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Original Research

Factors contributing to the development of pneumothorax and mortality in patients with COVID-19

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Abstract

Aim: Secondary spontaneous pneumothorax is caused by underlying lung disease, while barotraumatic pneumothorax results from mechanical ventilation. SARS-CoV2 (COVID-19) is a disease that is transmitted through droplets and affects many organs such as the lungs, brain, kidney, and liver. The lungs are the most affected organ and have the greatest influence on mortality. In SARS-CoV2 infection, progression of consolidations and expansion towards the upper lobes, the development of pleural or pericardial fluid, the development of lymphadenopathy, the presence of bronchiectasis, the development of cavitation, and pneumothorax are poor prognostic factors. In our study, we aimed to compare factors contributing to the development of pneumothorax in 29 patients who developed pneumothorax during the treatment of COVID-19 infection and follow-up.

Material and Methods: Age, gender, habits, co-morbid diseases, clinical, radiological, laboratory, treatment, mortality and morbidity results of 29 patients who developed pneumothorax during the treatment and follow-up of COVID-19 infection were evaluated. Patients were divided into two groups as deceased (Group1) and surviving (Group 2) patients. The results of the groups were compared.

Results: We found that mean age, lymphocyte elevation, mechanical ventilator applications, length of stay in the intensive care unit, and complication development after thoracostomy were more significant in Group 1 than in Group 2 ($p<0.05$), whereas gender, pneumothorax localization, blood group, Rh differences, and smoking were not significant ($p>0.05$).

Discussion: Although the number and ratio of the comparison criteria included in the study were in favor of Group 1, certain parameters were statistically significant. However, the development of pneumothorax is an important cause of mortality in SARS-CoV2 patients.

Keywords
Pneumothorax, Respiratory System, SARS-CoV2

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Introduction

Pneumothorax is the collection of air between the visceral and parietal pleura. It occurs spontaneously or for acquired reasons. Spontaneous pneumothorax can be classified as primary or secondary pneumothorax. While primary spontaneous pneumothorax that results from spontaneous rupture of a subpleural bleb or bulla occurs predominantly in young and thin males without underlying lung diseases. Secondary spontaneous pneumothorax is due to underlying lung disease, while barotraumatic pneumothorax is caused by mechanical ventilation. While symptoms such as shortness of breath and chest pain may occur, it may also progress to tachypnea, hypoxemia, cyanosis, hypotension, hypovolemia, and shock. Diagnosis is based on the physical examination findings and chest X-ray [1]. Treatment methods include observation, simple needle aspiration, pleural catheter, tube thoracostomy, and surgery [2].

SARS-CoV2 is a disease that is transmitted through droplets and affects many organs such as the lungs, brain, kidney, and liver. The lungs are the most affected organ and has the greatest effect on mortality [3]. The most common clinical findings are fever, dry cough, and fatigue. In severe cases, dyspnea, respiratory failure, and acute respiratory distress syndrome are seen [4].

Although the Real-Time Polymerase Chain Reaction (RT-PCR) test is the gold standard in the diagnosis of the disease, radiological demonstration of lung involvement is very important. However, radiological methods help in the diagnosis and follow-up of the disease [5]. In SARS-CoV2 infection, air bronchograms, vascular enlargements, bronchial dilatations, infiltrations, consolidations, nodular lesions, ground-glass opacities, pneumonia, hemorrhages, focal air bubbles, and pleural and parenchymal fibrotic bands develop in the lungs. Progression of consolidations and expansion towards the upper lobes, pleural-pericardial fluid, lymphadenopathy, bronchiectasis, cavitation, and pneumothorax are poor prognostic factors [6].

We aimed to determine the factors that were effective in the development of mortality in 29 patients who were treated and followed up due to COVID-19 infection and who developed pneumothorax during this period.

Material and Methods

Patients

The study was approved by the ethics committee approval (approval date and number: 03.12.2021/946). Patients who were followed up and treated for COVID-19 infection between 2020-2021 and developed pneumothorax during this period were evaluated retrospectively. Patients with a positive PCR who developed pneumothorax during service or intensive care follow-up and who were treated surgically or medically were included.

Procedures

The patients were divided into two groups as deceased (Group 1; 19) and surviving (Group 2; 10) patients. Age, gender, habits, symptoms, localization of the disease, radiological-laboratory findings, treatment methods, complications, accompanying pathologies, mortality, and morbidity were recorded. The groups were evaluated statistically.

