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Evaluation of Patients Treated in Intensıve Care Due to COVID-19: A Retrospective Study

Gökhan Kılınç iD **and Aslı Akcan Atasoy** iD

Department of Anesthesiology and Reanimation Intensive Care, Balıkesir Atatürk City Hospital, Balıkesir, Turkey

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Corresponding Author:
Gökhan Kılınç, MD
Department of Anesthesiology and Reanimation, Atatürk City Hospital, Gaziosmanpaşa Mahallesi, 209. Sok. No:2 6, 10100 Altıeylül/Balıkesir, Turkey.
Tel: +90-266-460-4000
Fax: +90-266-460-4045
Email: gkilinc35@hotmail.com

ORCID iDs
Gökhan Kılınç iD
https://orcid.org/0000-0001-7979-6993
Aslı Akcan Atasoy iD
https://orcid.org/0000-0001-8524-6904

Conflict of Interest.
No conflict of interest.

ABSTRACT

Background: The aim of this study is to report the demographic characteristics, clinical features, treatment protocols, comorbidities, imaging findings, prognosis and factors affecting mortality in critically ill patients with coronavirus disease 2019 (COVID-19) in the intensive care unit.

Materials and Methods: This retrospective cohort study consists of adult (≥18 years old) patients hospitalized in a tertiary hospital intensive care unit of with COVID-19. The independent effects of possible factors identified in previous analyzes on survival were analyzed using univariate and multivariate logistic regression analysis.

Results: The mean age of all patients was 70.2 ± 13.9 years. Of the 200 patients, 139 (69.5%) had died. White blood cells ($19.2 ± 76.1 × 10^9$ per L), neutrophil/lymphocyte ratio (15.4 ± 65.1), d-dimer (2,558.4 ± 4,574.2 ng/mL), ferritin (1,481.2 ± 4,447.4 µg/L) and C-reactive protein (CRP) (12.1 ± 11.9 mg/dL) levels were high at the time of admission. According to the results of univariate regression analysis; presence of additional disease (odds ratio [OR]: 3.837; $P = 0.015$), older age (OR: 1.027; $P = 0.015$), reverse transcriptase-polymerase chain reaction (RT-PCR) positivity (OR: 2.58; $P = 0.019$), higher heart rate (OR = 1.027; $P = 0.028$), higher APACHE II score (OR: 1.049; $P = 0.012$), higher sequential organ failure assessement (SOFA) score(OR: 1.479; $P = 0.014$), high d-dimer levels (OR: 3.180; $P < 0.001$) and high CRP levels (OR: 1.035; $P = 0.028$) increases the risk of death. When patients with full data for all variables in the multivariate logistic regression model were evaluated; positive RT-PCR (OR=4.105; $P = 0.005$), older age (OR: 1.033; $P = 0.024$), higher heart rate (OR: 1.042; $P = 0.006$), higher (SOFA) score (OR: 1.477; $P < 0.001$), high d-dimer levels at admission (OR: 3.459; $P = 0.002$) and diabetes mellitus (OR: 3.433; $P = 0.035$) increase the risk of death.

Conclusion: Mortality of critically ill patients with COVID-19 pneumonia was high (69.5%). Older patients and acute respiratory distress syndrome were at higher risk of death. High SOFA score, high d-dimer at admission, and presence of diabetes mellitus were associated with high mortality.

Keywords: COVID-19; Prognosis; Intensive care unit; RT-PCR, APACHE

INTRODUCTION

More than 500 million people in the world have been diagnosed with coronavirus disease 2019 (COVID-19) and more than 6 million patients have died. In Turkey, the diagnosis of COVID-19 has reached fifteen million and the number of deaths has reached one hundred thousand [1]. Patients infected with COVID-19 may present with symptoms ranging from mild to severe and a large proportion of the population is asymptomatic carriers. The most common initial symptoms of COVID-19 are cough, fever, fatigue, headache, myalgia, and diarrhea [2, 3]. Severe illness usually begins about 1 week after the onset of symptoms. Dyspnea is the most common symptom of severe disease and often accompanies hypoxemia [2, 4].

