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Characteristics of Lung Patients Diagnosed with COVID-19 Pneumonia in the Intensive Care Unit and Their Effects on Prognosis

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ABSTRACT

Introduction: There is no clear evidence of an increased risk of coronavirus disease-2019 (COVID-19) infection in chronic obstructive pulmonary disease (COPD) and asthma. However, COPD patients diagnosed with COVID-19 have a high risk of mortality. No significant effects of COVID-19 have been demonstrated on mortality in asthma patients. In the present study, the purpose was to retrospectively examine the effects of the asthma and COPD diagnosis of patients hospitalized in the intensive care unit (ICU) with the diagnosis of COVID-19 pneumonia on prognosis.

Methods: The study was designed in a retrospective and descriptive design. Among the patients who were diagnosed with COVID-19 pneumonia and hospitalized in our ICU between March 11, 2020-January 31, 2021, all patients who had a history of COPD and/or asthma were included in the study. Invasive mechanical ventilation (IMV) durations, ICU stays, and 28-day mortality rates of the patients were recorded from the hospital information system.

Results: A total of 276 intensive care patients diagnosed with COVID-19 were examined. The frequency of the presence of COPD or asthma was determined as 8.69% (n=24) and 4.35% (n=12), respectively. Although IMV was applied to 25% (n=6) of COPD patients at the time of admission to the ICU, IMV was not applied to any of the asthmatic patients. The duration of hospitalization was 15 (9-30) days in COPD patients and 15 (13-24) days in asthma patients. Mortality was 75% (n=18) in patients with COPD and 25% (n=3) in patients with asthma.

Conclusion: In this retrospective analysis, the incidence of asthma and COPD in patients with COVID-19 was found to be similar to the literature data. The length of stay in the ICU was similar in asthma and COPD patients and was longer compared to other studies. COPD patients with COVID-19 pneumonia had higher IMV and mortality rates than asthma patients.

Keywords: COVID-19, chronic obstructive pulmonary disease, asthma, mortality rate

Introduction

Coronavirus disease-2019 (COVID-19) pandemic appeared in Wuhan, China toward the end of 2019. The novel type of coronavirus that caused the pandemic was named severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) (1). It attaches to type 2 pneumocytes through the angiotensin converting enzyme-2 (ACE-2) receptors, enters the cells and creates infection after viral replication (2). COVID-19 pneumonia causes hyperinflammation and hypercoagulability and resulting in acute respiratory distress syndrome (3). It was reported in previous studies that it also causes approximately 4.5 million mortality worldwide, and this number is increasing with each passing day (4). It was shown that there is a relationship with clinical outcomes such as length of hospital stay, duration of mechanical ventilation, and mortality and patient characteristics such as age, gender, and comorbidities in the COVID-19 pandemic (5).

Chronic obstructive pulmonary disease (COPD) and asthma cause respiratory dysfunction by impairing lung functions and gas exchange. It is already known that asthma and COPD are common lung diseases in our society (6). Inter-country differences in the incidence of COVID-19 in these lung diseases were reported in previous studies, which also showed that the rates of COPD patients who contracted COVID-19 ranged from 2.0% to 17.7%. In their study, Leung et al. (7) reported that the release of ACE-2 is also high in COPD patients. It was also reported that both severe respiratory failure symptoms were seen more frequently and the mortality rate was higher in COVID-19 patients with COPD, while a systematic review and meta-analysis conducted in asthmatic patients

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reported that it did not cause increased mortality rates (7,8). Although it is known that asthma and COPD increase mortality in intensive care units (ICU), there are a limited number of intensive care studies on how COVID-19 progresses in asthma and COPD patients (7,9). In the present study, the purpose was to examine patients with COPD and asthma, which were reported to cause increased mortality in the ICU in patients hospitalized in the ICU with the diagnosis of COVID-19 pneumonia.

Methods

The study was approved by the University of Health Sciences Turkey, İzmir Tepecik Training and Research Hospital Clinical Research Ethics Committee (approval number: 2023/06-18, date: 13.07.2023).

The study had a retrospective and descriptive design. Among the patients who were diagnosed with COVID-19 pneumonia hospitalized in our ICU between March 11, 2020-January 31, 2021, all patients who had a history of COPD and/or asthma were included in the study, which was conducted in accordance with the Declaration of Helsinki Principles. Patients who were suggestive of COVID-19 both clinically and in imaging and who had positive real-time polymerase chain reaction test results were included in the study. Those with a diagnosis of malignancy and younger than 18 years were excluded from the study. Demographic data of the patients, clinical findings, laboratory parameters, Acute Physiology and Chronic Health Evaluation II (APACHE II) scores, data on non-invasive mechanical ventilation (IMV)/IMV applications, drug treatments, length of stay in ICU, and 28-day mortality rates were recorded from the hospital data system.