Statistics

IBM SPSS Statistics Base 22.0 program (IBM Corporation, Armonk, NY, USA) was used for data analysis. Continuous variables were expressed as mean±standard deviation, while categorical variables as number-ratio. Homogeneity analysis of variances was performed using Levene's test ($p>0.05$). The Shapiro-Wilk test was used to evaluate the normal distribution ($p>0.05$). The results were evaluated with the Mann-Whitney U and Fisher's exact tests. $P<0.05$ was considered significant.

Results

The total number of patients was 29. There were 19 (65%) patients in Group 1, and 10 (35%) in Group 2. When the groups were compared, the mean age had a significant effect on mortality in Group 1 compared to Group 2 ($p<0.05$). Gender, pneumothorax localization, blood group, Rh differences, and smoking were not significant (p>0, 05) (Table 1).

The complaints of the patients were dyspnea in 20 (69%), deterioration of general condition in 5 (17%), confusion + subarachnoid hemorrhage (SAH) + subdural hematoma (SDH) in 1 (3.5%), confusion + dyspnea + fever in 1 (3.5%), confusion + dyspnea in 1 (3.5%), and dyspnea + deteroration of general condition in 1 (3.5%). In Group 1, 11 (58%) patients had dyspnea, 4 (22%) deterioration of general condition, 1 (5%) confusion + SAH + SDH, 1 (5%) confusion + dyspnea + fever, 1 (5%) confusion+dyspnea, and 1 (5%) dyspnea + general condition

Table 1. Demographic distribution of patients with COVID-19 who developed pneumothorax

Variables	Total; 29	Group 1; 19	Group 2; 10	p-value
Male	21 (72%)	12 (63%)	9 (90%)	0.2008
Female	8 (28%)	7 (37%)	1 (10%)	
Right localization	20 (69%)	14 (74%)	6 (60%)	0.6749
Left localization	9 (31%)	5 (26%)	4 (40%)	
Mean age	59,82 ± 20,31	68,57 ± 5,93	43,2 ± 17,52	0.00124
Blood group A	12 (%41)	7 (37%)	5 (50%)	0.6 (A, B), 1 (A, AB), 0.6562 (A, 0), 0.5 (B, AB), 1 (B, 0), 0.5758 (AB, 0)
Blood group B	6 (21%)	5 (26%)	1 (10%)	
Blood group AB	4 (14%)	2 (11%)	2 (20%)	
Blood group 0	7 (24%)	5 (26%)	2 (20%)	
Rh+	22 (76%)	13 (68%)	9 (90%)	0.3667
Rh-	7 (24%)	6 (32%)	1 (10%)	
Smoking +	21 (72%)	14 (74%)	7 (70%)	1
Smoking -	8 (28%)	6 (26%)	3 (30%)	
Av. length of stay in ICU	14,62 ± 19,71	18,73 ± 21,57	13,5 ± 11,53	0.00308
Av. length of hospital stay	19,13 ± 18,92	22,10 ± 1,53	6,8 ± 13,20	0.12356
Co-morbid disease +	23 (79%)	19 (100%)	4 (40%)	0.0004
Co-morbid disease -	6 (21%)	-	6 (60%)	
Mech. ventilator +	18 (62%)	18 (95%)	0	< 0.00001
Mech. ventilator -	11 (38%)	1 (5%)	10 (100%)	
Culture +	15 (52%)	11 (61%)	4 (40%)	0.4497
Culture -	14 (48%)	8 (39%)	6 (60%)	
Tube thoracostomy +	22 (76%)	16 (84%)	6 (60%)	0.1929
Tube thoracostomy -	7 (24%)	3 (16%)	4 (40%)	
Comp. after TT +	18 (82%)	16 (84%)	2 (20%)	0.0021
Comp. after TT -	4 (18%)	-	4 (40%)	

Av: Average, ICU: Intensive Care Unit, Mech: Mechanical, TT: Tube thoracostomy, Comp: Complication, Hos: Hospital, +: Yes, -: No

deterioration. In group 2, 9 (90%) patients had dyspnea and 1 (10%) had general condition deterioration. When the groups were compared, dyspnea, general condition deterioration, and confusion were found to be more common in Group 1.

The diagnostic method for pneumothorax was mostly chest radiography (Figure 1).

23 (79%) patients had co-morbid diseases. When the groups were compared, the presence of co-morbid disease was more significant and effective in terms of mortality in group 1 than group 2 (p<0.05) (Tables 1, 2).

In laboratory examinations of the patients; When the groups were compared, neutrophil/lymphocyte elevation was more significant in Group 1 than Group 2 and was effective in mortality (p<0.05) (Table 3).

