission: P/F ≤100 and P/F >100. Patients were ventilated as per LPV protocol to keep tidal volume (VT) of 6–8 mL/kg predicted body weight (PBW), respiratory rate to maintain $PaCO_2$ at 35–50 mm Hg, plateau pressure <30 cm H_2O, peak inspiratory pressure (PIP) <40 cm H_2O, and positive end expiratory pressure (PEEP)-fractional inspired oxygen (FiO_2) combination to maintain PaO_2 >60 mm Hg or SpO_2 88–92%.

Patients receiving IMV at the time of PBT were on pressure regulated volume control (PRVC) mode with standard use of analgosedation and neuromuscular blocking agents. Patients receiving NIV at the time of PBT were on pressure control ventilation (PCV) and/or pressure support ventilation (PSV) mode without any use of sedation. The LPV protocol and PEEP were modified subsequently as per discretion of treating team if goals of oxygenation and ventilation were not met. Patients underwent prone ventilation according to standard institutional protocol and as per discretion of physician. However, it was challenging during the SARS-CoV-2 pandemic due to limited staffing of healthcare workers. Medical treatment and management of hypoxemic respiratory failure were carried out as per the Sir HNRFH COVID-19 management protocol. All patients received antivirals, steroids, vitamin B complex with zinc supplementation, and thromboprophylaxis. The study was approved by the Institutional Ethics Committee (IEC) at Sir HNRFH and Research Centre, Mumbai, India. The ethics committee waived off the need for informed consent from patients.

Data Collection

Data were abstracted from electronic medical record system (EMR) and included age, sex, comorbidities, sequential organ failure assessment (SOFA) score, P/F on admission and day of PBT, days from onset of SARS-CoV-2 symptoms to hospitalization, and number of days from admission to diagnosis of PBT.

Patients' data on inflammatory markers, such as serum CRP (<0.5 mg/dL), D-dimer (0–250 ng/mL), ferritin (30–400 ng/mL), LDH (≤250 U/L), IL-6 (0–7 pg/mL) on the day of admission, number of days on MV (NIV and/or IMV) preceding to diagnosis of PBT, ventilator variables on the day of PBT modes (PRVC, PCV, and PSV), highest peak inspiratory pressure PIP (cm H_2O), highest VT (mL/kg PBW), and highest PEEP (cm H_2O), were extracted from EMR. PBT was identified by presence of any of the following—subcutaneous emphysema, pneumothorax, and pneumomediastinum; the latter two were identified using chest X-ray and/or high-resolution chest computed tomographic (HRCT) scan. If a therapeutic intervention like a chest tube insertion was performed, it was included in the data collection.

Outcomes

Primary outcome was to identify clinical as well as radiological profile and inflammatory marker characteristic of SARS-CoV-2 pneumonia patients developing PBT on MV (IMV plus NIV). Secondary outcome was to identify length of hospital stay and survival at hospital discharge.

Statistical Analysis

Descriptive statistics included presentation of data as frequency (percentages) for categorical variables and analyzed for difference in distribution by Pearson's Chi-square and Fisher's exact test. Continuous data were presented as mean [standard deviations (SD)] and median [interquartile range (IQR)]. Quartiles (25th/75th) of a corresponding median have been mentioned during explanation in the text. A comparison of means and median between two groups was made by unpaired *t*-test and Mann-Whitney *U* test, respectively. A comparison of medians within the group between two time intervals was carried out by Wilcoxon's signed rank test. The statistical significance level was set at $p < 0.05$ (two-tailed). All analyses were conducted with MedCalc and SPSS version 23.0 statistical software.

Results

Baseline Characteristics (Table 1)

A total of 1,029 patients were admitted during study period out of which 45 required MV. Among these, 14 (31.1%) patients who developed PBT secondary to SARS-CoV-2 pneumonia were included in analysis. These 14 patients were divided into two groups of seven patients each on the basis of admission P/F ≤100 (median 80) and P/F >100 (median 222). The average age at the time of diagnosis was 57 and 51 years in P/F ≤100 and P/F >100 group, respectively. All patients in both the groups were male. Around 50% of patients in each group ($n = 7$ per group) had hypertension and diabetes mellitus; one patient had epilepsy in P/F >100 group. None of the patients had any chronic lung disease like bronchial asthma, ILD, COPD, bronchiectasis, and lung cancer. However, two patients in P/F ≤100 group had history of moderate smoking. Serum CRP, IL-6, ferritin, D-dimer, and LDH levels were markedly elevated as compared to the normal cutoff in all patients and the difference in the levels between the two groups was not statistically significant. The median time from symptom onset to hospitalization and SOFA score at admission was almost similar in both the groups.

