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Para-clinical and Epidemiological Features of COVID-19 in Deceased Patients: A Comparison with Treated Patients

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Abstract

Background: Patients with COVID-19 have shown a wide variety of symptoms and mortality rates in different communities.
Objectives: This study aimed to compare the epidemiological, clinical, and paraclinical features of patients with COVID-19 who have overcome the disease with patients who died.
Methods: All hospitalized patients admitted to Special Corona Hospital who had a positive real-time PCR test for SARS-CoV-2 from January to March 2020 were included in the study. Clinical characteristics, date of disease onset, hospital admission date, and the severity of COVID-19 were obtained from each patient's medical records. Independent sample *t*-test was used to compare continuous variables between the groups of the discharged and expired patients. The independence between categorical variables and the outcome was assessed by Chi-square or Fisher's exact tests.
Results: The order of essential variables for admission as the starting time are pH, WBC count, loss of consciousness, neutrophil count, base excess (BE), HCO_3, age, BUN, O_2 saturation, and lymphocyte count.
Conclusions: In the current study, the mortality rate of COVID-19 was 30% and was significantly associated with critical disease intensity, fever, chills, loss of consciousness, ischemic heart disease (IHD) history, Parkinson's disease, invasive O_2 therapy, and troponin level.

Keywords: COVID-19, Mortality, Death Causes, Treated Patients

1. Background

A novel coronavirus disease 2019 (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) that has a 79.5% similarity to SARS-CoV (SARS epidemic in 2003) and spread in individuals through various routes, such as droplets, airborne particles, feces, and oral mucosa (1, 2). Patients with COVID-19 have shown a wide range of symptoms, including asymptomatic to respiratory, gastrointestinal, neurological, etc. The most common clinical symptoms were fever, cough, and fatigue. Gastrointestinal symptoms such as nausea, anorexia, diarrhea, and vomiting are common, and even some patients have experienced gastrointestinal symptoms without respiratory symptoms (3, 4). The COVID-19 mortality rate at initial studies in China has been reported to be 2.3% (4). Further, On December 04, 2020, has proceeded in more than 165,000 dying worldwide with a universal mortality rate of 6.8%, and at this time, December 04, 2020, globally mortality reported by WHO is 2.3% (5). In July 2020, an experiment in Wuhan, China, revealed that older age, hypertension, and elevated lactate dehydrogenase (LDH) need accurate detection and immediate interference to stop the possible development of rigorous COVID-19. Severe male cases with heart damage, hyperglycemia, and high-dose corticosteroid use may be in great danger of death (6). An experiment in Italy revealed that of 3,988 critically ill patients admitted from February 20 to April 22, 2020, 50.4% of patients with COVID-19 had been discharged from the intensive care unit, 48.7% had died in the intensive care unit, and 0.8% were still in intensive care units (ICU) (7).

2. Objectives

Given the fact that the symptoms of the disease, its pathogenicity, and other features can be different in various situations and places, we aimed to compare the epidemiological, clinical, and paraclinical features of patients with COVID-19 who have overcome the disease with those patients who died in Ahvaz, Southwest of Iran.

3. Methods

All adult patients admitted to Special Corona Center with a diagnosis of COVID-19 over three months were included in this study. The current observational, retrospective investigation evaluated all hospitalized patients from January to March 2020 in Ahvaz city. Having clinical symptoms of COVID-19 and also positive real-time PCR for SARS-CoV-2 were the inclusion criteria. Therefore, subjects with negative laboratory results of SARS-CoV-2 were excluded from the study. All patients in this study lived in Ahvaz city during the COVID-19 outbreak. Demographic data, clinical characteristics (including medical history, history of exposure, symptoms, and laboratory findings) were extracted from each patient's medical records. The date of disease onset and hospital admission date, and the severity of COVID-19 were also noted. The onset date was defined as the day when the patients noticed any symptoms. The severity of COVID-19 was defined according to the diagnostic and treatment guideline for SARS-CoV-2 issued by the Chinese National Health Committee version 3 - 5 (8). The Ethical Approval Code is IR.AJUMS.REC.1399.088.

