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Original Article

Evaluation of Patients with COVID-19 Followed Up in Intensive Care Units in the Second Year of the Pandemic: A Multicenter Point Prevalence Study

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Abstract

OBJECTIVE: A 1-day point prevalence study was planned to obtain country data by determining the clinical characteristics, follow-up and treatment methods of coronavirus disease 2019 (COVID-19) cases that required intensive care unit (ICU) treatment in the second year of the pandemic.

MATERIAL AND METHODS: All patients who were hospitalized in the ICUs due to COVID-19 between March 11, 2022, 08.00 AM, and March 12, 2022, 08.00 AM, were included in the study. Demographic characteristics, intensive care and laboratory data, radiological characteristics, and follow-up results of the patients were recorded.

RESULTS: A total of 811 patients from 59 centers were included in the study, 59% of the cases were male, and the mean age was 74 ± 14 years. At least one comorbid disease was present in 94% of the cases, and hypertension was the most common. When ICU weight scores were examined, Acute Physiology and Chronic Health Evaluation-II: 19 (15-27) and Sequential Organ Failure Assessment: 7 (4-10) were seen. Sepsis was present in 37% (n = 298) of cases. PaO_2/FiO_2 ratios of the patients were 190 the highest and 150 the lowest and 51% of the cases were followed via invasive mechanical ventilation. On the study day, 73% bilateral involvement was seen on chest x-ray, and ground-glass opacities (52%) were the most common on chest tomography. There was growth in culture in 40% (n = 318) of the cases, and the most common growth was in the tracheal aspirate (42%).

CONCLUSION: The clinical course of COVID-19 is variable, and ICU follow-up was required due to advanced age, comorbidity, presence of respiratory symptoms, and widespread radiological involvement. The need for respiratory support and the presence of secondary infection are important issues to be considered in the follow-up. Despite the end of the second year of the pandemic and vaccination, the high severity of the disease as well as the need for follow-up in ICUs has shown that COVID-19 is an important health problem.

KEYWORDS: COVID-19, intensive care, intensive care unit, pandemic, follow-up
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INTRODUCTION

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first described in December 2019 in China and rapidly spread to other countries.[1] As of March 11, 2022, nearly 602 million confirmed COVID-19 cases have been reported globally; of these cases, 576 million recovered from the disease, and 6 million people died.[2] Coronavirus disease 2019 presents with a wide clinical spectrum ranging from asymptomatic illness to respiratory failure, and patients were followed up in the intensive care unit (ICU) for different causes such as severe pneumonia, sepsis, and acute respiratory distress syndrome (ARDS). Epidemiological and clinicopathological features of disease were evaluated worldwide. Reportedly, COVID-19

cases include 14% of severe illnesses and 6% of critical illnesses that required intensive care; 2% of these cases underwent invasive mechanical ventilation (IMV).[3] The ICU mortality rate ranges from 4 to 11%.[4,5] In Turkey, the data about ICU follow-up are limited. This study aimed to describe demographical and clinical characteristics, ventilation settings, treatment regimens, and outcomes in patients with COVID-19 who were followed up in ICUs. Thus, to obtain data on different ICUs in our country in the second year of the pandemic, a 1-day point prevalence study was planned via the Turkish Thoracic Society (TTS) Respiratory Failure and Intensive Care Association.

MATERIAL AND METHODS

This descriptive cross-sectional research was designed as a 1-day point prevalence study. The study was announced to the members practicing in the ICUs via mail through the societies (TTS and the Turkish Society of Intensive Care). Consent forms were shared with the centers that participated in the study. All cases of initial real-time polymerase chain reaction (RT-PCR)-positive cases hospitalized in the ICUs due to COVID-19 between March 11, 2022, 8:00 AM, and March 12, 2022, 8:00 AM, were included. The data were collected via e-mail from each center. The study was approved by the ethical committee of Health Sciences University İzmir Dr. Suat Seren Chest Disease and Thoracic Surgery Training and Research Hospital (March 10, 2022/10-14) and was in accordance with the Declaration of Helsinki.

Patients

According to the COVID-19 guidelines of the Ministry of Health, patients in ICUs should be followed up based on the following conditions:[6]

- Dyspnea and respiratory distress.
- Respiratory rate ≥30/min.
- PaO_2/FiO_2 ratio <300.
- Increased oxygen recruitment.
- SaO_2 <90% or PaO_2 <70 mm Hg despite 5 L/min oxygen therapy.
- Hypotension (systolic blood pressure <90 mm Hg and more than 40 mm Hg decrease from usual systolic blood pressure and mean arterial pressure <65 mm Hg), tachycardia >100/min.

