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# Presentations and Outcomes of COVID-19 Patients Hospitalized in Tertiary Intensive Care Unit

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## Summary

Now a day, Acute Respiratory Distress Syndrome (ARDS) due to COVID-19 is the most common cause of death in Intensive Care Units (ICU). Our study retrospectively reviewed the medical records of 72 consecutive adult patients treated in our ICU. Mortality rate was 22.2% (16/72), and the median length of ICU stay was 12 days.

Coexisting problems including cardio vascular disease were reported in 36 (50%) of 72 patients, lung diseases in 18 (25%) patients, chronicrenal failure in 14 (19.4%), and Chronic Lymphocytic Leukemia in 4 (4.5%) patients.

Our study showed that ARDS due to COVID-19 is still continuing to be a challenging problem and comprises the principal cause of deaths in ICUs.

**Keywords:** COVID-19; Third line intensive care; Morbidity; Mortality

## Background

After (COVID-19) was first diagnosed in December 2019 in Wuhan (China), it quickly evolved into a pandemic all over the world. Pandemic disease displays a clinic spectrum ranging from an asymptomatic condition to severe and critical disease [1]. Many multi centric studies reported that about 5 and 32% of hospitalized COVID-19 patients require intensive care unit treatment on admission [1-3].

ICU, and 30-88% of them require invasive mechanical ventilation support. Male sex, obesity, hypertension, coexisting cardio vascular problems, and diabetes are reported as risk factors forum favorable outcomes of these patients hospitalized in ICU. Previous studies showed that the mortality rate of the patients hospitalized in ICU ranges from 16 to 78% [4-8].

Our study aimed to evaluate the presentations and outcomes of the patients hospitalized in our intensive care unit due to COVID-19 disease.

## Material and Methods

### Study design

Were trospectively reviewed the demographic characteristics and past medical records of patients who underwent COVID-19 treatment in our ICU (September 2020). Our study was approved by the ethics committee of Ankara City Hospital and the Ministry of Health.

### Inclusion and exclusion criteria

Our study included all patients older than 18 years of age and suffered from acute respiratory distress due to COVID-19 in our ICU (Table 1). The length of hospital stay of all patients was longer than 24 hours. The diagnosis of COVID-19 was confirmed in a positive Reverse Transcription Polymerase Chain Reaction-PCR (RT-PCR) test in all patients. Patients with a length of hospital stay shorter than 24 hours were excluded from the study.

### Data sources and collection

All data, including past medical history, demographic features, examination, and laboratory results were obtained from the electronic recording system of our hospital. The files and follow-up forms of the patients were also analyzed as data. All laboratory data were submitted as part of the routine. SARS-CoV-2 infection was confirmed using RT-PCR in nasopharyngeal, oropharyngeal, endotracheal aspirate and bronchoalveolar lavage samples.

The date of the earliest symptom was recorded and accepted as the beginning of the COVID-19 disease. Patients with documented Hemoglobin A1C (HbA1C) value >6.5% (reference value was <5.7%) were accepted as diabetic regardless of pro drug prescription. All

**Table 1:** Demographic features of COVID-19 cases.

| Mean age | 18-40 years | 40-50 years | Over 50 | P value |
|---|---|---|---|---|
| | 39 | 48.6 (42.2-50) | 70.4 (52-92) | 0.39 |
| Number of Patients | 2 (2.7) | 20 (27.7) | 50 (69.4) | |
| Smoker number (n%) | 2 (100%) | 10 (50%) | 25 (50%) | 1.34 (0.33-5.0) |
| Male | 2 (2.7) | 16 (22.2) | 32 (44.4) | 0.03* |
| Female | - | 4 (5.5) | 18 (25) | Male:50 |
| | | | | Female:22 |

*Fifty of the 72 patients were male. The disease was more mortal in male ($p<0.05$).

patients accepted to the ICU unit underwent PA lung radio graphic examination with in the first 24 hours and chest computerized to mographic (CT) examination with in the first 48 hours [1-9]. All radiologic examinations were reported by specialist radiologists. The diagnosis of acute respiratory distress syndrome was based on radiologic findings according to berlin criteria including the presence of acute respiratory failure with bilateral pulmonary in filtrates, the ratio of arterial oxygen pressure to inspired oxygen fraction <300, and positive end-expiratory tension pressure >5 cm $H_2O$. Additionally, the presence of the positive end-expiratory pressure without cardiogenic Pulmonary Edema was included in the criteria [10-12].

