Clinical characteristics and outcomes of COVID-19 pneumonia patients from an intensive care unit in Faisalabad, Pakistan

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Abstract

Aim: To describe the clinical characteristics and outcomes of severe COVID-19 adult patients, with the exploration of risk factors for mortality in the hospital. Methods: This study included 20 adult patients diagnosed with COVID-19 in the ICU of DHQ Hospital Faisalabad (Pakistan) and were categorized into the survival group and death group according to the outcome. We retrieved demographics, clinical manifestations and signs, laboratory indicators, treatment measures, and clinical outcomes from the medical record, and summarized the clinical characteristics and outcomes of these patients. Results: The average age of patients was 70 ± 12 years, of which 40% were male. They were admitted to the ICU 11 days after the onset of symptoms. The most common symptoms on admission were cough (19 cases, 95%), fatigue or myalgia (18 cases, 90%), fever (17 cases, 85%), and dyspnea (16 cases, 80%). Eleven (55%) patients had underlying diseases, of which hypertension was the most common (11 cases, 55%), followed by cardiovascular disease (4 cases, 20%), and diabetes (3 cases, 15%). Six patients (30%) received invasive mechanical ventilation and continuous renal replacement therapy and eventually died. Acute heart injury was the most common complication (19 cases, 95%). Ten (50%) patients died between 2 and 19 days after admission to the ICU. Compared to dead patients, the average body weight of surviving patients was lower (61.70± 2.36 vs 68.60±7.15, P = 0.01), Glasgow Coma Scale score was higher (14.69±0.70 vs 12.70±2.45, P = 0.03), with fewer concurrent shocks (2 vs 10, P = 0.001) and acute respiratory distress syndrome (2 vs 10, P = 0.001). Conclusion: The mortality rate is high in patients with critical COVID-19 disease. Lower Glasgow Coma Scale, higher body weight, and decreased lymphocyte count appear to be potential risk factors for the death of COVID-19 patients in the ICU.

What is already known about this subject?

- Mortality rate is higher in critically ill COVID-19 patients, in Japanese, European, and American populations.
- Hypertension is the most commonly associated comorbidity in these patients.

What does this study contribute to the literature?

- Mortality rate is higher in critically ill COVID-19 patients and hypertension is the most commonly associated comorbidity, in South-Asian population also.
- Lower GCS score, higher body weight, and lymphocytopenia appear to be potential risk factors for the death of COVID-19 patients in the ICU.

1. INTRODUCTION

On March 11, 2020, due to the alarmingly increasing number of global cases of coronavirus disease 2019 (COVID-19), the World Health Organization declared the outbreak of severe acute respiratory syndrome

coronavirus 2 (SARS-CoV-2) as a pandemic.[1] As of August 18, 2020, the number of globally confirmed COVID-19 cases exceeded 21 million, the number of existing active cases was more than 6 million of which severe patients accounted for 1%, and the mortality rate in 216 countries and regions, based on the cases which had an outcome, was 5%.[2,3] With the spread of COVID-19 around the world, the intensive care unit (ICU) is one of the major rescue departments for severe pneumonia ensuing from COVID-19.[4]

Numerous studies have described preliminary findings of the epidemiology of COVID-19 patients,[5] clinical features, outcomes, and risk factors for death.[6-9] However, there are relatively few studies that have reported clinical characteristics and survival outcomes of COVID-19 critically ill patients. A retrospective study from Italy has published baseline characteristics of COVID-19 ICU hospitalized patients.[10] Similarly, two retrospective studies from Wuhan also described the severe clinical course and outcome of COVID-19 critically ill patients.[11,12] Another study from Wuhan has reported the poor outcomes in cancer patients infected with COVID-19.[13]

Current research shows that the mortality rate of SARS-CoV-2 pneumonia patients in the ICU is extremely high, which exerts significant pressure on hospital intensive care resources.[11,13] More evidence is required to better observe and summarize the characteristics and outcomes of COVID-19 ICU patients, which would be essential to guide the treatment of ICU patients and the rational allocation of intensive care resources. This study aimed to describe the demographics, survival status, clinical outcomes, and the risk factors of COVID-19 diagnosed patients who were admitted to the ICU of District Headquarter (DHQ) Hospital, Faisalabad (Pakistan) from May 10 to July 10, 2020.

