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The influence of pneumothorax, pneumomediastinum, and other factors on the mortality and morbidity in patients with viral infections

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Abstract

Aim: This study examines the effects of pneumothorax and pneumomediastinum on the mortality and morbidity of patients with respiratory virus infections. It analyses blood parameters and the Systemic Immune Inflammation Index (SII) in patients who acquired these complications compared to those who did not.

Materials and Methods: We conducted a retrospective assessment of 2246 COVID-19 patients who received treatment at our medical facility between August 2020 and February 2021. This study included a total of 118 patients who were admitted to the hospital due to a respiratory virus illness. The patients were categorised into two groups: one consisting of individuals who experienced pneumothorax and/or pneumomediastinum, and the other consisting of individuals who did not acquire these complications. Both groups had an equal number of participants. The study analysed many factors including metabolic profiles, hemogram results, length of hospital stay, SII levels, and the incidence of pneumothorax, with a focus on their association with morbidity and mortality outcomes.

Results: Significantly, female patients who experienced pneumothorax during COVID-19 treatment exhibited a worse mortality rate. Patients with pneumothorax had elevated leukocyte and neutrophil counts, along with heightened systemic immune-inflammation index (SII) and decreased levels of total protein and albumin. The data highlight the potential importance of specific blood measurements, as well as the presence of pneumothorax, as indications for death in patients with respiratory virus infections.

Conclusion: For enhanced patient outcomes, it is important to closely monitor and manage female patients who get pneumothorax after receiving therapy for respiratory virus infection.

Introduction

Coronaviruses are a specific category of viruses that have a positive polarity, are enclosed, and consist of a single-stranded ribonucleic acid (RNA). These viruses are responsible for causing diseases that affect the respiratory and gastrointestinal systems [1]. The COVID-19 illness, caused by the SARS-CoV-2 virus, was initially discovered in Wuhan, China in 2019. Coronaviruses replicate by attaching to angiotensin-converting enzyme-2 (ACE-2) receptors, enabling them to permeate the mucosa of the upper and lower respiratory tract [3]. Consequently, patients commonly display symptoms such as coughing, fever, chest pain, and tiredness. Significantly, in the initial phases of the pandemic, there was a rise in lung complications among patients, leading to a substantial surge in the utilisation of continuous positive airway pressure (CPAP) and mechanical ventilator devices for managing respiratory failure. This trend has led to a rise in the frequency of complications, particularly pneumothorax and pneumomediastinum [4].

Pneumothorax refers to the buildup of air or gas in the pleural space. The classification consists of three distinct subcategories: spontaneous, traumatic, and iatrogenic. Primary spontaneous pneumothorax, which refers to the collapse of the lung without any identifiable reason, and secondary spontaneous pneumothorax, which occurs owing to an underlying lung condition, are classified into two subcategories. Primary spontaneous pneumothorax typically occurs when a subpleural emphysematous bleb in the upper section of the lung ruptures. Iatrogenic pneumothorax can occur as a result of an invasive procedure or when a patient who is intubated and on a mechani-

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cal ventilator is subjected to elevated ventilator pressures. Pneumomediastinum refers to the occurrence of air within the mediastinum. It is observed in adult patients and newborn infants who are alive. Typically, it is a harmless and naturally resolving ailment. Pneumomediastinum can be caused by issues in the pharynx, tracheobronchial tree, or oesophagus. When there is a significant rise in pressure within the small air sacs of the lungs, called alveoli, the surrounding blood vessels can burst and air can leak into the tissue surrounding the blood vessels, causing a separation of the area in the middle of the chest known as the mediastinum.

Pneumothorax is commonly managed with tube thoracostomy, but pneumomediastinum is frequently managed conservatively. In the initial phases of the COVID-19 epidemic, a significant number of patients who were admitted to the hospital needed urgent care. The mortality rate for these patients was as high as 61.5% [5]. Consequently, the identification of risk factors for mortality in patients receiving intensive care and the implementation of targeted interventions have become crucial strategies for reducing COVID-19-related deaths. Blood tests, an essential diagnostic tool for assessing the severity of several medical conditions, have also demonstrated their utility in quantifying the extent of COVID-19 infection [6]. In addition to measuring neutrophil, lymphocyte, platelet, and monocyte counts, the systemic immune inflammation index (SII), which is generated by multiplying platelet, neutrophil, and lymphocyte counts, has demonstrated potential in predicting the prognosis of illnesses [7]. Research conducted in clinical settings has identified a correlation between the intensity of COVID-19 infection and the composition of immune system cells and proinflammatory cytokines [8]. This study aims to investigate the impact of SII, blood parameters, pneumothorax, and pneumomediastinum on the mortality and morbidity of COVID-19-infected patients. It specifically focuses on differentiating between patients who experienced these complications and those who did not.

