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A Survey for Predictors of Mortality among COVID-19 Patients: a Retrospective Study from Iran

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Abstract

***Background and Objective*:** In the current COVID-19 pandemic, disease diagnosis is essential for optimal management and timely isolation of infected cases in order to prevent further spread. The aim of this study is to assess of predictors of mortality among COVID-19 patients.

Material and Methods: In a retrospective study, 522 COVID-19 patients were enrolled in Razi hospital, Guilan Province, Iran. This hospital was the main center for the treatment of COVID-19 patients in Guilan province. Data gathering was performed by census sampling from March to August 2020. Simple and Multiple logistic regression analysis were applied to assess the relationships of clinical and demographic characteristics with in-hospital mortality.

Results: Multiple logistic regression showed that older age (aOR=1.04, 95%CI: 1.02 to 1.06, P<0.001), decreased O2 saturation (aOR=0.89, 95%CI: 0.86 to 0.92, P<0.001), having a dysrhythmia (aOR=2.97, 95%CI: 1.46 to 6.05, P=0.003), symptoms associated with heart failure (aOR=0.43, 95%CI: 0.18 to 0.99, P=0.048), and mixed drug antiviruses (aOR=2.44, 95%CI: 1.22 to 4.90, P=0.012) were mortality predictor variables among COVID-19 patients.

Conclusion: Therefore, special attention should be paid to the factors influencing the mortality of COVID-19 patients. It is recommended that older patients, dysrhythmia, and symptoms associated with heart failure be treated with extreme caution.

Keywords: Mortality [MeSH], Coronavirus [MeSH], COVID-19 [MeSH], SARS-CoV-2 [MeSH], Iran [MeSH]

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Highlights

- Older age, decreased O2 saturation, having a dysrhythmia, symptoms associated with heart failure, and mixed drug antiviruses were mortality predictor variables among COVID-19 patients.

Introduction

On December 8, 2019, some hospitals reported cases of idiopathic pneumonia in Wuhan, Hubei Province, China, which caused concern among public health professionals about the spread of a new disease in the world (1). The spread of the virus via human-to-human transmission led to a global pandemic (2). This pandemic has led to a major global challenge that has imposed significant costs on countries' economies and health systems (3).

Based on the World Health Organization, a total of 182,101,209 confirmed cases of COVID-19 had been identified around the world by July 2, 2021, out of which 3,950,876 died. In Iran, a total of 3,204,557 confirmed cases of COVID-19 had been identified around the world by July 2, 2021, out of which 84,264 died (4). Epidemiological evidence shows that the main route of transmission of the virus is through coughing or sneezing from person to person (2, 5, 6). The main clinical manifestations of COVID-19 include fever, dyspnea, and cough (7). However, these manifestations are various in different populations (8, 5). Comorbid conditions such as diabetes mellitus, respiratory, cardiovascular, and renal diseases, obesity and an older age group are known to be positively associated with poor outcomes among COVID-19 patients. One of the major concerns in COVID-19 patients is the involvement of the cardiovascular system, leading to plaque instability, vascular and myocardial inflammation. On the other hand, a previous history of cardiovascular disease increases the risk of adverse outcomes such as plaque instability, vascular and myocardial inflammation among COVID_19 patients (9). However, so far there is no effective and definitive drug treatment for COVID-19 patients (10). To optimize patient care and appropriately deploy health care resources during this pandemic, effective patient risk stratification is essential. However, the factors that predispose an individual to a higher risk of death from COVID-19 are poorly understood. To optimize patient care and appropriately deploy health care resources during this pandemic, effective patient risk stratification is essential.

Although the COVID-19 pandemic is still rampant and lots of information have been unfolding, narrow gaps in our understanding of the disease, and thus, aid decision-making by health care providers and administrators, more evidence is needed on the prevention, control, and treatment of COVID-19. Therefore, the present study aimed to assess of predictors of mortality among COVID-19 patients.

Materials and Methods

- ***Study design and subjects***

Five hundred and twenty-two (291 males and 231 females) with a diagnosis of COVID-19, hospitalized in Razi hospital, Guilan Province, Iran, from March to August 2020, were enrolled in a retrospective study. This hospital was the main center for the treatment of COVID-19 patients in Guilan province. In this study, patients with a definitive diagnosis of COVID-19 via Reverse transcription-polymerase chain reaction (RT-PCR) were included. Also, patients with incomplete medical records, who have been hospitalized more than once, or are still hospitalized, were excluded from the study.

- ***Ethical consideration***

This study was approved by Guilan University of Medical Sciences (IR.GUMS.REC.1399.206). After obtaining permission from the hospital administration, the researchers visited the hospital.