Eighteen (62%) patients underwent mechanical ventilation, while 11 (38%) did not need a ventilator. When the groups were compared, the need for mechanical ventilators was more significant in Group 1 than in Group 2 and was effective in the development of mortality (p<0.05) (Table 1).

While endotracheal aspiration and sputum cultures were positive in 15 (52%), there was no growth in 14 (48%) patients, 7 (24%) with growth had klebsiella and 8 (28%) had acinetobacter (Table 1).

Twenty-two (76%) patients underwent tube thoracostomy for therapeutic purposes, while 7 (24%) did not because of loculated pneumothorax due to adhesions. Complications developed in 18 (82%) patients after tube thoracostomy (TT). Eleven (61%) had prolonged air leak+empyema and 7 (39%) had prolonged air leak; 16 (84%) patients in Group 1 and 6 (60%) patients in Group 2 underwent TT, 11 (69%) patients in Group 1 had empyema+prolonged air leak and 5 (31%) had prolonged air leak, 2 (33%) patients in Group 2 had prolonged air leak. When the groups were compared, the presence of complications was more significant in Group 1 than in Group 2, which was effective in mortality (p<0.05) (Table 1).

While the mean length of stay was 19.13 ± 18.92, the mean duration of hospitalization in the intensive care unit was 14.62 ± 19.71. When the groups were compared, the length of stay in the intensive care unit was more significant in Group 1 than in Group 2, which was effective in mortality (p<0.05) (Table 1).

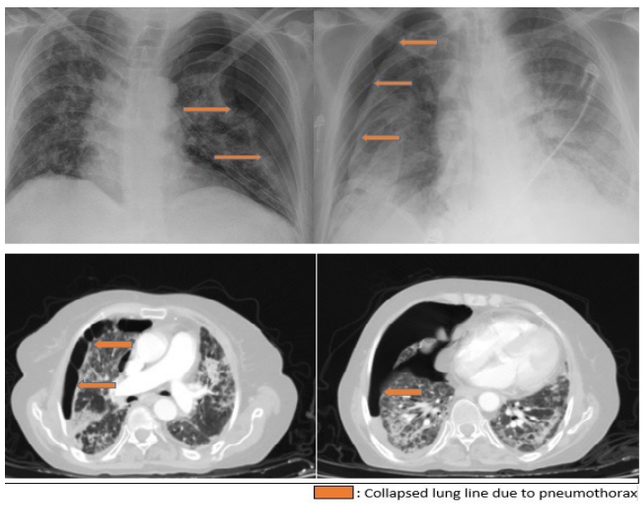

Figure 1. Images of patients who developed pneumothorax

Table 2. Co-morbid diseases of patients with COVID-19 developing pneumothorax

Co-morbid diseases	Total; 29	Group 1; 19	Group 2; 10	p-value
Fibromyalgia+HT+GER	1 (3,4%)	1 (5%)	-	
CKD +CHF+BPH	1 (3,4%)	1 (5%)	-	
HT+COPD+CKD	1 (3,4%)	1 (5%)	-	
AF+HT+DM	2 (7%)	1 (5%)	1 (10%)	
CAD+HT	2 (7%)	2 (10%)	-	
ARF	1 (3,4%)	1 (5%)	-	
Alzheimer+HT	1 (3,4%)	1 (5%)	-	
CAD+ CVD	1 (3,4%)	1 (5%)	-	
CAD+DM+HT	1 (3,4%)	1 (5%)	-	
HT	2 (7%)	1 (5%)	1 (10%)	0.0004
HT+DM	2 (7%)	2 (10%)	-	
HT+AF	1 (3,4%)	1 (5%)	-	
AF	1 (3,4%)	1 (5%)	-	
Histiocytosis X	1 (3,4%)	-	1 (10%)	
CVD	1 (3,4%)	1 (5%)	-	
DM	1 (3,4%)	-	1 (10%)	
CRF	1 (3,4%)	1 (5%)	-	
Alzheimer+HT	1 (3,4%)	1 (5%)	-	
CAD+DM+HT	1 (3,4%)	1 (5%)	-	
NO	6 (21%)	-	6 (60%)	

HT: Hypertension, GER: Gastroesophageal reflux, CKD: Chronic kidney disease, CHF: Congestive heart failure, BPH: Benign prostatic hyperplasia, COPD: Chronic obstructive pulmonary disease, AF: Atrial fibrillation, DM: Diabetes mellitus, CAD: Coronary artery disease, ARF: Acute renal failure, CVD: Cerebrovascular disease