Initially, the presence of 1.5 times increased serum creatinine levels in the laboratory results was accepted as a sign of acute kidney injury [13]. Cardiomyopathy diagnosis was based on the presence of the decreased ejection fraction <50% on the transthoracic echocardiogram (TECG), or the presence of the 10% relative decrease in base line ejection fraction compared to the result of a previous ECG within two years. Bloods tream infection was defined according to national healthcare guidelines [14].

## Results

A total of 72 SARS-CoV-2 positive patients were admitted to our intensive care unit between 1st October and 1st November 2020. Most (68(94.4%)) of the patients came from stable home conditions with their families. Four (5.5%) patients lived in a qualified care facility.

### Pre-existing co-morbidities

The coexistence of cardio vascular diseases was noted in 50(69.4%) of 72 patients and 20(27.7%) patients had underlying lung disease. Univariate analysis of the coexistent problems showed that only the coexistence of diabetes mellitus was the significant factor for prognosis.

Coexisting diseases were noted in 72 patients including hypertension (61.1%), hyperlipidemia (47.2%), diabetes mellitus (27.8%) and chronic renal failure (19.4%). The most common coexisting pulmonary problem was asthma or chronic obstructive pulmonary disease [1-3,15]. The weakened immunity was observed in six patients. The cause of the weakened immunity was malignancy in four patients and the presence of the kidney transplantation history in two patients.

Favipiravir had already started with prescription in 40(55.5%) patients before admission. Hydroxychloroquine was prescribed for 14(19.4%) patients for COVID-19. There were no patients using long-term hydroxychloroquine for other indications.

### Clinical features during admission

The most common presenting symptoms were fever (61.1%), dry cough (33.3%), and shortness of breath (86.1%), and of these symptoms, fever was statistically significantly higher over 50 years of age (Table 2). Non specific influenza-like symptoms including fatigue, myalgia, abdominal pain, nausea, and diarrhea were also frequently

encountered in our patients. Changes in the feelings of tasting and smelling were less commonly (16.6%) observed in our patients. ICU patients were more likely to have a fever, documented within 24 hours of admission, and higher temperatures recorded. Candida albicans was colonized in the blood culture of two patients connected to mechanical ventilators and Fluconazole was started.

Serratia marcescens were identified in a Deep Tracheal Aspirate (DTA) in one patient, and piperacillin-tazobactam and teicoplanin were administered intravenously.

Stenotrophomonas maltophilia was positive in DTA of two patients and meropenem and tigecycline treatments were started for these patients. Chest X-ray examinations commonly displayed pathologic findings in our patients. In consideration of the presenting symptoms, major of the patient's required hospitalization in the ICU. In consideration of the presenting symptoms, major of the patients required hospitalization in the ICU. Bilateral diffuse or irregular opacities were noted in all of the patients treated in ICU where as these findings were less common in other patients. Generally, patients treated in ICU underwent chest CT scanning within 24 hours. Clinical presentation features of the patients were detailed in table 2.

### Treatments

The patients most frequently received favipiravir treatment (100%) (Table 3). 2 ICU patients received tocilizumab (Interleukin-6 antagonist) and four patients received anakinra treatment (Interleukin-1 receptor human antagonist). In the ICU, hydroxyl chloroquine was given to 14 patients (19.4%), colchicines to 2 patient (2.7%), vitamin C to 20 patients daily 1000 mg (total 10 day) iv (27.7%), and 30 patients with Ceftriaxone Intravenous (41.6%). Cytokine filter was applied to six patients for three days when acute phase reactants from the femoral central catheter peaked. Intravenous gamma globulin was not given to any patient during the recovery period. The prone positioning application, which is in our institutional protocol, was used for all patients [15].