- ***Data collection***

Demographic and clinical characteristics, including age, sex, marital status, addiction,

smoking, alcoholism, history of hospitalization, number of comorbidities, cardiac diseases, Systolic Blood Pressure [SBP], Diastolic Blood Pressure [DBP], heart rate, O2 saturation, temperatures, respiration rate, cardiac manifestations (dysrhythmia, typical chest pain, pericardial effusion, inflammatory disorders of heart tissue, and symptoms associated with heart failure), treatments (antibiotics, antivirals, and bronchodilators), and clinical outcomes (survived and deceased) were collected.

- ***Statistical analysis***

Data analysis was carried out using SPSS version 16.0 (SPSS Inc., Chicago, IL, USA). Nominal variables were presented as numbers of cases and percentages, and continuous variables as median (interquartile range). Simple and Multiple logistic regression analysis (Enter method) were also applied to examine the relationships of clinical and demographic characteristics with in-hospital mortality. The Odds Ratio (OR) and 95% Confidence Interval (CI) were calculated. All statistical tests were two-sided and level of significance was set at 0.05.

Results

- ***Participant's characteristics***

The demographic characteristics, clinical features, cardiac manifestations, and treatments of the 522 study subjects were provided in Table 1. Of the survived patients, 51.8% were male, 15.4% were smokers, 11.7% were opium addicts, 40.1% had 2 or more than 2 comorbidities, 30.4% had cardiac disease, and 11.3% had dysrhythmia. Of the deceased patients, 59.3% were male, 6.5% were smokers, 7.3% were opium addicts, 35.3% had 2 or more than 2 comorbidities, 20.7% had cardiac disease, and 25.1% had dysrhythmia. The median age in the deceased group was greater than in the survived group (65.0 years vs. 58.0 years).

- ***Mortality predictor variables among COVID-19 patients***

As presented in Table 2, simple logistic regression showed that older age (OR= 1.03, 95%CI: 1.02 to 1.05, P <0.001), decreased O2 saturation (OR= 0.89, 95%CI= 0.87 to 0.92, P <0.001), having a dysrhythmia (OR= 2.62, 95%CI: 1.62 to 4.23, P <0.001), symptoms associated with heart failure (OR= 0.50, 95%CI: 0.27 to 0.90, P =0.022), and mixed drug antiviruses (OR= 2.05, 95%CI: 1.24 to 3.40, P =0.005) were important mortality predictor variables among COVID-19 patients. Older age increases the chance of mortality by 0.03. Decreased O2 saturation increases the probability of death by 0.11. Having a dysrhythmia increases 1.62 chance of death. Having symptoms associated with heart failure reduces the chance of death by 0.50. Also, mixed drug antiviruses increase the 1.05 chance of death

Multiple logistic regression showed that older age (aOR= 1.04, 95%CI: 1.02 to 1.06, P <0.001), decreased O2 saturation (aOR= 0.89, 95%CI: 0.86 to 0.92, P <0.001), having a dysrhythmia (aOR= 2.97, 95%CI: 1.46 to 6.05, P =0.003), symptoms associated with heart failure (aOR= 0.43, 95%CI: 0.18 to 0.99, P =0.048), and mixed drug antiviruses (aOR= 2.44, 95%CI: 1.22 to 4.90, P =0.012) were mortality predictor variables among COVID-19 patients. Older age increases the chance of mortality by 0.04. Decreased O2 saturation increases the probability of death by 0.11. Having a dysrhythmia increases 1.97 chance of death. Having symptoms associated with heart failure reduces the chance of death by 0.57. Also, mixed drug antiviruses increase the 1.44 chance of death (Table 2).

Table 1. Demographic characteristics, clinical features, cardiac manifestations, and treatments of COVID-19 patients (N=522).

