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ORIGINAL RESEARCH

Clinical and Laboratory Predictors of COVID-19-Related In-hospital Mortality; a Cross-sectional Study of 1000 Cases

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Abstract: **Introduction:** Identifying patients at risk for mortality and using appropriate treatment for each patient based on their situation could be an effective strategy in improving their outcome. This study aimed to evaluated the predictors of COVID-19 in-hospital mortality. **Methods:** This descriptive cross-sectional study was conducted on all adult COVID-19 patients who were managed in Imam-Reza and Sina Hospitals, Tabriz, Iran, from November 2020 until December 2021. The demographic, clinical, and laboratory characteristics of patients were evaluated and predictors of in-hospital mortality were identified using logistic regression model. **Results:** 1000 patients with the mean age of 56.34 ± 18.00 years were studied (65.7% male). There were significant associations between COVID-19 in-hospital mortality and hospitalization above five days (p = 0.001), white blood cell count (WBC) > 4000 Cells*10^3/mL (p < 0.01), aspartate aminotransferase (AST) above 40 IU/L (p = 0.001), alanine transaminase (ALT) above 40 IU/L (p = 0.001), creatinine above 1.4 mg/dL (p = 0.007), urea above 100 mg/dL (p = 0.024), and SaO2 below 80% (p = 0.001). Hospital stay above five days (OR: 3.473; 95%CI: 1.272 - 9.479; p = 0.15), AST above 40 IU/L (OR: 0.269, 95%CI: 0.179 - 0.402; p = 0.001), creatinine above 1.4 mg/dL (OR: 0.529; 95%CI: 0.344 - 0.813; p = 0.004), urea above 100 mg/dL (OR: 0.327, 95%CI: 0.189 - 0.567; p = 0.001), and SaO2 below 80% (OR: 8.754, 95%CI: 5.413 - 14.156; p = 0.001) were among the independent predictors of COVID-19 in-hospital mortality. **Conclusion:** The mortality rate of patients with COVID-19 in our study was 29.9%. Hospitalization of more than five days, AST above 40 IU/L, creatinine above 1.4 mg/dL, urea above 100 mg/dL and SaO2 < 80% were independent risk factors of in-hospital mortality among patients with COVID-19.

Keywords: COVID-19; Mortality; Prognosis; Respiratory Distress Syndrome

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1. Introduction

In December 2019, patients were diagnosed with pneumonia of unknown origin, later known as SARS-CoV-2 virus (severe acute respiratory syndrome coronavirus 2), in Wuhan, China (1, 2). The clinical manifestation of SARS-CoV-2 infection is mutable and includes asymptomatic disease, upper respiratory tract disorders, and in some cases, acute and severe fatal conditions. Therefore, to summarize the clinical manifestations and widespread consequences of SARS-CoV-2 infections, the WHO chose the specific name COVID-19 (Coronavirus disease 2019) for this disease (3-5).

The mortality rate is the most crucial factor in turning an infection into a public concern and the risk of developing a pandemic. Different viruses become epidemics each year, but very few of them become a public concern (6-8). Swine influenza A (H1N1 virus), severe acute respiratory syndrome

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(SARS), and Ebola (Zaire ebolavirus) have led to global concern in recent years due to high mortality (9, 10). As in the above cases, COVID-19 has received all the attention and has caused concern due to its high mortality rate (3, 11). For example, although the flu is widespread, its mortality rate is only 0.1%. Reports have also shown that COVID-19 is highly contagious and can spread via various routes (3, 5, 12).

The rate of infectivity is a significant factor, but the mortality rate from COVID-19 is not correctly estimated. Because when the initial mortality rate is reported, only patients with very severe condition are in the statistical population, and patients with mild to moderate disease are not included in the investigation (12). The rapid development of COVID-19 in Wuhan, China, has resulted in thousands of deaths (13), and the widespread virus worldwide has resulted in hundreds of thousands of patients (14). In Iran, WHO reports that there were about 10000 new cases of COVID-19 per day during the study, and death rate was about 400 cases daily (15).

More deaths were observed in patients with severe disease, and other patients in whom the disease symptoms were flu-like, improved quickly, and returned to everyday life (5). In addition, the difference between the clinical features of patients with severe and non-severe diseases has been rarely reported (16, 17). Also, in some studies, the clinical features of patients with severe diseases who died were compared with patients who survived after the infection. We hypothesized that assessing routine parameters such as vital signs and laboratory tests in COVID-19 patients, especially patients with severe disease, can help medical staff better manage patients. Therefore, this study aimed to design a predictive model of mortality in patients admitted with COVID-19, to identify patients with different conditions and use appropriate treatment for each patient based on their situation.

