RESEARCH ARTICLE

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Spontaneous pneumomediastinum and pneumothorax in COVID-19 patients: A tertiary care experience

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Abstract

Introduction: COVID-19 can occasionally complicate into spontaneous pneumothorax (SP) and/or spontaneous pneumomediastinum (SM). This study aims at exploring the occurrence of SP and or SM, risk factors, and outcomes in COVID-19 patients.

Materials and Methods: All patients with COVID-19, which complicated into SP and/or SM at Hamad Medical Corporation (the principal public healthcare provider in Qatar) from March to September 2020, were retrospectively enrolled. The clinical diagnosis was confirmed by CXR and CT. Between-group comparisons were performed by using Chi-square and t-test. Differences were considered statistically significant at $P \leq .05$.

Results: A total of 1100 patients were admitted, and 43 patients developed SP, SP + SM, or SM. Most patients were males (42/97.9%), and the most common comorbidity was diabetes mellitus (13/30.2%). All patients had acute respiratory distress syndrome (ARDS), and most patients had low lung compliance at the time of developing SP or SM. Twenty-two of the patients developed SP (51.2%), 11 patients had both SP and SM (25.6%), and 10 patients had SM only (23.3%). There was no significant difference in the development of SP or SM and patients' gender or blood group or whether patients were on invasive or noninvasive ventilation or even the mortality ($P > .05$). Lung compliance was significantly ($P < .05$) lower in patients complicated with SP and or SM. Patients with SP required significantly higher ($P < .001$) chest drain insertion.

Conclusion: Patients with severe COVID-19 pneumonia can complicate into SP and SM. These complications are more common in male diabetic patients. Patients with ARDS and having low lung compliance are at a higher risk of developing SP, SP + SM, or SM.

1 | INTRODUCTION

In late 2019, the occurrence of pneumonia of unknown origin was detected in China. Despite various mitigation and control measures, the disease has spread quickly and extensively across the world and was characterized by the World Health Organization as a global pandemic in early 2020.[1] Later, the disease was found to be caused by a novel coronavirus SARS-CoV-2 and was named coronavirus disease-2019 (COVID-19).[1] This pandemic resulted in significant morbidity, mortality, and financial losses globally.[1] COVID-19 pneumonia can frequently and rapidly complicate into ARDS, and such patients may require noninvasive and/or invasive forms of ventilation.[1,2] Spontaneous pneumothorax (SP) and or spontaneous pneumomediastinum (SM) are occasionally found clinical entities and occur in 1% to 2% of the COVID-19 patients without any traumatic cause. Initially, the occurrence of SP and SM was thought to be related to invasive ventilation-induced events but have recently been reported to occur without evidence of barotrauma or volume trauma. In addition, some cases have occurred even before the initiation of invasive mechanical ventilation.[3] SP and SM occur in 1% to 2% of all COVID-19 pneumonia patients having ARDS. The literature about the occurrence of SP and SM in COVID-19 patients is mainly in individual case reports and small case series. Moreover, no significant literature has been published from Gulf Cooperation Council (GCC) Countries.

The aim of our study was to examine the occurrence, risk factors, and outcome of COVID-19 patients complicating with SP and pneumomediastinum.

2 | MATERIALS AND METHODS

After obtaining permission for the study from the medical research department of our institution, all COVID-19 patients with pneumonia and or ARDS who developed a SP or pneumomediastinum (SM) from March to September 2020 were enrolled retrospectively in this study. The diagnosis of SP or SM was confirmed by chest x-ray and/or chest computerized tomography (CT). In addition, patients' demographic data, the severity of the disease, respiratory support mode, positive end-expiratory pressure, P/F ratios, lung compliance values, insertion of intercostal drains, and outcomes were recorded from the electronic health records retrospectively.

2.1 | Inclusion criteria

All adult COVID-19 patients admitted to our tertiary care hospital intensive care unit (a COVID-19 designated facility by the Ministry of Public Health [MoPH]) with the diagnosis of COVID-19 pneumonia complicating into SP and/ or pneumomediastinum.

2.2 | Exclusion criteria

In pediatric patients, pneumothorax or pneumomediastinum caused by iatrogenic reasons such as invasive procedures was excluded from the study.

