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# Characteristics and Outcomes of the Patients Infected with SARS-CoV-2 Admitted to Intensive Care Units: Erciyes University COVID-19 Center Experience

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ABSTRACT

**Objective:** This study aims to investigate the characteristics and outcomes of patients infected with SARS-CoV-2 admitted to the intensive care unit (ICU).

**Materials and Methods:** This study was performed retrospectively in a medical ICU. All patients admitted to were either laboratory-confirmed or clinically probable COVID-19 patients, and all patients admitted to our ICU during this period were enrolled in the study.

**Results:** We enrolled 47 patients. The mean age was 68.4±13.4 years and 66% of patients were male. The most common co-morbidities were hypertension (66%) and cardiovascular diseases (40%). The mean APACHE II score was 22.4±8.5, and the first-day median SOFA score was 5 (range: 1–12). *Hydroxychloroquine* was the most common drug prescribed (78.7%). All patients received at least one antibiotic other than Azithromycin as the most common drug was Piperacillin-Tazobactam (63.8%). Among 47 patients, 55.3% (28 patients) who were admitted to the ICU needed invasive mechanical ventilation. Prone positioning was used in 23% (6 patients) of mechanically ventilated patients. The mean positive end-expiratory pressure (PEEP) was 10±3 cm $H_2O$. The median $PaO_2/FiO_2$ ratio was 200 (range, 91–458). The most common ventilator mode was SIMV-PSV volume-controlled mode. ICU mortality rate was 34% (16 patients).

**Conclusion:** The most common reason to admit SARS-CoV-2 infected patients to our ICU was acute respiratory failure and hypoxemia during the first month of pandemics. COVID-19 patients have a high mortality rate when they develop severe disease.

**Keywords:** COVID-19, intensive care unit, SARS-CoV2, Erciyes University

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## INTRODUCTION

World Health Organization (WHO) declared severe acute respiratory syndrome (SARS-CoV-2) outbreak as a pandemic due to an increase in the global number of infected patients. These infected patients may develop coronavirus 2019 (COVID-19) disease. The first case was referred to the hospital on March 9, 2020, and the first death case related to COVID-19 occurred on March 17, 2020, when the total number of cases had reached 98 in Turkey (1) COVID-19 patients admitted to the ICUs frequently due to severity of the patients (2, 3). More than 2000 deaths occurred, and the number of the cases is well above 100.000 according to the Turkish Ministry of Health data. We admitted the first patient to ICU on 20 March 2020. Since then, we admitted SARS-CoV-2 patients to our ICU. Our ICU has 18 beds and totally dedicated to SARS-CoV-2 patients during the outbreak. ICU admission rates varied between 5% to 32% in China (2). More than 1500 ICU patients were reported from the Lombardy region, Italy (4).

There is still limited information about SARS-CoV-2 infected patients admitted to ICUs. There are significant variations between countries about the availability of ICU beds and ICU care. To our knowledge, there is no report so far for SARS-CoV-2 infected patients admitted to the ICUs in Turkey. Our single-center data may help to understand the characteristics of these patients in Turkey.

## MATERIALS and METHODS

This retrospective observational study was performed at the Medical ICU, dedicated to SARS-CoV-2 infected patients during the outbreak. All consecutive patients admitted to this ICU either with laboratory-confirmed or clinically possible cases were enrolled in this study. Ethics committee approval was received for this study from the Erciyes University Clinical Research Ethics Committee (Approval Date: April 06, 2020; Approval Number: 2020-199).

Diagnosis of COVID-19 disease was based on either laboratory confirmation or typical chest CT findings, according to the Radiological Society of North America Expert Consensus Statement (5). Laboratory confirmation for

SARS-Cov-2 was defined as a positive result of real-time reverse transcriptase–polymerase chain reaction (RT-PCR) assay of nasal, pharyngeal swabs or endotracheal aspirate according to the WHO guideline (6). Three patients were excluded from this study due to a lack of chest CT and negative RT-PCR tests. Three patients were excluded due to normal chest CT scan findings and negative RT-PCR tests.

### Data Collection

Clinical data reported in this study were collected from patient charts during their ICU stay. The recorded data included the following: age, sex, medical comorbidities, APACHE II and SOFA scores, routine laboratory blood tests, vital signs, drugs specifically given for COVID-19 disease treatment, antibiotics, ICU acquired infections, serum ferritin and D-Dimer levels, mode of respiratory support (invasive mechanical ventilation, noninvasive mechanical ventilation, oxygen mask), level of positive end-expiratory pressure (PEEP), the fraction of inspired oxygen ($FIO_2$), the arterial partial pressure of oxygen ($PaO_2$), $PaO_2/FIO_2$ ratio, the use of prone positioning, peak and plateau pressures on mechanical ventilation, fluid balance and vasopressor use. The number of patients who died were discharged and were still admitted in the ICU as of April 10, 2020, were recorded, and ICU length of stay also was determined.