2. Methods

2.1. Study design and setting

This descriptive cross-sectional study was conducted with the approval of the institutional ethics committee at Tabriz University of Medical Sciences (IR.TBZMED.REC.1399.950) in two Medical Research, Training and Treatment General Hospitals, Imam-Reza and Sina Hospitals, Tabriz, Iran, from November 2020 until December 2021. The data of all adult COVID-19 patients admitted in the mentioned hospitals during the study period were evaluated and predictors of in-hospital mortality were determined using logistic regression model.

2.2. Participants

The study included patients older than 18 years, with COVID-19 pneumonia, confirmed by reverse transcriptase-polymerase chain reaction (RT-PCR) for SARS-CoV-2. The sampling method was a complete census. The minimum number of samples is 1000 patients. The sample size was estimated based on the COVID-19 prevalence of 33% (18), a confidence interval of 95%, and a relative estimation error of 10%. Exclusion criteria were incomplete information recorded in the patient's medical record, discharge against medical advice, leaving the study in the middle of the study procedure, not willing to participate in the project, and negative PCR test (figure 1).

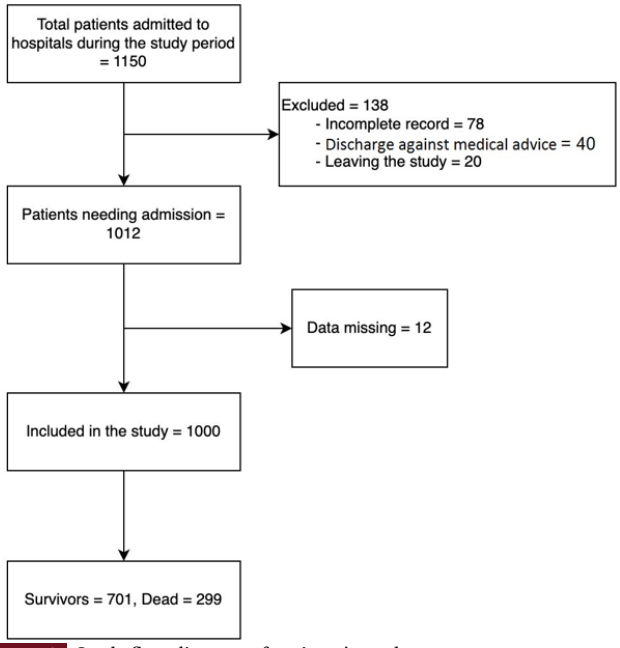

Figure 1: Study flow diagram of patients' enrolment.

2.3. Data gathering

Patients' demographic characteristics at the time of admission (age, sex, body mass index (BMI)), underlying disease, drug history, vital signs (blood pressure, heart rate (HR), respiration rate (RR), body temperature, O2 Saturation, AVPU level of consciousness), need for supplemental oxygen (via nasal cannula or mask), lung involvement on computed tomography (CT) scan, and the laboratory test results were recorded in the checklist. Laboratory findings included complete blood count (white blood cell (WBC), Neutrophil, Lymphocyte, Hemoglobin and Platelet counts), Liver functional enzymes (including Aspartate transaminase, Alanine transaminase, and Alkaline phosphatase), Creatinine, Urea, Coagulation status (including Prothrombin Time (PT), Partial Thromboplastin Time (PTT), and International Normalized Ratio (INR)), Venous blood gas analysis (including pH, PaCO2, and HCO3), and serum sodium (Na) and potassium (K) status. The patients were followed up during hospitalization (short-term follow-up of 30 days), and the duration

