A RETROSPECTIVE INVESTIGATION ON THE INCIDENCE, CLINICAL CHARACTERISTICS, AND OUTCOMES OF PNEUMOTHORAX IN HOSPITALIZED COVID-19 PATIENTS IN NORTH-EAST OF ROMANIA

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A RETROSPECTIVE INVESTIGATION ON THE INCIDENCE, CLINICAL CHARACTERISTICS, AND OUTCOMES OF PNEUMOTHORAX IN HOSPITALIZED COVID-19 PATIENTS IN NORTH-EAST OF ROMANIA (Abstract): The COVID-19 clinic ranges from asymptomatic to critical and fatal disease. Pneumothorax and pneumomediastinum are rare complications of COVID-19 infection but can occur at any time during the disease. The **aim** of this retrospective study was to analyze the impact of acute respiratory complications on patients diagnosed with SARS-CoV-2 infection. **Materials and methods:** 177 patients with COVID-19 were recruited to analyze the correlation between pneumothorax and demographics and general data of the patients. **Results:** In our study, pneumothorax or pneumomediastinum was much more frequent among younger, smoking individuals from urban environments. Moreover, the pneumothorax group had statistically significantly higher white blood cells and erythrocyte sedimentation rate values than the control group. The duration of hospitalization in patients who developed pneumothorax was similar to those who did not develop this complication. **Conclusions:** Patients experiencing this consequence had a significantly higher mortality rate compared to those in control groups. Although the precise origins of this complication remain unclear, individuals with preexisting pulmonary dysfunction appear to experience it more frequently. **Keywords:** COVID-19, COMPLICATION, PNEUMOTHORAX, PNEUMO-MEDIASTINUM, RETROSPECTIVE STUDY.

INTRODUCTION

In March 2020, the World Health Organization declared the COVID-19 pandemic. The Coronavirus disease 2019 (COVID-19) cause serious damage to the respiratory system. As a result of this damage air can pass into the intrapleural space or into the mediastinum and pneumothorax or pneumomediastinum can develop. Barotrauma, which includes pneumothorax or pneumomediastinum has been observed as an emerging complication in CODIV -19 patients (1, 2, 3). COVID-19 may cause spontaneous pneumothorax to the many progressive pathological changes in the lungs such as pneumonia, cystic changes or enlargement of blebs. Also, in clinically observed COVID-19 cases pneumothorax can develop without clinical or radiological parenchymal changes in the lung (4). Traumatic pneumo-

thorax results from injury to the pleura, as well iatrogenic pneumothorax result from injury to the pleura during medical procedures. Secondary spontaneous pneumothorax is a pneumothorax that occurs as a complications of underlying lung disease and the primary spontaneous pneumothorax is defined as pneumothorax in a healthy individual. Spontaneous pneumothorax and pneumomediastinum have been described as complications of COVID-19 with a wide incidence from 10% in patients with COVID-19-related acute respiratory distress syndrome, increasing to 24% in patients receiving mechanical ventilation (5). In another study by Geraci et al., the incidence of pneumothorax in COVID-19 was reported as 7.4% (6). Patients experiencing this consequence had a significantly higher mortality rate compared to those in control groups (7). Although the precise origins of this complication remain unclear, individuals with preexisting pulmonary dysfunction appear to experience it more frequently (7). In our study, we aimed to describe the clinical characteristics and outcomes of patients with pneumothorax or pneumomediastinum or both due to COVID-19 pneumonia.

MATERIALS AND METHODS

Study design. Patients were recruited for this retrospective study from the "Sfântul Ioan cel Nou" County Emergency Hospital from Suceava, designated for treating SARS-CoV-2 infections. The study included patients diagnosed with SARS-CoV-2 infection through PCR (polymerase chain reaction) testing from March 2020 to November 2020.

Ethical Approval. The study received approval from the Ethics Committee of the "Sfântul Ioan cel Nou" County Emergency Hospital from Suceava (No. 4/ 27.11.2020).

Patients. In the study interval, out of 28,678 admitted patients, 7,325 were confirmed with a diagnosis of Covid-19. Initially, the study included 113 patients confirmed with Covid-19 infection, pneumothorax, and/or pneumomediastinum. After excluding 7 patients with traumatic pneumothorax and 6 patients with iatrogenic pneumothorax, the study included 100 patients. The diagnosis of pneumothorax or pneumomediastinum was based on clinical symptomatology and confirmed by imaging. In the control group, we included only 77 patients out of 7212 who had a confirmed diagnosis of SARS-CoV-2 infection but no diagnosis of pneumothorax or pneumomediastinum. In the selection of patients for the control group several criteria of similarity were rigorously followed, such as hospital admission in the same period, data regarding the onset of COVID-19 disease, similar symptoms and demographic data such as environment of origin or smoking status. These patients also presented respiratory pathology in association such as chronic obstructive pulmonary disease, bronchiectasis, bronchial asthma or post-tuberculosis lung sequelae, so definite diagnosis of pre-existing lung damage. The inclusion criteria were age over 18 years, a diagnosis of SARS-CoV-2 infection, and pneumothorax. The exclusion criteria were age under 18, pregnant individuals, and the negation of a Covid-19 diagnosis.