### Statistical Analysis

SPSS 22.00 (Statistical Packages for Social Sciences; SPSS Inc. Chicago, Illinois, USA) was used for statistical analyses in this study. Any measurable data meeting the parametric requirement were expressed as arithmetic mean±standard deviation. A comparison of quantitative variables by groups was carried using a T-test for two independent samples for normal data and Mann-Whitney U test for non-normal data. The margin of error was assumed as $\alpha$=0.05 in all statistical analyses.

## RESULTS

From March 2020 to 22 April 2020, we admitted 53 patients to our COVID-19 ICU with the diagnosis of possible SARS-CoV-2. During this time frame, the total number of adult patients admitted to the hospital with possible COVID-19 infection was 431. The need for ICU admission was 12.2%. Three patients were excluded due to a lack of chest CT and negative RT-PCR tests. Three patients were excluded due to normal chest CT scan findings and negative RT-PCR tests. We report a total of 47 patients who were followed in the ICU. Table 1 shows the baseline demographic and clinical characteristics of the patients. Overall, 31 (66%) patients were male, and 16 (34%) were female. The mean age of the patients was 68.4±13.4 years. RT-PCR assay was positive in nine (19.1%) patients. The rest of the patients (70.2%) were diagnosed with clinical signs and chest CT scan findings.

A total of 42 (89.3%) of patients had at least one comorbidity. The most common comorbidities were hypertension (31 patients, 66%) and cardiovascular diseases (19 patients, 40%). Malignancies were present in 13 (27.7%) patients as the fourth most common comorbidity. The mean APACHE II score was 22.4±8.5 and the mean first day and last day SOFA scores were 5 (range: 1–12) and 7 (range: 1–15), respectively.

**Table 1.** Patient's demographic, laboratory and respiratory characteristics at admission

| | | Reference range |
|---|---|---|
| Age (mean±SD) | 68±13 | |
| Male, n (%) | 31 (66) | |
| Female, n (%) | 16 (34) | |
| APACHE II±SD | 22±8 | |
| Comorbidities, n (%) | | |
| Essential hypertension | 31 (66) | |
| Cardiovascular disease | 19 (40) | |
| Diabetes mellitus | 15 (32) | |
| Malignancy | 13 (28) | |
| COPD | 10 (21) | |
| Chronic kidney disease | 6 (13) | |
| Chronic liver disease | 6 (13) | |
| Other | 9 (19) | |
| Home oxygen use, no (%) | 6 (13) | |
| Heart rate, beats/min (mean±SD) | 110±15 | |
| MAP, mmHg (mean±SD) | 68±13 | |
| Respiratory rate, breaths/min (mean±SD) | 30±5 | |
| Admission laboratory values, mean (range) | | |
| AST, U/L | 33 (6–134) | 5–40 |
| ALT U/L | 29 (5–360) | 5–50 |
| White blood cell count, /µL | 11200 (3900–27000) | 4000–11000 |
| Absolute lymphocyte count, /µL | 1100 (120–4400) | 1000–3400 |
| Total bilirubin, mg/dL | 0.8 (0.1–5.1) | 0–1.5 |
| BUN, mg/dL | 33 (6–131) | 10–20 |
| Creatinine, mg/dL | 1.8 (0.2–5.5) | 0.6–1.2 |
| CRP, mg/L | 121 (1–400) | 0–10 |
| Ferritin, ng/mL | 725 (16–7100) | 30–400 |
| D-dimer, µg/L | 5100 (233–19190) | 0–500 |
| Respiratory parameters | | |
| Respiratory support, n (%) | | |
| Invasive mechanical ventilation, n (%) | 26 (55.3) | |
| Oxygen mask | 21 (44.7) | |
| Ventilatory and blood gas parameters, mean (range) | | |
| PEEP, cm $H_2O$ | 10.5 (6–18) | |
| $PaO_2/FiO_2$ ratio | 200 (91–458) | |
| $PaCO_2$, cm $H_2O$ | 33 (18–75) | |
| Ppeak, cm $H_2O$ | 25 (16–34) | |
| Pplat, cm $H_2O$ | 18 (8–28) | |

APACHE II: Acute Physiology and Chronic Health Evaluation; COPD: Chronic obstructive lung disease; MAP: Mean arterial pressure; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; BUN: Blood urea nitrogen; CRP: C reactive protein; PEEP: Positive end-expiratory pressure; $PaO_2$: Partial pressure of oxygen; $PaCO_2$: Partial pressure of carbon dioxide

