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Original Article

Clinical Features and Predictor of Mortality among Patients with COVID-19 in Shiraz, Iran

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Abstract

Introduction: This study aimed to identify the clinical features and predictor of mortality in patients hospitalized with Coronavirus disease 2019 (COVID-19) in southern Iran.

Methods: This cross-sectional study was performed on patients with COVID-19 admitted to Ali Asghar Hospital in Shiraz, Iran, in 2021. All patients with a definitive diagnosis of COVID-19 were included in the study. The required information was extracted from the patients' medical records.

Results: In this study, 619 patients with COVID-19 were included. Sixty-four patients (10.3%) died due to COVID-19, and 555 (89.7%) patients recovered. The clinical signs of breath shortness, muscle pain, low Oxygen saturation, and intubation were statistically significant between the two groups ($P<0.05$). The results of the multivariate logistic model showed that age >52 years, diabetes, and SaO_2 level less than 90% significantly increased the risk of death in COVID-19 hospitalized patients.

Conclusion: The results of the study showed that patients with SaO_2 levels less than 90% and over the age of 52 and those with diabetes had a higher risk of mortality from COVID-19. Therefore, identifying COVID-19 risk factors and deaths will have important implications for clinical management and disease reduction strategies.

Keywords: Coronavirus disease, Predictor, Mortality, Survival, Iran

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Introduction

Coronavirus disease 2019 (COVID-19) had a great impact on the society all over the world; due to COVID-19, comorbidity and mortality are high (1). Even many patients who were diagnosed with COVID-19 were hospitalized, and the mortality rate was high after vaccination (2). Although most of the COVID-19 patients have mild symptoms, some patients suffer severe complications following the COVID-19 disease such as respiratory failure, shock, and kidney, heart, and other organs failure, which increases the possibility of death in patients (3). Therefore, due to COVID-19, the death rate was about 30% in transplanted patients (4). While the mortality rate in patients with COVID-19 is around 2.3% and that in patients with severe COVID-19 is around 49%, despite the best treatment measures (5, 6). Respiratory symptoms are the most common symptoms reported in COVID-19 patients, and severe respiratory symptoms have a direct impact on the patient's hospitalization and mortality (7).

The most common symptoms of COVID-19 include fever, cough, fatigue, diarrhea, muscle and bone pain, chills, headache, nausea, and vomiting. Acute respiratory distress syndrome is one of the most common complications of COVID-19. In addition to the lungs, this virus also damages other organs, including the heart, kidney, liver, eyes, and nervous system (8). Old age, severity of COVID-19, and increase in C-reactive protein (CRP) level will increase the chance of death in these patients (9). The results of a meta-analysis study showed that acute kidney injury, chronic obstructive pulmonary disease (COPD), diabetes, hypertension, cardiovascular disease (CVD), cancer, increased D-dimer, male gender, older age, current smoker, and obesity are among the risk factors of mortality in COVID-19 patients (10). Also, higher temperature, higher leukocyte counts, and higher urea levels are predictors of mortality in COVID-19 patients (11).

The challenges of COVID-19 are numerous around the world, and it was a serious crisis in low- and middle-income countries due to low literacy, weak health care systems, and shortage of intensive

care beds (12). Many studies have been conducted on the risk factors, severity, and diagnosis of COVID-19. Lu et al. (2021) in China reported that patients with comorbidities; lower lymphocyte counts in hemogram, platelet count and serum albumin; high C-reactive protein level; and renal dysfunction had higher risk for COVID-19 death (13). In the study of Islam et al. (2020) in Bangladesh, the elderly and comorbidities such as COPD, diabetes mellitus (DM), coronary heart disease (CHD) and hypertension (HTN) were mortality risk factors in COVID-19 patients (14). Salari et al. (2021) demonstrated that obesity, higher levels of CRP, blood sugar, D-dimer, and lipid markers were the predictive factors of COVID-19-related mortality odds in Rasht, Iran (15). Zali et al. (2020) in Tehran showed that the highest rate of death related to COVID-19 was in patients over 65 years old, and those suffering from diabetes, cardiovascular diseases and cancer (16). The type and number of mortality risk factors in COVID-19 patients are different based on previous studies. Therefore, the objective of the present study was to investigate the risk factors of death in COVID-19 patients in Shiraz, Iran. The findings of this research can help to predict the severity of the disease and the risk of mortality, early identification of high-risk patients, and increase in knowledge for clinical interventions.