Statistical analysis. The data analysis was realized using *SPSS version 23.0* (Statistical Package for the Social Sciences, Chicago, Illinois). For continuous variables, the data were presented as median with interquartile range or as mean ± standard deviation (SD). For categorical variables, the data were presented as the

number of cases with percent frequency. Continuous normally distributed variables were compared by Independent Samples t-Test in case of two samples, or by One-Way ANOVA, in case of comparisons of more than two samples. Categorical comparisons were performed by Fisher's exact test or by Chi-square test.

RESULTS

Thus, we have enrolled in our study 177 patients (100 in the pneumothorax / pneumo-mediastinum group and 77 in the control group). Regarding the general characteristics of the two populations, we have observed that the patients included were predominantly males from urban area. There were no significantly statistical differences regarding the age of the two groups. Regarding the educational status, we can observe that most of the included individuals had a medium level of education, followed by the ones with high education.

Regarding the employee status, again no statistically significant differences could be observed, but it worth mentioning that the majority of them were retired, followed by full-time workers. Moreover, we can observe that in the pneumothorax group there was a higher prevalence of smoking and a lower BMI, compared to the control group (tab. I).

TABLE I.

General characteristics of the study groups

General characteristics		Pneumothorax Group (n = 100)	Control Group (n = 77)	p
Gender n (%)				
	Male	56 (56.0%)	49 (63.6%)	0.355
	Female	44 (44.0%)	28 (36.4%)	
Living environment, n (%)				
	Rural	41 (41.0%)	25 (32.5%)	0.275
	Urban	59 (59.0%)	52 (67.5%)	
Age, years (mean ± DS)		59.98±13.95	64.11± 15. 18	0.066
Education status, n (%)				
	No education	10 (10.0%)	2 (2.6%)	0.070
	Medium level of education	40 (40.0%)	51 (66.2%)	0.001
	High level of education	32 (32.0%)	23 (29.9%)	0.870
	Unspecified	18 (18.0%)	1 (1.3%)	0.000
Employee status, n (%)				
	Household	8 (8.0%)	3 (3.9%)	0.353
	Full-time	43 (43%)	28 (36.4%)	0.440
	Retired	49 (49%)	46 (59.7%)	0.173
Alcohol consumption, n (%)		4 (4.0%)	1 (1.3%)	0.389
Smoking, n (%)		41 (41.0%)	23 (29.9%)	0.083
BMI (kg/m^2)		25.06 (22.40; 32.00)	27.98 ±5.14	0.157
Days of hospitalization (mean± SD)		14.00 (8.75; 18.25)	13.37±7.05	0.070

The prevalence of COVID-19 infection types within the pneumothorax group, where the moderate form exhibited the highest prevalence, succeeded by the severe form, and the mild type was the least frequent. In contrast, the control group showed the highest prevalence in the severe form, followed by the moderate and mild types (tab. II).

TABLE II.
Types of the COVID-19 infection within the study groups

Type of disease	Pneumothorax Group (n = 100)	Control Group (n = 77)	p
Mild	19	13	0.844
Moderate	42	30	0.758
Severe	39	34	0.539

When evaluating the symptomatology of the patients, we observed statistically significant differences regarding nausea, ageusia, anosmia, myalgia, and asthenia, these symptoms being more frequent in the pneumothorax group compared to the control group. Regarding the cough, we can observe that the dry one was more prevalent in the pneumothorax group compared to the control group. Statistical significance was also observed for almost all the classes of dyspnea (tab. III).

TABLE III.
Associated symptomatology in the two studied groups

Symptomatology		Pneumothorax Group (n = 100)	Control Group (n = 77)	p
Nausea		26 (26.0%)	7 (9.1%)	0.006
Vomiting		4 (4.0%)	5 (6.5%)	0.505
Ageusia		24 (24.0%)	3 (3.9%)	0.000
Anosmia		25 (25.0%)	6 (7.8%)	0.003
Myalgia		63 (63.0%)	24 (31.2%)	0.000
Headache		60 (60.0%)	16 (20.8%)	0.000
Asthenia		87 (87.0%)	42 (54.5%)	0.000
Thoracic pain		46 (46.0%)	30 (39.0)	0.363
Cough	Dry	64 (64.0%)	37 (48.1%)	0.401
	Productive	10 (10.0%)	17 (22.1%)	0.042
Dyspnea	MRC 0	17 (17.0%)	25 (32.5%)	0.021
	MRC 1	29 (29.0%)	9 (11.7%)	0.006
	MRC 2	25 (25.0%)	18 (23.4%)	0.861
	MRC 3	21 (21.0%)	8 (10.4%)	0.067
	MRC 4	8 (8.0%)	17 (22.1%)	0.009

We can observe that in the pneumothorax group there are statistically significant higher values of the while blood cells and erythrocyte sedimentation rate compared

to the control group. Moreover, it worth mentioning that the number of platelets, urea and creatinine were higher in the pneumothorax group compared to the control, but without statistical significance (tab. IV).