3.1. Statistical Analysis

Independent sample *t*-test was used to compare continuous variables between the groups of the discharged and expired patients. The independence between categorical variables and the outcome was assessed by chi-square or Fisher's exact tests. The Kaplan-Meyer curve was plotted to visualize the development of survival probabilities for two different starting time-points, hospital admission and clinical symptoms diagnosis. Moreover, the log-rank test was used to investigate the difference in the two starting time-point curves' survival probabilities. Survival analysis was utilized to assess the impact of various variables on time to death/discharge data. In this dataset, dying from COVID-19 was considered the event, and discharge was assumed to be the right censoring. When the number of covariates and factors exceeds the number of observations, routine and standard survival analysis approaches, such as Cox's proportional hazard regression, do not result in adequate and reliable estimations (9).

4. Results

Of all 97 cases with COVID-19, 30 (30.9%) died, and 67 (69.1%) were discharged after recovery. The distribution of variables across the two groups of cases is shown in Table 1 and 2. Death from COVID-19 was significantly associated with critical disease intensity ($P < 0.001$), loss of consciousness ($P = 0.001$), ischemic heart disease (IHD) ($P = 0.005$), Parkinson ($p = 0.028$), invasive O_2 support ($P < 0.001$), and non-negative Troponin ($P = 0.016$). Dead individuals were almost 11 years older than those discharged ($P = 0.001$). Discharging from COVID-19 was associated with the lower mean of respiratory rate (RR), blood sugar (BS), BUN, AST, total and direct bilirubin, neutrophil count, and sodium. Moreover, discharging is affiliated with higher O_2 saturation, higher lymphocyte count, and neutral pH, higher HCO_3, and base excess (BE) (Table 2).

The survival probability quartiles in two different starting times of admission and presentation of symptoms are shown in Table 3. The starting time for admission was recorded for all patients, while only 77 (79%) cases remembered the day when the first COVID-19 symptoms appeared. Based on the Kaplan-Meier (Product Limit) approach, the mean survival time with admission and beginning of symptom as the starting times was 11.92 days and 20.87 days, respectively. Moreover, 25% of the cases survived 26 days and 17 days after the beginning of symptoms and admission, respectively. The median and third quartile survival time after admission was 12 days and eight days, respectively. The median and third quartile survival time after symptoms were 22 days 16 days, respectively. In other words, 50% of the cases died between days 16 and 26 after diagnosing their clinical symptoms. Also, half of the patients died between days eight and 17 after their first admission. The log-rank test showed a significant difference in the two survival probabilities (chi-square = 17.39, DF = 1, $P < 0.001$).

The results of the random survival forest are shown in Figures 1 and 2. The order of essential variables for admission as the starting time is shown in Figure 1, in which pH, WBC count, loss of consciousness, neutrophil count, BE, HCO_3, age, BUN, O_2 saturation, and lymphocyte count were at the top list. Moreover, some critical variables for symptom recognition as the starting time were BUN, lymphocyte count, loss of consciousness, IHD, Cerebrovascular accident (CVA), CVA, age, and AST. Other variables are shown in detail in Figure 2.

5. Discussion

In the current study, the mortality rate of COVID-19 was 30% and was significantly associated with critical disease

Table 3. Means and Quartiles for Survival Time in the Hour

Quantity and Start From	Estimate Hour (Day)	Std. Error	95% Confidence Interval	
Mean				
Admission	286.119 (11.92)	25.933	235.29	336.949
Symptom	500.899 (20.87)	40.712	421.103	580.695
First quartile				
Admission	408 (17)	55.118		
Symptom	624 (26)	69.561		
Median				
Admission	288 (12)	24.79		
Symptom	528 (22)	35.195		
Third quartile				
Admission	192 (8)	29.869		
Symptom	384 (16)	39.123		

intensity, fever, chills, loss of consciousness, IHD history, Parkinson's disease, invasive O_2 therapy, and troponin levels. According to several studies, coronavirus infection, similar to some viral infections, may be associated with heart damage. A study of 400 patients admitted to Wuhan, China, found that about one-fifth of patients with COVID-19 had heart disease, which increases mortality (10). Severe and sudden inflammation of the heart muscle causes arrhythmia and impairs the heart's ability to pump blood efficiently. Therefore, patients with a history of cardiovascular disease and hypertension are at higher risk of death than normal individuals (11). Moreover, fatty plaques in the arteries of the heart of people with or without cardiovascular disease symptoms may become unstable due to fever and inflammation, leading to vascular occlusion and cardiovascular problems (12).