Approximately 5 - 15% of patients with COVID-19 infection require intensive care surveillance and respiratory support. Intensive care units (ICUs) have an important role in the management of most of these patients, but the mortality rate in this group is high. Mortality is even higher in patients who need invasive mechanical ventilator therapy [5]. Most patients with severe COVID-19 have lymphopenia and some have thromboembolic complications as well as central or peripheral nervous system disorders [6-8]. Severe COVID-19 can also cause of acute organ damage in addition to cardiac arrhythmias, rhabdomyolysis, coagulopathy and shock [9]. These organ failures may be associated with clinical and laboratory manifestations of inflammation, including high fever, thrombocytopenia, hyperferritinemia, and high levels of C-reactive protein (CRP) and interleukin-6 [10]. Patients should have chest radiographs and usually show bilateral consolidations or ground glass opacities [11].

In this report, we aimed to explain the demographic characteristics, comorbidities, treatment protocols, clinical outcomes and factors affecting mortality of critically ill patients admitted to the ICU of our hospital due to COVID-19.

MATERIALS AND METHODS

1. Study design

This retrospective cohort study consists of adult patients (≥18 years old) hospitalized in the ICU of Balıkesir Atatürk City Hospital. All adult patients diagnosed with COVID-19, according to World Health Organization (WHO) guidance, were screened and included those who died or were discharged between 1 April 2020 (*i.e.*, when the first patients were admitted) and 1 July 2020.

Patients with COVID-19 infection or clinically and radiologically confirmed COVID-19 infection admitted to adult ICUs were included in the study. The researchers analyzed only the anonymized data.

The case definition was made according to the definitions of the WHO COVID-19. WHO suggests that COVID-19 be suspected in patients with acute respiratory illness and fever, plus travel to or residence in a location reporting community transmission, or contact with a confirmed or probable COVID-19 case in the 14 days before symptom onset; and in patients with severe acute respiratory illness who require hospitalisation without an alternative diagnosis that fully explains the clinical presentation.
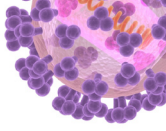
A confirmed case of COVID-19 was identified by a positive result on the reverse transcriptase-polymerase chain reaction (RT-PCR) test or rapid antibody test of a sample collected from a nasopharyngeal swab or endotracheal aspirate. During Severe acute respiratory syndrome coronavirus 2 RT-PCR, we used Bio-speedy RT-qPCR kit (Bioeksen, İstanbul, Turkey), that detects Orf1ab (N genes) (FAM) and RNaseP (internal control) (HEX). Patient data were obtained from electronic data stored in software on hospital computers.

2.Ethics statement

Ethical clearance for this study was obtained from the Balıkesir University Faculty of Medicine Institutional Review Board (IRB number is KY-2020–01.01) and the need for informed consent was waived by the committee. And also necessary permissions were obtained from Republic of Turkey Ministry of Health for the study.

3. Data collection

The files of all patients over the age of 18 who were hospitalizedd in the ICU with a prediagnosis of COVID-19 were scanned retrospectively. Demographic data such as age and sex, chronic diseases, laboratory values (blood cell count, neutrophil/lymphocyte ratio, international normalized ratio (INR), aspartate aminotransferase, alanine aminotransferase, d-dimer, creatinine, lactate, ferritin, fibrinogen, CRP, procalcitonin, radiological findings (Computed tomography and chest X-ray), acute physiologic assessment and chronic health evaluation (APACHE)-II and the sequential organ failure assessment (SOFA) scores, vital signs (heart rate, respiratory rate, blood pressure) at admission to the ICU, RT-PCR results, need for mechanical ventilation, length of stay in the ICU, 28-day survival and exit status from the ICU were examined. To identify COVID-19 infection, respiratory samples, including nasal and pharyngeal swabs, were collected from all patients at admission and during their stay. The data were obtained from the data processing center and analyzed by anonymization.

Sepsis and septic shock were defined and managed according to established guidelines [12] and Republic of Turkey Ministry of Health recommendations for the treatment of COVID-19 patients [13].