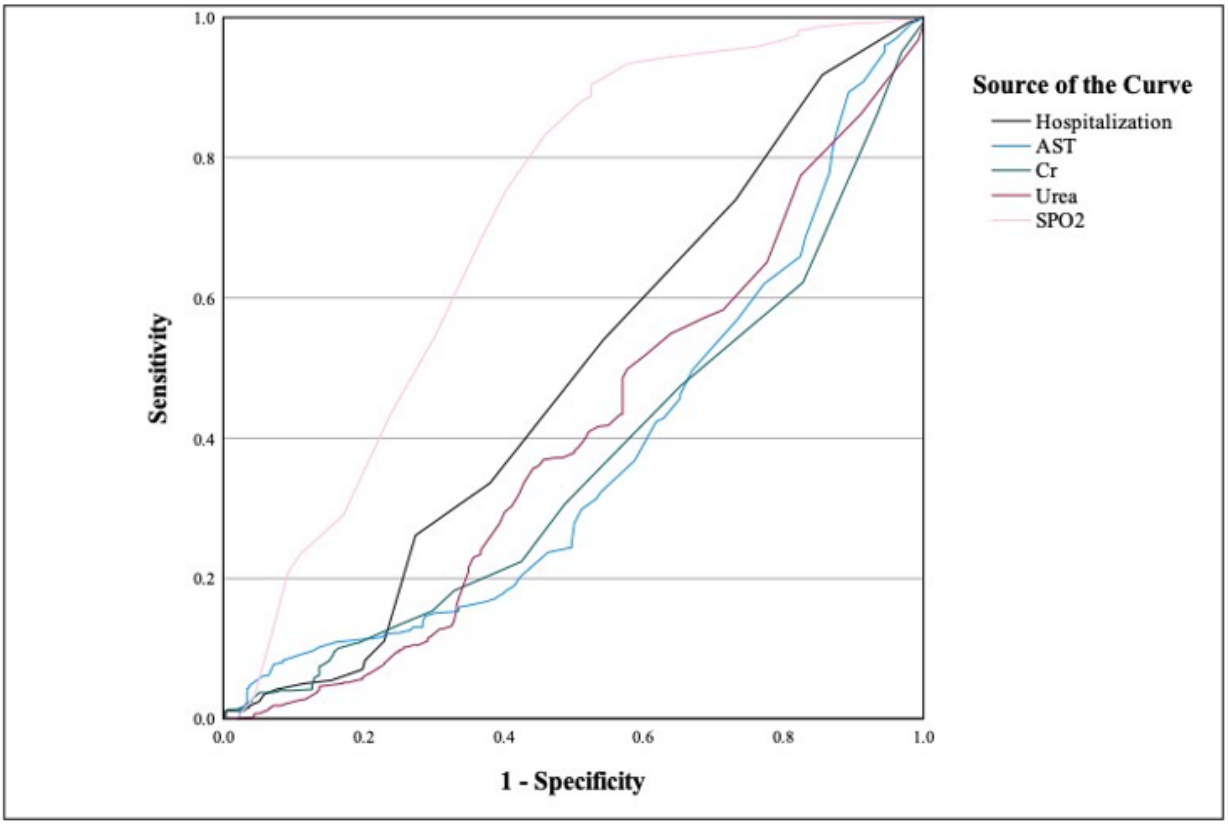

Figure 2: Area under the receiver operating characteristic (ROC) curve of hospital stay above five days (P value: 0.435), aspartate aminotransferase (AST) above 40 IU/L (P value: 0.001), creatinine above 1.4 mg/dL (P value: 0.001), urea above 100 mg/dL (P value: 0.001), and SaO2 below 80% (P value: 0.001) in predicting the in-hospital mortality of COVID-19 patients.

of hospitalization, intubation, intensive care unit (ICU) hospitalization, and outcome, including death or survival, were assessed.

2.4. Outcome

The study's primary outcome was patient mortality during the hospitalization period or within 30 days from admission.

2.5. Statistical analysis

All data were entered into the SPSS 21. Normal data distribution was assessed using Kolmogorov-Smirnov test. For the descriptive data, mean ± standard deviation was used to report the findings in the case of normal data distribution. In case of non-normal data distribution, the median was used, and for qualitative variables frequency (percentage) was reported. The Independent sample's T-test was used to compare quantitative data if the data distribution was normal, and the Mann Whitney U test was used if it was non-normal. The Chi-square test was used to compare qualitative data. The receiver operating characteristic (ROC) curve was used to determine the predictive value of each of the studied variables. Area under the ROC curve (AUC), cut-off point, sensitivity, specificity, positive predictive value, negative predictive value, positive and negative likelihood ratios, and J point were reported. In all cases, a P value less than 0.05 was considered significant. Logistic regression and Odds Ratio were used to determine the value of each variable and their coefficients to create the model. The primary bias of the study was missing data, to address this problem we excluded patients with missing data. The comparison was made between patients who survived and those who died.