### Complications

Pneumothorax was the most common complication and was noted in four patients. The striking point for these patients was subcutaneous emphysema occurrence on the day of hospitalization (Table 4). All but two of the patients hospitalized in the ICU developed acute respiratory distress syndrome. No patients were treated with intravenous pulmonary vasodilators or extracorporeal membrane oxygenation. Arrhythmias also developed in the ICU patient: 8 Supraventricular tachycardia, 2 atrial fibrillation or atrial flutter, and 6 bradycardia were recorded (Table 4).

### Results

Mortality due to COVID-19 was noted in 16(22%) of the patients treated in ICU during a month period. Four patients were discharged to previously stayed nursing homes. Forty-eight patients were discharged to the COVID-19 ward. The median age of 24 patients who died or were discharged to the nursing homes was 75. The median length of hospital stay for all patients was 12 days (range 4-21 days). Thirty-two of the patients treated in ICU required mechanical ventilation support

**Table 2:** Clinical presentations of COVID-19 cases.

| Obesity | | | |
|---|---|---|---|
| Age | 18-40 years (n%) | 40-50 years (n%) | Over 50 age (n%) |
| BMI >30 | 2(2.7) | 16(22.2) | 40(55.5) |
| BMI <30 | - | 4(5.5) | 10(13.8) |
| Cardio vascular diseases | 18-40 years (n%) | 40-50 years (n%) | Over 50 age (n%) |
| Hypertension | 2(2.7) | 12(16.6) | 30(41.6) |
| Hyperlipidemia | - | 10(13.8) | 24(33.3) |
| Diabetes | - | 8(11.1) | 20(27.7) |
| Chronic kidney disease | - | 4(5.5) | 10(13.8) |
| Coronaryartery disease | - | 4(5.5) | 10(13.8) |
| Arrthytmia | - | 2(2.7) | 6(8.3) |
| Heart failure | - | 2(2.7) | 8(11.1) |
| Cerebro vasculary disease | - | 2(2.7) | 6(8.3) |
| Pulmonary diseases | 18-40 years (n%) | 40-50 years (n%) | Over 50age (n%) |
| COPD/asthma | 2(2.7) | 6(8.3) | 12(16.6) |
| Cardio vascular Medication | 18-40 years (n%) | 40-50 years (n%) | Over 50age (n%) |
| Statins | - | 10(13.8) | 12(16.6) |
| Calcium channel blockers | - | 4(5.5) | 10(13.8) |
| Beta-blockers | - | 2(2.7) | 8(11.1) |
| Diuretics | - | 2(2.7) | 10(13.8) |
| ARB (Angiotens in receptor blocker) | - | 4(5.5) | 12(16.6) |
| ACE-1(Angiotensine converting enzyme inhibition) | - | 4(5.5) | 6(8.3) |
| Digoxin | - | 2(2.7) | 4(5.5) |
| Inhaled respiratory medication | 2(2.7) | 6(8.3) | 12(16.6) |
| Steroidinhaler | - | 6(8.3) | 10(13.8) |
| LABA (Long effectivebron codilaltator) | - | - | 6(8.3) |
| SABA (Short effectivebron codilaltator) | - | - | 6(8.3) |
| Immuno suppressants | 18-40 years (n%) | 40-50 years (n%) | Over 50 age (n%) |
| Oral glucocorticoids(Pulse steroid aplications) | - | 8(11.1) | 20(27.7) |
| Hydroxy chloroquine | 2(2.7) | 4(5.5) | 8(11.1) |
| Cytocine filter applications | 2(2.7) | 4(5.5) | - |

for a median of 17 days (13-29) and 2(2.7%) patients underwent a tracheostomy.