The difference in the median duration from admission to the diagnosis of PBT between P/F ≤100 [median 8 (3/14)] and P/F >100 group [median 6 (4/30)] was statistically not significant. The median P/F on the day of PBT was 58 and 77 of P/F ≤100 and P/F >100 groups, respectively. The reduction in P/F between the two time intervals, i.e., from the time of admission to the development of PBT in the P/F ≤100 group (27.5%), was statistically not significant, while that in the P/F >100 group, the reduction was statistically significant (65.3%, $p = 0.028$).

Table 1: Baseline demographic and clinical characteristics of patients with PBT and SARS-CoV-2 pneumonia

Baseline parameters	*P/F ≤100 (n = 7)*	*P/F >100 (n = 7)*
Age (years) Mean (SD)	57.1 (13.1)	51.4[NS] (15.1)
Gender (male) [*n* (%)]	7 (100)	7 (100)
Hypertension [*n* (%)]	3 (42.9)	3 (42.9)
Diabetes mellitus [*n* (%)]	2 (28.6)	2 (28.6)
Epilepsy [*n* (%)]	0	1[NS] (14.3)
Days from symptom onset to hospitalization Median (IQR)	6 (6)	7[NS] (5)
SOFA score on admission Median (IQR)	4 (6)	3[NS] (2)
P/F on admission Median (IQR)	80 (46)	222[a] (102)
P/F on day of PBT Median (IQR)	58 (45)	77[NS] (55)
Days from admission to diagnosis of PBT Median (IQR)	8 (11)	6[NS] (26)
Inflammatory markers Median (IQR) on admission		
CRP (mg/dL) Median (IQR)	11.2 (25.4)	3.7[NS] (9.15)
D-dimer (ng/mL) Median (IQR)	7,805 (23,920)	4,346[NS] (4,683)
Ferritin (ng/mL) Median (IQR)	822 (471)	1,836[NS] (4,368)
LDH (U/L) Median (IQR)	527 (264)	641[NS] (214)
IL-6 (pg/mL) Median (IQR)	158 (461)	77[NS] (654)

CRP, C-reactive protein; IL-6, interleukin 6; IQR, interquartile range; LDH, lactate dehydrogenase; P/F, PaO_2/FiO_2; PBT, pulmonary baro trauma; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation; SOFA, sequential organ failure assessment score; [NS]Nonsignificant; [a]$p = 0.001$

SI conversion factors: CRP (mg/dL)—multiply by 95.24 for nmol/L, D-dimer (ng/mL)—multiply by 1 for µg/L, ferritin (ng/mL)—multiply 2.247 for pmol/L, and LDH (U/L)—multiply by 0.0167 for µkat/L

Ventilation Characteristics (Table 2)

At the time of occurrence of PBT of the 12/14 (85.7%) patients on IMV, seven were of P/F ≤100 group and five of P/F >100 group, while 2/14 (14.3%) of the latter group were on NIV.

The median duration of preceding MV (IMV plus NIV) was 5 (5/16) days in patients who suffered PBT in P/F ≤100 group. Though no patient had NIV use at the time of PBT in this group, these patients had received NIV prior to initiation of IMV for a median 4 (0/5) days. In P/F >100 group, the median duration of preceding MV (IMV plus NIV) was 4 (0/16) days. In this group, only two patients were on NIV at the time of occurrence of PBT and median duration of NIV was 4 (2/10) days (including NIV use prior to use of IMV in five subjects and ongoing NIV use in two subjects). There was no statistical significant difference in duration of MV (IMV plus NIV) between both the groups. The median time for occurrence of PBT after onset of IMV was 4 (1/14) and 3.0 (2/9) days in P/F ≤100 and P/F >100 groups, respectively, and the difference between the two durations was statistically not significant. Majority, i.e., five and four patients each of P/F ≤100 and P/F >100 group, respectively, developed PBT between first and sixth days (9/12, 75%). PIPs of both the groups were markedly elevated; however, that of P/F >100 group (28 cm H_2O) was 20% ($p = 0.002$) less then P/F ≤100 group (36 cm H_2O). The median highest VT and median highest PEEP on the day of the development of PBT did not differ between the two groups.

