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Clinical characteristics and risk factors of patients with COVID-19 developing barotrauma

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ABSTRACT

Background: At our hospital, people with COVID-19 (coronavirus disease 2019) had a high rate of pulmonary barotrauma. Therefore, the current study looked at barotrauma in COVID-19 patients getting invasive and non-invasive positive pressure ventilation to assess its prevalence, clinical results, and features.

Methodology: Our retrospective cohort study comprised of adult COVID-19 pneumonia patients who visited our tertiary care hospital between April 2020 and September 2021 and developed barotrauma.

Results: Sixty-eight patients were included in this study. Subcutaneous emphysema was the most frequent type of barotrauma, reported at 67.6%; pneumomediastinum, reported at 61.8%; pneumothorax, reported at 47.1%. The most frequent device associated with barotrauma was CPAP (51.5%). Among the 68 patients, 27.9% were discharged without supplemental oxygen, while 4.4% were discharged on oxygen. 76.5% of the patients expired because of COVID pneumonia and its complications.

In addition, 38.2% of the patients required invasive mechanical breathing, and 77.9% of the patients were admitted to the ICU.

Conclusion: Barotrauma in COVID-19 can pose a serious risk factor leading to mortality. Also, using CPAP was linked to a higher risk of barotrauma.

Keywords: *COVID-19, Barotrauma, CPAP, BiPAP, NIV, pneumothorax*

INTRODUCTION

The latest worldwide pandemic was caused by a new coronavirus that was later called SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2). Acute respiratory distress syndrome and respiratory failure are the most common complications seen in severe cases of COVID pneumonia. Less common complications include secondary infections, hypoxic encephalopathy, acute cardiac injury, acute kidney injury, acute liver injury, shock, and barotrauma [1-5].

Barotrauma is tissue damage secondary to the pressure gradient between an unvented body cavity, surrounding air/fluid interface, or across a tissue plane [6]. The clinical manifestations of barotrauma comprise pneumothorax, pneumomediastinum, and subcutaneous emphysema. Despite the rarity of barotrauma in viral pneumonia, we have seen a higher prevalence of it in patients with COVID-19 illness. [7-9].

Incidence of spontaneous pneumothorax was found to be 0.66% in COVID-19 patients. [10]. The prevalence of pneumothorax among COVID-19 patients in the intensive care unit (ICU) has been 2% [11]. Up to 15% of COVID-19 patients on mechanical ventilation experience barotrauma. Additionally, there is strong evidence linking acute respiratory distress syndrome (ARDS) and the emergence of secondary pneumothorax in patients receiving mechanical ventilation as a risk factor for mortality [12-14]. Our aim is to describe the clinical traits and risk variables that could raise the possibility of barotrauma.

MATERIALS AND METHODOLOGY

A retrospective cohort analysis was performed on the characteristics and risk factors of patients with COVID-19 developing barotrauma in Dr. Ziauddin Hospital North Nazimabad, a tertiary care hospital in Karachi, Pakistan, from April 2020 through September 2021.

A rapid antigen assay, PCR on a nasopharyngeal swab, and radiological imaging features were used to diagnose COVID-19 pneumonia. Patients with COVID-19 pneumonia who were older than 18 years old were included as cases. The exclusion criteria for our study comprised incomplete medical records.

Procedure

Our study was endorsed by the institutional Clinical Review Committee (CRC) and carried out under the code of ethics. According to the institutional protocol, patients were initially treated with intravenous methylprednisolone or dexamethasone, low molecular weight heparins, tocilizumab, and/or remdesivir if needed.

Data Collection

Electronic medical records of all the patients admitted with COVID-19 pneumonia during the study duration were collected. A detailed chart review was carried out on patient socio-demographics, comorbidities, clinical features, radiological findings, laboratory parameters, and clinical outcomes. Informed consent was waived as the study was based on pre-existing retrospective data. A manual review of patients' charts was also carried out to ensure accurate data collection. One thousand eight hundred ninety electronic charts were reviewed and studied, out of which 1822 patients were excluded, and 68 were included. Out of the Eighty-seven patients who developed barotrauma; 68 were included in the study and 19 were excluded based on the exclusion criteria.

Outcome

The patient's discharge and death were outlined as the primary outcomes of interest. We divided discharged as those discharged in room air and discharged requiring supplemental oxygen. The necessity for ICU stay and invasive mechanical ventilator support were all other outcomes of interest.