## Discussion

A new acute respiratory illness began to spread from a sea food market in Wuhan, China on December 31st, 2009 [5-15]. Mortality rates were reported as 17.5% - 21% in the researchers conducted up to date. The mortality rate of our patients treated in ICU was higher than the ones reported in previous studies. The high mortality rate of our series could be explained by the limited number of mechanical ventilation devices in our ICU. As the Anesthesia Reanimation Clinic, We could reserve mechanical ventilation support for only patients with the most serious clinical scenario. In this group, the mortality rates reported within the United States (US) were (45% -50%) [13,15-17]. The US has tackled this situation by placing patients who do not require care at the ICU leve lintore habilitation or long-term acute care.

The effect of glucocorticoids has been extensively studied in patients with SARS and MERS in the past. During the SARS outbreak in 2003, it became the primary immune modulatory therapy with mixed results. Although glucocorticoids improved fever and oxygenation in many cases, other studies showed adverse reactions, including delayed virus clearance or even further worsening of the disease. Currently, glucocorticoids are used to suppress cytokine storm symptoms and improve ARDS. Because of the overall poor clinical support for glucocorticoids therapy, the current WHO guide line does not support glucocorticoids use for the treatment of viral pneumonia and ARDS for COVID-19 cases without concurrent conditions such as chronic obstructive pulmonary disease or asthma that would in dependently require glucocorticoids use [4,13,18].

### Chloroquine and hydroxychloroquine

Chloroquine (CQ) and hydroxychloroquine (HCQ) have been used for decades as the primary choice for prophylaxis and treatment of malaria but also have had effects on the *Marburg virus*, *zika virus*, *dengue virus*, *ebola virus*, and SARS. CQ blocks viral infection by altering the endosome pH that is required for viral particles to bind to the cell surface receptor. CQ also interferes with the glycosylation of SARS cellular receptors, specifically ACE2. Its immune modulatory, anti-inflammatory, and the anti viral mechanism works synergistically, making it a choice for its efficacy and side-effect profile [13,16,19].

An early clinical trial conducted in patients with COVID-19 in China showed better clinical outcomes and earlier viral clearance in patients treated with CQ compared to control groups [13,14]. Based on these positive findings, Chinese experts recommended that patients with mild, moderate, and severe cases of COVID-19 pneumonia be treated with 500 mg CQ twice per day for 10 days [13,14,20].