The current study declared that increased old age correlated with death in subjects suffering from COVID-19. In most studies, older age has been stated as a related predictor of fatality in SARS-CoV-2 and COVID-19 (13, 14). Opal in 2005 revealed that T-cell and B-cell function and the overproduction of interleukins become further acting by age, leading to a lack in control of viral replication and more extensive proinflammatory responses with harmful consequences (15).

We found that patient discharging was associated with higher O_2 saturation, lymphocyte count, atrial blood pH, HCO_3, and BE. Moreover, the higher mean of BS, BUN, total and direct bilirubin, neutrophil count, and sodium was associated with a higher discharge rate. Other essential studies confirm the mentioned factors in our study, and the results are somehow consistent (6, 14, 16). Li et al. in Wuhan in March 2020 presented that male gender, older subject, leukocytosis, cardiac injury, high blood glucose were associated with death in patients with severe COVID-19 (11). Similarly, in February 2020, Yang found that the increased risk of death of COVID-19 patients with pneumonia is considerable with older patients, duration from the onset of symptoms to ICU admission, ratio of PaO_2 to FiO_2, total bilirubin concentration, and lactate concentration (17).

The mean survival time with admission and symptom starting was approximately 12 and 21 days in the current research, respectively. Another study revealed the patient information based algorithm (PIBA) considered the death rate according to data of the subjects in Wuhan and then in other cities overall China. They calculated the predicted days from hospital admission to death was 13, and the mortality rate of COVID-19 varies from 0.75% to 3% and may decrease in the future (18). the study predicted the force of continuous exposure to coronavirus on the fatality rate gain and was used in Germany, China, France, United Kingdom, Iran, Italy, and Spain, for modeling. Regarding Iran, Italy, and Spain, the fatality rate will increase to 10% with an extra 3 - 10 days of exposure (19). However, for the dead time, the results are not consistent in different studies, and some have reported death up to 57 days after symptom onset (20).

Nevertheless, we found that cases have a higher probability of discharge when the clinical symptoms are diagnosed before the admission time. Finally, our results indicated that pH, WBC count, loss of consciousness, neutrophil count, BE, HCO_3, age, BUN, O_2 saturation, and lymphocyte count were at the top list of factors that affect the prognosis of the disease. Moreover, some critical variables for symptom recognition at the starting time were as follows: BUN, lymphocyte count, loss of consciousness,