Table 2: Mechanical ventilation characteristics of patients with PBT and SARS-CoV-2 pneumonia

Ventilator parameters	*P/F ≤100 (n = 7)*	*P/F >100 (n = 7)*
NIV patients on day of PBT; PCV or PS (*n* = 2) *n* (%)	0	2 (28)
IMV patients on day of PBT; PRVC (*n* = 12) *n* (%)	7 (100)	5 (72)
Days on MV (IMV + NIV) preceding PBT Median (IQR)	5 (11)	4[NS] (16)
Days on NIV preceding PBT Median (IQR)	4 (5)	4[NS] (8)
Days from initiation of IMV to the occurrence of PBT Median (IQR)	4 (13)	3[NS] (7)[a]
Highest VT on the day of PBT (mL) Median (IQR)	420 (30)	420[NS] (70)
Highest PIP on the day of PBT (cm H_2O) median (IQR)	36 (2)	28[b] (4)
Highest PEEP on the day of PBT (cm H_2O)	6 (7)	6[NS] (2)

NIV, noninvasive ventilation; [NS]Nonsignificant; P/F, PaO_2/FiO_2; PBT, pulmonary barotrauma; PBW, predicted body weight; PCV, pressure control ventilation; PEEP, positive-end expiratory pressure; PIP, peak inspiratory pressure; PRVC, pressure-regulated volume controlled; PS, pressure support; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation; VT, tidal volume; [a]median (IQR) $n = 5$; [b]$p = 0.002$

Radiological Characteristics (Table 3)

Amongst patients in P/F ≤100 group, all seven (100 %) had pneumothorax, while three (42%) also had subcutaneous emphysema. Among patients in P/F >100 group, six (85%) had pneumothorax, three (42%) had subcutaneous emphysema, and four (57%) had pneumomediastinum (Fig. 1). All patients ($n = 14$) had a HRCT chest with 100% prevalence of diffuse ground glass opacity along with diffuse pulmonary involvement. The overall incidence of pneumothorax was higher in patient with P/F ≤100 as compared to P/F >100 group (100 vs 85%). Intercostal chest drain insertion was required in all the cases in P/F ≤100 group and in five cases in P/F >100 group. Two patients of P/F >100 group on NIV were managed conservatively.

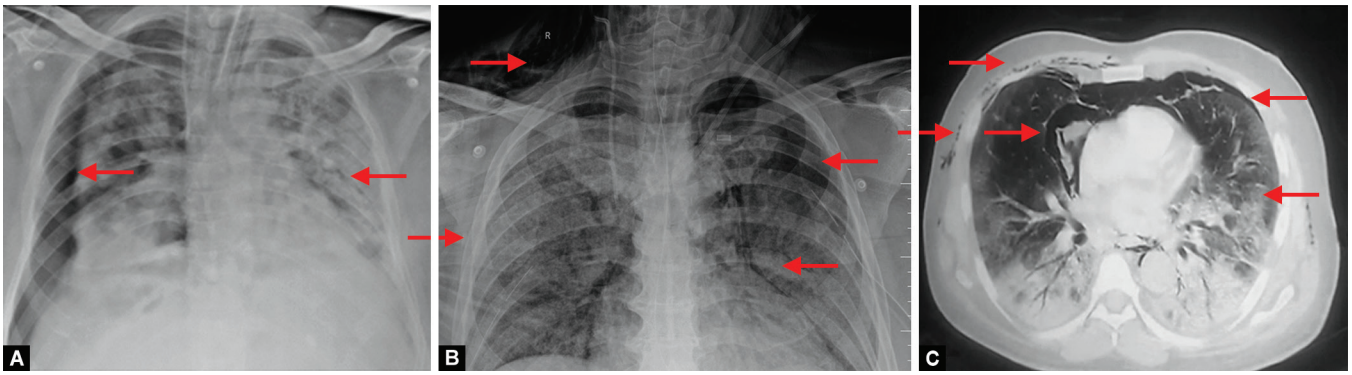
Outcomes

The overall survival at hospital discharge was 4/14 (28.6%) in patients following PBT. This included one patient (14.2%) in P/F ≤100 group and three patients (42%) in P/F >100 group. The median

Table 3: Radiological characteristics and outcome of patients with PBT and SARS-CoV-2 pneumonia

HRCT findings and chest X-ray findings	*P/F ≤100 (n = 7)*	*P/F >100 (n = 7)*
Pneumothorax *n* (%)	7 (100)	6 (85)
Pneumomediastinum *n* (%)	0	4 (57)
Subcutaneous emphysema *n* (%)	3 (42)	3 (42)
Ground-glass opacity *n* (%)	7 (100)	7 (100)
Diffuse involvement *n* (%)	7 (100)	7 (100)
Pleural thickening *n* (%)	6 (85)	3 (42)
Localized involvement *n* (%)	0	0
Cystic lesion *n* (%)	0	0
Cavitary lesion *n* (%)	0	0
Chest tube insertion *n* (%)	7 (100)	5 (71.4)
Outcomes		
Survival at hospital discharge *n* (%)	1 (14.2)	03 (42)
Length of hospital stay Median (IQR)	11 (21)	25^{NS} (31)