4. Statistical analysis

Statistical analyses were performed using statistical software (SPSS 25.0, IBM Corporation, Armonk, Chicago, IL, USA). Descriptive statistics were used to summarize the data; results are reported as means and standard deviations. Categorical variables were summarized as numbers and percentages. Conformity of continuous variables to normal distribution was examined. Student's t-test was used for the comparison of normally distributed variables in 2 independent groups, and the Mann Whitney U-test was used for non-normally distributed variables. The difference in frequency between the groups was compared using the chi-square and fisher test. The independent effects of possible factors identified in previous analyzes on survival were analyzed using univariate and multivariate logistic regression analysis. $P < 0.05$ was considered statistically significant. Significant in univariate analyzes, P-value close to type 1 error value (with $P = 0.25$ cut off value) and correlation matrix of regression coefficients below 0.6; age, comorbidity, renal replacement therapy, presence of nodules in computerized tomography, diagnosis, contact history, pulmonary disease, diabetes mellitus, hypertension, RT-PCR positivity and d-dimer, APACHE II score, SOFA score, respiratory rate, fever, heart rate, lymphocyte, CRP values were included in the multivariate analysis.

RESULTS

1. Epidemiological and clinical manifestations

Between April 1 and July 1, 2020; a total of 1,443 patients with a prediagnosis of COVID-19 were hospitalized in our hospital. 200 adult patients (18 years of age or older) were admitted to the ICU with either laboratory-confirmed COVID-19 infection or clinical/radiologically-confirmed COVID-19 infection (**Fig. 1**). The mean age of all patients was 70.2 ± 13.9 years, the mean age of discharged patients was 66.5 ± 15.8 years and the mean age of patients who died was 71.8 ± 12.8 years. 93 (46.5%) were female, 107 (53.5%) were male (**Table 1**). The mean body mass index was 25.9 ± 3.19. While 61 (30.5%) of the patients survived, 139 (69.5%) died. 185 (92.5%) patients had chronical disease. The most common comorbidities were hypertension (45.0%), cardiac disease (35.0%) and lung disease (27.1%). The most common symptoms during intensive care hospitalization were dyspnea in 174 (87.0%) patients, fever in 107 (53.5%) and cough in 97 (48.5%) (**Table 1**). There was a history of smoking in 89 (44.5%) of the patients, but there was no statistically significant difference between the two groups in smoking patients (P = 0.370) (**Table 1**). APACHE II and SOFA scores were found to be high. APACHE II and SOFA scores of non-survivor patients were significantly higher than those of surviving patients (P = 0.011 and P <0.001). The data are shown in **Table 1**.

Seventy seven (38.5%) were admitted from the emergency department, 69 (34.5%) from the hospital and 54 (27.0%) from other hospitals (**Table 2**). The most common reasons for hospitalization were respiratory failure in 166 (83.0%) and sepsis developing secondary to COVID-19 in 17 (8.5%) patients.

2. Laboratory and computed tomography finding

White blood cells (19.2 ± 76.1 × 10^9 per L) and neutrophil/lymphocyte ratio (15.4 ± 65.1) were high at the time of admission. d-dimer (2,558.4 ± 4,574.2 ng/mL), ferritin (1,481.2 ± 4,447.4 μg/L) and CRP levels (12.1 ± 11.9 mg/dL) were also found high in the patients. At the same time, CRP levels of patients who died were significantly higher than survived (**Table 3**).
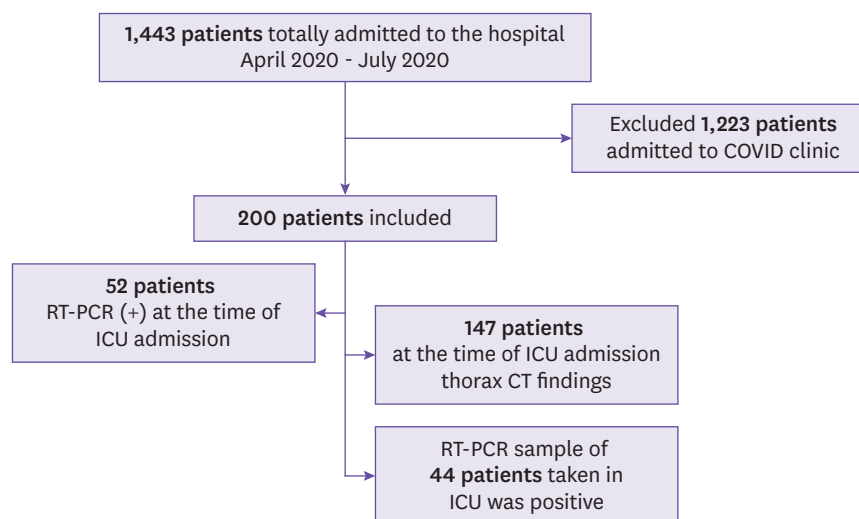