2.3 | Statistical analysis

Data were entered in SPSS version 23. Categorical variables were reported as frequency (n) and percentage (%), whereas continuous variables were reported as mean and standard deviation (SD). The Kolmogorov-Smirnov test proved these variables to be normally distributed. Comparisons between the groups were performed by chi-square test for categorical variables and the t-test for continuous variables. Differences were considered statistically significant at $P \leq .05$.

3 | RESULTS

During the study period, a total of 1100 COVID-19 patients were admitted to the intensive care unit of our hospital, and only 43 patients (3.9%) had SP and/or SM. The majority of the patients were male (42/97.7%), and the most frequent comorbidity was diabetes mellitus (13/30.2%). Blood group "A" was the most frequent, whereas type "O" blood group was the least frequent in patients who developed SP and SM. (Table 1) Most of the patients had sequential organ failure assessment (SOFA) score of less than 6 (37/86%). In the majority of patients (35/81.4%), the partial pressure of oxygen to fraction of inspired oxygen ratio (P/F) was less than 150, making the diagnosis of ARDS clear. Thirty-nine (90.7%) patients were intubated and ventilated, 12 (27.9%) patients received oxygen via high flow nasal cannula (HFNC), and 27 (62.8%) patients received noninvasive ventilation (NIV) (Table 1). In the majority of patients, the positive end-expiratory pressure (PEEP) was less than 10 cm of H_2O. Thirty-four patients (79%) had low lung compliance of less or equal to 25 mL/cm of H_2O (Table 1). Twenty-nine (67.4%) patients required intercostal drain insertion as a management of their pneumothorax (Table 1).

Twenty-two (52.4%) patients had only pneumothorax (SP), 11 (26.2%) had both pneumothorax and pneumomediastinum (SP and SM), whereas 10 (23.3%) patients had pneumomediastinum only (SM) (Table 2). There was no significant difference in the occurrence of SP and SM according to gender and blood group ($P = .11$ and 0.34,

TABLE 1 Patients' characteristics

Variables		Frequency (n)	Percentage (%)
Gender	Male	42	97.7
	Female	1	2.3
Comorbidities	DM	13	30.2
	HTN	10	23.3
	CAD	2	4.7
	CKD	5	11.6
	CRI	4	9.3
	Hyperlipidemia	3	7
	CLD	1	2.3
	Others	21	48.9
Blood groups	A+	17	39.5
	A−	1	2.3
	B+	11	25.6
	B−	3	7
	O+	10	23.3
	O−	1	2.3
SOFA * score	<6	37	86
	7 to 12	5	11.6
	>12	1	2.3
P/F ratio	<150	35	81.4
	>150	8	18.8
HFNC	12	27.9	
NIV	27	62.8	
Intubation	39	90.7	
Chest drain	29	67.4	
PEEP	None	3	7.0
	≤10	25	58.1
	>10	15	34.9
Lung compliance (mL/cm H_2O)	≥40	3	7.0
	>25	6	14.0
	<25	20	79.0
Mortality	No	21	48.8
	Yes	22	51.2

Abbreviations: CAD, coronary artery disease; CKD, chronic kidney disease; CLD, chronic liver disease; CRI, chronic respiratory illness; DM, diabetes mellitus; HFNC, high flow nasal cannula; HTN, hypertension; NIV, noninvasive ventilation; PEEP, positive end expiratory pressure/cmH$_2$0; SOFA, Sequential organ failure Assessment score.

respectively). The SOFA score on admission was significantly low ($P < .03$) in patients who developed SP, SP + SM, and SM. There was no significant difference in the patient's comorbidities and development of SP, SP + SM, and SM (Table 2). There was no significant difference in the mode of ventilation or respiratory support, namely HFNC, NIV, or intubation and invasive ventilation and development of SP, SP + SM, and SM ($P = .4/.9/.7$ respectively). The level of PEEP was not associated with or increased the risk of development of SP, SP + SM, or SM ($P = .4$) (Table 2). Prone position was not associated with significantly increased risk for development of SP, SP + SM, or

SM ($P = .4$). Lung compliance was significantly low ($P = .05$) in patients developing SP, SP + SM, or SM. Patients developing SP required significantly higher ($P < .001$) chest drain insertion as a therapeutic approach compared to SP + SM or SM (Table 2). The mean age of our patients developing SP, SP + SM, or SM was 51.5 years. The P/F ratio was 115 ± 49.80 (Table 3). Mechanical ventilation days were 25.37 ± 18.4, SOFA score on admission was 3.5 ± 2.44, whereas the worst SOFA score was 11.70 ± 4.49 (Table 3). Our patients' length of intensive care unit (ICU) stay was 39.30 ± 32.09 days and hospital stay was 60.49 ± 55.18 days (Table 3).