Table 3. Laboratory values of patients with COVID-19 who developed pneumothorax

Variables	Total; 29	Group 1; 19	Group 2; 10	z-score	p-value
Average leukocytes	13,9 ± 6,9	12,75 ± 6,1	16,23 ± 8,3	0.10	0.92
Average. neutrophil	9,7 ± 4,3	8,4 ± 3,4	11 ± 5	0.21	0.82
Average lymphocyte	1,10 ± 0,5	0,94 ± 0,6	1,26 ± 0,4	-0.71	0.47
Average Neut/lymph	11,27 ± 7,4	13,75 ± 6,6	8,39 ± 7,8	2.48	0.01
Average platelet	215,413 ± 90,7	227,36 ± 94,6	192,7 ± 82,6	0.80	0.42
Average hematocrit	36,80 ± 6,6	33,58 ± 6,4	40,03 ± 5,4	-0.12	0.90
Average d-dimer	1783 ± 3492	1563 ± 2690	762,7 ± 419,7	0.64	0.52
Average ferritin	966 ± 775	1091 ± 797,4	729,1 ± 708,6	1.12	0.26
Average sodium	135,68 ± 3,4	135,26 ± 2,9	136,5 ± 4,3	-1.51	0.13
Average chlorine	103,13 ± 4,6	103,05 ± 4,6	103,03 ± 4,9	0	1
Average potassium	4,42 ± 0,7	4,50 ± 0,7	4,21 ± 0,7	0.73	0.45
Average ALT	99,31 ± 353,2	132,26 ± 435,8	36,7 ± 39,1	0.45	0.64
Average AST	180,13 ± 774,2	260,68 ± 955,2	27,1 ± 14,5	1	0.31
Average CRP	97,31 ± 75,4	114,06 ± 70,08	82 ± 81,4	-0.16	0.87
Average lactate	1,96 ± 0,6	2,47 ± 1,3	1,88 ± 0,3	1.33	0.18
Average LDH	420,82 ± 278,3	430,10 ± 280	430,2 ± 289	0.39	0.69

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, CRP: C-reactive protein, LDH: Lactate dehydrogenase, Neut: Neutrophil, lymph; lymphocyte

Discussion

Secondary spontaneous pneumothorax develops secondary to underlying lung disease. Even minimal pneumothorax causes severe respiratory distress in patients due to impaired existing lung functions. Iatrogenic pneumothorax develops after transthoracic or transbronchial needle biopsies, central venous catheter placement, thoracentesis, pleural biopsy, and barotrauma. In our study, one patient in Group 1 had COPD and 18 were mechanically ventilated. All patients had pneumothorax that developed due to secondary reasons after the lung parenchyma damage following COVID-19. Both underlying co-morbid diseases and mechanical ventilator applications were found to be significant in the development of mortality in patients who developed pneumothorax [1].

In COVID-19, the most affected organ is the lung. The clinical course is more severe and fatal in patients with chronic lung or other chronic diseases. Progression of consolidations, enlargement to the upper lobes, pleural-pericardial fluid, lymphadenopathy, presence of bronchiectasis, development of cavitation, and pneumothorax are poor prognostic factors. In such cases, the management of patients hospitalized or requiring intensive care due to COVID-19 becomes more important [6]. In our study, 19 patients in Group 1 and 4 patients in Group 2 had co-morbid diseases. The presence of co-morbid disease was more significant in Group 1 than in Group 2, which was effective in mortality.

Gender and smoking are associated with the severity of the clinical condition in COVID-19. This may be related to the high level of angiotensin-converting enzyme 2, the SARS-CoV-2 receptor, in smokers [11]. Although there are conflicting rates between gender and COVID-19, the high number of smoking in men increases the incidence of COVID-19 [7]. In our study, the mean age was 59.82 ± 20.31 years, and the rate of male patients was 72%, while the rate of female patients was 28%. While male gender and aging were significant in the development of mortality, blood group and Rh differences were not significant in mortality.

Zhang et al. reported the rate of active smoking as 3.4% in 58 severe COVID-19 patients, 0% in 82 non-severe COVID-19 patients, and 3.7% in former smokers [8]. In a case series of 1099 cases, the rate of active smoking was reported as 16.9% and 5.2% in former smokers in severe patients, while it was 11.8% in non-severe patients and 1.3% in smokers. The need for mechanical ventilation and the mortality rate have been reported as 25.5% in active smokers and 7.6% in passive smokers (those exposed to cigarette smoke) [4]. In Liu et al.'s study of 78 cases, a history of smoking was reported in 27.3% in severe patients and 3.0% in the stable group [9]. In many different studies, there has been an association between smoking and COVID-19 [10]. In our study, 14 patients in Group 1 patients were smokers and 7 patients in Group 2 were smokers. Unlike the literature, smoking was not statistically significant in the development of mortality. This may be due to the fact that the study was limited to patients with pneumothorax.