Main Points

- Coronavirus disease 2019 (COVID-19) patients were followed up in intensive care units for different causes, such as severe pneumonia, sepsis, and acute respiratory distress syndrome.
- The clinical features of the COVID-19 patients in the intensive care unit (ICU) during the second year of the pandemic were as follows: majority of the patients were over 65 years old and had comorbid diseases, ICU severity scores were high, and PaO_2/FiO_2 ratios were in lower limits.
- The clinical course of COVID-19 is variable, and ICU follow-up is required due to advanced age, comorbidity, the presence of respiratory symptoms, and radiological extensive involvement.

- Development of acute organ dysfunction such as acute kidney injury, impaired acute liver function tests, confusion, and acute bleeding diathesis.
- Patients with immunosuppression.
- Increased troponin levels and arrhythmia.
- Lactate >2 mmol.
- Presence of capillary return disorder and cutis marmorata.

Assessments

Data on case demographics (age and gender), COVID-19 PCR results, comorbidities, symptoms, ICU duration, chest x-ray and computed tomography (CT) features, Acute Physiology and Chronic Health Evaluation II (APACHE II) and Sequential Organ Failure Assessment (SOFA) scores, PaO_2/FiO_2 ratio, type of respiratory support therapy (nasal oxygen, mask oxygen, high flow oxygen, noninvasive ventilation [NIV], IMV), accompanying conditions (sepsis, septic shock, ARDS), complete blood count and CRP, types of medical treatment (antibiotics, corticosteroids, anticytokine), and follow-up results were obtained at study day.

Clinical suspicion of infection and an increase in inflammatory markers that were consistent with culture positivity (tracheal aspirate, blood, urine, and wound samples) were defined as non-COVID-19 secondary infections.

Statistical Analysis

The statistical analysis was performed using Statistical Package for the Social Sciences Statistics software for Windows, version 21.0 (IBM Corp., Armonk, NY, USA). Descriptive analyses were done for the patients' demographics and clinical data. Student's *t*-test was performed for continuous variables with normally distributed values, and the values were defined as the mean ± standard deviation (SD). The Mann–Whitney *U*-test was used for non-normally distributed continuous values, and the results were shown as median and 25%-75% as interquartile ratio (IQR). Counts and percentages were used when applicable.

RESULTS

A total of 811 cases from 59 centers were included in the study. Table 1 shows the demographic characteristics and radiologic features of patients on study day. Four hundred eighty-two (59%) of the cases were male, and the median age was 74 years. Nearly all of the cases had at least 1 comorbidity; hypertension (57%), diabetes mellitus (31%), coronary artery disease (26%), and chronic obstructive pulmonary disease (COPD) (20%), were the most frequent comorbidities. Of the cases, 73% were vaccinated for COVID-19, and on study day, 77% of the cases COVID PCR tests were positive. Of the patients, 780 (96%) had symptoms of COVID-19 at ICU admission, and dyspnea was the most common symptom. The laboratory data of the cases followed up in ICUs in the second year of the pandemic are shown in Table 1. Although most of the cases had bilateral involvement on the chest x-ray, the most common finding on the thorax CT was ground-glass opacities.

The ICU data and type of respiratory support of the cases followed up in the ICUs in the second year of the pandemic

Table 1. Demographic Characteristics and Initial Symptoms of Cases Followed in the Intensive Care Units (n = 811)

Age, year, mean ± SD	74 ± 14
Male, n (%)	482 (59)
Comorbidity, n (%)	763 (94)
COPD	164 (20)
HT	462 (57)
CVD	214 (26)
AF	109 (13)
CHF	161 (20)
DM	252 (31)
Alzheimer's	145 (18)
CVD	116 (14)
Malignancy	122 (15)
COVID vaccine, n (%)	591 (73)
Last COVID-19 PCR result, positive; n (%)	619 (77)
Presence of symptoms at admission, n (%)	780 (96)
Fever	161 (20)
Cough	362 (45)
Dyspnea	692 (85)
Leucocyte count, 10^9 L, median (25-75)	10205 (7100-14700)
Lymhocyte count, median (25-75)	710 (400-1150)
CRP (mg/dL), median (25-75)	108 (48-171)
Involvement on chest x-ray, n (%)	
Unilateral	161 (20)
Bilateral	590 (73)
Lesion on thorax CT, n (%)	
Ground-glass opacity	394 (52)
Consolidation	180 (24)
Fibrosis	19 (3)