TABLE IV.

Laboratory tests in the two studied groups

Laboratory values	Pneumothorax Group (n = 100)	Control Group (n = 77)	p
WBC	10.52 ± 4.12×10^3/mm^3	7.77 ± 3.62 ×10^3/mm^3	0.000
PLT	256.66 ± 96.38	219.00 (161.50; 309.00)	0.318
ESR	99.50 (78.00; 124.00)	59.81 ± 39.35	0.000
CRP	11.64 (3.31; 24.15)	20.18 (6.64; 45.56)	0.422
Urea (mg/ dL)	45.00 (34.00; 62.75)	38.00 (29.30; 62.55)	0.606
Creatinine (mg/ dL)	0.90 (0.74; 1.24)	0.89 (0.68; 1.20)	0.101
GFR (ml/min/1.73 m^2)	78.86± 33.65	84.05 ± 28.14	0.315

WBC – white blood cells, PLT – platelets, ESR – erythrocyte sedimentation rate, CRP – C reactive protein, GFR – glomerular filtration rate

DISCUSSION

The study aimed to quantify the number of patients who developed pneumothorax following SARS-CoV-2 infection and identify the risk factors that caused the development of sars-cov-2. In our study, the incidence of SARS-CoV-2 infection was 25.46% among patients hospitalized at the "Sfântul Ioan cel Nou" County Emergency Hospital Suceava, from March 2020 to February 2021. In addition, the incidence of pneumothorax in patients with COVID-19 was 1.36%. Studies reveal that patients with this infection encounter pneumothorax much more frequently than those with other respiratory infections, with an incidence of 10% among those with severe forms of the disease (2). In the cases included in the study, the incidence of pneumothorax was approximately the same for both moderate (42%) and severe (39%) forms of the disease, but without significant statistical significance. On the other hand, data from the literature show strong correlations between the severe form of the disease and the occurrence of complications such as pneumothorax (9).

Moreover, a systematic review published in 2020, which included 9 observational studies, highlights that the rate of pneumothorax would be higher among men (10, 11, 12). This can also be observed among the patients included in our study (56% *vs.* 44%). One possible cause for this difference between sexes is that smoking is more common among men. Regarding the symptoms, patients most frequently presented to the hospital with dyspnea (83%), myalgia (63%), headache (60%), asthenia (87%), anterior chest pain (46%), and dry cough (64%).

Smoking is a well-known risk factor for respiratory diseases. The patients included in the study with pneumothorax had a much higher smoking rate than the control group (41% vs. 29.9%). Still, there was no statistically significant correlation between smoking and this complication arising from SARS-CoV-2 infection. Even though smoking is considered an emerging risk

factor for pulmonary pathologies such as chronic obstructive pulmonary disease, studies in the literature have failed to identify a correlation between this habit and the occurrence of pneumothorax in patients with COVID-19 (12, 13).

The urban environment is another risk factor involved in the development of pneumothorax in COVID-19 patients. It seems that existing pollution, lifestyle, sedentary behavior, and diet-factors predominant in cities-negatively influence the progression of COVID-19. From a future perspective, this idea should be further explored to see if the number of pneumothorax cases is higher in industrialized cities compared to smaller towns (14).

Increased white blood cell counts and inflammatory markers like CRP and ESR indicate an inflammatory status, which prolongs the healing period of lung infections and increases the risk of complications (15). In the case of patients monitored at the "Sfântul Ioan cel Nou" County Emergency Hospital Suceava, it is observed that both white blood cells and ESR have a much higher value among patients with pneumothorax, while the CRP value is lower in these patients.

Throughout the pandemic, several studies have emerged highlighting that obese patients were much more prone to complications associated with SARS-CoV-2 infection than normal-weight patients. Abdominal adipose tissue predominantly hinders respiratory movements, leading to greater respiratory effort. Furthermore, obesity is considered a factor that maintains the inflammatory status, promoting the occurrence of numerous complications (16). However, our study did not find a statistically significant correlation between BMI and the occurrence of pneumothorax.

Another particularity of our study would be the duration of hospitalization, although pneumothorax typically results in a higher number of hospitalization days, the two groups showed no statistically significant differences (10).

CONCLUSIONS

Since 2020, infection with the SARS-CoV-2 virus has caused numerous deaths due to associated complications. One of the most severe complications encountered in these patients was pneumothorax, which led to an increased length of hospitalization and, consequently, to exposure to the risk of developing superadded respiratory infections or even those associated with medical procedures. In our study, it seems that this complication was much more frequent among younger, smoking individuals from urban environments.

CONFLICT OF INTEREST AND FUNDING

The authors declare that there is no conflict of interest, and they received no specific funding.

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