	Survived (n=247)	Deceased (n=275)
Demographic characteristics		
Age	58.0 (45.0 – 70.0)	65.0 (56.0 – 76.0)
Male sex	128 (51.8)	163 (59.3)
Marital Status (married)	236 (95.5)	273 (99.3)
Smoking	38 (15.4)	18 (6.5)
Alcohol	5 (2.0)	2 (0.7)
Opium	29 (11.7)	20 (7.3)
Clinical features		
History of hospitalization	43 (17.4)	56 (20.4)
No. of comorbidities		
0	61 (24.7)	89 (32.4)
1	87 (35.2)	89 (32.4)
≥2	99 (40.1)	97 (35.3)
Cardiac diseases	75 (30.4)	57 (20.7)
SBP (mmHg)	120.0 (110.0 – 130.0)	110.0 (100.0 – 130.0)
DBP (mmHg)	70.0 (60.0 – 80.0)	70.0 (60.0 – 80.0)
Heart rate (beats per minute)	82.0 (78.0 – 90.0)	84.0 (79.0 – 90.0)
O_2 Saturation	92.0 (90.0 – 96.0)	84.5 (70.2 – 92.0)
Temperatures (°C)	37.0 (37.0 – 38.0)	37.0 (37.0 – 37.8)
Respiration rate	18.0 (16.0 – 20.0)	20.0 (18.0 – 22.0)
Cardiac manifestations		
Dysrhythmia	28 (11.3)	69 (25.1)
Typical chest pain	6 (2.4)	3 (1.1)
Pericardial effusion	4 (1.6)	2 (0.7)
Inflammatory disorders of heart tissue	1 (0.4)	2 (0.7)
Symptoms associated with heart failure	32 (13.0)	19 (6.9)
Treatments		
Antibiotic drug		
No	32 (13.0)	55 (20.0)
Single	109 (44.1)	78 (28.4)
Mixed	106 (42.9)	142 (51.6)
Antiviral drugs		
No	42 (17.0)	51 (18.5)
Single	144 (58.3)	72 (26.2)
Mixed	61 (24.7)	152 (55.3)
Bronchodilator drugs	104 (42.1)	129 (46.9)

SBP: Systolic Blood Pressure; **DBP:** Diastolic Blood Pressure.
Values are given as number (percentage) for categorical variables and as median (interquartile range) for continuous variables.

Table 2. Mortality predictor variables among COVID-19 patients (N=522).

	Simple Logistic Regression		Simple Logistic Regression	
	OR (95% CI)	*p*	aOR (95% CI)	*p*
Demographic characteristics				
Age	1.03 (1.02 – 1.05)	<0.001	1.04 (1.02 – 1.06)	<0.001
Male sex	1.35 (0.96 – 1.91)	0.087	1.55 (0.95 – 2.51)	0.077
Marital Status (married vs single)	6.36 (1.40 – 28.99)	0.017	3.60 (0.41 – 31.60)	0.248
Current smoker	0.39 (0.21 – 0.69)	0.002	0.56 (0.21 – 1.47)	0.239
Alcohol drinker	0.35 (0.07 – 1.84)	0.218	2.45 (0.33 – 18.26)	0.383
Opium user	0.59 (0.32 – 1.07)	0.083	0.66 (0.25 – 1.72)	0.066
Clinical features				
History of hospitalization	1.21 (0.78 – 1.89)	0.390	1.13 (0.64 – 2.00)	0.682
No. of comorbidities				
0	1		1	
1	0.70 (0.45 – 1.09)	0.114	0.79 (0.43 – 1.46)	0.456
≥2	0.67 (0.44 – 1.03)	0.069	0.72 (0.39 – 1.33)	0.295
SBP (mmHg)	0.99 (0.98 – 1.00)	0.007	0.99 (0.98 – 1.01)	0.360
DBP (mmHg)	0.98 (0.96 – 0.99)	0.002	0.99 (0.96 – 1.02)	0.430
Heart rate (beats per minute)	1.02 (1.00 – 1.03)	0.007	1.01 (0.99 – 1.02)	0.479
O_2 Saturation	0.89 (0.87 – 0.92)	<0.001	0.89 (0.86 – 0.92)	<0.001
Temperatures (°C)	0.82 (0.65 – 1.04)	0.100	0.98 (0.72 – 1.35)	0.915
Respiration rate	1.11 (1.06 – 1.16)	<0.001	1.02 (0.95 – 1.08)	0.635
Cardiac manifestations				
Dysrhythmia	2.62 (1.62 – 4.23)	<0.001	2.97 (1.46 – 6.05)	0.003
Typical chest pain	0.44 (0.11 – 1.79)	0.253	0.43 (0.07 – 2.64)	0.363
Pericardial effusion	0.45 (0.08 – 2.45)	0.352	1.14 (0.16 – 8.08)	0.893
Inflammatory disorders of heart tissue	1.80 (0.16 – 20.00)	0.631	1.59 (0.09 – 26.83)	0.750
Symptoms associated with heart failure	0.50 (0.27 – 0.90)	0.022	0.43 (0.18 – 0.99)	0.048
Treatments				
Antibiotic drug				
No	1		1	
Single	0.42 (0.25 – 0.70)	0.001	0.55 (0.27 – 1.11)	0.094
Mixed	0.78 (0.47 – 1.29)	0.332	1.34 (0.68 – 2.64)	0.401
Antiviral drugs				
No	1		1	
Single	0.41 (0.25 – 0.68)	<0.001	0.80 (0.41 – 1.56)	0.510
Mixed	2.05 (1.24 – 3.40)	0.005	2.44 (1.22 – 4.90)	0.012
Bronchodilator drugs	1.21 (0.86 – 1.72)	0.271	1.10 (0.69 – 1.77)	0.691

OR: Odds Ratio; **aOR:** Adjusted Odds Ratio; **CI:** Confidence Interval; **SBP:** Systolic Blood Pressure; **DBP:** Diastolic Blood Pressure.