AF, atrial fibrillation; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; CT, computed tomography; CVD, cardiovascular disease; DM, diabetes mellitus; HT, hypertension; PCR, polymerase chain reaction.

are shown in Table 2. On ICU admission, the APACHE-II and SOFA scores were 19 (15-27) and 5 (4-10), respectively. On study day, half of the cases were intubated and followed up with IMV for a median of 8 days, and 298 (37%) of cases had sepsis. Extracorporeal membrane oxygenation (ECMO) was applied to 1 of 811 patients, and 8 of the cases were in a prone position on the study day. Culture positivity was observed in 40% (318) of the cases; the most common positivity was detected in the tracheal aspirate specimen (42%), and *Acinetobacter baumanii* was identified frequently. On study day, 89 (11%) patients died in ICUs, 28 (4%) were discharged, and 693 (86%) were still in ICUs Table 2 shows the treatment procedures, infection status, and outcomes of the cases followed up in ICUs.

Table 2. Intensive Care Unit Data, Treatments and Outcomes of the Cases Followed in the Intensive Care Unit in the Second Year of the Pandemic (n = 811)

ICU duration, day, median (25-75)	9 (3-16)
APACHE II score, median (25-75)	19 (15-27)
SOFA score, median (25-75)	7 (4-10)
Lowest PaO_2/FiO_2, median (25-75)	150 (100-220)
Respiratory support therapies, n (%)	
Room air	12 (1)
Nasal O_2	109 (13)
Mask O_2	38 (5)
Reservoir oxygen mask	62 (8)
HFO	105 (13)
NIMV	70 (9)
IMV	415 (51)
HFO (day), median (25-75)	3 (2-6)
NIV (day), median (25-75)	2 (2-5)
IMV (day), median (25-75)	8 (3-18)
Tracheostomy, n (%)	63 (8)
Tracheostomy (day), median (25-75)	12 (6-21)
Sepsis, n (%)	298 (37)
Dialysis, n (%)	68 (8)
ECMO, n (%)	1 (0.1)
Prone position, n (%)	65 (8)
Anticytokine therapy (anakinra), n (%)	17 (2)
Pulse/mini pulse corticosteroid, n (%)	163 (20)
Anticoagulant, n (%)	753 (92)
Vasopressor, n (%)	283 (35)
Antibiotic therapy, n (%)	653 (82)
Antibiotic duration, median (25-75)	5 (3-9)
Culture positivity, n (%)	318 (40)
Source of infection, n (%)	
Tracheal aspirate	139 (42)
Blood	128 (38)
Urine	62 (19)
Wound	4 (1)
Pathogen, n (%)	
Acinetobacter baumanii	84 (10)
Klebsiella pneumoniae	50 (6)
Candida spp.	39 (5)
Pseudomonas aeruginosa	15 (2)
Result, n (%)	
Exitus	89 (11)
Discharge from ICU	28 (4)
Continued ICU stay	693 (86)

APACHE, acute physiology and chronic health evaluation; ECMO, extracorporeal membrane oxygenation; HFO, high-flow oxygen; ICU, intensive care unit; IMV, invasive mechanical ventilation; NIV, noninvasive ventilation; PaO_2/FiO_2, arterial oxygen tension/fraction of inspired oxygen; SOFA, sequential organ failure assessment.

DISCUSSION

The present study evaluated the clinical features of patients with COVID-19 in various ICUs during the second year of the pandemic. Most of the patients were over 65 years old and had comorbid diseases; their ICU severity scores were high, and PaO_2/FiO_2 ratios were in lower limits. The clinical course of COVID-19 is variable, and ICU follow-up is required owing to advanced age, comorbidity, the presence of respiratory symptoms, and extensive radiological involvement.

As reported in the ICU data of different countries, the cases followed up in ICUs due to severe COVID-19 were 60%-80% male, and the mean age was 60-70 years.[3,7,8] Consistent with these data, most of the patients hospitalized in the ICUs in our country were male and of elderly age. In a meta-analysis of 8 studies that involved 1816 patients,COPD, cardiovascular disease, and hypertension were found to be risk factors for severe illnesses and ICU admission.[9] Similarly, a prospective, multicentre cohort study, from 63 ICUs enrolled patients over 18 years old with RT-PCR-confirmed COVID-19 who were on IMV and showed hypertension and obesity as the main comorbidities.[10] Jain and Yuan[9] reported that the most prevalent symptoms of severe COVID-19 were cough, fever, and fatigue. Moreover, cough, fever, and dyspnea were common in ICU patients. Dyspnea was found to be the only symptom that is associated with both severe disease and ICU admission. Similarly, in our study, dyspnea was observed in most patients during ICU admission.