TABLE 2   Variables affecting the patients' outcome

Variable		Pneumothorax	Pneumothorax+ Pneumomediastinum	Pneumomediastinum	P value
		22(51.2%)	11(25.6%)	10(23.3%)	
Gender	Male	22(52.4%)	11(26.2%)	9(21.4%)	.11
	Female	0(0.0%)	0(0.0%)	1(3.4%)	
Blood groups	A+	9(52.9%)	6(35.3%)	2(11.8%)	.34
	A−	0(0.0%)	1(100%)	0(0.0%)	
	B+	5(45.5%)	2(18.2%)	4(36.4%)	
	B−	2(66.7%)	1(33.3%)	0(0.0%)	
	O+	6(60.0%)	1(10.0%)	3(30.0%)	
	O−	0(0.0%)	0(0.0%)	1(100%)	
SOFA * score	<6	22(59.5%)	9(24.3%)	6(16.2%)	.03[a]
	7 to 12	0(0.0%)	2 (40.0%)	3(60.0%)	
	>12	0(0.0%)	0(0.0%)	1(100%)	
Comorbidities	DM	7(53.8%)	3(23.1%)	3(23.1%)	.9
	HTN	4(40.0%)	2(20.0%)	4(40.0%)	.3
	CAD	1(50.0%)	1(50.0%)	0(0.0%)	.6
	CKD	2(40.0%)	2(40.0%)	1(20.0%)	.7
	CRI	2 (50.0%)	1(25.0%)	1(25.0%) (25.0%)	.9
	Hyper	2(66.7%)	1(33.3%)	0(0.0%)	.4
	CLD	1(100%)	0(0.0%)	0(0.0%)	
Chest drain		18(62.1%)	11(37.9%)	0(0.0%)	.001[a]
Intubation		19(48.7%)	11(28.2%)	9(23.1%)	.4
P/F ratio	<150	19(44.18%)	8(18.60%)	8(18.60%)	.7
	>150	3(37.5%)	3(37.5%)	2(25.0%)	
NIV		14(51.9%)	7(25.9%)	6(22.2%)	.9
HFNC		6(50.0%)	4(33.3%)	2(16.7%)	.7
Prone position		16(47.1%)	10(29.4%)	8(23.5%)	.4
PEEP	None	3(100%)	0(0.0%)	0(0.0%)	.4
	≤10	11(44.0%)	7(28.0%)	7(28.0%)	
	>10	8(53.3%)	4(26.7%)	3(20.0%)	
Compliance (mL/cm H_2O)	≥40	3(100%)	0(0.0%)	0(0.0%)	.05[a]
	>25	2(33.3%)	4(66.7%)	0(0.0%)	
	≤25	17(50.0%)	7(20.6%)	10(29.4%)	
Mortality		10(45.5%)	7(31.8%)	5(22.7%)	.61

[a]Sequential organ failure Assessment score.
Abbreviations: CAD, coronary artery disease; CKD, chronic kidney disease; CLD, chronic liver disease; CRI, chronic respiratory illness; DM, diabetes mellitus; HFNC, high flow nasal cannula; HTN, hypertension; NIV, noninvasive ventilation; PEEP, positive end expiratory pressure/cm$H_2$0.

TABLE 3   Descriptive statistics

Variable	Number	Mean	Std deviation
Age (years)	43	51.5	13.30
P/F ratio at intubation	43	15.59	49.80
Mechanical ventilation (days)	43	25.37	18.4
SOFA score on admission	43	3.53	2.44
Worst SOFA score	43	11.70	4.49
ICU stay (days)	43	39.30	32.09
Hospital stay (days)	43	60.49	55.18

The mortality in patients complicated by SP + SM or SM was 51.2% (22 Patients) (Table 1), but there was no difference in mortality if patients complicated with SP or SP + SM or SM ($P = .61$) (Table 2).