Statistical Analysis

The data were analyzed with the SPSS 22.0 statistical package (SPSS, USA) and were presented as number of cases, percentage, or median (median-minimum and maximum). A p-value <0.05 was considered statistically significant.

Results

A total of 276 patients with COVID-19 pneumonia were reviewed for the study, and 28 patients were found to have a history of COPD and asthma. Three patients had an additional diagnosis of malignancy, and one patient was younger than 18 years. These 4 patients were excluded from the study, and 24 patients were included. A total of 24 (8.69%) of the patients had COPD and 12 (4.35%) had asthma (Table 1). When the patient's age was evaluated, the median age of patients with COPD was 77 (73-80), and the age of patients with asthma was 68.5 (57-75). Among the patients diagnosed with COPD, 19 (79.1%) were male and 5 (20.9%) were female. Two (16.7%) patients with asthma were male and 10 (83.3%) were female. The APACHE II score of asthma patients was 16.0 (10-22) and 16.5 (11-22) in COPD patients. The time elapsed between the onset of symptoms and admission to the ICU was recorded as 6 (3-8) days in COPD patients and 9 (8-15) days in asthma patients. The patients were also evaluated in terms of accompanying chronic diseases. In COPD patients, hypertension was detected in 13 (54%), diabetes mellitus (DM) in 8 (33%), heart disease in 12 (50%), cancer in 1 (4%), chronic liver disease in 3 (12%), and chronic kidney disease in 1 (4%) patient. In asthma patients, hypertension was detected in 7 (58%), DM in 4 (33%), heart disease in 1 (8%), cancer in 1 (8%), chronic liver disease in 1 (8%), and chronic kidney disease in 0 (0%) patients. Hypertension was the most common comorbidity in both COPD and asthma patients. The second most common comorbidity was heart disease in COPD patients, a and DM patients with asthama. The duration of hospitalization was 15 (9-30) days in COPD patients and 15 (13-24) days in asthma patients. Regarding the respiratory support treatments of COPD patients admitted to the ICU, 16 (66%) received oxygen only, 2 (8%) received NIV or high-flow oxygen treatment, and 6 (25%) received IMV treatment. Similarly, when respiratory support treatments of asthma patients were evaluated during hospitalization, there were 10 (83%) patients who received oxygen only, 2 (16%) patients who received NIV or high-flow oxygen treatment, and 0 (0%) patients who received IMV treatment. When the IMV treatments received by the patients during admission to the ICU were evaluated, there were 6 (25%) COPD patients and no patients who received IMV during admission with asthma. When re-evaluated on the 7th day in terms of the IMV treatments received, it was found that 19 (82%) of the hospitalized patients received IMV treatment. Although this rate was 15 (83%) in COPD patients, it was found in 4 (80%) patients with asthma (Table 1).

When the medical treatments received for COVID-19 were evaluated, the frequency of medical treatment in patients with COPD was favipiravir (Toyama Chemical, Japan) in 20 (83%) patients, steroid (Dexamethasone-Decort, Deva Holding, Turkey) in 16 (66%) patients, convalescent plasma in 11 (45%) patients, and tocilizumab (Hoffmann-La Roche and Chugai, Japan) in 3 (12%) patients. The frequency of medical treatment in asthmatic patients was favipravir in 10 (83%) patients, steroid in 8 (66%) patients, convalescent plasma in 6 (50%) patients, and tocilizumab in 1 (8%) patient (Table 1).

When 28-day mortality was evaluated in both groups, mortality was 75% (n=18) in patients with COPD and 25% (n=3) in patients with asthma (Table 1).

The laboratory parameters of the patients during hospitalization are given in Table 2. C-reactive protein (CRP), lactate dehydrogenase (LDH), D-dimer and troponin values, which are widely accepted as mortality predictors for COVID-19, were higher in the COPD patient group (Table 2).

Discussion

This retrospective descriptive study was conducted on patients with COPD and asthma who were admitted to the ICU because of COVID-19 and obtained two important results. The first important point was that the incidence of COPD and asthma among patients with COVID-19 was substantial and similar to other studies in the literature. In studies conducted in Italy and New York including hospitalized patients, it was reported that the incidence of COPD varied between 2.4% and 14% in patients with a diagnosis of COVID-19 (7,9) The frequency of asthma shows significant differences between countries. It was shown that this rate was approximately 1-1.5% in China, and 5-6% in Spain, Brazil, Israel and Switzerland (10). Another remarkable point was the high mortality rate in COPD patients in our cohort. In another retrospective study that included hospitalized patients similar to our study, the mortality of patients with COVID + COPD was reported as 46.34% (11).