Materials and Methods

This is a retrospective cross-sectional study that analyzes the risk factors for mortality in patients with COVID-19. The study population included all COVID-19 patients who were admitted and hospitalized in Ali Asghar Hospital in Shiraz, Iran, between April 1 and November 30, 2021. In Iran, the fourth and fifth delta waves were in this period. Inclusion criteria were age older than 18 years and positive diagnosis of COVID-19 confirmed by reverse transcription polymerase chain reaction (RT-PCR) method for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in at least one biological sample of nasal swab or throats. Exclusion criteria were an infectious disease other than SARS-CoV2, pregnancy, and incomplete medical record information. A total of 652 COVID-19 patients were admitted during the study period; 13 patients were excluded due to incomplete medical record information and 20 patients due to pregnancy.

Data were extracted from patients' records, using a case report form. The case report form included age; sex; clinical characteristics of patients such as oxygen saturation, intubation, fever, shortness of breath, muscle pain, weakness, and headache; and concomitant diseases such as cancer, high blood pressure, high blood lipids, weak immune system, heart failure, myocardial infarction (MI), and cerebrovascular disease (CVA).

Blood samples were taken from all patients at the beginning of admission to the hospital, and the usual blood tests including white blood cell count (WBC), lymphocyte count (LYM), neutrophil count (NEU), platelet count (Plt), Red blood cells (RBC), and hemoglobin were recorded. In addition, blood biochemistry, coagulation, and serology parameters such as creatinine, blood urea nitrogen (BUN), serum potassium, serum sodium, aspartate aminotransferase (AST), fasting blood sugar (FBS), creatinine phosphokinase (CPK), D-dimer, and C-reactive protein (CRP) were evaluated.

In this study, the patient's outcome included recovery, discharge, and death. The criteria for patient discharge was based on the protocol for diagnosis and treatment of COVID-19 version 7 (17). Survivors were patients who were discharged alive from the hospital. Non-survivors were patients who died during the study and due to COVID-19. Also, the selection of these clinical features was based on the opinions of infectious disease experts and previous studies (13-16).

Descriptive statistics of frequency (percentage) were used for all categorical variables in total patients, survivors and non-survivors. Chi-square test and Fisher's exact test were used to determine whether there is a significant relationship between the variables classified in the two groups of survivors and non-survivors. Mean and standard deviation were used to describe the measured data, and independent t-test was used to compare them. A multivariate logistic test was also performed to identify the variables predicting mortality due to COVID-19. Statistical analyses were performed using IBM SPSS version 21, and a p-value less than 0.05 was considered statistically significant.

This study was approved by Shiraz University of Medical Sciences with ethics code of IR.SUMS.REC.1399.158. Also, all patients were free to participate in the study, and the informed consent was obtained from all the patients who participated in the study; all of them were assured of the confidentiality of their responses.