4 | DISCUSSION

SP was first described by Laennec, and a few years later, Hamman reported a case series in 1939.[4] SP and SM are a rare complication in COVID-19 infection, pneumonia, and acute respiratory distress.[1]

SM is the presence of air in the mediastinum, it can be spontaneous or traumatic, and it can begin or life threatening when the air spread in the mediastinum and pleural cavities, causing pressure on the mediastinal structure leading to hemodynamic collapse.[5] Pathophysiology of occurrence of SM is explained by the Macklin phenomenon. It is the occurrence of a large pressure gradient between the margin of lung alveoli and the lung interstitium, resulting in air escape into the surrounding bronco-alveolar sheath and can extend into the pleural spaces.[6] SP and SM occurred in 1% to 2% of all COVID-19 pneumonia patients and reported that the SP occurs mainly during rest, whereas SM develops once patients start to ambulate or physical activity.[7] SP and SM commonly occur in Males.[8] Male patients were the majority in our study as well.

In our patient population, a majority had SP (51.2%), followed by SP + SM (25.6) and only SM (23.3%). Martinelli et al reported SP frequent in their COVID-19 patients followed by SM (60 and 11 patients, respectively).[9] Noppen and Sahni both reported that asthma, chronic Obstructive pulmonary disease (COPD), and tobacco-chewing are the risk factors for the development of SP and SM.[10,11] In our study, there was no impact on patients' comorbidities on the development of SP or SM or both. Martinelli et al did not find any correlation between the development of SP or SM and the comorbidities.[9] Patients with blood group "A" are at a higher risk of getting COVID-19 infection compared to the other blood groups.[12] In our patients, however, SP and SM occurred more frequently in patients with blood group "A," but there was no significant correlation between the patients' blood group and SP and SM development.

Our patients' disease severity score (SOFA score < 6) was low on admission, the worst SOFA score was higher (11.7) as these patients were complicated with SP and SM.

As described in the literature,[3,9] SP and SM can develop without invasive ventilation, but the majority of the patients were intubated and ventilated. In our study, also most of the patients were intubated and ventilated.

The majority of our patients had ARDS according to the P/F ratio and low lung compliance; this might have triggered the lung parenchymal changes and bullae formation, causing air leak, complicating into the development of SP and SM.[13]

More than 60% of our patients with SP and SM required treatment with intercostal drain insertion and predominantly were with SP. Literature also suggests that both conservative or chest drain guided management for SP and SM in COVID-19 patients.[3,9,13]

The literature describes that COVID-19 pneumonia complicated by the development of SP and SM increases mortality.[3,13] In our patient series, there was increased mortality of COVID-19 patients complicated with SP and SM. There was no significant difference in mortality whether patient complicated with SP or SP + SM or SM. Although Martinelli et al reported lower mortality in their COVID-19 patients complicated with SP and SM and suggested that development of SP and SM will not increase the mortality.[9]

5 | CONCLUSION

COVID-19 pneumonia can complicate into pneumothorax and pneumomediastinum. Our study indicated that patients' gender, blood group, comorbidities, level of PEEP, or prone position did not increase the risk of development of SP and SM in COVID-19 patients. PEEP level and prone positioning were not associated with increased risk of SP or SM. Low lung compliance due to ARDS is a risk factor for the development of SP and SM in COVID-19 patients. SP and SM increase the mortality in COVID-19 patients; there was no significant difference in mortality in patients who developed SP only or SP + SM or SM only.

CONFLICT OF INTEREST
The authors declare that they have no competing interests.

AUTHORS' CONTRIBUTIONS
Conceptualization: Nissar Shaikh, Gamal Al Ameri.
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Data Integrity: The corresponding author confirm that he had full access to all of the data in the study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.
Final Draft Editing: Hazem Daeri.
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All authors read and approved the final manuscript.

CONSENT FOR PUBLICATION
Not applicable.

TRANSPARENCY STATEMENT
This manuscript is an honest, accurate, and transparent account of the study being reported; no important aspects of the study have been omitted; and no any discrepancies from the study as planned have been explained.

DATA AVAILABILITY STATEMENT
All data generated or analyzed during this study are included in this published article.

ETHICS STATEMENT
The project has been approved by the Medical Research Center (MRC) IRB in Hamad Medical Corporation (MRC-01-20-866). The

study has been conducted in accordance with the ethical standards noted in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. No consents were obtained due to the retrospective nature of the study.

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