Figure 1. Flow diagram of patient's selection for retrospective cohort study.
COVID, coronavirus disease; RT-PCR, reverse transcriptase-polymerase chain reaction; ICU, intensive care unit; CT, computed tomography.

Table 1. Demographics and clinical characteristics of COVID-19 patients at admission to intensive care unit

	Survivors (n = 61)	Non-survivors (n = 139)	Total (n = 200)	P-value
Age	66.5 ± 15.8	71.8 ± 12.8	70.2 ± 13.9	0.013
Sex (%)				0.263
Female	32 (52.5)	61 (43.9)	93 (46.5)	
Male	29 (47.5)	78 (56.1)	107 (53.5)	
BMI (kg/m²)	25.6 ± 3.3	26.1 ± 3.2	25.9 ± 3.2	0.370
Smoke (%)	24 (39.3)	65 (46.8)	89 (44.5)	0.331
APACHE II score	21.2 ± 8.2	24.6 ± 8.6	23.6 ± 8.6	0.011
SOFA score	4.6 ± 2.0	5.9 ± 2.0	5.5 ± 2.1	<0.001
Fever (°C)	36.7 ± 0.6	36.9 ± 0.7	36.9 ± 0.7	0.199
Respiratory Rate	23 ± 2.4	23.5 ± 2.9	23.4 ± 2.8	0.217
Heart rate	95.8 ± 13.5	100.2 ± 12.7	98.9 ± 13.1	0.026
MAP (mm/Hg)	59.4 ± 7.3	59.7 ± 7.6	59.6 ± 7.4	0.852
SpO₂	89.4 ± 1.6	89.1 ± 2.6	89.2 ± 2.4	0.474
RT-PCR (%)	9 (17.3)	43 (82.7)	52 (26.0)	0.016
Comorbidity (%)	52 (82.2)	133 (95.7)	185 (92.5)	0.017
Hypertension	23 (37.7)	67 (48.2)	90 (45.0)	0.170
Diabetes	6 (9.8)	26 (18.7)	32 (16.0)	0.115
Cardiac Disease	19 (31.1)	51 (36.7)	70 (35.0)	0.449
Pulmonary Disease	13 (21.3)	41 (29.7)	54 (27.1)	0.219
Malignancy	9 (14.8)	26 (18.7)	35 (17.5)	0.498
Chronic Kidney Injury	8 (13.1)	15 (10.8)	23 (11.5)	0.635
Immune Deficiency (%)	6 (9.8)	16 (11.5)	22 (11.0)	0.727
Symptom (n) (%)	51 (83.6)	123 (88.5)	174 (87.0)	0.344
Fever	29 (47.5)	78 (56.1)	107 (53.5)	0.263
Dispnea	51 (83.6)	123 (88.5)	174 (87.0)	0.344
Cough	34 (55.7)	63 (45.3)	97 (48.5)	0.175
Fatigue	18 (29.5)	47 (33.8)	65 (32.5)	0.550

COVID-19, coronavirus disease 2019; BMI, body mass index; APACHE II, acute physiology and chronic health evaluation II; SOFA, sequential organ failure assessment; MAP, mean arteriel pressure; SpO₂, saturation of peripheral oxygen; RT-PCR, reverse transcriptase-polymerase chain reaction.