2. METHODS

2.1 Inclusion criteria

According to the diagnostic and classification criteria of the National Institute of Health [NIH] Pakistan,[14] following criteria were used to enroll the patients admitted in the ICU of DHQ Hospital, Faisalabad due to COVID-19 associated pneumonia:

1. Age $>$ 18 years.
2. Patients who met the diagnostic criteria of NIH Pakistan for COVID-19 infection, which are as follows:
3. Clinical manifestations including fever and pulmonary symptoms (cough, shortness of breath, chest pain, and tightness).
4. Radiological findings of consolidation, ground-glass opacities (GGOs) either on chest X-ray or high-resolution computed tomography (HRCT).
5. Real-time fluorescent reverse transcription-polymerase chain reaction (RT-PCR) of respiratory samples (nasal/oropharyngeal swab or tracheal secretions) positive for SARS-CoV-2. The laboratory confirmation of SARS-CoV-2 infection was carried out by the local health department.

2.2 Exclusion criteria

Following patients were excluded from the study:

1. Patients with negative detection of novel coronavirus nucleic acid.
2. Heart failure with pulmonary edema (non-COVID heart disease).
3. Allergic pneumonia (acute or chronic eosinophilic pneumonia).
4. Patient refusal to be enrolled in the study.

2.3 Sample size

Twenty eligible confirmed cases of COVID-19 patients were available to be enrolled in the study in the above time period.

2.4 Study design

This was a retrospective, cross-sectional, descriptive study conducted at the ICU of DHQ Faisalabad (Pakistan) from during the above time period.

The facility was designated as a referral center by the provincial health department to cater to approximately 13 million population from the surrounding districts. The patients from these districts were referred to this facility for the management of COVID-19 patients.

2.5 Data collection and procedure

A standardized data collection form was used to obtain patients' demographics, clinical manifestations and signs, laboratory indicators, treatment measures, and clinical outcomes from their electronic medical records. This data form is a revision of the NIH Pakistan Severe Acute Respiratory and Emerging Infections Association Case Record Form Version.[14] The recorded data included:

1. Demographics: Age, gender, body mass.
2. Underlying diseases: Chronic obstructive pulmonary disease, chronic kidney disease, cardiovascular disease, hypertension, diabetes, cerebrovascular disease, chronic liver disease, tumor.
3. Symptoms from onset to admission: Fever, cough, dyspnea, fatigue or myalgia, diarrhea.
4. Vital signs at admission to ICU: Heart rate, respiratory rate, oxygen saturation, Glasgow Coma Scale (GCS) score.
5. Laboratory tests at admission: Blood routine, coagulation profile, liver and kidney function tests, myocardial enzyme spectrum, atrial natriuretic peptide (BNP), infection indicators (C-reactive protein, procalcitonin).
6. Therapies: Continuous renal replacement therapy (CRRT), oxygen inhalation, noninvasive mechanical ventilation (NIV), invasive mechanical ventilation (IMV).
7. Complications: Acute respiratory distress syndrome (ARDS), acute heart injury, shock.
8. Hospital stay: Duration of stay in hospital prior to admission to ICU, duration of stay in ICU.

2.6 Operational definitions

According to the provisional guidelines of the NIH Pakistan,[14] following definitions were employed in the study.

Moderate Disease: Patients diagnosed with COVID-19 infection with any one of the following features:

1. Respiratory rate [?] 30/min at rest.
2. Oxygen saturation (SpO2) [?] 93% on room air.
3. Arterial oxygen partial pressure (PaO2) /oxygen uptake concentration (FiO2) [?] 300.

Severe Disease: Patients with moderate disease criteria plus any one of the following:

1. Oxygen requirement of more than 10 liters for 90% saturation.
2. 50% of lung involvement on either chest X-ray or HRCT.
3. CRP $>$ 10 mg/L, D-dimer $>$ 1000 mg/mL, serum ferritin $>$ 1000 ng/mL.
4. Secondary infection (diagnosed by blood culture and sensitivity test or raised procalcitonin).
5. Arterial oxygen partial pressure (PaO2)/oxygen uptake concentration (FiO2) [PaO2/FiO2] (PF ratio) $<$ 118 mmHg.

Critical Disease: Patients with severe disease and any one of the following were labeled as having critical disease:

1. Shock
2. Acute Respiratory Distress Syndrome (ARDS)
3. Cardiac injury
4. Multi-organ dysfunction

Shock: Persistent hypotension despite volume resuscitation, requiring vasopressor to maintain mean arterial pressure (MAP) $\pm$ 65 mmHg and serum lactate level $>$ 2 mmol/L.[15]

ARDS: As per the Berlin Definition of ARDS:[16]

1. Onset: Within one week of a known clinical consultation.
2. Respiratory failure not fully explained by cardiac failure or fluid overload.
3. Bilateral opacities not fully explained by fluid overload, lobar or lung collapse or nodules.
4. Oxygen impairment with PF ratio < 300 mmHg.