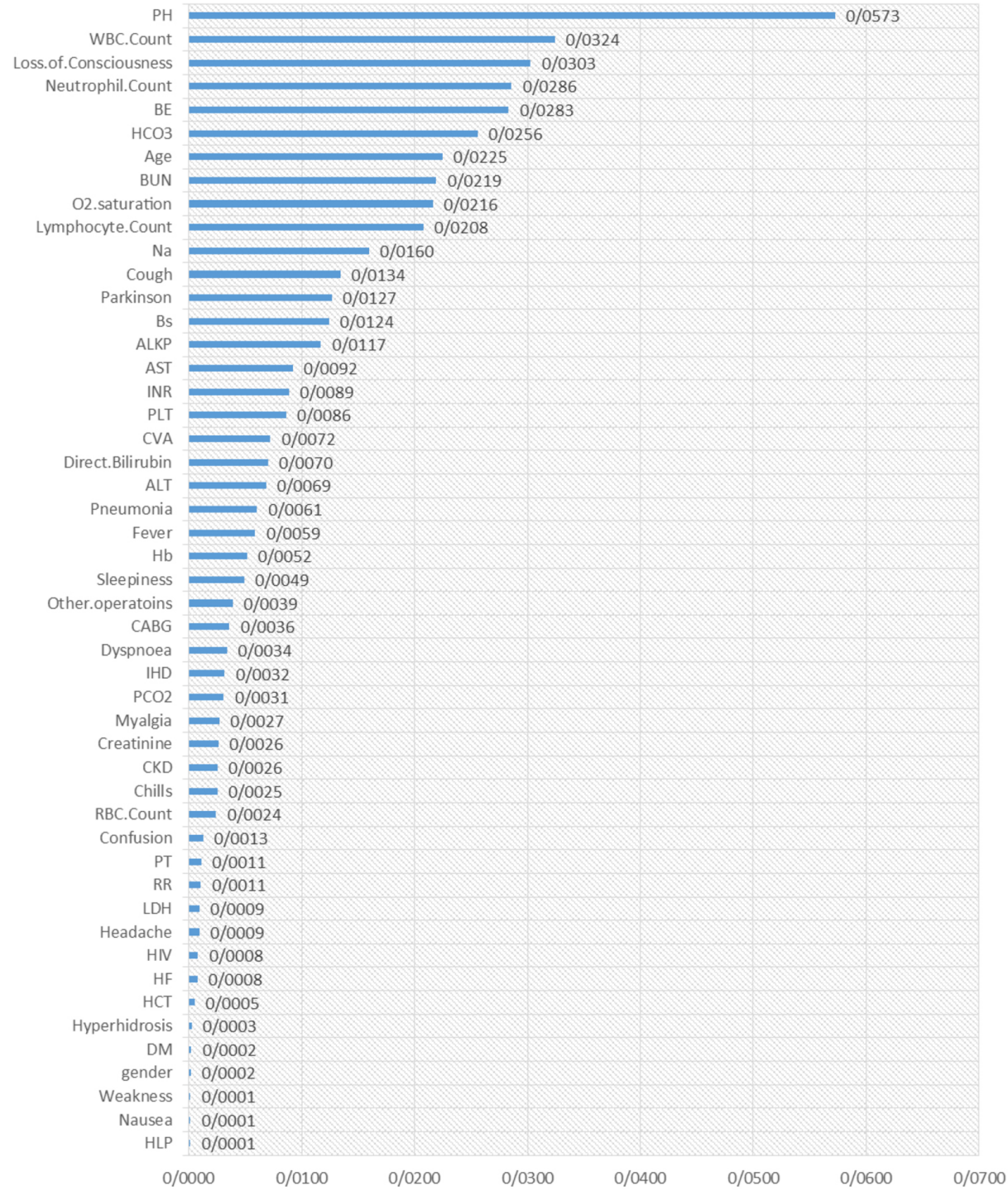

Figure 1. Variable importance resulted by random survival forest for classifying cases into dead and discharged for those with admission as the starting time.

IHD, CVA, age, and AST. It is necessary to mention that most of the mentioned factors are the same in many studies but vary in importance. Garcia et al. reported creatinine, D-dimer, lactate, potassium, arterial pO_2/FIO_2 (P/F ra-