Materials and Methods

This study has been approved by the non-invasive clinical research ethics committee (Fırat University Non-invasive Research Ethics Committee, decision No.2021-01-18, dated January 14, 2021) and the Ministry of Health's general directorate of health services scientific research platform (decision No. 2020-12-19T16-06-06, dated December 21, 2020). Furthermore, the patient or the patient's family has given written informed consent for the utilisation and disclosure of patient data. The study adhered to the criteria outlined in the Helsinki Declaration.

Data gathering: A retrospective assessment of medical records was performed on a total of 2,246 patients who received COVID-19 infection treatment at our institution between August 16, 2020, and February 16, 2021 Patients with positive SARS-CoV-2 polymerase chain reaction (PCR) test results from oropharyngeal and nasopharyngeal swab samples, as well as 118 patients with multifocal ground glass opacities and peripherally distributed consolidation patterns on tomography images, were included [9]. Patients whose COVID-19 diagnosis lacked clinical clarity and whose PCR findings failed to establish infection were excluded from the research.

Upon admission to the hospital with a COVID-19 infection, 118 patients were categorised into two categories. Group 1 consisted of 59 patient who experienced complications during their therapy, such as pneumothorax, pneumomediastinum and subcutaneous emphysema. Group 2 comprised 59 patients who were admitted to the hospital for viral infection but did not experience pneumothorax, pneumomediastinum and subcutaneous emphysema during their treatment. In both groups, we assessed the occurrence of pneumothorax and pneumomediastinum, intubation status, length of stay in the general ward and intensive care unit, laboratory results, and the systemic immune inflammation index (SII). The objective of the study was to examine the influence of these factors on the rates of death and illness during the course of treatment.

Statistical analysis

Data were meticulously analyzed using SPSS for Windows, version 22.0 (SPSS Inc., Chicago, IL, USA). The assumption of normality for continuous variables was assessed by the Kolmogorov-Smirnov test, supplemented by visual inspection of histograms and Q-Q plots for a more comprehensive evaluation. The Levene test was employed to verify the homogeneity of variances, ensuring the appropriateness of subsequent parametric tests. Continuous data were expressed as mean ± standard deviation (SD) for variables conforming to a normal distribution and as median with interquartile range (IQR) for those exhibiting skewed distributions. Categorical data were summarized using frequencies and percentages.

For comparisons involving continuous data, the Student's t-test was utilized for variables with normal distributions and homogeneity of variances between two independent groups. In contrast, the Mann-Whitney U test was reserved for variables that did not satisfy these conditions. Pearson's chi-square or, where necessary due to small expected cell counts, Fisher's exact tests were applied to examine the associations between categorical variables.

To elucidate the relationships between risk factors and clinical outcomes, both univariate and multivariate logistic regression analyses were conducted. The multivariate model was constructed using variables with p-values less than 0.10 in the univariate analysis to capture potential predictors. A stepwise backward elimination process was used to refine the model, with the retention of variables based on the likelihood ratio test with an entry and removal significance level set at $p<0.05$ and $p>0.10$, respectively. For all inferential statistics, a 2-tailed significance level of $p<0.05$ was considered statistically significant.

Several potential hypotheses are as follows:

1. A correlation exists among categorical variables.
2. Risk factors exert a substantial impact on clinical outcomes.
3. Specific factors exhibit substantial predictive power towards the outcome variables within the framework of multivariate logistic regression.

Results

With a mean age of 64.9% and ages ranging from 32 to 97, 118 patients were admitted to the hospital due to the COVID-19 infection. Of these patients, 59 were named group 1, with complications such as pneumotorax, pneumomediastinum and subcutaneous amphysema. Group 2 consisted of 59 patients who did not develop these complications. The length of hospitalisation varied from 1 to 55 days. 115 of these patients required treatment in the intensive care unit, compared to three who were attended to in the main ward. In the pneumothorax group, comprising 32 patients, the average time since admittance until intubation was 8.2 days; four patients remained unventilated during this time. Out of the total count, 22 patients who presented to the emergency room with respiratory failure due to pneumothorax required immediate admission to the intensive care unit; of these, only one needed intubation. In addition, after an average of 7.7 days, eleven of fourteen pneumothorax patients admitted to the general ward were transferred to the intensive care unit. Three patients remained who did not require acute care. The pneumothorax group exhibited an average duration of stay of 6.5 days in the general ward, contrast with a critical care unit stay of 17 days.