Table 2. Intensive care treatment times and the need for renal replacement of COVID-19 patients

	Survivors (n = 61)	Non-survivors (n = 139)	All (n = 200)	P-value
Renal replacement therapy (%)	20 (30.5)	64 (69.5)	84 (42.0)	0.080
Length of stay in intensive care (days)	19.6 ± 18.3	8.5 ± 9.5	11.9 ± 3.8	<0.001
Duration of mechanical ventilation (days)	2.8 ± 7.3	4.7 ± 7.2	4.1 ± 7.3	0.080
Duration of non-invasive mechanical ventilation (days)	0.6 ± 1.4	0.5 ± 1.3	0.6 ± 1.3	0.508

COVID-19, coronavirus disease 2019.

Table 3. Laboratory parameters of COVID-19 patients at admission to intensive care unit

	Survivors (n = 61)	Non-survivors (n = 139)	Total (n = 200)	P-value
White blood cell count, × 10⁹ per L	23.3 ± 109.6	17.3 ± 55.8	19.2 ± 76.1	0.613
Lymphocyte count, × 10⁹ per L	2.2 ± 1.1	1.86 ± 1.6	1.9 ± 1.5	0.112
Platelet count, × 10⁹ per L	302.1 ± 183.9	277.6 ± 181.1	285.1 ± 181.9	0.381
Neutrophilto lymphocyte ratio	16.4 ± 89.4	15.1 ± 51.1	15.4 ± 65.1	0.889
INR	1.7 ± 1.9	1.54 ± 0.7	1.6 ± 1.2	0.470
Aspartate aminotransferase, U/L	91.4 ± 158.8	208.5 ± 883.9	172.8 ± 743.2	0.306
Alanine aminotransferase, U/L	78.1 ± 171.4	117.9 ± 368.8	105.7 ± 321.5	0.421
d-dimer, ng/mL	1,110.8 ± 1,471.7	3,206.5 ± 5,294.6	2,558.4 ± 4,574.2	<0.001
Creatinine, mg/dL	2.3 ± 2.4	2.7 ± 1.8	2.6 ± 2.1	0.264
Lactate, µg/L	2.1 ± 0.7	2.2 ± 0.8	2.1 ± 0.7	0.553
Ferritin, µg/L	624.3 ± 807.8	1,921.1 ± 5,395.9	1,481.2 ± 4,447.4	0.014
Fibrinojen, mg/dL	646.6 ± 206.7	625.1 ± 227.2	632.3 ± 220.1	0.545
C reactive protein, mg/dL	9.2 ± 9.4	13.4 ± 12.7	12.1 ± 11.9	0.012
Procalcitonin, ng/mL	6.7 ± 9.2	9.7 ± 15.6	8.8 ± 14.1	0.159

COVID-19, coronavirus disease 2019; INR, international normalized ratio.

Table 4. Radiologic findings of COVID-19 patients at admission to intensive care unit

	Survivors (n = 61)	Non-survivors (n = 139)	All (n = 200)	*P*-value
Radiography (%)	20 (32.7)	46 (33.0)	66 (33.0)	0.966
Patohologic findings	17 (27.8)	37 (26.6)	54 (27.0)	0.855
Bilateral infiltrates	13 (21.3)	27 (19.4)	40 (20.0)	0.759
Pleural effusion	0 (0.0)	5 (3.59)	5 (2.5)	0.326
Irregular opacities	10 (16.3)	28 (20.1)	38 (19.0)	0.534
CT (%)	61 (100)	138 (99.2)	199 (99.5)	0.98
Pleural effusion	27 (45.0)	64 (46.3)	91 (45.5)	0.858
Bilateral ground glass opacification	52 (86.6)	127 (91.3)	179 (85.9)	0.312
Nodules	12 (20.0)	64 (32.6)	91 (45.5)	0.072

COVID-19, coronavirus disease 2019; CT, computed tomography.

Procalcitonin (8.8 ± 14.1 ng/mL), aspartate aminotransferase (AST) (172.8 ± 743.2 U/L), alanine transaminase (ALT) (105.7 ± 321.5 U/L) and creatinine (2.6 ± 2.1 mg/dL) levels at the time of hospitalization values were also high. Lymphocyte count (1.9 ± 1.5 × 10^9 per L) and platelet count (285.1 ± 181.9 × 10^9 per L) were normal and there was no significant difference between the two groups (**Table 3**). RT-PCR results were positive in only 52 (26.0%) of the patients in the ICU. RT-PCR sample taken in the ICU of 44 patients was positive. The rate of positive RT-PCR results in patients who died was significantly higher than in patients who survived (*P* = 0.016) (**Table 1**).