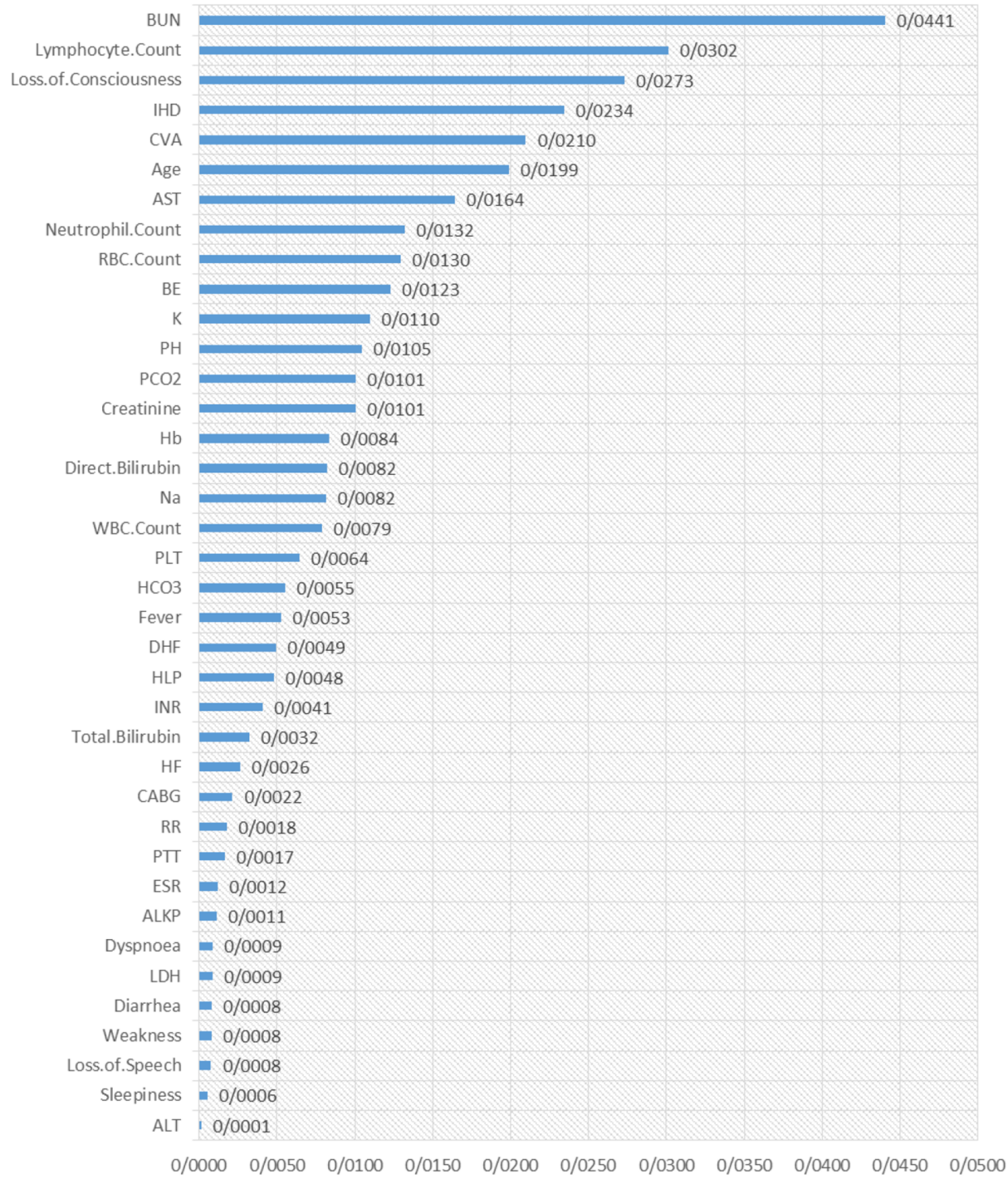

Figure 2. Variable importance resulted by random survival forest for classifying cases into dead and discharged for those with symptoms as the starting time.

tio), and alveolar-arterial gradient at admission and IHD as prognostic factors in patients with COVID-19 (20). Another study by Cummings et al. indicated that chronic pulmonary disease, chronic cardiovascular disease, older

age, and elevated interleukin-6 and D-dimer levels at admission are the most substantial prognostic factors in patients with COVID-19 (21).

5.1. Conclusions

We hypothesize that the survival probability when symptom diagnosis is considered symptom diagnosis was considered the starting time is higher than that of admission time. In other words, cases had a higher probability of discharge when the clinical signs are diagnosed before than at the time of admission. Further, genetics, immune response, health care system, and other factors may affect the prognosis and change the most critical factors affecting the COVID-19 COVID_19 prognosis in different regions.

Footnotes

Authors' Contribution: Study concept and design: A.D, H.B; Acquisition of data: H.B, M.V; Analysis and interpretation of data: P.A; Drafting of the manuscript: R.K; Critical revision of the manuscript for important intellectual content: A.D, M.M; Statistical analysis: P.A; Administrative, technical, and material support: M.M, M.P, A.F; Study supervision: A.D.

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Table 1. Distribution of Categorical Variables in Two Groups of Dead and Discharged COVID-19 Cases