Within the control group, a total of 24 patients underwent intubation around 5.8 days following their admission to the hospital. As a result of requiring critical care, these patients were transferred to the intensive care unit after spending an average of 3.7 days on the general ward. Their average stay in the intensive care unit was 15.2 days. The average hospitalisation time for this group was 17.2 days.

A total of 28 out of 36 patients (78%) who experienced pneumothorax and pneumomediastinum as a result of COVID-19 treatment unfortunately passed away. On the other hand, five patients (14%) were released after making a satisfactory recovery, while three patients (8%) were transferred to different hospital facilities. Table 1 provides comprehensive data regarding the issues that arose in these people.

Out of the total number of patients, ten experienced right pneumothorax, five experienced left pneumothorax, and two experienced bilateral pneumothorax. Thirteen patients diagnosed with pneumothorax underwent tube thoracostomies, whereas four patients with mild pneumothorax were managed conservatively by oxygen therapy. The thoracic drains of patients who underwent tube thoracostomies were typically removed after an average of 5.4 days.

Table 2 presents a juxtaposition of patient data from the pneumothorax group and the control group. All patients with pneumothorax exhibited elevated blood glucose levels, with certain individuals seeing a doubling of their values. Urea levels, leukocyte counts, neutrophil counts, SII values, and death rates in COVID-19 patients with pneumothorax exhibited a substantial increase compared to the control group. However, total protein and albumin levels were significantly lower in these patients (Table 3).

A univariate logistic regression analysis was conducted (Table 4) to determine the parameters that contribute to the probability of pneumothorax in COVID-19 patients. Potential risk factors for pneumothorax in COVID-19 patients include decreased levels of total protein and albumin, as well as increased leukocyte counts, neutrophil counts, and SII values. Only factors with p-values less than 0.10 were considered in the multivariate logistic regression analysis. The resulting findings are presented in the table below. The multivariate analysis utilising the

Table 1. Complication distribution in patients.

Complications in patients		Patients, n(%)	Deceased patients, n(%)
Isolated	Right pnx	2 (3.4%)	0
	Left pnx	1 (1.7%)	0
	Pneumomediastinum	2 (3.4%)	2 (100%)
	Sce	4 (6.8%)	2 (50%)
Pnx + Sce	Bilateral pnx + Sce	1 (1.7%)	1 (100%)
	Sağ pnx + Sce	4 (6.8%)	0 (0%)
Pnomomediastinum +	Right pnx	3 (5.1%)	2 (66.7%)
	Left pnx	1 (1.7%)	1 (100%)
	Sce	21 (35.6%)	16 (76.2%)
	Bilateral pnx + Sce	2 (3.4%)	1 (50%)
	Left pnx+ Sce	7 (11.9%)	6 (85.7%)
	Right pnx + Sce	11 (18.6%)	10 (90.9%)
Total		59	41(69.5%)

Pnx, pneumothorax; Sce, subcutaneous emphysema.

Table 2. Shows the patient data from the two groups.

Groups	Subgroups	Patients (n=59)	Control (n=59)
Age, mean±SD (minimum-maximum)		63.8 (33-97)	66 (32-93)
Age groups	20-40 years	3 (5%)	4 (6.7%)
	41-60 years	21 (35.5%)	17 (28.8%)
	61-80 years	29 (49.1%)	30 (50.8%)
	>80 years	6 (10.1%)	8 (13.5%)
Gender	Male	35 (59.3%)	27 (45.8%)
	Female	24 (40.7%)	32 (54.2%)
Number of days stay in	Hospital	19	17.2
	Service	4.8	3.6
	Intensive care	17.6	15.1
Blood parameters	Glucose (mg/dl)	204	185
	Urea (mg/dl)	75.1	64
	Creatinine (mg/dl)	1.00	1.14
	Total protein(g/dl)	57.03	63.5
	LDH (U/L)	508.9	507
	Ferritin (µg/L)	539.8	490.7
	CRP (mg/L)	107.4	135
	Procalcitonin (µg/L)	0.77	0.62
	D-dimer (µg/ml)	2.64	2.07
	WBC $x10^9$/L	14.74	12.48
	Lymphocyte $x10^9$/L	0.81	0.88
	Neutrophil $x10^9$/L	14.54	10.87
	Platelets $x10^9$/L	262.4	277.9
SII		8123	5255
Died patients		41 (69.5%)	19 (32.2%)

Pnx, pneumothorax; LDH, Lactate dehydrogenase; CRP, C-reactive protein; WBC, White blood cells; SII, Systemic Immune Inflammatory Index.