Discussion

Based on findings of the present study, older age, decreased O2 saturation, having a dysrhythmia, symptoms associated with heart failure, and mixed drug antiviruses were mortality predictor variables among COVID-19 patients.

In the present study, older age was mortality predictor variables among COVID-19 patients. Consistent with this finding, a cohort study in the USA found a direct and significant association between age and mortality among COVID-19 patients. They also found that patients over the age of 60 had a higher probability of mortality than others (11). Another study in China showed that old age is a risk factor for poor prognosis in COVID-19 patients (12). Also, the results of a study showed that age-based frailty is one of the important predictors of mortality and complications from COVID-19 (13). Obviously, age-dependent defects in immune cells occur with age, which has been proposed as a theory for higher mortality in older people. Also, the presence of various types of comorbidities in older people is another cause of this high mortality (12). Therefore, it is important to pay attention to the high-risk populations of COVID-19 patients due to the high probability of mortality. This pandemic has suggested that the management of vulnerable populations might be successful when data-driven policies and strategies are adopted.

Another predictor of mortality among COVID-19 patients was decreased O2 saturation. Consistent with this finding, studies from the USA (14) and Iran (15) showed that decreased O2 saturation is an important predictor of mortality among COVID-19 patients. Also, one study found that the mortality rate was higher among patients with O2 saturation less than 93% compared with O2 saturation above 93% (16). Therefore, due to the importance of assessing O2 saturation in predicting mortality among COVID-19 patients, it is suggested that patients with lower levels of O2 saturation receive special attention when receiving emergency care.

In this study, having a dysrhythmia was mortality predictor variables among COVID-19 patients. In this regard, the findings of a study in Germany showed that dysrhythmias were the most common cardiac complication among COVID-19 patients. On the other hand, the presence of dysrhythmias has been associated with increased length of stay in hospital and higher mortality among COVID-19 patients (17). On the other hand, some reports indicate a significant increase in QT interval by hydroxychloroquine, which is even greater when combined with azithromycin (18, 19). However, due to the discrepancy between these findings, dysrhythmias cannot be considered as the main cause of higher mortality among COVID-19 patients but can be confirmed as an effective factor. Therefore, further studies in this area are necessary.

Another predictor of mortality among COVID-19 patients was symptoms associated with heart failure. Consistent with this finding, a study showed that mortality was higher among COVID-19 patients with heart failure than in other patients (20). SARS-COV-2 Found inside macrophages and endothelial cells. In addition, evidence of active virus replication within the myocardium has been shown at autopsy. Thus, widespread inflammation and increased micro and macrovascular thrombosis may predispose to cardiac manifestations and myocarditis. However, the level of myocardial damage is reflected by an increase in troponin concentration, which has been associated with an increased risk of mortality among COVID-19 patients (21). In general, it is strongly recommended that patients with chronic or underlying diseases avoid any close contact with others in the community, especially in patients with COVID-19 due to the long incubation period of COVID-19 and asymptomatic carriers of COVID-19. Therefore, special attention to patients with underlying diseases during the COVID-19 pandemic is very important (22).

In the present study, mixed drug antiviruses were mortality predictor variables among COVID-19 patients. Consistent with this finding, the results of a systematic review and meta-analysis showed

that the use of chloroquine and hydroxychloroquine for COVID-19 patients not only did not reduce mortality but also increased mortality when combined with azithromycin (23). In contrast, studies in Belgium (24) and the USA (25) have shown that treatment with hydroxychloroquine combined with azithromycin reduces mortality among COVID-19 patients. Therefore, due to the contradictions in this field, further studies are needed.

The present study has several limitations. Due to incomplete clinical records, there is no history of symptom changes that could limit our analysis. Also, the present study had a retrospective design in which the effect of treatments in patients is not reported. Additional large-scale studies are required to determine mortality among hospitalized COVID-19 patients with other associated comorbid conditions. It is suggested that researchers evaluate other predictors of mortality in COVID-19 patients in future studies, including laboratory tests.

Conclusion

Overall, special attention should be paid to the factors influencing the mortality of COVID-19 patients. It is recommended that older patients, dysrhythmia, and symptoms associated with heart failure be treated with extreme caution.

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Conflict of interest disclosure

The authors have no conflicts of interest to declare for this study.

Ethics approval statement

This study was approved by Guilan University of Medical Sciences (IR.GUMS.REC.1399.206). After obtaining permission from the hospital administration, the researchers visited the hospital.

Patient consent statement

The researchers explained the objectives of the present study to the participants and received informed consent from them.

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