Variable	Outcome, No. (%)		P-Value
	Discharge, 67 (69.1%)	Death, 30 (30.9%)	
Gender			0.812
Female	24 (35.80)	10 (33.30)	
Male	43 (64.20)	20 (66.70)	
Tobacco and alcohol	5 (7.50)	4 (13.30)	0.452
Sign and Symptoms			
Cough	55 (82.10)	20 (66.7)	0.118
Dyspnea	26 (38.80)	15 (50.00)	0.302
Orthopnea	2 (3.0)	0 (0.0)	0.999
Paroxysmal nocturnal dyspnea (PND)	2 (3.0)	0 (0.0)	0.999
Sore throat	4 (6.00)	0 (0.00)	0.308
Chest pain	4 (6.00)	1 (3.30)	0.677
Fever	46 (68.70)	13 (43.30)	0.018
Chills	29 (43.30)	7 (23.30)	0.060
Tachypnea	2 (3.00)	0 (0.00)	0.999
Loss of speech	0 (0.00)	1 (3.30)	0.309
Dizzying	3 (4.50)	0 (0.00)	0.550
Runny nose	1 (1.50)	0 (0.00)	0.999
Level of consciousness (LOC)	0 (0.00)	6 (20.00)	0.001
Hyperhidrosis	3 (4.50)	1 (3.30)	0.793
Weakness	19 (28.40)	8 (26.70)	0.864
Lethargy	19 (28.40)	8 (26.70)	0.864
Sleepiness	0 (0.00)	1 (3.30)	0.309
Hemoptysis	1 (1.50)	0 (0.00)	0.999
Myalgia	27 (40.30)	7 (23.30)	0.106
Vomiting	6 (9.00)	3 (10.00)	0.870
Nausea	14 (20.90)	4 (13.30)	0.376
Anorexia	9 (13.40)	5 (16.70)	0.675
Constipation	2 (3.00)	1 (3.30)	0.927
Diarrhea	8 (11.90)	2 (6.70)	0.430
Stomachache	1 (1.50)	1 (3.30)	0.550
Dry mouth	1 (1.50)	0 (0.0)	0.999
Delusion	0 (0.0)	1 (3.30)	0.309
Confusion	0 (0.00)	1 (3.30)	0.309
Headache	14 (20.90)	2 (6.70)	0.137
Past medical history			
Coronary artery bypass graft (CABG)	5 (7.50)	4 (13.30)	0.357
Other operations	3 (4.50)	3 (10.0)	0.297
Operation mediastinum	1 (1.50)	0 (0.0)	0.999

Chronic obstructive pulmonary disease (COPD)	2 (3.00)	1 (3.30)	0.927
Diabetes mellitus (DM)	15 (22.40)	11 (36.70)	0.142
Hypertension (HTN or HT)	21 (31.30)	11 (36.70)	0.606
Heart failure	2 (3.00)	3 (10.00)	0.149
Ischemic heart disease (IHD)	6 (9.00)	9 (30.00)	0.005
Dengue hemorrhagic fever (DHF)	1 (1.50)	1 (3.30)	0.525
Cerebrovascular accident (CVA)	1 (1.50)	3 (10.00)	0.086
Congestive heart failure (CHF)	0 (0.00)	1 (3.30)	0.309
Hyperlipidemia	3 (4.50)	2 (6.70)	0.643
Sinusitis	1 (1.50)	0 (0.00)	0.999
End-stage renal disease (ESRD)	2 (3.0)	0 (0.0)	0.999
Chronic kidney disease (CKD)	1 (1.50)	2 (6.70)	0.225
Asthma	5 (7.50)	0 (0.00)	0.320
Pneumonia	0 (0.00)	1 (3.30)	0.309
Allergy	1 (1.50)	0 (0.00)	0.999
Tuberculosis (TB)	0 (0.00)	1 (3.30)	0.309
Fatty liver	1 (1.50)	1 (3.30)	0.525
Bedridden	0 (0.00)	1 (3.30)	0.309
Cardiomegaly	0 (0.00)	1 (3.30)	0.309
Hyperthyroidism	2 (3.00)	0 (0.00)	0.999
Rheumatoid arthritis	1 (1.50)	0 (0.00)	0.999
Acute kidney injury (AKI)	0 (0.00)	2 (6.70)	0.093
Auto Immune hepatitis	1 (1.50)	0 (0.00)	0.999
Parkinson	0 (0.00)	3 (10.00)	0.028
Gout	1 (1.50)	0 (0.00)	0.999
Human immunodeficiency viruses (HIV)	0 (0.00)	1 (3.30)	0.309
Pacemaker	1 (1.50)	0 (0.00)	0.999
Kidney transplant patients	1 (1.50)	0 (0.00)	0.999
Critical criterion			
Ventilator	1 (1.50)	15 (50.0)	<0.001
Shock	0 (0.00)	1 (3.30)	0.999
ICU/ multi organ failure	2 (3.00)	5 (16.70)	0.606
Ventilator & multi organ failure	64 (95.5)	9 (30.0)	0.018
O_2 support			<0.001
Invasive	3 (4.50)	25 (83.30)	
Noninvasive	17 (25.40)	5 (16.70)	
Spontaneous	47 (70.10)	0 (0.00)	
Treatments			
Antiviral	59 (88.1)	20 (66.7)	0.012
Antibiotic	42 (62.70)	25 (83.30)	0.042
Corticosteroid	54 (80.60)	22 (73.30)	0.422
Positive troponin	0 (0.00)	3 (15.80)	0.016
Aware of the transmission source	9 (13.40)	4 (13.30)	0.989