199 patients had thorax computed tomography (CT) imaging. 179 (85.9%) patients had bilateral ground glass opacity. Pleural effusion and nodular appearance were present in 91 (45.5%) of the patients. There was no patient with normal CT findings. Other findings are shown in **Table 4**.

3. Treatment and outcomes

All patients were diagnosed with acute respiratory distress syndrome (ARDS) and 7 patients were diagnosed with sepsis. 154 (78.2%) of the patients were treated with hydroxychloroquine sulfate (Plaquenil, Sanofi, İstanbul, Turkey), 178 (89.9%) of them were treated with antibiotics and all of the patients were treated with antiviral drugs (oseltamivir [Tamiflu, Roche Basel, Switzerland]; lopinavir/ritonavir [Kaletra, AbbVie, Ludwigshafen, Germany; favipiravir [Favira, Novelfarma, İstanbul, Turkey]. Mesenchymal stem cell therapy was applied to 4 (2.0%) patients. Convalescen plasma therapy was applied to 8 (4.0%) patients. 135 (67.5%) of the patients received vasopressor treatment. Renal replacement therapy was administered to 40 (20.0%) of 84 (42.0%) patients with renal failure (**Table 5**).

Table 5. Specific treatment and intensive care unit support of COVID-19 patients until study end point

	All Patient (n = 200)
Spesific treatment	
Hydroxychloroquine	154 (78.2%)
Azithromycin	178 (89.9%)
Antiviral (Enfluvir, Kaletra, Favipiravir)	200 (100.0%)
Mesenchymal stem cell	4 (2.0%)
Convalescent plasma therapy	8 (4.0%)
Vasopressor	135 (67.5%)
Renal replacement therapy	40 (20.0%)
Length of stay in intensive care	11.9 ± 3.8 days
Invasive mechanical ventilation	157 (78.5%)
Duration of invasive mechanical ventilation	4.1 ± 7.3 days

COVID-19, coronavirus disease 2019.

Table 6. Risk factors associated with in-hospital death of COVID-19 patients treated in intensive care unit

	Univariable OR (95% CI)	P-value	Multivariable OR (95% CI)	P-value
RT- PCR	2.58 (1.170 - 5.724)	0.019	4.105 (1.516 - 11.115)	0.005
Contact History	2.221 (0.802 - 6.148)	0.125		
Age	1.027 (1.005 - 1.049)	0.015	1.033 (1.004 - 1.062)	0.024
Apache II score	1.049 (1.011 - 1.089)	0.012		
SOFA score	1.479 (1.225 - 1.786)	0.014	1.477 (1.195 - 1.827)	<0.001
Fever	1.366 (0.848 - 2.202)	0.200		
Respiratory rate	1.075 (0.958 - 1.205)	0.218		
Heart rate	1.027 (1.003 - 1.051)	0.028	1.042 (1.012 - 1.073)	0.006
Lymphocyte	0.859 (0.710 - 1040)	0.119		
d-dimer	3.180 (1.679 - 6.023)	<0.001	3.459 (1.569 - 7.627)	0.002
CRP	1.035 (1.004 - 1.067)	0.028		
Procalcitonin	1.018 (0.987 - 1.051)	0.249		
Fibrinogen	1 (0.998 - 1.001)	0.542		
Ferritin	1 (1 - 1.001)	0.129		
Comorbidity	3.837 (1.301 - 11.315)	0.015		
Lung disease	1.561 (0.765 - 3.185)	0.221		
Diabetes	2.109 (0.820 - 5.423)	0.121	3.433 (1.090 - 10.808)	0.035
RRT	1.749 (0.932 - 3.285)	0.082		
CT nodules	1.935 (0.937 - 4.0)	0.075		

-2 Log likelihood: 173,848, Cox & Snell R Square:0,269, Nagelkerke R Square:0,380.
COVID-19, coronavirus disease 2019; OR, odds ratio; CI, confidence interval; RT-PCR, reverse transcriptase-polymerase chain reaction; APACHE II, acute physiologic assessment and chronic health evaluation II; SOFA, sequential organ failure assessment; CRP, c-reactive protein; RRT, renal replacement therapy; CT, computed tomography.