**Table 3:** COVID-19 cases clinical features and laboratory results with radiological findings.

| Characteristic Symptoms (n%) | 18-40 years (n%) | 40-50 years (n%) | Over 50 age (n%) | P value |
|---|---|---|---|---|
| Fever | 2(2.7) | 12(16.6) | 30(41.6) | - |
| Dysnpnea | 2(2.7) | 20(27.7) | 40(55.5) | |
| Tremor | - | 10(13.8) | - | - |
| Dry Cough | - | 24(33.3) | - | |
| Productive Cough | - | 8(11.1) | 20(27.7) | - |
| Pain/pressure on chest | - | 4(5.5) | 10(13.8) | - |
| Fatique | - | 4(5.5) | 10(13.8) | - |
| Myalgia | - | 2(2.7) | 6(8.3) | - |
| Atralgia | - | 2(2.7) | 8(11.1) | - |
| Headache | - | 2(2.7) | 6(8.3) | - |
| Sorethroat | 1(2.7) | 12(16.6) | 30(41.6) | - |
| NasalCongestion /Rinore | - | 10(13.8) | - | - |
| Nausea | - | 24(33.3) | - | - |
| Vomiting | - | 24(33.3) | - | - |
| Diarrhea | - | 4(5.5) | 10(13.8) | - |
| Smell/tastealterations | 2(2.7) | 6(8.3) | 4(5.5) | |
| VitalSigns | | | | |
| First 24 HoursTemperature> 38,2°C | | 10(13.8) | 6(8.3) | - |
| $SaO_2$: under 90 (%) | 2(2.7) | 16(22.2) | 24(33.3) | |
| <94 RR | - | 4(5.5) | 10 (13.8) | - |
| Laboratoryresults | 18-40 years (n,%) | 40-50 years (n,%) | Over 50age (n,%) | pvalue |
| Leucocyte | 5.6 (4.3–7.8) | 5.7 (4.4–8.1) | 5.2 (4.0–7.0) | 0.4 |
| ANC absoluteneutrophilcount | 3.890 (2.705-5.835) | 3.875 (2.630-5.725) | 4.140 (2.930-6.430) | 0.47 |
| AbsoluteLymphocytecount | 910 (580–1.235) | 915 (592–1.335) | 890 (520–1.090) | 1(2.7) |
| Platelet | 194 (160–256) | 198 (162–265) | 183 (157–250) | 0.4 |
| Sodium, mmol/L | 136 (133–138) | 136 (132–139) | 136 (134–137) | 1.00 |
| Potassium, mmol/L | 3.8 (3.7–4.2) | 3.9 (3.7–4.2) | 3.8 (3.6–4.0) | 0.31 |
| Creatinin, mg/dL | 0.89 (0.67-1.07) | 0.89 (0.73-1.07) | 01.32 (0.66-2.67) | 0.69 |
| Glucose, mg/dL | 108 (98–124) | 107 (96–120) | 115 (102–147) | 0.18 |
| AST, U/L | 45.5 (31.8-63.5) | 45.0 (29.0–59.5) | 52.0 (38.0–82.0) | 0.04 |
| ALT, U/L | 36.5 (23.8–56.2) | 35.0 (22.5–51.5) | 49.0 (34.0–58.0) | 0.09 |
| CK, total, U/L | 119 (55–360) | 53 (48–70) | 282 (174–774) | 0.01 |
| LDH, U/L | 394 (251–492) | 344 (250–442) | 430 (299–522) | 0.03 |
| CRP >0.5 µg/L | 136 (50-187.8) | 121 (50-180.8) | 150 (50-190) | 0.14 |
| IL-6 >5 pg/mL | 7.2 (4-7.42) | 3.68 (3.2-5.4) | 5.06(4-8.42) | 0.43 |
| Procalcitonin >0.16 µg/L | 2.50 (1.08-3.35) | 4.21 (2.35-4.43) | 7.42 (4-8.56) | 1.00 |
| D-dimer >0.5 mg/L | 3.2 | 4.35 (1.9-5.5) | 5.6 (3.2-13.8) | 1.00 |
| Troponin >45 ng/L | 22.3 | 54.6 | 62.1 | 0.53 |
| Radiology, (%) Chest x-ray | 18-40 years (n%) | 40-50 years (n%) | Over 50age (n%) | P value |
| Common/irregular bilateralin filtrations | 2(2.7) | 12(16.6) | 30(41.6) | <0.05 |
| Focus consolidation | - | 10(13.8) | 20(27.7) | - |
| Pleural effusions | 2(2.7) | 12(16.6) | 24(33.3) | |
| Clear | - | - | 2(2.7) | - |
| Computed to mography chest | 18-40 years (n%) | 40-50 years (n%) | Over 50age (n%) | pvalue |
| Diffuse/multifocal/GGO/opacities | 2(2.7) | 4(5.5) | 10(13.8) | - |
| Common consolidations | - | 2(2.7) | 20 (27.7) | - |
| Focus consolidations | 2(2.7) | 16(22.2) | 24(33.3) | 0.01 |

‡ Reference Ranges: Leucocyter, 4.0-11.0 K/µL; ANC, 1.700–6.700 cell/µL; ALC, 1.000–3.000 cell/µL; platelet, 150-400 K/µL; sodium, 135-145 mmol/L; potasium, 3.5-5.5 mmol/L; creatinin, 0.67-1.17 mg/dL; glucose, 70-100 mg/dL; AST, 10-50 U/L; ALT, 10-50 U/L; CK, total <190 U/L; LDH, 135-225 U/L; ferritine 30-400 ng/mL; CRP <0,5 ng/dL; IL-6, <5 pg/mL; procalsitonine, <0.5 ng/mL; D-dimer, <0,5 µg/mL; troponine <0,055 ng/mL.