Chau et al's[11] study in 2004 showed the relationship between the initial chest radiograph and the clinical outcome of patients with severe acute respiratory syndrome (SARS). Their results showed that bilateral disease and involvement of more than 2 zones on the chest radiograph were associated with poor clinical outcomes. Patients with bilateral involvement had a higher rate of ICU admission, assisted ventilation, and mortality in comparison with those with unilateral involvement. Similarly, bilateral involvement in chest x-ray has been reported to be more common in patients in ICUs.[3,12,13] In our population, bilateral involvement in chest x-rays was detected frequently. Moreover, typical thorax CT features of COVID-19 were clearly defined as ground-glass opacities, with or without consolidations, in peripheral lung regions, and multifocal bilateral distribution. In most of the studies, such as ours, the common CT finding in ICU patients was ground-glass opacities.[13,14]

Based on the intensive care data from different countries, IMV support ranged from 28%-100%.[3,7,8,12,13,15] Patients included in our study were severe cases and half of them required IMV; thus, the APACHE II and SOFA scores of the present study were higher than the other studies.[3,8,13,16] This may be due to the clinical characteristics of the patients admitted to the ICUs and the differences in ICU capacities in various countries. Additionally, the lower rates of PaO_2/FiO_2 ratio also led to IMV support. A lower PaO_2/FiO_2 ratio at ICU admission was reported as an independent risk factor for mortality.[7] In previous studies, the use of NIV was reported to be 2%-11%, and the rate was similar in our data.[3,7,8,13] This might be related to the prevalent application of NIV in the ward and intermediate ICU.

The data about bacterial and fungal coinfection in patients with COVID-19 show that their number is increasing over time, and coinfections were associated with a high mortality rate and a longer course of ICU stay. Bardi et al[17] evaluated the epidemiological, clinical, and microbiological features and outcomes of ICU-acquired infections in their study which included 140 patients. The COVID-19-related nosocomial infection during ICU stay was defined as 41%. Furthermore, the nosocomial infections tended to be late complications occurring after 7 days of ICU stay.[17] Nosocomial infections in ICU patients vary across a wide spectrum comprising such as ventilator-associated pneumonia, tracheobronchitis, catheter-related bloodstream infections, and urinary tract infections. In the present study, the most common microbiological isolates were *A. baumannii* and *Klebsiella pneumonia*. Previous studies showed that immunomodulatory therapies, including tocilizumab and glucocorticoids, were associated with coinfections in patients with COVID-19.[18,19] Moreover, higher APACHE II score at ICU admission was associated with infection.[17] Interestingly, in our study, the rate of patients using antibiotics was higher than that of patients with culture positivity, i.e., 82% and 40%, respectively. This might be associated with the increased tendency to initiate empirical antibiotics by clinicians in ICUs.

Previous studies reported different ICU mortalities as follows: 16%-31%.[7,13,16] A multicenter retrospective study reported COVID-19 mortality rate of 4.5% in our country. This study defined that male patients with severe pneumonia, multiorgan dysfunction, malignancy, sepsis, and interstitial lung diseases were at increased risk of mortality.[20] The mortality rate was twice as high as in the present study, which might be related to the fact that our study included only patients in ICUs.

This study has some limitations. First, it is a cross-sectional 1-day point prevalence study and only shows the results on study day. It does not give information on the changing conditions in the follow-up of the patients. However, the results may be interpreted as a representation of severe COVID-19 and ICUs. Second, due to the multicenter nature of the study, the data may be heterogeneous due to the different structures of ICUs. However, considering that 59 different centers were evaluated, the results can provide important data on the ICUs in the whole country. To the best of our knowledge, this is the first and most widespread study that evaluates ICU patients with COVID-19.

In conclusion, this multicenter study showed that in the second year of the pandemic, the majority of the patients in ICUs were of elderly age and had comorbid diseases, high ICU severity scores, and high intubation rates. The clinical course of COVID-19 is variable, and ICU follow-up is required because of advanced age, comorbidity, the presence of respiratory symptoms, and extensive radiological involvement. Despite the end of the second year of the pandemic and vaccination, the severity of the disease is high enough to require follow-up in ICUs, which shows that COVID-19 continues to be an important health problem.

Ethics Committee Approval: The study was approved by the ethical committee of Health Sciences University Izmir Dr. Suat Seren

Chest Disease and Thoracic Surgery Training and Research Hospital (Approval No:10-14 Date: 10.03.2022).

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