When the duration of hospitalization in the ICU was examined, the mean ICU stay was 11.9 ± 3.8 days and the ICU hospitalization days of the surviving patients were longer (19.6 ± 18.3 days, P <0.05). 157 (78.5%) patients received invasive mechanical ventilation therapy. While the duration of invasive mechanical ventilation was 4.1 ± 7.3 days, it was 0.6 ± 1.3 days in patients who underwent non-invasive mechanical ventilation. At admission, the respiratory rate was 23.4 ± 2.8/min, SpO_2 value was 89.2 ± 2.4, and heart rate was 98.9 ± 13.1 beat/min.

Acute kidney injury developed in 84 (42.0%) patients during the ICU stay and this rate was statistically higher in patients who died (P = 0.080) (**Table 1**).

According to the results of univariate regression analysis; presence of additional disease (OR: 3.837; P = 0.015), older age (OR: 1.027; P = 0.015), RT-PCR positivity (OR: 2.58; P = 0.019), higher APACHE II score (OR: 1.049; P = 0.012) and higher SOFA score (OR: 1.479; P = 0.014), higher heart rate (OR: 1.027; P = 0.028), high d-dimer levels (OR: 3.180; P <0.001) and high CRP levels (OR: 1.035; P = 0.028) increases the risk of death (**Table 6**).

When patients with full data for all variables in the multivariate logistic regression model were evaluated; positive RT-PCR (OR: 4.105; P = 0.005), older age (OR: 1.033; P = 0.024), higher SOFA score (OR: 1.477; P <0.001), high d-dimer levels at admission (OR: 3.459; P = 0.002) and the presence of diabetes mellitus (OR: 3.433; P = 0.035), high heart rate (OR: 1.042; P = 0.006) increase the risk of death rates (**Table 6**).

DISCUSSION

In this report, we summarize the clinical features, treatment protocols and clinical results in critically ill patients who were followed up in the ICU due to the prediagnosis of COVID-19. In our study, most of the patients were hospitalized in the ICU due to respiratory failure. Most

of the patients were admitted directly from the emergency room to the ICU. First of all, like previous studies, this study confirmed that increasing age is also associated with death in the ICU due to COVID-19.

The most common symptoms during ICU admission were dyspnea (87.0%), fever (53.5%) and cough (48.5%). In studies conducted in the United States, Netherlands, and Italy the most common symptoms were dyspnea, fever and cough, as in our study [14-16].

In a cohort of 1,500 critical ICU patients with COVID-19 in Lombardy, Italy, 68% of patients had at least one comorbidity. Hypertension was the most common comorbidity (49.0%) [14]. In a study conducted in United States, 1,738 patients had at least one comorbidity such as hypertension, diabetes and chronic lung disease. Hypertension (59.7%) and diabetes (38.9%) were seen most frequently [15]. In a meta-analysis examining 87 studies, it was stated that comorbidities play a very important role in hospitalized COVID-19 patient deaths. The most common comorbidity is hypertension and diabetes mellitus is one of the most important markers of mortality [17]. Patients with both type 1 and type 2 diabetes are associated with significant increases in the risk of COVID-19 disease compared to the risks seen in people of the same age [18]. 92.5% of our patients had at least one comorbidity and hypertension was the most common comorbiidity, as in other studies. We found that the presence of diabetes was associated with high mortality.