Cardiac Injury: Cardiac injury is diagnosed if the serum level of a cardiac marker (such as high-sensitivity troponin I) is higher than the 99^{th} percentile upper reference limit, or the ECG and echocardiogram show new abnormalities.[17]

Multi-organ Dysfunction: Acute life-threatening organ dysfunction with any of the following signs:

1. Altered mental status
2. Reduced urine output
3. Shortness of breath or increased respiratory failure
4. Signs of impending shock or circulatory failure
5. Decrease oxygen saturation
6. Lab evidence of coagulopathy
7. Thrombocytopenia
8. Acidosis
9. Raised lactate level
10. Deranged liver function and renal function

2.7 Data Analysis

Continuous variables were expressed as means with standard deviation and 95% confidence interval. Categorical variables were expressed as frequencies (percentages) with 95% confidence interval. Where appropriate, the t-test and chi-square test (Fisher's exact test where required) were used to compare the differences between the survival and death groups. Single-factor logistic analysis was used to explore the risk factors associated with hospital deaths. If the number of events was too small to calculate the odds ratio or there was collinearity between the variables, the variable was excluded from the univariate logistic analysis. $P < 0.05$ was considered statistically significant unless otherwise stated.

3. RESULTS

3.1 Demographics

Twenty eligible patients diagnosed with severe COVID-19 pneumonia were admitted to the ICU of DHQ Hospital Faisalabad during the above mentioned duration. The mean age of the patients was 70±12 years (35 to 85 years), 40% of them were male. The mean duration of symptoms before admission to the ICU DHQ Hospital was 11±9 days. The most common symptom on admission was cough. Other common symptoms include fatigue or myalgia (n=18, 90%), fever (n=17, 85%), and dyspnea (n=16, 80%). Six (30%) patients had more than one underlying disease. More than 50% (n=11, 55%) of patients had underlying diseases, of which hypertension was the most common (n=11, 55%), followed by cardiovascular diseases (n=4, 20%) and diabetes (n=3, 15%). Ten patients died during the ICU hospitalization (hereinafter referred to as "death group"), and 10 patients recovered and were discharged (hereinafter referred to as "survival group"). Table 1 represents the demographics, clinical characteristics, and laboratory indicators of the patients in each group.

3.2 Laboratory indicators

Laboratory parameters showed that 11 patients (55%) developed lymphopenia (lymphocyte count $< 0.8\times10^9$/L), of which eight patients eventually died ($P = 0.07$). The baseline lymphocyte count of the survival group was significantly higher than that of the death group. Among the survivors, the lymphocyte count was the lowest on days 1 to 3 after hospitalization, however, improved during hospitalization, while persistent lymphopenia was observed in the death group. The white blood cell count in the death group showed a rising trend, and its mean value began to be higher than that in the survival group from 4 to 6 days after admission to the ICU DHQ Hospital Faisalabad.

The serum creatinine and blood urea nitrogen in the death group were significantly higher than those in the survival group, and the urine volume continued to decrease after 4 to 6 days of admission to the ICU. The D-dimer increased at admission to 6.91 ± 11.17 mg/mL in all patients, and 15 (75%) patients had D-dimer > 1 mg/mL. Half of the patients had blood urea nitrogen > 7.1 μmol/L. The D-dimer of the survival group was significantly lower than that of the death group and began to show a downward trend from 9 to 11 days after admission to the ICU. Most patients had increased lactate dehydrogenase (LDH) (17 cases, 85%) and BNP (15 cases, 75%) at the time of admission, respectively 539.15±455.85 U/L and 5696.53±8832.56 pg/mL.

In all patients, C-reactive protein (CRP) was elevated to 101.46±65.60 mg/L. The CRP in the survival group showed a significant downward trend after the admission to the ICU, while the CRP in the death group increased as the disease worsened. The majority of the patients (17 cases, 85%) had high procalcitonin (ProCT), 0.31±0.42 ng/mL, of which 8 (40%) patients had 0.1 [?] ProCT < 0.25 ng/mL and 7 (35%) patients had 0.25 [?] ProCT < 0.5 ng/mL. Figure 1 shows the trends of laboratory indicators in the patients from the time of admission to the ICU.

3.3 ICU treatment and clinical outcomes

The duration of stay in ICU was 15+-11 days. Most patients (n=19, 95%) required oxygen inhalation in the ICU. Fourteen patients (70%) required NIV support. All 10 patients in the death group received NIV treatment, of which six (30%) received further IMV treatment. Six patients receiving IMV also received CRRT due to multi-organ dysfunction. Acute heart injury was the most common complication (n=19, 95%), followed by shock (n=12, 60%), ARDS (n=12, 60%), and pneumothorax (n=2, 10%). The death group patients were all considered complicated with shock and ARDS, and the probability of complicating shock and ARDS in the death group was significantly higher than that in the survival group (100% vs 20%, P = 0.001; 100% vs 20%, P = 0.001). Table 2 represents the treatment measures, complications, and clinical outcomes of the patients.