Statistical Analysis

We calculated frequencies and percentages of the baseline characteristics of the participants, including demographics, comorbidities, clinical features, laboratory parameters, and biochemical markers. The median and interquartile ranges were computed for continuous variables. Patient survival analysis was done for development of barotrauma until discharge, the need for admission to the intensive care unit, assisted mechanical ventilation, and death via Kaplan-Meier Curve. A P-value of less than 0.05 was used to determine statistical significance, and data were analyzed using IBM SPSS Version 26.

RESULTS

In our study, individuals with barotrauma were 61.36 years old on average table-1.

TABLE 1: Demographic characteristics.

Demographics	
	Number of patients (percentage)
Age (mean ± SD)	61.36 (11.56)
Gender	
Male	47 (69.1)
Female	21 (39.9)
Comorbidities	
Diabetes mellitus	33 (48.5)
Hypertension	36 (52.9)
Chronic liver disease	2 (3.6)
Asthma or COPD	5 (7.4)
Ischemic heart disease	16 (23.5)
Tobacco use	4 (5.9)
End-stage renal disease	1 (1.5)
Chronic liver disease	1 (1.5)
Malignancy	0
Symptoms	
Fever	59 (86.8)
Cough	48 (70.6)
Shortness of breath	66 (88.2)
Gastrointestinal Symptoms	10 (14.7)
Anorexia	9 (13.2)
Runny nose	0
Lethargy	31 (45.6)
Myalgia	16 (23.5)
Headache	3 (4.4)
Anosmia	3 (4.4)
Treatment	
Dexamethasone	34 (50)
Methylprednisolone	21 (30.9)
Tocilizumab	44 (61.8)
Remdesivir	56 (82.4)

Abbreviations

SD Standard deviation; COPD chronic obstructive pulmonary disease.

Male patients made up the majority of those who experienced barotrauma (69.1%). Hypertension (52.9%) was the most common comorbidity, followed by diabetes mellitus (48.5) and ischemic heart disease (23.5). End-stage renal disease and chronic liver disease were the least frequent comorbidities. Shortness of breath (88.2%) and fever (86.8%) were the most frequently reported symptoms by patients, followed by cough (70.6%), lethargy (45.6%), and myalgia (23.5%). Headache and insomnia were the least reported symptoms. Laboratory presentation is defined in table-2.

TABLE 2: Baseline Blood Counts and Biochemical Markers

Laboratory parameters	
	Median (IQR)
Hemoglobin (g/dL)	12.950 (11.60-13.775)
White Blood Cells (x 109/L)	12.90 (9.60-18.40)
Lymphocyte (%)	6 (4-11)
Neutrophils (%)	88 (82.25-92)
Neutrophil to Lymphocyte ratio	15.08 (7.2175-23.1875)
Platelets	241 (202.25-311)
Alanine aminotransferase	30.5 (22.25-55.5)
Aspartate aminotransferase ST (U/L)	39.50 (28.25-60.75)
Gamma-Glutamyl transferase (IU/L)	53.0 (26.75-108.25)
Urea	43 (28.25-67.75)
Creatinine	1.02 (0.86-1.29)
Serum Bicarbonate	23.0 (20.0-25.0)
Partial pressure of oxygen	55.35 (34.75-69.0)
Partial pressure of co2	37.85 (30.25-45.0)
Arterial pH	7.37 (7.10-7.43)
C-reactive protein (mg/L)	128.26 (81.89-189.78)
Lactate Dehydrogenase (U/L)	587 (418.25-730.0)
D-dimer (ng/mL FEU)	1389 (631-12586.25)
Procalcitonin (ng/mL)	0.28 (0.13-0.553)
Pro-BNP (pg/mL)	377.25 (94.86-843.50)
Ferritin (µg/L)	973 (559.5-1895.75)

Abbreviations

ALT alanine transaminase; AST aspartate transaminase, GGT Gamma-Glutamyl Transferase; LDH lactate dehydrogenase; SD Standard Deviation; CRP C-reactive protein; IQR Interquartile range; FEU Fibrinogen equivalent units CO2 Carbon dioxide; BNP Brain natriuretic peptide.

Types of barotraumas are defined in table-3.