**Table 2.** Treatments and clinical parameters

| Drugs used for COVID-19 disease | n | % |
|---|---|---|
| *Hydroxychloroquine* | 37 | 78.7 |
| *Azithromycin* | 33 | 70.2 |
| Oseltamivir | 36 | 76.6 |
| Lopinavir-Ritonavir | 23 | 48.9 |
| Favipiravir | 12 | 25.5 |
| Tocilizumab | 1 | 2.1 |
| Steroids | 7 | 13.9 |
| Antibiotics, n (%) | | |
| Piperacillin-Tazobactam | 30 | 63.8 |
| Ceftriaxone | 4 | 8.5 |
| Clarithromycin | 7 | 13.9 |
| Meropenem | 4 | 8.5 |
| Ampicillin-sulbactam | 2 | 4.3 |
| Other antibiotics | 8 | 17.0 |
| Vasopressors, n (%) | 8 | 17.0 |
| CRRT, n (%) | 2 | 4.3 |
| Hemodialysis, n (%) | 6 | 12.7 |
| Prone position, n (%) | 6 | 23.0 |
| Nutrition, n (%) | | |
| Oral/enteral | 31 | 66 |
| Parenteral | 1 | 2.1 |
| No nutrition | 15 | 32.0 |
| Fluid balance, (range) ml | 5150 | -400–21440 |
| ICU length of stay, (range) days | 5.4 | 1–20 |
| Mortality, n (%) | 16 | 34.0 |

COVID-19: Coronavirus 2019; CRRT: Continuous renal replacement therapy; ICU: Intensive care unit

Lymphocytopenia (<1000/µL) was observed in 25 (53.2%) patients although the mean lymphocyte count is normal. Mean ferritin levels were high, 725 ng/mL (range, 16–7103), and mean D-dimer levels were also high as5100 µg/L (range 233–19190).

Drugs used for the treatment of COVID-19 disease along with other treatments are shown in Table 2. *Hydroxychloroquine* was the most common drug prescribed (37 patients, 78.7%). All patients received at least one antibiotic other than Azithromycin as the most common was Piperacillin-Tazobactam (30 patients, 63.8%). High dose vitamin C (50 mg/kg) for three days was administered to five (10.6%) patients as a part of a prospective randomized multicenter study. Noradrenaline was administered to eight (17%) patients.

Oral/enteral nutrition was given to 31 (66%) patients, one patient received only parenteral nutrition, and one patient received both parenteral and oral/enteral nutrition. Overall, 15 (32%) patients did not receive any type of nutrition during the ICU course.

Intermittent hemodialysis was used in six (12.7%) patients. Three (6%) patients were on chronic hemodialysis. Continuous renal replacement therapy was used two (4%) patients, and these two patients received cytokine removal therapy with a modified AN-69 filter. The mean net fluid balance was 5110 mL (range, -400 to 21440 mL).

As nosocomial infections, two (4%) patients developed ventilator-associated pneumonia, two (4%) patients developed hospital-acquired pneumonia and two (4%) had primary bacteremia.

Among 47 patients, 26 (55.3%) who were admitted to the ICU needed invasive respiratory support. The rest of the patients (21 patients, 44.7%) received mask oxygen. Non-invasive ventilatory support or high flow nasal oxygen treatment was given to none of the patients. Prone positioning was used in six of 26 (23%) mechanically ventilated patients. The mean positive end-expiratory pressure (PEEP) was 10±3 cm $H_2O$. PEEP levels as high as 18 cm $H_2O$ were applied. The median $PaO_2/FIO_2$ ratio was 200 (range, 91–458). The most common ventilatory mode was SIMV-PSV volume-controlled mode, which was applied to 25 of 26 mechanically ventilated patients. Pressure controlled mode was used in only one patient. Other respiratory parameters are shown in Table 1. Dornase alpha was used in three patients for secretion management.

As of April 22, 2020, the mean length of stay in the ICU was 5.4 (range, 1–20) days, and 16 (34%) patients died in the ICU. Until April 22, 2020, nine (19%) patients were still in ICU.

## DISCUSSION

In this case series of critically ill patients admitted to Erciyes University hospital ICU in Kayseri, Turkey, confirmed cases of COVID-19 with either laboratory or chest CT findings and clinical signs from March 2020 to 22 April 2020 are presented. The majority were older men, intubation and mechanical ventilation was used more than half of them, requiring high levels of PEEP. Intensive care unit mortality rate was 34%. All of the patients were admitted to ICU with the diagnosis of acute respiratory failure and/or low arterial oxygen saturation. Endotracheal intubation and invasive mechanical ventilation were needed in 55% of the patients, and the rest of them were given nasal or face mask oxygen. Any lower respiratory bacterial infections were not identified on admission from blood, endotracheal aspirate and urine cultures, but 16% of the patients developed nosocomial infections during the hospital course.