3.4 Risk factors for death

Half of the patients (10 patients) died between 2 and 19 days after admission to the ICU. Figure 2 shows the clinical course and outcome of each patient. Compared with dead patients, the average weight of the surviving patients was lower (61.70+-2.36 vs 68.60+-7.15 kg, P = 0.01), and the GCS score was higher (14.69+-0.70 vs 12.70+-2.45, P = 0.03). Univariate logistic analysis showed that increased body weight (OR=1.39, 95% CI: 1.01˜1.93) and decreased lymphocyte count (OR=0.11, 95% CI: 0.01˜0.84) were significantly associated with death among the patients. Table 3 represents the association of various factors with death in the regression model.

4 DISCUSSION

Our study reports the analysis of clinical characteristics and outcomes of 20 confirmed COVID-19 patients characterized by severe disease. Nine (45%) of these patients died within 35 days of admission to the hospital.

Our critically ill patients with COVID-19 were older which is in line with other studies.[8,18] In previous studies involving severe COVID-19 patients, most common symptoms were fever, cough, fatigue, and dyspnea.[6-8,9,11,18] Similarly, the incidence of cough, fatigue or myalgia, fever, and dyspnea on admission in our study were 95% (n=19), 90% (n=18), 85% (n=17) and 80% (n=16) respectively. In these patients mean duration of symptoms was 11+-9 days from onset to ICU admission, and the previous studies reported similar (from 7-12 days) duration of symptoms prior to ICU admission.[5,7,9,11]

More than half of the patients (n=11, 55%) in our center had underlying diseases, similar to the data reported by the study from Wuhan (n=64, 46%).[8] However, a much higher percentage of patients has been reported in other studies.[7,18] Similar to the previous studies,[8,18] hypertension was the most common comorbidity, followed by cardiovascular disease and diabetes in our study. This requires more follow-up data for the observation of hypertension, the hypertension treatment received by the patient, and the assessment of high-risk factors.

With regards to laboratory indicators, 11 (55%) patients in our center developed lymphocytopenia on admission, and it mainly occurred in the death group (n=8). Decreased lymphocyte count was significantly associated with the death of COVID-19 patients in ICU. This is consistent with the results of a single factor analysis of the retrospective study from Wuhan.[8] Previous studies of Severe Acute Respiratory Syndrome [SARS] and Middle East Respiratory Syndrome [MERS] have also found lymphopenia in their studies. Studies have confirmed that lymphopenia is one of the earliest changes in SARS and a reliable prognostic indicator of SARS.[19] In addition, studies have also shown that MERS coronavirus can induce T cell apoptosis through the activation of apoptotic pathways.[20] In several previous studies on moderate disease patients infected with SARS-CoV-2, only 35%[6] and 40%[5] of patients had mild lymphopenia, whereas in other studies severe SARS-CoV-2 associated lymphopenia occurred in more than 70%[12] and 80%[11] of the infected patients, suggesting that lymphopenia may reflect the severity of SARS-CoV-2 infection.

Most critically ill patients in our center had an increased LDH (n=17, 85%) when they were admitted, slightly higher than the 76%[6] and 67%[5] observed in patients from the other studies. All patients in our study had elevated D-dimers on admission, and 15 (75%) patients had D-dimers > 1 mg/L. However, in the study of moderate disease COVID-19 patients, only 36% had an increase in D-dimer.[6] Another early study from Wuhan also showed that ICU patients had a higher level of D-dimer (median D-dimer level of 2.4 mg/L) than non-ICU patients (median D-dimer level of 0.5 mg/L). Studies have also found that D-dimer > 1 mg/L has been associated with increased mortality of patients.[5] Our study did not observe differences between survival and death groups in terms of D-dimer, which may be related to small sample size. The CRP of all patients in our study was increased to 101.46+-65.60 mg/L, which was much higher than the average CRP in moderate disease COVID-19 patients, 51.4+-41.8 mg/L.[6] The probability of CRP increase (100%) was also higher in our study than that of moderate disease COVID-19 patients, 60.7%[18] and 86%.[6] Similarly, the probability of elevated ProCT (85%, n=17) was much higher in our study than the 6% to 30% probability found in moderate disease COVID-19 patient studies.[6,5,18] It is, therefore, suggested that secondary bacterial infection may be a complication in severe patients and cannot be disregarded.