Table 3. The comparison of patient data from two groups.

Data		Patient (n=59)	Control (n=59)	p
Gender, n(%)	Female	24(40.7%)	32(54.2%)	0.140
	Male	35(59.3%)	27(45.8%)	
Age, X±SD		63.86±14.29	65.86±14.26	0.440
Length of stay in	Hospital, med(IQR)	18(15)	16(10)	0.357
	Service, med(IQR)	4.5(4.5)	3(3)	0.276
	Intensive care, med(IQR)	16(14)	13(10)	0.256
Intubation day, med(IQR)		5(8)	5(5.5)	0.921
Day of discharge or ex, med(IQR)		16(24)	16(10)	0.260
Mortality, n(%)	Surviving	18(30.5%)	40 (67.8%)	<0.001
	Ex	41(69.5%)	19 (32.2%)	
Blood parameters	Glucose (mg/dl), med(IQR)	179(109)	162 (105)	0.117
	Urea (mg/dl), med(IQR)	64(41)	54.2 (33.6)	0.015
	Creatinine (mg/dl), med(IQR)	0.8(0.55)	0.85 (0.62)	0.081
	Total protein(g/dl), X±SD	57.04±7.98	63.53±5.14	<0.001
	Albümin(g/dl), X±SD	27.60±4.69	31.32±3.39	<0.001
	Laktat dehidrogenaz(U/L) (LDH), med(IQR)	449(288)	455(303)	0.590
	Ferritin (µg/L), med(IQR)	420.5(675)	450(408)	0.422
	D-dimer (µg/ml), med(IQR)	1.5(1.64)	1.15(1.82)	0.164
	Leukocyte x10^9/L(WBC), med(IQR)	13.6(6)	11.1(9)	0.028
	Lymphocyte x10^9/L (Lym), med(IQR)	0.56(0.5)	0.63(0.48)	0.162
	Neutrophil x10^9/L (Neu), med(IQR)	12(5.94)	9.21(7.8)	0.016
	Platelets x10^9/L (Plt), X±SD	262.4±118.22	277.8±119.31	0.483
SII, med(IQR)		5136.5(7761.5)	3893.5(5680.5)	0.045

Continuous variables are expressed as either the mean ± standard deviation (SD) or median (interquartile range) and categorical variables are expressed as either frequency (percentage). Continuous variables were compared with student t test or mann whitney u test, and categorical variables were compared using Pearson's chi-square test or fisher exact test. Statistically significant p-values are in bold. SD, Standart deviation; LDH, Laktat dehidrogenaz; SII, Systemic Immune Inflammatory Index.

Table 4. Logistic regression analysis for risk variables for pneumothorax.

Pnx	Univariate Logistic Regression					Multivariate Logistic Regression				
	Wald	p	OR	%95 CI for OR		Wald	p	OR	%95 CI for OR	
				Lower	Upper				Lower	Upper
Age	0.584	0.445	0,990	0.965	1.016					
Gender(ref:female)	2.161	0.142	1.728	0.833	3.585					
Glucose (mg/dl)	1.110	0.292	1.002	0.998	1.006					
Urea (mg/dl)	2.002	0.157	1.007	0.997	1.017					
Creatinine (mg/dl)	0.830	0.362	0.814	0.522	1.268					
T.protein (g/dl)	18.06	<0.001	0.860	0.802	0.922	13.24	<0.001	0.820	0.737	0.913
Albumin (g/dl)	16.72	<0.001	0.793	0.709	0.886	3.886	0.049	0.840	0.707	0.999
LDH (U/L)	0.003	0.958	1.000	0.998	1.002					
Ferritin (µg/L)	2.429	0.119	1.001	1.000	1.002					
D-dimer (µg/ml)	1.148	0.278	1.081	0.939	1.244					
Leukocyte x10^9/L	3.110	0.078	1.055	0.994	1.120	0.100	0.752	1.021	0.898	1.160
Lymphocyte x10^9/L	0.115	0.735	0.940	0.659	1.342					
Neutrophil x10^9/L	3.984	0.046	1.065	1.001	1.132	0.445	0.505	1.039	0.928	1.164
Platelets x10^9/L	0.499	0.480	0.999	0.996	1.002					
SII	5.936	0.015	1.001	1.000	1.002	3,056	0.080	1.001	1.000	1.002