Results

Of the 619 examined patients, 555 (89.7%) were discharged from the hospital alive, and 64 (10.3%) died in the hospital. Most patients were men (61.7%), and their age was less than or equal to 52 years (75.9%). The most common clinical characteristics

Table 1: Comparison of clinical characteristics and comorbidities in the two groups

Variables	Total (n=619) N (%)	Survivors (n=555) N (%)	No survivors (n=64) N (%)	P value
Age				<0.001
≤52 years	470 (75.9)	439 (79.1)	31 (48.4)	
>52 years	149 (24.1)	116 (20.9)	33 (51.6)	
Sex				0.20
Male	382 (61.7)	347 (62.5)	35 (54.7)	
Female	237 (38.3)	208 (37.5)	29 (45.3)	
SaO_2				<0.001
≤90 %	160 (26.8)	122 (76.3)	38 (23.8)	
Intubation				<0.001
Yes	18(4.8)	4 (22.2)	14 (77.8)	
Fever				0.208
Yes	333 (53.8)	295 (53.2)	38 (59.4)	
No	286 (46.2)	260 (46.8)	26 (40.6)	
Shortness of breath				0.009
Yes	465 (75.1)	409 (73.7)	56 (87.5)	
No	154 (24.9)	146 (26.3)	8 (12.5)	
Muscular pain				0.016
Yes	202 (32.6)	189 (34.1)	13 (20.3)	
No	417 (67.4)	366 (65.9)	51 (79.7)	
Weakness				0.052
Yes	138 (22.3)	118 (21.3)	20 (31.2)	
No	481 (77.7)	437 (78.7)	44 (68.8)	
Headache				0.075
Yes	89 (14.4)	84 (15.1)	5 (7.8)	
No	530 (85.6)	471 (84.9)	59 (92.2)	
cancer				<0.001
Yes	14 (2.3)	10 (1.8)	4 (6.2)	
No	605 (97.7)	545 (98.2)	60 (93.8)	
Hypertension				<0.001
Yes	203 (32.8)	169 (30.5)	34 (53.1)	
No	416 (67.2)	386 (69.5)	30 (46.9)	
Hyperlipidemia				0.020
Yes	100 (16.2)	87 (15.7)	13 (20.3)	
No	519 (83.8)	468 (84.3)	51 (79.7)	
Diabetes				0.016
Yes	29 (4.7)	22 (4)	7 (10.9)	
No	590 (95.3)	533 (96)	57 (89.1)	
Immune compromised				0.012
Yes	10 (1.6)	6 (1.1)	4 (6.2)	
No	609 (98.4)	549 (98.9)	60 (93.8)	
Heart failure				< 0.001
Yes	72 (11.6)	52 (9.4)	20 (31.2)	
No	547 (88.4)	503 (90.6)	44 (68.8)	
MI				0.06
Yes	87 (14.1)	71 (12.8)	16 (25)	
No	532 (85.9)	484 (87.2)	48 (75)	
CVA				0.048
Yes	9 (1.5)	6 (1.1)	3 (4.7)	
No	610 (98.5)	549 (98.9)	61 (95.3)	

Data described by frequency (Percent); SaO_2: Oxygen saturation; MI: Myocardial infarction; CVA: Cerebro Vascular Accident. Level of significance was P<0.05.

of the patients were shortness of breath (75.1%), fever (53.8%), and muscle pain (32.6%), respectively. In terms of comorbidities, most patients in this study had high blood pressure (32.8%) (Table 1).

Mortality of COVID-19 was significantly higher in patients over 52 years of age (P<0.001). Also, patients who died due to COVID-19 had significantly lower blood oxygen saturation (≤90% SaO2) than the surviving group (P<0.001). In addition, tracheal intubation in non-survivors group was significantly more than the survivors (P<0.001). Comorbidities including cancer, hypertension, hyperlipidemia, diabetes, immune system weakness, heart failure, and cerebrovascular disease were significantly higher in the non-survivor group (Table 1).

Laboratory parameters of survivors and non-survivors of COVID-19 were compared. The results showed that WBC, NEU, BUN, AST, FBS, CPK, and D-dimer parameters were significantly higher in non-survivors than survivors. On the other hand, lymphocyte count (LYM), Plt, RBC, and Hemoglobin parameters were significantly higher in the survivor group than in the non-survivor group. No significant difference was observed in creatinine, potassium, sodium, and CRP values between the two groups of survivors and non-survivors (Table 2).