3. Results

3.1. Baseline and Clinical findings

1000 patients with the mean age of 56.34 ± 18.00 (range: 18 - 96) years were studied (65.7% male). The most frequent underlying disease was hypertension (32.2%). Of all patients, 29.9% died during admission. The demographic and clinical findings of the studied patients are compared between survived and non-survived cases in table 1. Results showed that the mean age of dead patients was significantly higher (59.36 ± 18.40 vs. 55.05 ± 17.68 years; p = 0.001), and the rate of mortality was significantly lower in females than in males

Table 1: Comparing the demographic and clinical findings between survived and non-survived cases

Variable	Alive (n=701)	Dead (n=299)	Dead (n=1000)	P
Age (year)				
Mean ± SD	55.05±17.68	59.36±18.40	56.34±18.00	0.001
Sex				
Male	443 (63.2)	214 (71.6)	657 (65.7)	0.011
Female	258 (36.8)	85 (28.4)	343 (34.3)	
Underlying Disease				
HTN	233 (33.2)	89 (29.8)	322 (32.2)	0.198
DM	92 (13.1)	40 (13.4)	132 (13.2)	0.212
HLP	11 (1.6)	6 (2.0)	17 (1.7)	0.134
Hypothyroidism	14 (2.0)	9 (3.0)	23 (2.3)	0.313
CAD	6 (0.9)	0 00.0)	6 (0.6)	0.219
CVA	4 (0.6)	5 (1.7)	9 (0.9)	0.192
CRF	16 (2.3)	9 (3.0)	25 (2.5)	0.217
Vital Signs				
HR (beats/min)	91.41±13.41	94.61±13.93	92.37±13.64	0.001
RR (breath/min)	22.05±9.79	23.28±8.67	22.42±9.48	0.031
BT	37.24±0.53	37.31±0.56	37.26±0.54	0.030
SBP (mmHg)	119.82±15.21	121.46±22.96	120.31±17.89	0.128
DBP (mmHg)	74.79±9.04	75.39±12.16	74.97±10.007	0.225
SPO2 (%)	90.32±4.77	84.41±8.17	88.55±6.57	0.001
Hospitalization (Day)				
Mean ± SD	5.52±4.19	6.23±5.00	5.73±4.45	0.016

* Data were analyzed using Independent-Sample t Test and Chi-Square and presented as mean ± standard deviation (SD) and frequency (%). ** HTN: Hypertension; DM: Diabetes mellitus; HLP: Hyperlipidemia; CAD: Coronary artery disease; CVA: Cerebrovascular accident; CRF: Chronic renal disease; HR: Heart rate; RR: Respiratory rate; BT: Body temperature; SBP: Systolic blood pressure; DBP: Diastolic blood pressure.

(28.4% vs. 71.6%; p = 0.011). The mean HR (94.61±13.93 vs. 91.41±13.41/minute; p = 0.001), RR (23.28 ± 8.67 vs. 22.05 ± 9.79/minute; p = 0.031), and temperature (37.31 ± 0.56 vs. 37.4 ± 0.53 Celsius; p = 0.001) were significantly higher in dead patients; however, the value of SaO2 (84.41±8.17 vs. 90.3±4.77%; p=0.001) was lower in dead cases. The length of hospitalization in dead patients was significantly longer (6.23 ± 5.00 vs. 5.52 ± 4.19 days; p=0.016).

3.2. Laboratory findings

Laboratory and paraclinical findings of the patients are shown in Table 2. The results showed that the values of WBC (8.27±7.71 vs. 7.53±5.29 cells*10^3; p = 0.009), neutrophils (81.68±9.90% vs. 78.93±12.19%; p=0.001), ALT (60.82±66.04 vs. 46.11±47.48 IU/L; p=0.001), AST (56.46±75.00 vs. 41.73±38.55 IU/L; p=0.001), creatinine (1.56±1.34 vs. 1.23±12.1 mg/dL; p=0.001), and urea (62.85±54.98 vs. 42.98±32.62; p=0.001) were significantly higher in dead patients.

3.3. Predictors of Mortality

There were significant associations between COVID-19 in-hospital mortality and hospitalization above five days (p = 0.001), WBC > 4000 Cells*10^3/mL (p < 0.01), AST above 40 IU/L (p = 0.001), ALT above 40 IU/L (p = 0.001), creatinine above 1.4 mg/dL (p = 0.007), urea above 100 mg/dL (p = 0.024), and SaO2 below 80% (p = 0.001) (table 3).