Wald Test statistics; OR odds radio; CI, Confidence interval. Statistically significant p-values are in bold. Pnx, pneumothorax; LDH, Laktat dehidrogenaz; SII, Systemic Immune Inflammatory Index.

Enter approach identified reductions in total protein and albumin as variables that increase the risk of pneumothorax in COVID-19 patients. The study found that an elevation in SII was identified as a risk factor for pneumothorax, although it was only considered marginally significant ($p<0.10$).

A further study using univariate logistic regression was conducted to examine the factors that influence mortality.

Table 5. Univariate logistic regression analysis for factors hypothesized to influence mortality.

Mortality	Univariate Logistic Regression					Multivariate Logistic Regression				
	Wald	p	OR	%95 CI for OR		Wald	p	OR	%95 CI for OR	
				Lower	Upper				Lower	Upper
Age	0.032	0.857	0.998	0.973	1.023					
Gender(ref:female)	4.101	0.043	0.467	0.224	0.976	8.602	0,003	0.226	0.084	0.611
Pnx	15.595	<0.001	4.795	2.203	10.440	8.890	0.003	4.962	1.731	14.224
Glucose (mg/dl)	3,916	0.048	1.005	1.000	1.009	0.951	0.329	1.003	0.997	1.009
Urea (mg/dl)	4.838	0.028	1.012	1.001	1.023	0.215	0.643	1.003	0.990	1.016
Creatinine (mg/dl)	0.057	0.811	1.053	0.690	1.607					
T.protein (g/dl)	10.359	0.001	0.908	0.856	0.963	0.017	0.897	0.994	0.913	1.083
Albumin (g/dl)	12.970	<0.001	0.830	0.750	0.918	3.121	0.077	0.875	0.755	1.015
LDH (U/L)	2.352	0.125	1.001	1.000	1.003					
Ferritin (µg/L)	2.456	0.117	1.001	1.000	1.002					
D-dimer (µg/ml)	0.261	0.610	1.036	0.904	1.188					
Leukocyte $x10^9$/L	0.517	0.472	1.020	0.966	1.078					
Lymphocyte $x10^9$/L	1.932	0.165	1.382	0.876	2.179					
Neutrophil $x10^9$/L	1.309	0.252	1.028	0.980	1.078					
Platelets $x10^9$/L	0.696	0.404	0.999	0.996	1.002					
SII	0.013	0.910	1.000	1.000	1.000					

Wald, test statistics; OR, odds radio; CI, Confidence interval; Statistically significant p-values are in bold. LDH, Laktat dehidrogenaz; SII, Systemic Immune Inflammatory Index.

The results are presented in Table 5. The univariate investigation identified several variables that were shown to be associated with an increased risk of death. These variables include female gender, pneumothorax, high glucose levels, elevated urea levels, and decreased total protein and albumin levels. The statistical analysis showed a significance level of p=0.10 for these associations. The factors were subsequently examined in a multivariate logistic regression analysis, and the results are presented in the table below. By employing the Enter approach in multivariate analysis, it was found that being female and having a pneumothorax were identified as variables that increase the risk of death. Additionally, a reduction in albumin levels was determined to be a factor that has a borderline significant influence (with a p-value between 0.05 and 0.10) on the risk of mortality.