HRCT, high-resolution chest computed tomographic; IQR, interquartile range; NS Nonsignificant; PBT, pulmonary barotrauma; P/F, PaO2/FiO2; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2



Figs 1A to C: Radiological findings of the lung in SARS-CoV-2 Pneumonia. (A) Anterior posterior view chest radiograph (CXR)-A large right pneumothorax (arrow) and some leftward tracheal shift. Bilateral wide spread bilateral alveolar opacity (arrow) is typical common radiographic feature of SARS-CoV-2 infection; (B) Anterior posterior view (CXR)-A pneumomediastinum (arrow), subcutaneous emphysema in the neck (arrow). A large left pneumothorax (arrow) and bilateral diffuse ground glass opacifications (arrow); (C) Axial computed tomography single image of the thorax acquired in SARS-CoV-2 patient showing right-sided pneumothorax (arrow) with subcutaneous emphysema (arrow). Areas of bibasal consolidations with air bronchogram and diffuse ground glass densities with crazy paving pattern (arrow), noted in rest of the lungs, as seen commonly bilaterally with predominant involvement of posterior and peripheral lung parenchyma

length of hospital stay was 11 (6/27) and 25 (8/39) days in P/F ≤100 and P/F >100 groups, respectively; however, the difference did not reach statistical significance.

Discussion

The present study focuses on PBT, in subset of patients with SARS-CoV-2 pneumonia requiring IMV or NIV. PBT is defined as the development of air outside the tracheobronchial tree resulting from presumptive alveolar rupture and manifested by at least one of the following: pneumothorax, pneumomediastinum, and subcutaneous emphysema.[7,8] In our study, the total incidence of pneumothorax was 1.2% (13/1,029), subcutaneous emphysema was 0.5% (6/1,029), and pneumomediastinum was 0.3% (4/1,029). This is in accordance with previously published reports.[9,10] The overall incidence of pneumothorax in the SARS-CoV-2 infected patients as per recently published study from UK was 0.43%.[11]

There are currently only few published case reports of spontaneous pneumomediastinum in the setting of SARS-CoV-2 pneumonia.[12,13] In the present study, all patients were male with more than one comorbidity but no underlying lung disease, with average onset of symptoms to hospitalization around 7 days and had elevated inflammatory markers.

MV appears to be a predominant risk factor for the development of PBT with SARS-CoV-2 pneumonia.[14] In the present study, 45 patients were on MV and out of which 14 developed PBT i.e. 31%. Specific for IMV, in our case series 12 patients were on IMV with LPV and developed PBT, i.e., 26.7% (12/45). Similar finding has also been reported by McGuinness et al. wherein 24% (145/601) patients of SARS-CoV-2 pneumonia on IMV developed PBT.[14]

Aiodfi et al. have reported two cases of SARS-CoV-2 pneumonia who developed pneumothorax on day 4, while on MV.[15] On the contrary, Wang et al. have reported a SARS-CoV-2 pneumonia case who developed spontaneous pneumothorax,

pneumomediastinum, and subcutaneous emphysema without being exposed to MV suggesting that positive pressure ventilation alone cannot explain this association.[16] However, in our study, two patients of SARS-CoV-2 pneumonia in P/F >100 group [2/14 (14.2%)] who developed PBT without being subjected to IMV or very high PEEP. Both these patients on NIV survived. This is contrary to the retrospective case series by Pattupara et al. wherein two patients with confirmed SARS-CoV-2 infection developed PBT on NIV and did not survive.[17]

Most physicians believe that usually PBT occurs late in the course of ARDS.[18] Gammon et al. observed that the majority of PBT occurred within 6 days after the onset of acute lung injury or ARDS.[19] Similar to these reports, in the present study, PBT occurred at median eighth (3/14) and sixth (4/30) days from admission in P/F ≤100 and P/F >100 groups, respectively. With respect to the start of IMV, Aiodfi et al.[15] have documented development of PBT by fourth day after MV. In the present study, two patients of P/F ≤100 group developed PBT on 14th and 19th day and one of P/F >100 group on 14th day, while rest all developed earliest by first day and late by sixth day from the start of IMV.