TABLE 3: Barotrauma Type

Type of Barotrauma	Frequency (Percentages)
Pneumothorax	32 (47.1)
Pneumomediastinum	42 (61.8)
Subcutaneous Emphysema	46 (67.6)

Sites of barotrauma are given in table-4, associated devices in table-5, devices used in table-6, CPAP pressure settings in table-7, BiPAP pressure settings in table-8, ventilator parameters in table-9 and outcomes in table-10.

TABLE 4: Barotrauma site

Site of Barotrauma	Frequency (Percentages)
Right Lung	17 (25)
Left Lung	13 (19.1)
Bilateral	38 (55.9)

TABLE 5: Oxygen device at the time of barotrauma

Oxygen device at the time of barotrauma	Frequency (Percentages)
Non-re-breather Mask	5 (7.4)
CPAP	35 (51.5)
BiPAP	23 (33.8)
Invasive Ventilator	4 (5.9)
HFNO	1 (1.5)

Abbreviations
CPAP, continuous positive airway pressure; BiPAP, Bilevel positive airway pressure; HFNO, high-flow nasal oxygen.

TABLE 6: Type of devices used

Type of Devices used	Frequency (Percentages)
Non-re-breather Mask	39 (57.4)
CPAP	39 (57.4)
BiPAP	27 (39.7)
Invasive Ventilator	26 (38.2)
HFNO	29 (42.6)

Abbreviations
CPAP, continuous positive airway pressure; BiPAP, Bilevel positive airway pressure; HFNO, high-flow nasal oxygen.

TABLE 7: CPAP pressure settings

CPAP Pressures	Frequency (Percentages)
5-8	6 (8.8)
9-12	19 (27.9)
13-16	10 (14.7)

Abbreviations
CPAP; Continuous positive airway pressure.

TABLE 8: BiPAP pressure settings

BiPAP Pressures	Frequency (Percentages)
Low (EPAP min 4-6) (IPAP max 10-14)	9 (13.2)
Medium (EPAP min 7-10) (IPAP max 15-20)	9 (13.2)
High (EPAP min >10) (IPAP max >20)	5 (7.4)

Abbreviations, BiPAP; Bilevel positive airway pressure.

TABLE 9: Ventilatory parameters

Ventilatory Parameters	
Ventilator Mode	
CMV	1 (1.5)
SIMV	3 (4.4)
Tidal Volume	
280	1 (1.5)
400	2 (2.9)
600	1 (1.5)
FiO2	
90	1 (1.5)
100	3 (4.4)
PEEP	
4	1 (1.5)
5	1 (1.5)
6	2 (2.9)

Abbreviations, CMV; Control mode ventilation, SIMV; Synchronized intermittent mandatory ventilation, FiO2; Fraction of inspired oxygen, PEEP; Positive end-expiratory pressure.

TABLE 10: Outcome

Outcome	Number of patients (percentage)
Discharged	19 (27.9)
Discharged on oxygen	3 (4.4)
LAMA	4 (5.9)
Expired	52 (76.5)
ICU admission	53 (77.9)
IMV	26 (38.2)

Abbreviations, LAMA Leave against medical advice; ICU Intensive care unit; IMV Invasive mechanical ventilation.

DISCUSSION

There is still limited information on the typical traits of COVID-19 patients at risk of developing barotrauma from Pakistan, despite the fact that it is widely acknowledged as one of the main consequences of COVID-19 linked to mortality in these individuals. One characteristic consistent among various research on COVID patients with barotrauma and our study was an age group, typically between the fifth and sixth decade [15–25]. Data reported barotrauma predominantly in males, a finding consistent with our results [15-29]. Hypertension, diabetes mellitus, and ischemic heart disease were common pre-existing conditions in these studies, which favor the findings of our study [17,20,21,23,24]. Similarly, these studies' common symptoms reported among barotrauma patients were shortness of breath, fever, and cough [17,20,21]. The mortality rate varies between 60% and 87% in a few studies [15,20,23,24,25] and 36% to 46% in others [21,27]. Patients of COVID-19 with barotrauma show higher mortality when compared with non-barotrauma patients [31,16,22,28]. This study reported a slightly higher median white cell count (12.9) compared to other studies (10.9-12.1) [16.17,21,23], whereas the lymphocyte count in these studies ranged from 1.2 to 7.7 [21,23], a finding matching the results of this study. Likewise, the neutrophil percentage was between 83.8 to 90 [16,23], which matches our results of 88 percent.