Mechanical ventilation is the main supportive treatment for COVID-19 critically ill patients. In our study, only six patients (30%) received further IMV treatment, which is much lower than reported in other ICU patients: 88% (Lombardy, Italy),[10] 47% (Wuhan),[8] 42% (Wuhan),[11] and 30% (Wuhan).[7] Non-invasive ventilation was used more frequently, with 70% of patients receiving NIV in our study, as compared to the rate of NIV use in other ICU studies: 42% (Wuhan),[8] 56% (Wuhan),[11] and 62% (Wuhan).[7]

Acute hypoxemic respiratory failure caused by ARDS has been found to be the most common complication (60% to 70% of patients admitted to the ICU), followed by shock (30%), myocardial dysfunction (20% to 30%) and acute kidney disease injury (10%˜30%) [5,6 9-11].[7-11] In our study, acute heart injury was the most common (19 cases, 95%), followed by ARDS (12 cases, 60%), shock (12 cases, 60%), and pneumothorax (2 cases, 10%). A study of mild disease COVID-19 patients in Wuhan reported that 53% of patients in their cohort died of respiratory failure, 7% died of shock (probably caused by fulminant myocarditis), and 33% of patients died of both conditions.[21] In our study, the 10 patients in the death group were all complicated with shock and ARDS. The probability of death and ARDS in the death group was much higher than that in the survival group. Due to the limited sample size, this study failed to show the association of concurrent ARDS or shock with the death of patients. We speculate that concurrent ARDS and shock may be related to the death of severe COVID-19 patients. Due to the limitation of sample size and lack of laboratory data, our study found that only increased BMI and decreased lymphocyte count were significantly associated with an increased chance of death in patients with COVID-19 in the ICU.

This study had several limitations. Firstly, the study was conducted in a single center and was limited by the time of follow-up. Only 20 patients with serious and critical COVID-19 disease patients were included. Smaller sample size may reduce the reliability of the statistical analysis. Secondly, there was a lack of detailed medical and treatment information during the hospitalization of patients, such as mechanical ventilation parameters, blood gases, patient medication, imaging examinations, and other supportive treatments. Finally, this is a retrospective study that failed to include adequate laboratory tests on all patients,

including interleukin 6, serum ferritin, etc., resulting in an inability to assess their role in predicting hospital deaths. The findings of our study can be utilized by future studies to further investigate the clinical course and outcome of COVID-19 patients hospitalized in ICU. However, a prospective multicenter study with a larger sample size is necessitated to further explore the factors associated with nosocomial death in severe COVID-19 patients.

5. CONCLUSION

In summary, critically ill patients with COVID-19 tend to be relatively older. Hypertension is the most common underlying condition in critical COVIID-19 patients. The mortality rate is high in critical COVID-19 patients. Lower GCS score, higher body weight, and decreased lymphocyte count appear to be potential risk factors for the death of COVID-19 patients in the ICU.

REFERENCES

1. Waris A, Atta U, Ali M, Asmat A, Baset A. COVID-19 outbreak: current scenario of Pakistan. *New Microbes New Infect* . 2020;35:100681. doi:10.1016/j.nmni.2020.100681
2. World Health Organization. Coronavirus disease (COVID-19) pandemic. 2020; https://www.who.int/emergencies/diseases/novel-coronavirus-2019. Accessed 19 August, 2020.
3. Worldometer. Coronavirus. COVID-19 Coronavirus pandemic. 2020; https://www.worldometers.info/coronavirus/?utm_campaign=homeAdUOA?Si. Accessed 19 August, 2020.
4. Diaz-Ballve L, Risso-Vasquez A, Rios F. Coronavirus disease 2019 (COVID-19) aspects of interest for critical care - narrative review. *Rev Arg de Ter Int* . 2020;Suppl 1:1-11.
5. Chen N, Zhou M, Dong X et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *The Lancet* . 2020;395(10223):507-513. doi:10.1016/s0140-6736(20)30211-7
6. Huang C, Wang Y, Li X et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet* . 2020;395(10223):497-506. doi:10.1016/s0140-6736(20)30183-5
7. Wang D, Hu B, Hu C et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. *JAMA* . 2020;323(11):1061-1069. doi:10.1001/jama.2020.1585
8. Guan W, Ni Z, Hu Y et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *NEJM* . 2020;382(18):1708-1720. doi:10.1056/nejmoa2002032
9. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. *Intensive Care Med* . 2020;46(5):846-848. doi:10.1007/s00134-020- 05991-x
10. Grasselli G, Zangrillo A, Zanella A et al. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. *JAMA* . 2020;323(16):1574-1581. doi:10.1001/jama.2020.5394
11. Yang X, Yu Y, Xu J et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *The Lancet Respiratory Medicine* . 2020;8(5):475-481. doi:10.1016/s2213-2600(20)30079-5
12. Wang Y, Lu X, Li Y et al. Clinical Course and Outcomes of 344 Intensive Care Patients with COVID-19. *Am J Respir Crit Care Med* . 2020;201(11):1430-1434. doi:10.1164/rccm.202003-0736le
13. Zhang L, Zhu F, Xie L et al. Clinical characteristics of COVID-19-infected cancer patients: a retrospective case study in three hospitals within Wuhan, China. *Annals of Oncology* . 2020;31(7):894-901. doi:10.1016/j.annonc.2020.03.296
14. National Institute of Health (NIH), Islamic Republic of Pakistan. COVID-19. 2020; https://www.nih.org.pk/novel-coranavirus-2019-ncov/. Accessed March 27, 2020.
15. World Health Organization. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected: interim guidance 13 March 2020. 2020; https://apps.who.int/iris/handle/10665/331446. Accessed March 27, 2020.