The development of PBT has been associated with the ventilator settings, including mode, lung compliance below 30 mL/cm H_2O PIP, plateau pressures above 35 cm H_2O, higher PEEP, and higher VT.[18–20] In our cases series of SARS-Cov-2 patients, any statistical significant difference in the incidence of pneumothorax between both the groups on MV was not observed. This is despite the fact that patients with P/F >100 group had PIP 20% significantly less than that of P/F ≤100 group (28 vs 36 cm H_2O). Things that may increase PIP could be increased secretions, bronchospasm, kinking of ventilation tubing, and decreased lung compliance. Another observation from our study was that the P/F drop from the day of admission to the day of development of PBT for P/F ≤100 group was 27.5%, while for P/F >100 group, it was 65.3%. This drop in the latter group may correlate with the development of PBT almost around same time as that of former group. The drop in P/F may be due to the worsening disease which may have led to decreased lung compliance and increase PIP.

While on MV, a higher level of applied PEEP (>5 cm H_2O) is traditionally used to improve hypoxemia in patients with acute lung injury, ARDS, or other types of hypoxemic respiratory failure,[20] Eisner et al. have observed that patients with worse lung condition required higher PEEP for oxygenation which in turn was related to an increased risk of barotrauma.[20,21] However, in our present study, in both the groups of SARS-CoV-2, the median PEEP applied was 6 cm H_2O, which was less than usually required for ARDS patients (10–20 cm H_2O), still they developed PBT. This finding points to a multifactorial etiology of PBT in these cases, rather than pointing exclusively role of high airway pressures. We were required to accept higher peak pressures in certain cases in order to achieve adequate oxygenation or ventilation. Though these were aberrations from LPV strategy, it was logistically not possible to prone all patients as soon as their ventilator needs escalated.

The radiological findings of these patients showed different degrees of ground glass opacities, areas of consolidation, and diffuse involvement on HRCT scan consistent with what has been reported in the literature.[22] These findings were not predictive of any pattern and were not different in any way between the groups. In the present study, incidence of pneumomediastinum was more in P/F >100 group, while the pneumothorax was seen more in P/F ≤100 group.

All the above-mentioned observations correlate with recently published studies, in that the pathophysiology of SARS-CoV-2 pneumonia-related acute lung injury is claimed to be complex in nature. One such mechanism being a cytokine storm that causes destruction of the alveoli and pulmonary endothelium with pulmonary microthrombosis is associated with high mortality.[23,24] This destruction may lead to spontaneous pneumomediastinum through previously described Macklin's phenomenon. Macklin reported how alveolar air which is released from alveolar rupture tracks along peribronchial vascular sheaths toward the mediastinum and rupture through the mediastinal pleura leads to the development of pneumothorax.[25] Further research would be necessary to clarify the basis of these findings better. The limitations of our study were a retrospective review of EMR that was dependent on the available documentation wherein we could not analyze for some patients lung compliance and plateau pressure from the records. As high plateau pressure (>35 cm H_2O) is also a risk factor for PBT, it is one of our major limitations. Also it was difficult to determine from the EMR ventilator dyssynchrony on MV. Another limitation is small sample size of the study.

Thus, in the present study, two cases of invasive ventilation each in P/F ≤100 and P/F >100 group and two of NIV in P/F >100 group survived. It is important to recognize that to this date, there is no specific recommendation on the timing and optimal settings of MV in patients with SARS-CoV-2 pneumonia. Since PBT is not related only to ventilator parameters, commencement of early antiviral and anti-inflammatory medication with use of noninvasive devices like high-flow nasal cannula (HFNC) may provide a multi-pronged approach to help reducing worsening of disease and the incidence of PBT in these patients.

Conclusion

PBT is a rare but life-threatening complication of SARS-CoV-2 pneumonia. It may occur early during the course of the disease in patients receiving IMV or NIV despite low PEEP and low VT ventilation. All these patients had elevated inflammatory markers at presentation and there was significant drop in P/F at the time of the development of PBT even in patients with P/F >100 at admission, suggesting the possibility of disease severity a major predictor of PBT. Since the pathogenesis is multifactorial, development of PBT increases length of hospital stay and reduces survival in these patients. Clinicians should be vigilant about the diagnosis of PBT in patients with SARS-CoV-2 pneumonia.

Orcid

Ketan V Kargirwar https://orcid.org/0000-0001-7091-1844
Darshana Rathod https://orcid.org/0000-0002-5446-6768
Vivek Kumar https://orcid.org/0000-0002-6914-5422
Mayur Patel https://orcid.org/0000-0002-4315-5016
Mehul Shah https://orcid.org/0000-0002-0720-7632
Himanshu Choudhury https://orcid.org/0000-0003-2620-264X
Kavita Shalia https://orcid.org/0000-0003-1302-6114

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