In previous studies, d-dimer levels have been commonly found to be elevated in patients with COVID-19, and d-dimer levels have been associated with disease severity. It is a prognostic marker for hospital mortality in COVID-19 patients. d-dimer levels greater than 2,000 ng/mL have been associated with mortality [19, 20]. d-dimer levels were significantly higher in patients who died in our study compared to those who survived. Most patients exhibited a hyperinflammatory profile with high CRP, ferritin and procalcitonin levels. CRP levels were found to be significantly higher in nonsurvivor patients compared to survivor patients. Similar results were obtained in a study conducted in Turkey [21]. Disease severity scores were found to be high for APACHE II and SOFA scores. The APACHE II and SOFA scores of the patients who died were statistically significantly higher than those of the patients who survived. Various studies have also shown that higher SOFA and APACHE II scores are associated with mortality in admission to the ICU [21-23]. Other studies suggest that the APACHE II score may be better at predicting mortality among severely ill patients [24].

Vazopressors was required 67.5% of the patients, 42.0% of the population developed acute kidney injury (AKI) and 20.8% of the population received renal replacement therapy (RRT). In different studies, the incidence of AKI was between 12.3% and 50.2% [25-27]. It has been observed that there is a positive correlation between high CRP levels and RRT [27].

Most patients (78.5%) admitted to the ICU needed invasive mechanical ventilation. Series published from Italy (88.0%), United States (71.0%), Spain (77.0%) and Sweden (86.5%) had similar results [14, 28-30].

RT-PCR results were positive in only 52 of the patients in the ICU. RT-PCR sample of 44 patients taken at the ICU was positive and the mortality of RT-PCR positive patients was found to be higher. Many factors can affect the reliability of the RT-PCR test, such as the quality of sample collection, the day of the disease, the sampling site, the stages of infection, and the quality of the PCR tests used. Diagnostic RT-PCR test sensitivity can range from

45.0% to 67.0% [31]. In the diagnosis of COVID-19, clinical findings should be evaluated together with laboratory and radiological findings.

CT with the COVID-19 Reporting and Data System (CO-RADS) is a reliable, practical and rapid method for diagnosing and evaluating COVID-19 in symptomatic individuals and excluding pulmonary fibrosis in follow-up in patients recovering from COVID-19 infection [32]. There was no normal CT finding in our patients, and bilateral ground glass opacity was the most common.

According to the results of our study, the case fatality rate was 69.5%. Previous reports have described different mortality rates in patients admitted to the ICU, ranging from 16.0% to 78.0% [2, 4, 33, 34]. In a meta-analysis evaluating 32 studies, the ICU mortality rate among COVID-19 patients was 30.6%. The mortality rate was higher (59.6%) when only mechanically ventilated patients were considered [35]. In a meta-analysis including 43,128 patients admitted to the ICU with COVID-19, the ICU mortality rate was found to be 35.5%. In the study, steroids (especially dexamethasone) improved survival in patients who were oxygen dependent or who received mechanical respiratory support in the later stages of the pandemic; It has been stated that other drugs such as chloroquine, azithromycin, lopinavir/ritonavir and remdesivir have no effect and the management of COVID-19 has probably evolved over the years with changes in approaches to oxygen therapy, fluids and anticoagulation management. For this reason, it has been emphasized that while mortality rates are higher in the early stages of the pandemic, they may be lower in the following periods, and that there may be a change in mortality due to the fact that the study deals with studies involving a wide process [36]. In our study, our mortality rates may be high, since the use of corticosteroids and different anticoagulants was not included in the routine treatment protocols and included the early stages of the pandemic.

In addition, additional factors such as critical care admission criteria for patients, underlying health characteristics of patients, and a significant lack of consistency in reporting without reporting on the severity of critical illness or the nature or intensity of treatments, critical care service (such as intensive care beds per capita), critical care mortality and may cause different results between studies.

Our study has some limitations such as being retrospective and missing some data such as mechanical ventilation. It is the only hospital data consisting of patients admitted to the hospital; Collecting standardized data for a larger cohort will help further define clinical presentation, natural history, and risk factors. In addition, comparing different periods of the pandemic with different treatment protocols may yield healthier results.

In conclusion, the mortality of critically ill patients with COVID-19 pneumonia is high. ARDS and elderly patients are at high risk of death. Higher SOFA score, higher D-dimer levels at admission, higher heart rate, positive RT-PCR and presence of diabetes mellitus are associated with high mortality. The severity of COVID-19 pneumonia places a huge strain on hospital critical care resources, especially when adequate staffing or resources are not provided.

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