Based on the results of multivariate logistic regression analysis, hospital stay above five days (OR: 3.473; 95%CI: 1.272 - 9.479; p = 0.15), AST above 40 IU/L (OR: 0.269, 95%CI: 0.179 - 0.402; p = 0.001), creatinine above 1.4 mg/dL (OR: 0.529; 95%CI: 0.344 - 0.813; p = 0.004), urea above 100 mg/dL (OR: 0.327, 95%CI: 0.189 - 0.567; p = 0.001), and SaO2 below 80% (OR: 8.754, 95%CI: 5.413 - 14.156; p = 0.001) were among the independent predictors of COVID-19 in-hospital mortality (Table 4).

To evaluate the diagnostic value of independent risk factors of mortality, the ROC Curve analysis was used (Figure 2 and Table 5). SaO2 has an excellent diagnostic value for predicting in-hospital mortality of COVID-19 patients in cut-off point of 85.5% (67.7% sensitivity, and 56.3% specificity).

4. Discussion

In this study, which was performed to design a prediction model for hospital mortality in admitted COVID-19 patients, 1000 patients who referred to Imam Reza and Sina Hospitals in Tabriz were studied. The mean age of the patients was 56.34 years, and 65.7% of the patients were male. The mortality rate was 29.9%. Evaluation of demographic character-

Table 2: Comparing the laboratory findings on admission between survived and non-survived cases

Variable	Alive (n=701)	Dead (n=299)	Dead (n=1000)	P
WBC (Cells*10^3/mL)	7.53±5.29	8.27±7.71	7.75±6.12	0.009
Neutrophil (%)	78.93±12.19	81.68±9.90	79.75±11.62	0.001
Lymphocyte (%)	20.88±12.27	18.00±10.04	20.02±11.72	0.001
Hb (g/dL)	13.46±1.94	12.27±2.15	13.11±2.08	0.061
Plt (Cells*10^3/mL)	235.53±100.71	235.99±119.43	241.05±106.92	0.110
AST (IU/L)	46.11±47.48	60.82±66.04	50.51±54.09	0.001
ALT (IU/L)	41.73±38.55	56.46±75.00	46.13±52.58	0.001
AlkP (IU/L)	205.01±148.65	203.61±136.81	204.59±145.14	0.443
Cr (mg/dL)	1.23±1.12	1.56±1.34	1.33±1.20	0.001
Urea (mg/dL)	42.98±32.62	62.85±54.98	48.92±41.60	0.001
PT (sec)	14.13±3.97	14.49±4.29	14.24±4.07	0.111
PTT (sec)	37.73±11.04	41.85±14.50	38.97±12.31	0.101
INR	1.14±0.35	1.17±0.38	1.15±0.36	0.126
Na (mEq/L)	140.14±3.94	141.07±4.46	140.42±4.12	0.301
K (mEq/L)	4.24±0.47	4.30±0.46	4.26±0.46	0.231
pH	7.40±0.03	7.39±0.03	7.40±0.03	0.150
HCO_3- (mEq/L)	25.13±6.66	24.71±6.60	25.01±6.64	0.179
$PaCO_2$ (mmHg)	41.48±12.61	43.12±13.74	41.97±12.97	0.835
CRP				
0	273 (38.9)	133 (44.5)	406 (40.6)	
+1	254 (36.2)	64 (21.4)	318 (31.8)	
+2	136 (19.4)	88 (29.4)	224 (22.4)	0.746
+3	16 (2.3)	7 (2.3)	23 (2.3)	
+4	22 (3.1)	7 (2.3)	29 (2.9)	

* Data were analyzed using Independent-Sample t Test and Chi-Square and presented as mean ± SD and frequency (%).
** WBC: White Blood Cell; Hb: Hemoglobin; Plt: Platelet; AST: Aspartate aminotransferase; ALT: Alanine transaminase; AlkP: Alkaline Phosphatase; Cr: Creatinine; PT: Prothrombin Time; PTT: Partial Thromboplastin Time; INR: International Normalized Ratio; Na: Sodium; K: Potassium; CRP: C-Reactive Protein.

istics of the studied patients showed that the mean age of the deceased patients was significantly higher (59.36±18.40 vs. 55.05±17.68; p=0.001), and mostly male patients died (71.6% vs. 28.4%; p = 0.011). Assessment of clinical signs also showed that the level of SaO2 was significantly lower in dead patients. The results showed that hospitalization over five days, AST above 40 IU/L, creatinine above 1.4 mg/dL, urea above 100 mg/dL, and SaO2 below 80% were the independent risk factors of in-hospital mortality among COVID-19 patients.