The results of multivariate logistic model showed that age more than 52 years [OR=5.78 (95% CI: 1.06 -31.57)], Diabetes [OR=5.91 (95% CI: 1.61-21.62)] and SaO2 level less than 90% [OR=4.37 (95% CI: 1.47-12.0)] would increase the chance of mortality in COVID-19 (Table 3).

Discussion

The COVID-19 pandemics with subsequent morbidity and mortality and the economic burden imposed on the community mandated the scientists and health care workers to conduct extensive studies to investigate risk factors contributing to transmission, morbidity, and mortality of COVID-19 to control the

Table 2: Comparison of the laboratory parameters between the survivors and non-survivors

Laboratory parameters	Survivors, (n=555) Mean (SD)	No survivors, (n=64) Mean (SD)	P value
WBC (×10^3/mm3)	5852.0 (2689.7)	8088.5 (3996.9)	<0.001
LYM (×10^3/mm3)	1520.6 (1279.4)	1072.31 (881.5)	0.001
NEU (×10^3/mm3)	4498.8 (3433.8)	7838.94 (5632.1)	<0.001
Plt (×10^9/L)	243626.0 (114229.2)	151652.3 (132843.4)	0.001
RBC (mill/cu mm)	4.9 (0.72)	4.6 (0.81)	0.006
Haemoglobin (g/L)	13.95 (1.9)	13.4 (2.1)	0.004
Creatinine (mg/dl)	1.32 (1.3)	1.46 (0.72)	0.440
BUN (mg/dl)	16.02 (9.6)	26.8 (17.2)	<0.001
Serum potassium (mmol/L)	3.09 (0.97)	3.25 (1.13)	0.337
Serum sodium (mg/L)	139.4 (3.89)	138 (4.84)	0.095
AST (U/L)	34.9 (28.68)	60.63 (58.27)	<0.001
FBS (mg/dl)	125.8 (66.6)	177.1 (104.8)	<0.001
CPK (U/L)	125.83 (119.8)	305.5 (250.8)	<0.001
D-dimer (µg/L)	1408.6 (1559)	4177.0 (3568)	0.032
CRP (mg/l)	10.21 (10.7)	11.74 (9.3)	0.447

Data presented as mean (standard deviation); WBC=White blood cell count; LYM: Lymphocyte count; NEU: Neutrophil count; Plt: Platelet count; RBC: Red Blood Cell count; BUN: Blood Urea Nitrogen; AST: Aspartate Aminotransferase; FBS: Fasting Blood Sugar; CPK: Creatine Phosphokinase; CRP: C-reactive protein. Level of significance was P<0.05.

Table 3: Multivariable logistic regression to identify the factors associated with in-hospital death from COVID-19

Variable	OR	CI 95%	P value
Age			
≤52	ref		
>52	5.78	1.06-31.57	0.04
SaO_2			
≤90%	ref		
>90%	4.34	1.47-12.0	0.008
Diabetes			
No	ref		
Yes	5.91	1.61-21.62	0.007

OR: Odds ratio; CI: Confidence Interval; SaO_2: Oxygen Saturation; Level of significance was P<0.05.

global pandemics better (1, 2). In the present study, we evaluated the clinical features and risk factors of mortality in COVID-19 patients admitted in Aliasghar hospital in Shiraz, southern Iran.

This study showed that age older than 52 years was a risk factor for mortality in COVID-19, which confirms the result of previous studies that have indicated aging as a risk factor for advanced COVID-19 and mortality. It has been proposed that a weaker immune response in the elderly may explain the high mortality rate. In fact, compromised body immunity of the elderly patients could not win the fight with COVID-19; rather, it leads to the worst outcome (14, 18-20).