Discussion

Coronavirus infections, particularly COVID-19, have recently garnered global attention, as the virus's level of aggression has been gradually diminishing. COVID-19 poses a significant threat, particularly to the older population, who have underlying chronic illnesses and weakened immune systems [10]. The COVID-19 infection can manifest with a diverse array of clinical signs, ranging from those without any noticeable symptoms to cases with severe illness. Around 14-17% of individuals will get acute respiratory distress syndrome (ARDS), while approximately 5% may develop septic shock or multiple organ failure [11]. This study found that death rates in the pneumothorax group were significantly higher, and levels of leukocytes, neutrophils, urea, and the Systemic Immune Inflammation Index (SII) were also significantly greater compared to the control group. In addition, the total protein and albumin levels of these patients were significantly lower compared to the control group. Protein and albumin levels in patients may decrease as a result of various factors, such as decreased appetite, nausea and vomiting, systemic inflammation related to sickness, and some medications used in treatment. Pneumothorax, characterised by the presence of air in the pleural space due to leaking from the lungs, is a rare complication in COVID-19 patients. It occurs more frequently in individuals with a history of severe disease, especially when mechanical ventilation is employed. Pneumothorax is a notable consequence in individuals with COVID-19 and may be linked to a heightened likelihood of mortality. Nevertheless, variations in sample sizes and research methodology across different studies in this field may lead to inconclusive findings.

This study focuses on a particular group of people and a specific period of the COVID-19 pandemic, providing valuable insights on how COVID-19 complications have changed over time. During this specific time period, there is a distinct chance to closely monitor alterations in the virus's path and the efficacy of medical interventions. Most previous studies have not investigated the correlation between the Systemic Immune-Inflammation Index (SII) and the occurrence of pneumothorax and pneumomediastinum in COVID-19 patients. Therefore, our study's examination of the potential of SII as a prognostic indicator is significant. This technique has the potential to enhance our comprehension of the influence of inflammation and immune response on disease outcomes. The present study undertakes a comprehensive investigation of a wide range of blood parameters in relation to the outcomes of pneumothorax and pneumomediastinum. Our research indicates that there is a higher likelihood of death when levels of total protein and albumin are lower. This discovery highlights a gap in the existing body of knowledge. Our study examines the gender disparities in death rates after the occurrence of pneumothorax in individuals with COVID-19. The elevated mortality rate observed in female patients, as indicated by our data, brings attention

to a facet that has not been adequately investigated in previous studies.

In 2021, Amit Chopra and colleagues documented that approximately 13% of COVID-19 patients who were on mechanical ventilation experienced pneumothorax. Furthermore, these patients exhibited a greater mortality rate in comparison to those who did not develop pneumothorax [12]. Furthermore, Woon H. Chong and colleagues reported a mortality rate of 74.2% in individuals with COVID-19 who also had pneumothorax [13]. Our study found that persons with pneumothorax experienced a more severe clinical progression and a higher mortality rate (69%) compared to the control group (32%). In addition, COVID-19 patients receiving treatment in the critical care unit had an average duration of respiratory support of around 13 days, accompanied by a mortality rate of approximately 67% [14]. In our study, the average duration of intubation in the pneumothorax group was 13.5 days, and the death rate was 69.5%.

Fever, cough, and shortness of breath are prevalent clinical manifestations in individuals with COVID-19. Blood tests often reveal a decline in lymphocyte and eosinophil levels, accompanied by an increase in leukocyte and neutrophil counts. Elevations in C-reactive protein (CRP), lactate dehydrogenase (LDH), aspartate aminotransferase (AST), and alanine aminotransferase (ALT) levels have been observed [15,16]. We observed elevated leukocyte and neutrophil levels, along with decreased lymphocyte levels, namely in the pneumothorax group, consisting of 28 patients. A majority of patients in the pneumothorax group exhibited elevated levels of CRP, ALT, and AST, whereas most of them had decreased levels of glucose, D-dimer, ferritin, urea, and albumin.

The univariate logistic regression analysis in this investigation identified female gender, pneumothorax, elevated glucose and urea levels, and decreased total protein and albumin levels as potential risk factors associated with mortality in COVID-19 patients. The variables with p-values of 0.10 in the initial logistic regression analysis were subsequently included in the multivariate logistic regression analysis. The results revealed that being female and having a pneumothorax were factors that increased the risk of mortality. Additionally, low albumin levels were found to have a borderline significant impact on mortality risk, with a p-value between 0.05 and 0.10. Multiple studies have indicated that being female is associated with a higher risk of mortality in individuals with COVID-19. Takahashi T et al. conducted a study on 1,099 individuals with COVID-19 and found that the mortality rate was higher among female patients compared to male patients [17]. A further study revealed that females infected with COVID-19 exhibited a more pronounced immunological reaction compared to males, potentially leading to more severe symptoms of the illness [18]. The underlying factors contributing to this gender gap in outcomes, however, remain partially unknown and necessitate further investigation.