Pneumothorax, pleuritic chest pain, tachypnea, and dyspnea are common findings. Physical examination findings may be normal in mild and moderate pneumothorax [11]. However, moderate or even mild pneumothorax can cause serious problems in patients with underlying lung disease. Vital capacity is reduced in large pneumothoraxes. Tachycardia is the most common finding [12]. The most common complaints in COVID-19 are fever, fatigue, dry cough, anorexia, myalgia, dyspnea, and expectoration. Especially high fever, cough, and dyspnea indicate severe cases and pneumonia [4, 13]. In some studies, the rate of cases showing no clinical symptoms despite PCR positivity was reported as 1% [13]. Fever was reported as the most common symptom. Cough is observed in 2/3 of the cases. Cough is generally described as dry and, less frequently, with expectoration of sputum. Anosmia and hyposmia are reported as early diagnosis findings [13, 14]. In the study of Zhou et al., fever persisted for a median of 12 days (8-13 days), and the cough continued for 19 days [15]. In our study, when the groups were compared , dyspnea, general condition deterioration, and confusion were more important in Group 1.

The diagnosis of pneumothorax is made by chest X-ray. In secondary pneumothorax, the lung may partially collapse due to adhesions between the lung and the chest wall, and loculated pneumothorax is seen on the radiograph. Computed tomography gives nearly 100% results in pneumothorax [16]. In our study, 7 of the patients had loculated pneumothorax.

In COVID-19, the RT-PCR test is the gold standard in diagnosis. Although chest radiography is not sensitive in the early period to show the ground-glass opacity, it should be used as an initial method in young patients. Thin-section thorax computed tomography is important in the early detection and follow-up of the disease [14, 17]. In our patients, the diagnostic method for pneumothorax was mostly chest radiography.

There is no obvious specific laboratory finding in pneumothorax. The most common laboratory findings in Coronavirus disease-19 are lymphocytopenia (83.2%), thrombocytopenia (36.2%), and leukopenia [4]. Elevated C-reactive protein (CRP), liver function tests (ALT/AST), and D-dimer have also been frequently reported [17, 18]. Severe lymphocytopenia, which persisted at initial diagnosis and throughout the disease, was associated with mortality. Elevated D-dimer, serum ferritin, troponin I, and LDH are poor prognostic factors associated with severity and mortality [10, 18-20]. In a prospective study of 61 patients with COVID-19, serious illness and intensive care hospitalization were significant in the group with advanced age (≥50 years) and neutrophil/lymphocyte ratio ≥ 3.13 [21]. In our study, when the groups were compared, lymphocyte/neutrophil ratio and advanced age were found to be more significant, which was effective in mortality ($p<0.05$).

The main purpose of treatment in pneumothorax is to remove the air in the pleural cavity and to prevent recurrences. Tube thoracostomy is the most preferred and applied intervention method. Common complications associated with tube thoracostomy are prolonged air leak, bleeding, diaphragmatic injury, and empyema [2, 12, 16,]. In our study, 16 (%) patients in Group 1 patients and 6 (%) patients in Group 2 patients underwent therapeutic tube thoracostomy, 11 (69%) patients had empyema+prolonged air leak and 5 (31%) had prolonged air leak in Group 1, while 2 patients (33%) had prolonged air leak in Group 2. When the groups were compared, the presence of complications was more significant in Group 1 than Group 2. The mean hospital stay of group 1 was 22.10 ± 21.53 days,

while it was 6.8 ± 13.20 days in Group 2. While the mean length of stay in the intensive care of Group 1 patients was 18.73 ± 21.57 days, it was 13.5 ± 11.53 in Group 2. When the groups were compared, the length of stay in the intensive care unit was more significant in Group 1 than Group 2.

Conclusion

SARS-CoV2 is a disease that causes multiorgan failure but is mostly mortal due to lung damage. Many factors affect the course of the disease. We think that advanced age, comorbid diseases, mechanical ventilator applications, increased length of stay in the intensive care unit, neutrophil/lymphocyte ratios, developed infections and prolonged air leaks after tube thoracostomy are important factors contributing to mortality.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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