Table 1. General characteristics of the patients

	COPD and asthmatic patients (n=36)	Patients with asthama (n=12)	Patients with COPD (n=24)
Age, year	75 (69-79)	68.5 (57-75)	77 (73-80)
Gender (female/male)	15 (23.8%)/21 (86.2%)	10 (83.3%)/2 (16.7%)	5 (20.9%)/19 (79.1%)
APACHE II	16.50 (11-22)	16 (10-22)	16.5 (11-22)
The number of days between symptom onset and admission to intensive care unit	7 (5-10)	9 (8-15)	6 (3-8)
Concomitant chronic diseases			
Hypertension	20 (55%)	7 (58)	13 (54)
Diabetes mellitus	12 (33%)	4 (33)	8 (33)
Chronic heart disease	13 (36%)	1 (8)	12 (50)
Cancer	2 (5%)	1 (8)	1 (4)
Chronic liver disease	4 (11%)	1 (8)	3 (12)
Chronic kidney disease	12)	0 (0)	1 (4)
Respiratory support treatment on admission (n, %)			
Oxygen only	26 (72%)	10 (83)	16 (66)
NIMV and/or HFNC	4 (11%)	2 (16)	2 (8)
IMV	6 (16%)	0 (0)	6 (25)
Other treatments			
Favipiravir	30 (83%)	10 (83)	20 (83)
Steroid	24 (66%)	8 (66)	16 (66)
Convalescent plasma	17 (47%)	6 (50)	11 (45)
Tocilizumab	4 (11%)	1 (8)	3 (12)
Patients who received IMV on the 7th day in the intensive care unit [n=23, (%)]	19 (82%)	4 (80)	15 (83)
28-day mortality			
Yes/no (%)	21/15 (58%)	3 (25)	18 (75)
The length of the stay in intensive care unit (days)	12 (8-20)		
The length of stay in hospital (days)	15 (10-30)	15 (13-24)	15 (9-30)

COPD: Chronic obstructive pulmonary disease, APACHE II: Acute Physiology and Chronic Health Evaluation II, NIMV: Non-invasive mechanical ventilation, HFNC: High-flow nasal cannula, IMV: Invasive mechanical ventilation

Table 2. Laboratory values of the patients at admission

	All patients (n=36)	Patients with asthama (n=12)	Patients with COPD (n=24)
Hemoglobin (g/dL)	11.9 (10.4-13.3)	11.8 (10.5-12.2)	12.2 (10.4-14.4)
Neutrophil (/µL) $\times 10^9$	8.5 (5.8-11.0)	7.05 (3.6-9.2)	9.2 (6.3-12.7)
Lymphocyte (/µL) $\times 10^9$	0.50 (0.40-0.70)	0.5 (0.5-0.7)	0.5 (0.32-0.70)
Creatinine (mg/dL)	1.2 (1.0-1.7)	1.0 (0.6-1.2)	1.5 (1.0-2.0)
C-reactive protein (mg/L)	163 (97-221)	118 (72-210)	132 (68-199)
Procalcitonin (ng/mL)	0.19 (0.11-0.26)	0.22 (0.16-0.26)	0.15 (0.11-0.26)
Lactate dehydrogenase (U/L)	518 (341-781)	513 (347-537)	628 (302-827)
D-dimer (µg/L)	1540 (640-3710)	1030 (522(1825)	1830 (830-4170)
Troponin (ng/L)	22 (8-164)	9.5 (7-23)	89 (10-674)
Blood lactate level (mmol/L)	1.4 (1.1-2.1)	1.5 (1.1-1.8)	1.3 (1.1-2.4)
pO_2 (mmHg)	66 (47-75)	53 (45-66)	68 (47-80)
pCO_2 (mmHg)	41 (32-48)	43 (38-51)	39 (31-45)
pH	7.38 (7.28-7.47)	7.48 (7.34-7.49)	7.36 (7.25-7.40)

COPD: Chronic obstructive pulmonary disease, pO_2: Partial oxygen pressure, pCO_2: Partial carbon dioxide pressure

Although COVID-19 causes approximately 3.4 percent mortality worldwide, mortality is higher in critically ill patients in need of an ICU (12,13). In a systemic review and meta-analysis of Alqahtani et al. (14), it was reported that patients with COPD diagnosis as a comorbidity had more severe COVID-19 infection and mortality rates were higher than those without COVID-19. It is also emphasized that high mortality may occur because of vascular damage and thrombosis in COPD patients (13). SARS-CoV-2 uses ACE-2 as a receptor for intracellular entry (2). It is already known that the excretion of ACE-2, which is used as a receptor, is high in COPD patients, and although this is considered to be one of the reasons for the high mortality rate, it has not yet been proven (8). It was shown that COVID-19 does not cause increased mortality in patients with asthma (9).