16. Dubb R, Hekler M, Kaltwasser A. Bauchlagerung von Intensivpatienten - Gibt es neue Trends?. *Intensiv* . 2004;12(01):4-8. doi:10.1055/s-2004-812696
17. Gao C, Wang Y, Gu X et al. Association Between Cardiac Injury and Mortality in Hospitalized Patients Infected With Avian Influenza A (H7N9) Virus. *Crit Care Med* . 2020;48(4):451-458. doi:10.1097/ccm.0000000000004207
18. Fu L, Wang B, Yuan T et al. Clinical characteristics of coronavirus disease 2019 (COVID-19) in China: A systematic review and meta-analysis. *Journal of Infection* . 2020;80(6):656-665. doi:10.1016/j.jinf.2020.03.041
19. Ding Y, He L, Zhang Q et al. Organ distribution of severe acute respiratory syndrome(SARS) associated coronavirus(SARS-CoV) in SARS patients: implications for pathogenesis and virus transmission pathways. *J Pathol* . 2004;203(2):622-630. doi:10.1002/path.1560
20. Chu H, Zhou J, Ho-Yin Wong B et al. Productive replication of Middle East respiratory syndrome coronavirus in monocyte-derived dendritic cells modulates innate immune response. *Virology* . 2014;454:197-205. doi:10.1016/j.virol.2014.02.018
21. Wang X, Liu W, Zhao J et al. Clinical characteristics of 80 hospitalized frontline medical workers infected with COVID-19 in Wuhan, China. *Journal of Hospital Infection* . 2020;105(3):399-403. doi:10.1016/j.jhin.2020.04.019**TABLE 1** Demographics, clinical characteristics, and laboratory indicators of the patients

Parameter	**Total (n =20)**	**Survival group (n =10)**	**Death group (n =10)**	**P value**
Age (year)	69.75±12.00	69.80±7.79	69.70±15.60	0.99
Gender	Gender	Gender	Gender	Gender
Male	8 (40%)	3 (30%)	5 (50%)	0.65
Female	12 (60%)	7 (70%)	5 (50%)	
Weight (kg)	65.15±6.28	61.70±2.36	68.60±7.15	0.01
BMI	24.45±1.84	24.12±2.03	24.78±1.67	0.44
Comorbidities	Comorbidities	Comorbidities	Comorbidities	Comorbidities
COPD	2 (10%)	1 (10%)	1 (10%)	1
Chronic kidney disease	1 (5%)	0 (0%)	1 (10%)	1
Cardiovascular disease	4 (20%)	2 (20%)	2 (20%)	1
Hypertension	11 (55%)	6 (60%)	5 (50%)	1
Diabetes	3 (15%)	2 (20%)	1 (10%)	1
Cerebral vascular disease	2 (10%)	1 (10%)	1 (10%)	1
Clinical manifestations and signs	Clinical manifestations and signs	Clinical manifestations and signs	Clinical manifestations and signs	Clinical manifestations and signs
Fever	17 (85%)	8 (80%)	9 (90%)	1
Cough	19 (95%)	10 (100%)	9 (90%)	1
Dyspnea	16 (80%)	10 (100%)	6 (60%)	0.09
Fatigue or myalgia	18 (90%)	10 (100%)	8 (80%)	0.47
Diarrhea	3 (15%)	1 (10%)	2 (20%)	1
Vital Signs	Vital Signs	Vital Signs	Vital Signs	Vital Signs
Oxygen saturation (%)	85.55 ±10.30	(84.10±13.82)	(89.00±4.42)	0.3
Respiratory rate	29.30±7.21	30.70±8.17	27.90±6.21	0.4
Respiratory rate > 24/min	14 (70%)	7 (70%)	7 (70%)	1