Elsaaran H et el. reported the neutrophil-to-lymphocyte ratio to be 17.5 [16], which is closer to our results of 15.08. One study found ABGs of patients on the day of barotrauma as PO2 54mmHg, PCO2 44.3mmHg, and a PH of 7.37; these results closely resembled our findings of 55.35, 37.85, and 7.37, respectively [23]. LDH levels reported in our study were lower than 600 U/L, whereas those reported in other studies ranged from 600 to 1000 [16,20,21]. Procalcitonin levels in other studies ranged from 0.97 to 1.21 ng/mL [21,23], whereas our values were significantly lower. Other researchers also found markedly raised ferritin levels than our results [20,21,23]. Subcutaneous emphysema was the most common type of barotrauma in two other studies similar to ours, although the other types varied in percentage [15,28].

Regarding the site of barotrauma, the most common finding was a right-sided injury in the published literature [18,22,24,29]; however, this differs from our finding of bilateral lung involvement. Bilateral lung involvement was supported by Hamouri S et al. [17]. Most studies showed that most patients developing barotrauma were on IMV (65-100%) [15,16,22,25], contradicting our findings. However, one study reported that 33% of barotrauma patients were on IMV [17], which is closely associated with our results. The data seems divided regarding the device used, with some studies showing CPAP as the most frequently used [17,28], whereas others showed IMV as the most frequent device used in barotrauma patients [15,30]. CPAP's most commonly used pressure settings were 8 to 16 cmH2O [15,21,28]. The mean PEEP on IMV was greater than or equal to 10 cmH2O in barotrauma patients [15,20,24,28], while our study reported 6 cmH2O or below values. There is insufficient data regarding preferred BIPAP settings, ventilator modes, tidal volumes, FiO2 levels, and treatment of COVID-19 patients with barotrauma in existing studies to compare to ours, making our research among the few contributing new data regarding this, especially in our region. However, our study had many limitations, like a comparatively small sample size that cannot be generalized to the total population. Being a retrospective cohort, the study meant insufficient data for some participants that had to be excluded. And the absence of a control group.

CONCLUSION

Barotrauma in COVID-19 can pose a serious risk factor leading to mortality. Use of CPAP was linked to an increased risk of developing barotrauma. Further research on a larger sample size is required to help establish the typical characteristics of barotrauma patients to help detect the ones at risk of developing this complication and therefore change the treatment plan.

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REFERENCES

1. Chen G, Wu D, Guo W, et al. Clinical and immunological features of severe and moderate coronavirus disease 2019. J Clin Invest. 2020;130(5):2620-9.
2. Xu Z, Shi L, Wang Y, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med. 2020;8(4):420-2.
3. Gomersall CD, Joynt GM, Lam P, et al. Short-term outcome of critically ill patients with severe acute respiratory syndrome. Intensive Care Med. 2004;30(3):381-7.
4. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med. 2020;8(5):475-81.
5. McGuinness G, Zhan C, Rosenberg N, et al. Increased Incidence of Barotrauma in Patients with COVID-19 on Invasive Mechanical Ventilation. Radiology. 2020;297(2):E252-E62.
6. Battisti AS, Haftel A, Murphy-Lavoie HM. Barotrauma. StatPearls. Treasure Island (FL): StatPearls Publishing Copyright © 2022, StatPearls Publishing LLC.; 2022.
7. Hazariwala V, Hadid H, Kirsch D, et al. Spontaneous pneumomediastinum, pneumopericardium, pneumothorax and subcutaneous emphysema in patients with

COVID-19 pneumonia, a case report. J Cardiothorac Surg. 2020;15(1):301.