In their meta-analysis, Fang et al. (15) reported that although the frequency of COPD among those with COVID-19 was between 2.0% and 17.7% (average around 2-4%), it was found to be higher at 8.6% in our patient cohort. This can be explained by the fact that our hospital was declared as a pandemic hospital (ward and intensive care) since the early period of the pandemic and that there was a chest diseases center nearby. Although it is a matter of debate why the prevalence of COPD was low in the current pandemic, it was emphasized that it may be because of the disease itself or its treatment modality. However, these remained at the level of hypotheses and could not be proven (13). In previous studies conducted with hospitalized patients with serious diseases, the frequency of asthma was shown to vary between 0.9% and 9% (16,17), but the frequency of asthma was found to be 4.3% in our cohort, which is consistent with the literature data.

The time between symptom onset and ICU admission was found to be consistent with the mean time (6-12 days) reported in the literature in COPD patients (18). Our rate of IMV application during admission to the ICU was found to be higher compared to the literature data (18). This may be because of ICU admission during the period when patients deteriorated to the point of intubation because of limited ICU beds. There was no patient who needed IMV at the time of ICU admission in our asthma patients.

It was reported in a systematic review that the length of stay in COPD patients was 8 days (19). In the present study, the reason why the hospital stay was longer in both asthma and COPD patients compared to the literature data can be explained by the admission of patients requiring ICU admission during the period when they deteriorated to the point of intubation because of limited ICU beds. A significant rate of our cohort had additional chronic diseases. We think that this may be a reason for the longer length of stay.

Hypertension, DM, and chronic heart disease were the most common comorbidities in both patient groups. In the literature, it has been shown that these additional diseases frequently accompany COVID-19 (5). The prevalence of chronic heart disease may be one of the reasons for the high mortality rate, especially in patients with COPD.

When the additional treatments applied because of COVID-19 were evaluated, it was seen that the favipravir treatment was used in almost all patients. This can be explained by the direct inclusion of favipravir treatment in the COVID-19 Treatment Guideline of the Ministry of Health until recently. The small cohort group that did not receive this treatment was in the period before favipravir entered the treatment guideline.

The second most common treatment seems to be steroids. It is seen that approximately two-thirds of the patients are administered steroids. The RECOVERY Collaborative Group conducted a randomized controlled trial of dexamethasone in hospitalized patients with COVID-19 and reported that 28-day mortality was lower in the dexamethasone group than in the usual care group (20). After their study, dexamethasone (or equivalent methylprednisolone) was included in the treatment guide of the Ministry of Health. This treatment was not given to one-third of patients because some of the patient cohort coincided with the period before the study of the RECOVERY Collaborative Group.

Convalescent plasma treatment was used as a part of treatment in many studies and was recommended in the treatment guide of the Ministry of Health in the early period of the COVID-19 pandemic. Convalescent plasma treatment was used in approximately half of our patients in both cohorts (21,22). In the current situation, the frequency of use has decreased significantly because of the debate about its effectiveness and the fact that it is not recommended to be given outside of a certain period (i.e., the first 5-7 days of the disease).

Low lymphocyte, CRP, troponin, LDH, and D-dimer elevation are shown to be predictors of poor prognosis in COVID-19 patients. Laboratory data were also found to be compatible with the literature in this study cohort. The current situation develops secondary to the inflammation caused by COVID-19 (17,19). Ferritin, which is also considered as an acute phase reactant, was shown to increase in COVID-19 infection and its height will be evaluated as a predictor of mortality (17). In the present study, ferritin values were not studied in the majority of our patients at admission to the ICU, and therefore, they could not be presented as data.

Study Limitations

The limitations of the study were that it had a retrospective and single-center design. However, although it was single-center, it included the evaluation of 276 tertiary intensive care patients.

Conclusion

The frequency of COPD and asthma is high in patients hospitalized in ICU because of COVID-19. High mortality and IMV rates were found in patients with COPD during intensive care. A closer follow-up of these patient groups is important. Further studies are needed to elucidate the etiology of poor prognosis in COPD patients.

Ethics Committee Approval: The study was approved by the University of Health Sciences Turkey, İzmir Tepecik Training and Research Hospital Clinical Research Ethics Committee (approval number: 2023/06-18, date: 13.07.2023).

Informed Consent: Retrospective study.

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