**Table 4:** COVID-19 complications, interventions and results.

| Mean age | 18-40 years (n%) | 40-50 years (n%) | Over 50 age (n%) | P values |
|---|---|---|---|---|
| Nasal cannula | - | 2(2.7) | 8(11.1) | - |
| High flownasal cannula | 2(2.7) | 14(19.4) | 20(27.7) | 0.01 |
| $O_2$ mask | 2(2.7) | 12(16.6) | 24(38.8) | - |
| Mechanical respiratory support (CPAP) | - | 10(13.8) | 20(27.7) | - |
| Mean mechanical ventilation | 12 (2-33) gün | | | |
| İnterventions (%) | 18-40 years (n,%) | 40-50 years (n,%) | Over 50age (n,%) | P values |
| Paralytic agent usage | 2(2.7) | 12(16.6) | 30(41.6) | - |
| Prone positioning | 2(2.7) | 10(13.8) | 32(44.4) | - |
| Tracheostomy | 2(2.7) | - | - | |
| Vaso pressor usage | 2(2.7) | 8(11.1) | 20(27.7) | 0.01 |
| Treatment | | | | |
| Aziytromycine | - | 4(5.5) | 10(13.8) | - |
| Favipir | 72 (%100) | | | |
| Hydroxychloroquine | - | 2(2.7) | 8(11.1) | - |
| Sistemik glukokortikoidler | 2(2.7) | 20(27.7) | 20(27.7) | - |
| Tocilizumab | 2(2.7) | - | - | - |
| No antimicrobial drug | 2(2.7) | 10(13.8) | 20(27.7) | 0.01 |
| Antifungal drug | - | 4(5.5) | 10(13.8) | - |
| Hospital stay (days) | 24(4–15) | 16(4–13) | 26(4–20) | - |

Although our sample size is small, this difference in mortality can be attributed to sudden increases in clinical severity. Patient volumes did not exceed normal levels. Disease severity was higher in the population in our study group; 50% (36/72) of patients required only high-pressure nasal cannula. Complementary oxygen therapy was available to all of them at the time of admission. In addition, a significant number of patients were considered favipiravir treated patients, which lowers the mortality rate. Recent preliminary data and clinical studies suggest that the use of favipiravir may be associated with a reduction in mortality [4,19-21]. One of the patients who received the cytokine filter survived and two died. Cytokine filter treatment success was 33.3% in our study.

Complementary oxygen therapy was available to all of them at In our study, the presenting symptoms and laboratory findings of the patients were noted from previous studies published in China [4-7,22]. As seen in previous studies, respiratory complaints were the most common symptoms; However, in our study, cough or respiratory symptoms were found to be absent in 6 (8.3%) patients. This finding demonstrates the importance of capturing non-respiratory symptoms in COVID-19 screening questionnaires [22-23]. In our study, there was no safe place to isolate 6 patients (8.3%) at home due to crowded living conditions, and we could not take the patients out of the hospital because their relatives were afraid of infectiousness and transmission. These conditions also prolonged hospital stays enormously.

## Conclusion

Our study has some limitations. The poor general condition of the patient increased the death toll. Probably because of early and determined public health interventions in our society, the mortality rate was low because drug treatments were initiated earlier [24-25]. This observational study was not developed or designed to analyze the treatment efficacy of given experimental therapies. Therefore, the length of hospital stay is weighted according to the patients. However, there are factors and treatments that affect mortality. We also wanted to reveal the effects of the treatments given in our study. In summary, we found the overall mortality rate high in the tertiary COVID-19 ICU.

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