The majority of patients had comorbidities before ICU admission and the most common ones were hypertension, cardiovascular diseases and diabetes mellitus, as indicated in other studies (2). Lymphocytopenia was common as it was reported before although our patients mean lymphocyte count was above 1000 (2, 7). Lymphocytopenia was also common in critically ill patients with MERS infection (8). Lymphocytopenia is secondary to lymphocyte apoptosis.

Our ICU admission rate was 12.2% and was higher than the study from Lombardy, Italy (9%) and ICU admission rates reported to be between 5% to 7% from China (2, 4, 9).

Our rates of invasive mechanical ventilation are higher than the numbers reported with two studies from Wuhan, China (42% and 30%) (9, 10) but less than the reports from Lombardi, Italy (88%) and Washington State, the USA (71%) (4, 11). Our lower rate of

invasive mechanical ventilation compared to the other studies from Lombardi, Italy (88%) and Seattle, Washington State, USA (75%) may be related to better oxygenation (mean P/F ratio of 200) of our patients (4, 7).

NIMV use was reported in a considerable number of patients in other studies (10, 11). We did not use high flow nasal cannula oxygen (HFNO) or non-invasive ventilation (NIMV) at the beginning due to concerns about viral contamination. Currently, we are using both HFNO and NIMV in our negative pressure rooms. NIMV is not recommended for patients during pandemic influenza A H1N1 (PIAH1N1) virus infection. NIMV initially can improve oxygenation, but since it does not change the course of the disease, and may cause delay for endotracheal intubation, it was not recommended during PIAH1N1. NIMV also may increase the risk of respiratory pathogen transmission (12).

The mortality rate in our case series is 34%. The mortality rates reported in different critically ill patient population are 26% from Lombardy, Italy, 50% from Seattle, Washington State, the USA, and 61.5% from Wuhan, China (4, 7, 9). Our mortality rate is higher than the study conducted in Italian, probably because 58% of the patients were still in the ICU during the report time. Higher mortality rates from the other two studies are probably related to the severity of their patients. Their patients were required more invasive mechanical ventilation and more vasopressors (7, 9).

Patients required high oxygen levels and high PEEP levels after initiation of mechanical ventilation with mean plateau pressures of 18 cm $H_2O$ and mean driving pressures of 8 cm $H_2O$. PEEP levels as high 18 cm $H_2O$ were applied to the patients. The mean PEEP level in our study was 10 cm $H_2O$. These pressures are lower compared to the other studies from Italy and the USA (4, 7). Their patients also required more invasive mechanical ventilation with more severe hypoxemia. This may be explained by which patients were admitted to the ICU. We probably had a lower threshold for ICU transfer of the patients. Extubation was performed in 11 of 26 invasively ventilated patients, and three patients were required re-intubation within 72 hours but then successfully extubated. The mean age of extubated patients was 67.8 (24–77) years, which is similar to the mean age of all patients suggesting age may not be an indicator of extubation in COVID-19 patients. Bronchoscopy was not performed for these patients. Three patients had copious secretions that may need bronchoscopy. We had to replace endotracheal tubes and dornase alpha, which is recombinant human deoxyribonuclease I (rhDNase), an enzyme that selectively cleaves DNA in these patients. Dornase alpha did effectively helped to remove secretions.

Steroids were administered to seven patients. One patient received for cerebral edema and six of them received as part of ARDS treatment. None of these patients were in shock.

The vasopressor requirement in our patients was less compared to the other studies (7, 9, 11). Echocardiography was performed in all patients requiring high dose vasopressors, and we did not find any significant myocardial dysfunction suggesting shock related to infection. Shock should be related to COVID-19 infection because all initial cultures were negative. Less use of vasopressors may be related to vasopressor use thresholds and severity of the patients. These studies also reported a higher number of Invasive mechanical ventilation requirements.

We used *Hydroxychloroquine*, *azithromycin*, oseltamivir, lopinavir-ritonavir and favipiravir based on the recommendations from the Turkish Ministry of Health even though there is no clear scientific evidence about these drugs (13). We did not specifically follow the side effects of the drugs, but we did not observe any significant one. We do have sufficient information to report the effects of these drugs. Tocilizumab was administered to only one patient who had signs of the cytokine storm.

Our study has significant limitations. This was in retrospective nature from a single center. We decided to publish to provide objective data and the urgent timeline. To our knowledge, this is the first case series of COVID-19 infection from Turkey. The second limitation was that 19% of the patients were still in the ICU during the time period, which may significantly affect the results.

This is an early experience of the COVID-19 pandemic in Turkey similar to other countries with a high mortality rate. Patients with co-existing conditions and older age are at higher risk for severe disease.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the Erciyes University Clinical Research Ethics Committee (date: April 06, 2020; number: 2020-199).

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

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