Parameter	**Total (n =20)**	**Survival group (n =10)**	**Death group (n =10)**	**P value**
Heart rate	97.95±16.72	99.50±16.94	96.40±17.25	0.69
GCS score	13.65±2.01	14.69±0.70	12.70±2.45	0.03
Duration	Duration	Duration	Duration	Duration
Days from onset to ICU admission	11.15±9.45	8.10±9.47	14.20±8.93	0.16
Days in the general ward prior to ICU admission	5.55±6.86	4.50±5.78	6.60±7.96	0.51
Days from onset to hospitalization	9.35±6.34	8.20±3.08	10.50±8.52	0.43
Days from onset to dyspnea	9.95±6.63	7.22±7.50	12.40±4.89	0.09
Laboratory indicators	Laboratory indicators	Laboratory indicators	Laboratory indicators	Laboratory indicators
WBC (×10^9/L)	8.70±5.13	9.12±5.87	8.29±4.56	0.73
< 4	1 (5%)	0 (0%)	1 (10%)	1
4-10	14 (70%)	8 (80%)	6 (60%)	0.63
> 10	5 (25%)	2 (20%)	3 (30%)	1
NEU (%)	82.40±10.44	80.70±9.11	84.10±11.86	0.48
Lymphocyte count (×10^9/L)	0.95±0.91	1.01±0.49	0.89±1.22	0.78
< 0.8	11 (55%)	3 (30%)	8 (80%)	0.07
Hemoglobin (g/L)	128.20±18.49	126.60±14.19	126.80±22.68	0.71
Anemia	3 (15%)	1 (10%)	2 (20%)	1
PT (s)	13.76±1.10	13.70±1.07	13.82±1.19	0.81
APTT (s)	95.26±18.18	94.83±15.30	95.70±21.53	0.92
D-Dimer (mg/mL)	6.91±11.17	5.16±7.46	8.65±14.17	0.5
> 0.5 to [?]1	5 (25%)	2 (20%)	3 (30%)	1
> 1	15 (75%)	8 (80%)	7 (70%)	1
ALT (U/L)	59.96±96.75	73.30±129.15	46.60±51.82	0.55
> 40	6 (30%)	3 (30%)	3 (30%)	1
AST (U/L)	69.75±83.40	41.80±30.07	97.70±109.74	0.14
> 40	8 (40%)	3 (30%)	5 (50%)	0.66
TBIΛ (μμoλ/Λ)	13.62±7.89	12.69±4.80	14.55±10.32	0.61
> 17.1	2 (10%)	1 (10%)	1 (10%)	1
Albumin (g/L)	34.92±2.77	34.92±3.35	34.91±2.23	0.99
BϒN (μμoλ/Λ)	7.22±3.81	5.76±3.03	8.69±4.08	0.09
> 7.1	10 (50%)	4 (40%)	6 (60%)	0.66
CK (U/L)	96.15±52.84	100.90±47.30	91.40±60.05	0.7
> 185	2 (10%)	1 (10%)	1 (10%)	1
CK-MB (U/L)	16.40±8.59	17.70±9.33	15.10±8.06	0.51
LDH (U/L)	539.15±455.85	574.30±604.95	504.0±264.52	0.74
> 245	17 (85%)	9 (90%)	8 (80%)	1
BNP (pg/mL)	5696.53±8832.56	2991.77±2441.31	8401.28±11936.46	0.18
> 400	15 (75%)	8 (80%)	7 (70%)	1
CRP (mg/L)	101.46±65.60	114.58±74.25	88.33±56.47	0.39
ProCT (ng/mL)	0.31±0.42	0.37±0.58	0.25±0.14	0.53
<0.1	3 (15%)	2 (20%)	1 (10%)	1
0.1-0.25	8 (40%)	4 (40%)	4 (40%)	1

Parameter	Total (n =20)	Survival group (n =10)	Death group (n =10)	P value
0.25-0.5	7 (35%)	3 (30%)	4 (40%)	1
[?]0.5	2 (10%)	1 (10%)	1 (10%)	1

The data are shown as mean (variance, SD) or n (%). P value was calculated by t test or chi-square test, wherever appropriate.

BMI: Body mass index. COPD: Chronic obstructive pulmonary disease. GCS: Glasgow Coma Sale. WBC: White blood cell. NEU%: Percentage of neutrophils. PT: Prothrombin time. APTT: Activated partial thromboplastin time. ALT: Alanine transaminase. AST: Glutamic oxaloacetic transaminase. TBIL: Total bilirubin. BUN: Blood urea nitrogen. CK: Creatine kinase. CK-MB: Creatine kinase isoenzyme. LDH: Lactate dehydrogenase. BNP: B-type natriuretic peptide. CRP: C-reactive protein. ProCT: Procalcitonin.