Numerous predictive models have been published in recent studies to estimate the risk of nosocomial mortality in patients with COVID-19 in eastern and western countries; especially the 4C mortality score, which includes age, sex, number of comorbidities, respiration rate, oxygen saturation, level of consciousness, urea, and c-reactive protein (CRP), which were evaluated in a cohort of 35,000 patients and had an excellent prediction power (AUC = 0.79) (19). In the present study, patients with COVID-19 who died had a higher mean age than other patients. Consistent with the present study, studies conducted in China and the United States also introduced a high age as a risk factor for in-hospital mortality but compared to the above studies, the mortality rate in our patients was lower, which seems to be due to differences in demographic variables (4, 20, 21).

Recent studies have examined various variables in predicting mortality in patients with COVID-19 with mild to severe disease and ICU admission. For example, the data of 4711 patients with COVID-19 were investigated in a study by Altschul et al., and the results showed a classification scale for mortality of COVID-19 patients with six variables (age, SPO2, mean arterial pressure (MAP), urea, CRP, and INR) at the time of admission (22). In the study by Liang et al., ten variables (including radiographic chest abnormalities, age, hemoptysis, dyspnea, unconsciousness, number of comorbidities, history of cancer, neutrophil to lymphocyte ratio, lactate dehydrogenase (LDH), and direct bilirubin) were evaluated. The results showed that these variables are good predictors of mortality risk in COVID-19 patients (23). The study by Knight et al. also reported a mortality prediction scale consisting of 8 variables (age, sex, number of comorbidities, respiration rate, SPO2, level of consciousness, urea, and CRP), the evaluation of which is a good criterion in the initial clinical examination of patients at hospitalization to predict mortality (19). Consistent with the above studies, the methods used in studies that used machine learning to predict mortality showed

Table 3: Univariate logistic regression analysis of COVID-19 mortality risk factors

Variable	Alive (n=701)	Dead (n=299)	OR (95% CI)	P
Age (year)				
< 60	390 (55.6)	150 (50.2)	-	0.096
60 - 80	260 (37.1)	111 (37.1)	1.754 (0.932 - 3.304)	0.082
> 80	51 (7.3)	38 (12.7)	2.340 (0.892 - 6.138)	0.084
RR (/minute)				
> 20	5 (1.6)	2 (1.7)	0.747 (0.106 - 5.282)	0.770
Hospitalizations (day)				
< 5	647 (93)	233 (80.1)	-	0.001
5 - 10	40 (5.7)	49 (16.8)	4.401 (1.955 - 9.906)	0.001
> 10	9 (1.3)	9 (3.1)	4.006 (0.843 - 19.043)	0.081
WBC (Cells*10^3/mL)				
< 4	56 (8.0)	56 (18.7)	0.717 (0.212 - 1.989)	0.016
4 - 10	531 (75.7)	170 (56.9)	0.295 (0.128 - 0.687)	0.004
> 10	114 (16.3)	73 (24.4)	0.354 (0.121 - 1.034)	0.058
Neutrophil (%)				
< 18	0	0	-	-
18 - 63	69 (9.8)	12 (4.0)	-	-
> 63	632 (90.2)	287 (96.0)	0.625 (0.205 - 1.908)	0.409
AST (IU/L)				
> 40	209 (29.8)	151 (50.5)	6.190 (3.170 - 12.085)	0.001
ALT (IU/L)				
> 40	305 (43.5)	121 (40.5)	0.287 (0.141 - 0.582)	0.001
Creatinine (mg/dL)				
> 1.4	96 (13.7)	77 (25.8)	2.673 (1.313 - 5.444)	0.007
Urea (mg/dL)				
> 100	38 (5.4)	54 (18.1)	2.764 (1.146 - 6.668)	0.024
O2 Saturation (%)				
< 60	0 (0.0)	0 (0.0)	-	-
60 - 80	37 (5.3)	102 (34.1)	1.289 (0.891 - 4.313)	0.003
> 80	664 (84.7)	197 (65.9)	0.095 (0.039 - 0.228)	0.001

* Data are presented as frequency (%). CI: confidence interval; OR: Odds Ratio; RR: Respiratory rate; WBC: White blood cells; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase.