Disease intensity			
Weakly	0 (0.00)	1 (5.30)	0.999
Mild	50 (74.6)	0 (0.00)	0.001
Severe	14 (20.9)	1 (3.3)	0.001
Critical	3 (4.5)	29 (96.7)	0.001

Table 2. Distribution of Continuous Variables in Two Groups of Dead and Discharged COVID-19 Cases

Outcome	Mean (SD)	P-Value
Creatine kinase-MB (CK-MB)		0.792
Discharge	22.750 (19.441)	
Death	25.000 (10.412)	
Respiratory rate		0.043
Discharge	23.552 (7.163)	
Death	26.767 (7.016)	
Age		0.001
Discharge	51.930 (15.088)	
Death	62.830 (15.295)	
O_2 Sat.		< 0.001
Discharge	94.896 (4.537)	
Death	87.000 (11.117)	
Blood sugar		0.020
Discharge	130.091 (82.084)	
Death	204.286 (124.959)	
Creatinine		0.329
Discharge	1.603 (2.442)	
Death	2.097 (1.882)	
BUN		< 0.001
Discharge	19.761 (14.075)	
Death	46.933 (41.666)	
Aspartate aminotransferase (AST)		0.052
Discharge	50.344 (34.088)	
Death	155.643 (417.416)	
Alanine aminotransferase (ALT)		0.154
Discharge	32.361 (35.944)	
Death	50.750 (85.117)	
Total bilirubin		0.016
Discharge	0.995 (0.471)	
Death	1.311 (0.725)	
Direct bilirubin		0.035
Discharge	0.300 (0.350)	
Death	0.536 (0.685)	
Alkaline phosphatase		0.472
Discharge	195.684 (121.418)	
Death	173.333 (69.822)	
Lactate dehydrogenase (LDH)		0.216
Discharge	596.072 (274.847)	
Death	686.134 (323.019)	

WBC count		0.165
Discharge	8.065 (9.220)	
Death	10.663 (6.313)	
Neutrophil count		< 0.001
Discharge	67.003 (12.973)	
Death	77.323 (10.445)	
Lymphocyte count		< 0.001
Discharge	27.024 (13.045)	
Death	15.847 (8.364)	
RBC count		0.127
Discharge	4.509 (0.566)	
Death	4.295 (0.741)	
Hemoglobin		0.071
Discharge	13.021 (1.717)	
Death	12.260 (2.238)	
Hematocrit		0.139
Discharge	37.975 (4.626)	
Death	36.197 (6.631)	
Platelet count		0.458
Discharge	171.726 (54.449)	
Death	161.778 (65.304)	
Prothrombin Time (PT)		0.144
Discharge	12.586 (2.527)	
Death	13.423 (2.038)	
Partial Thromboplastin Time (PTT)		0.452
Discharge	37.426 (18.649)	
Death	40.423 (11.197)	
International normalized ratio (INR)		0.077
Discharge	1.141 (0.288)	
Death	1.272 (0.334)	
Erythrocyte sedimentation rate (ESR)		0.281
Discharge	42.490 (25.876)	
Death	51.444 (39.057)	
pH		< 0.001
Discharge	7.404 (0.057)	
Death	7.288 (0.194)	
PCO_2		0.942
Discharge	44.321 (8.284)	
Death	44.145 (13.913)	
HCO_3		0.001
Discharge	26.135 (4.202)	
Death	21.919 (6.369)	
Na		0.010

	Discharge	135.739 (2.769)	
	Death	138.267 (6.565)	
K			0.828
	Discharge	4.099 (0.564)	
	Death	4.130 (0.823)	
P			0.441
	Discharge	4.267 (1.791)	
	Death	5.290 (2.813)	
Ca			0.739
	Discharge	9.057 (1.162)	
	Death	8.900 (0.811)	
Mg			0.328
	Discharge	2.025 (0.287)	
	Death	2.550 (0.943)	