8. Volpi S, Ali JM, Suleman A, et al.. Pneumomediastinum in COVID-19 patients: a case series of a rare complication. Eur J Cardiothorac Surg. 2020;58(3):646-7.
9. Udi J, Lang CN, Zotzmann V, et al. Incidence of Barotrauma in Patients With COVID-19 Pneumonia During Prolonged Invasive Mechanical Ventilation - A Case-Control Study. J Intensive Care Med. 2021;36(4):477-83.
10. Zantah M, Dominguez Castillo E, Townsend R, et al. Pneumothorax in COVID-19 disease-incidence and clinical characteristics. Respir Res. 2020;21(1):236.
11. Chan JF, Yuan S, Kok KH, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet. 2020;395(10223):514-23.
12. Bajema KL, Oster AM, McGovern OL, et al. Persons Evaluated for 2019 Novel Coronavirus - United States, January 2020. MMWR Morb Mortal Wkly Rep. 2020;69(6):166-70.
13. Chen N, Zhou M, Dong X, Qu J, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395(10223):507-13.
14. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. Jama. 2020;323(11):1061-9.
15. Rajdev K, Spanel AJ, McMillan S, et al. Pulmonary barotrauma in COVID-19 patients with ARDS on invasive and non-invasive positive pressure ventilation. Journal of intensive care medicine. 2021 Sep;36(9):1013-7.
16. Elsaaran H, AlQinai S, AlTarrah D, et al. Prevalence and risk factors of barotrauma in Covid-19 patients admitted to an intensive care unit in Kuwait; a retrospective cohort study. Annals of Medicine and Surgery. 2021 Mar 1;63:102141.
17. Hamouri S, Samrah SM, Albawaih O, et al. Pulmonary barotrauma in COVID-19 patients: invasive versus non-invasive positive pressure ventilation. International journal of general medicine. 2021;14:2017.
18. Chong WH, Saha BK, Hu K, et al. The incidence, clinical characteristics, and outcomes of pneumothorax in hospitalized COVID-19 patients: a systematic review. Heart & Lung. 2021 Sep 1;50(5):599-608.
19. Belletti A, Palumbo D, Zangrillo A, et al. Predictors of pneumothorax/pneumomediastinum in mechanically ventilated COVID-19 patients. Journal of cardiothoracic and vascular anesthesia. 2021 Dec 1;35(12):3642-51.
20. Sethi SM, Ahmed AS, Hanif S, et al. Subcutaneous emphysema and pneumomediastinum in patients with COVID-19 disease; case series from a tertiary care hospital in Pakistan. Epidemiology & Infection. 2021;149.
21. Manna S, Maron SZ, Cedillo MA, et al. Spontaneous subcutaneous emphysema and pneumomediastinum in non-intubated patients with COVID-19. Clinical imaging. 2020 Nov 1;67:207-13.
22. Chopra A, Al-Tarbsheh AH, Shah NJ, et al. Pneumothorax in critically ill patients with COVID-19 infection: incidence, clinical characteristics and outcomes in a case-control multicenter study. Respiratory medicine. 2021 Aug 1;184:106464.
23. Cut TG, Tudoran C, Lazureanu VE, et al. Spontaneous pneumomediastinum, pneumothorax, pneumopericardium and subcutaneous emphysema—Not so uncommon complications in Patients with COVID-19 pulmonary infection—A series of cases. Journal of clinical medicine. 2021 Jan;10(7):1346.
24. Wong K, Kim DH, Iakovou A, et al. Pneumothorax in COVID-19 acute respiratory distress syndrome: Case series. Cureus. 2020 Nov 28;12(11).
25. Tacconi F, Rogliani P, Leonardis F, et al. Incidence of pneumomediastinum in COVID-19: a single-center comparison between 1st and 2nd wave. Respiratory Investigation. 2021 Sep 1;59(5):661-5.
26. Edwards JA, Breitman I, Bienstock J, et al. Pulmonary barotrauma in mechanically ventilated coronavirus disease 2019 patients: a case series. Annals of Medicine and Surgery. 2021 Jan 1;61:24-9.
27. Rodriguez-Arciniega TG, Sierra-Diaz E, Flores-Martinez JA, et al. Frequency and risk factors for spontaneous pneumomediastinum in COVID-19 patients. Frontiers in Medicine. 2021 Apr 9;8:405.
28. Jones E, Gould A, Pillay TD, et al. Subcutaneous emphysema, pneumomediastinum, and pneumothorax in critically ill patients with coronavirus disease 2019: a retrospective cohort study. Critical care explorations. 2020 Sep;2(9).
29. Özdemir S, Bilgi DÖ, Köse S, et al. Pneumothorax in patients with coronavirus disease 2019 pneumonia with invasive mechanical ventilation. Interactive

CardioVascular and Thoracic Surgery. 2021 Mar;32(3):351-5.
30. Kahn MR, Watson RL, Thetford JT, et al. High incidence of barotrauma in patients with severe coronavirus disease 2019. Journal of intensive care medicine. 2021 Jun;36(6):646-54.
31. Guven BB, Erturk T, Kompe Ö, et al. Serious complications in COVID-19 ARDS cases: pneumothorax, pneumomediastinum, subcutaneous emphysema and haemothorax. Epidemiology & Infection. 2021;149.