We also indicated that the mortality rate was higher in COVID-19 patients who suffered from an underlying disease like hypertension, diabetes, heart failure, hyperlipidemia, immune suppression, cancer, and CVA. According to recent studies, comorbidities like hypertension, diabetes mellitus, and cardiovascular disease were regarded as risk factors for mortality in COVID-19 (13, 21-24). Some studies also showed that hyperlipidemia could be a risk factor for mortality in COVID-19 (24).

Our data showed that the need for intubation and mechanical ventilation was significantly higher in the non-survivors group compared to the survivors group, which is compatible with previous studies (25, 26). The most common sign of COVID-19 patients in our study was fever (53.8%), but the difference in the rate of fever was not statistically significant between the two groups. The most common symptoms of COVID-19 patients were shortness of breath (75.1%), muscular pain (32.6%), weakness (22.3%), and headache (14.4%), respectively. The most common sign and symptoms of COVID-19 disease reported in other series were fever and cough, and some patients complained of sneezing, anosmia, weakness, and fatigue (25-27).

In our study, the mean platelet count differed significantly in survivors and non-survivors (243626.0 vs. 151652.3, P<0.001), and those who died of COVID-19 disease had lower platelet levels. Our data confirm the results of previous studies that thrombocytopenia acts as a risk factor for disease severity and mortality in COVID-19 patients (28).

High WBC counts and elevated plasma levels of d-dimer, creatine phosphokinase (CPK), and Aspartate Aminotransferase (AST) are indicators of rapid progression of COVID-19 disease (15, 29-31). We also indicated that WBC and especially neutrophil count, d-dimer, CPK, and AST plasma levels were significantly higher in the non-survivors than in the survivors. We also demonstrated that the lymphocyte count was significantly lower in non-survivors of COVID-19. In contrast to previous studies (32), we could not find a significant association between elevated CRP levels and mortality.

According to our study, anemia and elevated fasting blood sugar (FBS) levels can be regarded as the risk factors for mortality since the non-survivors had significantly lower hemoglobin and higher FBS levels (33). We also indicated that blood urea nitrogen level was significantly higher in non-survivors than the survivors (26.8 vs. 16.0 mg/dl); however, the creatinine level did not differ significantly between the two groups.

The male to female ratio was 1.6: 1, which is relatively similar to other studies conducted in this region (34, 35). According to our data, the mortality rate was higher in male patients compared to femaleones. Still, the result was not statistically significant, and we could not regard the male sex as a risk factor for mortality in COVID-19 disease. This finding is in contrast with previous studies that showed men were more likely to need intensive care and also die of COVID-19 (36, 37).

The significance of our study compared to previous studies conducted in Iran was its high sample size. All the patients were gathered from Aliasghar hospital, the largest center that managed the COVID-19 patients in southern Iran. All the lab data were analyzed in the same laboratory and personnel, which decreased the chance of measurement (instrument) bias. The limitation of this study was the incomplete medical records of some patients and the retrospective design of the study, which limited access to some of the epidemiologic features of patients. We recommend prospective cohort studies to better define morbidity and mortality risk factors in COVID-19 disease. The results from our study highlight the need for public health intervention to reduce the risk of COVID-19.

Conclusion

The result of this study demonstrated that age and previous disease are more prone to death due to Covid-19. Leukocytosis, neutrophilia, lymphopenia, and elevated CPK, D-dimer, BUN, and AST levels can be indicators of disease progression and mortality. Identifying these prognostic factors and finding therapeutic options to better control comorbidities and manage abnormal laboratory findings will improve the patients' survival from COVID-19 and provides important insights into disease pathogenicity, health care practices, and public health policies.

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Availability of Data and Materials
The datasets used are available on reasonable request.

Ethics Approval and Consent to Participate
This study was approved by Shiraz University of Medical Sciences with the code number of 98-01-106-22013 and ethics committee code number of IR.SUMS.REC.1399.158 in accordance with the guidelines of the National Ethics Committee and COPE regulations.

Conflict of Interest: None declared.

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