Chen T. et al [19] found that elevated levels of glucose, urea, creatinine, and LDH, together with decreased levels of total protein and albumin, were associated with a higher likelihood of mortality in COVID-19 patients. A further investigation revealed that elevated concentrations of urea, creatinine, lactate dehydrogenase, and glucose, together with diminished levels of total protein and albumin, were linked to a heightened likelihood of mortality [20].

Pneumomediastinum is a medical condition characterised by the accumulation of air in the mediastinal region, which typically resolves spontaneously. Pneumomediastinum, similar to pneumothorax, is a rare occurrence in COVID-19 patients, but it can happen in extreme cases, especially in individuals who need mechanical ventilation. The precise method by which pneumomediastinum develops remains unknown. However, it is believed that air is released from ruptured alveoli, which occurs due to increased fragility of the surrounding tissues. This air then travels through the sheath that surrounds the bronchial and vascular structures, eventually accumulating in the mediastinal region [21,22].

Although pneumothorax affects only 1% of COVID-19 patients, the occurrence of both pneumothorax and pneumomediastinum is higher in COVID-19 patients who require intubation [23,24]. COVID-19 patients have an elevation in coughing episodes, heightened respiratory effort in the lungs, and a higher reliance on positive pressure ventilation. These factors are believed to be contributing factors to the rise in pneumothorax and pneumomediastinum cases in these patients [25]. Animal studies have demonstrated that coughing can cause inflammation in the airways, specifically neutrophilic airway inflammation, and can also lead to stress and damage in the respiratory tract epithelium due to increased sensitivity to coughing [26]. This article is limited in that it solely focuses on patients with viral respiratory tract infections who experienced complications such as pneumothorax or pneumomediastinum.

It is important to note that patients with mild pneumonia who are being monitored at home after initial diagnosis may also experience pneumothorax and pneumomediastinum as the disease progresses. The occurrence of pneumothorax, pneumomediastinum, and subcutaneous emphysema in individuals with COVID-19 can result in the destruction and spontaneous rupture of the alveoli. Additionally, positive pressure air from respiratory support equipment can also induce damage and rupture of the alveoli. Individuals afflicted with COVID-19 pneumonia experience the onset of respiratory failure. The patients' condition aligns with the ARDS criteria established by the Berlin criteria [27]. In such instances, the suggested mechanical breathing therapies for ARDS are advised. The recommended ventilation strategy for ARDS is pulmonary protective ventilation, regardless of the mechanism of ventilation used.7.8 Pneumoprotective ventilation aims to achieve sufficient oxygenation while minimising the risk of ventilator-induced lung injury [28].

The Systemic Immune Inflammation Index (SII) is a valuable metric that utilises a ratio to assess the severity of disease and predict the prognosis of COVID-19 patients. High SII readings may be associated with severe disease and a poorer prognosis, making SII an important indicator for monitoring and managing COVID-19 patients. Research findings indicate that persons with elevated SII levels, decreased albumin levels, increased ferritin levels,

and lymphopenia are more likely to experience worsened illness progression, higher chances of being admitted to the critical care unit, the need for intubation, and a higher mortality rate [29].

To summarise, our analysis has identified specific characteristics associated with the occurrence of pneumothorax and pneumomediastinum in COVID-19 patients. These include reduced levels of total protein and albumin, elevated counts of leukocytes and neutrophils, and increased SII values. These issues exacerbate respiratory and circulatory ailments, deteriorating the overall health of patients and raising the likelihood of mortality. Significantly elevated levels of urea, neutrophils, leukocytes, and SII, especially in individuals with pneumothorax, substantially raise mortality rates. It is crucial to closely monitor patients for these symptoms in order to promptly intervene and provide therapy.

Moreover, our research indicates that gender, namely female gender, may influence the probability of experiencing pneumothorax while infected with COVID-19. Therefore, closely observing female patients, including their nutritional status and blood parameters, could enhance therapy results.

Conclusion

In conclusion, it is necessary to continuously monitor these indicators and tailor treatment choices in order to assess the impact of pneumothorax and pneumomediastinum on the morbidity and mortality of COVID-19 patients. This study underscores the significance of further research and practical implementations in this domain.

Ethical approval

Ethical approval was received for this study from Fırat University Non-Interventional Clinical Research Ethics Committee (session date: 14.01.2021, session number: 2021/01-18).

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