TABLE 2 Treatments, complications, and clinical outcomes of the patients

Treatment and Outcome	Total (n =20)	Survival group (n =10)	Death group (n =10)	P value
Treatments	Treatments	Treatments	Treatments	Treatments
CRRT	6 (30%)	0 (0%)	6 (60%)	0.01
Oxygen Therapies	19 (95%)	10 (100%)	9 (90%)	1
NIV	14 (70%)	4 (40%)	10 (100%)	0.01
IMV	6 (30%)	0 (0%)	6 (60%)	0.01
Outcomes	Outcomes	Outcomes	Outcomes	Outcomes
Length of ICU stay (day)	14.65±11.25	20.60±12.83	8.70±4.90	0.01
Total hospital stay (day)	20.70±12.21	26.20±13.30	15.20±8.40	0.04
Shock	12 (60%)	2 (20%)	10 (100%)	<0.01
ARDS	12 (60%)	2 (20%)	10 (100%)	<0.01
Acute cardiac injury	19 (95%)	10 (100%)	9 (90%)	1
Pneumothorax	2 (10%)	0 (0%)	2 (20%)	0.47

CRRT: Continuous renal replacement therapy. NIV: Non-invasive mechanical ventilation.

IMV: Invasive mechanical ventilation. ARDS: Acute respiratory distress syndrome.

TABLE 3 Univariate logistic analysis of risk factors associated with death

Parameter	OR	95% CI	P value
Age	1	0.93-1.08	0.99
Male vs Female	0.43	0.06-2.60	0.37
Weight	1.39	1.01-1.93	0.05
BMI	1.23	0.74-2.05	0.42
With vs Without comorbidity			
COPD	1	0.05-18.57	1
Cardiovascular disease	1	0.11-8.95	1
Hypertension	0.67	0.11-3.93	0.65
Diabetes	0.44	0.02-5.53	0.54

Parameter	**OR**	**95% CI**	**P value**
Cerebral vascular disease	1	0.05-18.57	1
Clinical Characteristics			
Fever vs no fever	0.44	0.03-5.88	0.54
Diarrhea vs no diarrhea	0.44	0.03-5.88	0.54
Oxygen saturation	1.08	0.96-1.37	0.38
Respiratory rate > 24/min	1	0.14-7.16	1
Heart rate	0.99	0.93-1.04	0.6
GCS score	0.33	0.06-0.83	0.09
Days from onset to ICU admission	1.08	0.98-1.24	0.16
Days in the general ward prior to ICU admission	1.05	0.92-1.23	0.49
Laboratory Parameters			
Blood complete ($\times 10^9$/L)			
4-10	0.38	0.04-2.61	0.34
> 10	1.71	0.22-16.09	0.61
Neutrophil (%)	1.03	0.95-1.14	0.46
Lymphocyte count <0.8×109/L	0.11	0.01-0.84	0.03
Anemia vs no anemia	0.44	0.03-5.88	0.54
PT	1.11	0.48-2.70	0.8
APTT	1	0.95-1.06	0.91
D-Dimer > 1 mg/mL	0.58	0.58-0.06	061
ALT > 40 U/L	1	0.14-7.16	1
Albumin	1	0.71-1.40	0.99
BΥN > 7.1 μμολ/Λ	0.58	0.06-4.54	0.61
CK > 185 U/L	1	0.05-18.58	1
LDH > 245 U/L	0.44	0.02-5.53	0.54
BNP > 400 pg/mL	0.58	0.06-4.54	0.61
CRP	1	0.98-1.01	0.37
ProCT (ng/mL)			
< 0.1	0.44	0.02-5.53	0.54
0.1-0.25	1	0.16-6.20	1
0.25-0.5	1.56	0.24-10.82	0.64
[?] 0.5	1	0.04-28.00	1

OR: Odds ratio. CI: Confidence interval. BMI: Body mass index.

COPD: Chronic obstructive pulmonary disease. GCS: Glasgow Coma Scale.

PT: Prothrombin time. APTT: Activated partial thromboplastin time.

ALT: Alanine transaminase. BUN: Blood urea nitrogen. CK: Creatine kinase.

LDH: Lactate dehydrogenase. BNP: B-type natriuretic peptide.

CRP: C-reactive protein. ProCT: Procalcitonin.

FIGURE 1 Tracking of main laboratory markers from time of admission to the ICU

Temporal changes in laboratory markers from the admission in the patients. The diagraphs show the changes of leukocyte count (A), neutrophil percentage (B), lymphocyte count (C), D- dimer (D), urea nitrogen (E), C- reactive protein (F), serum creatinine (G), and urine volume (H) in 20 patients with length of the stay. The blue line represents the survival group and the red line the death group.

FIGURE 2 Clinical course and outcome of 20 COVID-19 ICU patients