Table 4: Multivariate logistic regression analysis of COVID-19 mortality risk factors

Variable	OR (95% CI)	P-value
Hospitalization > 5 Days	3.473 (1.272 - 9.479)	0.015
AST > 40 IU/L	0.269 (0.179 - 0.402)	0.001
Creatinine > 1.4 mg/dL	0.529 (0.344 - 0.813)	0.004
Urea > 100 mg/dL	0.327 (0.189 - 0.567)	0.001
SPO_2 < 80%	8.754 (5.413 - 14.156)	0.001

OR: odds ratio; CI: confidence interval; AST: Aspartate aminotransferase.

Table 5: Diagnostic value of independent risk factors of COVID-19 mortality

Variable	AUC (95% CI)	P-value	Cut off point	Sensitivity	Specificity
Hospitalization	0.484 (0.443-0.526)	0.439	-	-	-
AST	0.374 (0.328-0.403)	0.001	36.5	61.9	57.6
Creatinine	0.366 (0.335-0.414)	0.001	1.05	48.8	69.4
Urea	0.402 (0.362-0.442)	0.001	71	29.6	89.4
SPO2	0.705 (0.666-0.745)	0.001	85.5	67.7	56.3

AUC: area under the receiver operating characteristic curve; CI: confidence interval; AST: Aspartate aminotransferase.

that the above variables in COVID-19 patients admitted to the ICU are good predictors of mortality (24).

In recent studies, the nutritional status of patients with COVID-19 with severe disease was evaluated using mNUTRIC criteria at the time of hospitalization, and the results showed that the risk of mortality in patients with high nutritional risk, based on the above criteria, is twice as high as patients with low nutritional risk (25). However, in the present study, the nutritional status of the patients was not studied, and it is better to be considered in future studies.

By comparing the present study's findings with previous studies, we can say that the clinical and paraclinical characteristics of patients and risk factors are different, which seems to be due to differences in the number of samples, demographic characteristics, and status of patients on admission. In addition, logistic regression and ROC curve analyses were used to Identify the factors affecting inpatient mortality. However, risk regression models or standard Cox proportional hazard models were used in some of the other studies (26, 27). Another reason for the difference between the present study and other studies is the age of the patients. In the present study, young and middle-aged patients were studied, while in other studies, elderly patients with a mean age over 60 years were studied (22, 24, 25, 28-30).

In a multicenter study conducted by Gupta et al. on 2215 patients in the United States, nine risk factors (including age, sex, BMI, coronary artery disease (CAD), active cancers, hypoxemia, hepatic impairment, renal impairment, and the number of hospital ICU beds) were introduced as predictors of 28-day patient mortality (29). In the present study, SPO2, Urea, creatinine, AST, and hospitalization were the factors that predicted the mortality of patients. In contrast, studies have used non-COVID-19 predictive criteria, including the Waterlow score, to predict short-term mortality and length of hospital stay in elderly patients. Waterlow score is a multidimensional criterion for evaluating bed sores, calculated based on age, nutritional status, weight, patient movement, sex, smoking, comorbidities, and medications used (30).

5. Limitations and strengths

One of the strengths of this study is the large sample size and evaluation of demographic variables, vital signs, and laboratory findings of patients with COVID-19. In addition, the assessment of mortality risk in patients based on patients' clinical and laboratory findings also increases the applicability of the results of the present study to other patients. Limitations of the present study include: Some of the patients' tests were not completely performed and they were excluded from the study. Some patients were discharged against medical advice or referred to other centers, and their information could not be fully verified and they were excluded from the study. Also, we didn't evaluate and report the severity of disease.

6. Conclusion

The mortality rate of patients with COVID-19 in our study was 29.9%. Hospitalization of more than five days, AST above 40 IU/L, creatinine above 1.4 mg/dL, urea above 100 mg/dL, and SaO2 < 80% were the independent risk factors of in-hospital mortality of patients with COVID-19.

7. Declarations

7.1. Acknowledgments

The researchers acknowledge all study participants and staff of the toxicology ward in the Hospitals for their support from the beginning to the end of the research process.

7.2. Data availability

It can be available after legal permits.

7.3. Authors' contributions

All authors participated in the conception and design, acquisition of data, analysis and interpretation of data, drafting of the article, review of the article, and finding approval.

7.4. Funding and supports

None.

7.5. Conflict of interest

No potential and actual conflicts of interest were present during our investigation.

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