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The Impact of Significant Risk Factors on the Mortality Rate of Hospitalized COVID-19 Patients in the Iranian Population

Nasrin Milani[1], Mohammad Reza Rouhbakhsh Zahmatkesh[2], *Mona Kabiri[3]

[1]*Department of Internal Medicine, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.*
[2] *School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.*
[3]*Nanotechnology Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran.*

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ABSTRACT

Introduction:
The present study aimed to assess the respiratory signs and laboratory parameters in COVID-19 patients based on recovery or mortality during hospitalization in the Iranian population.

Materials and Methods:
623 patients over 16 years of age with confirmed COVID-19 infection using polymerase chain reaction test who were admitted to the COVID-19 wards of Imam Reza Hospital from 2020 to 2022 were included in this study. The vital signs and paraclinical parameters such as liver and renal function tests as well as hematological and inflammatory markers were evaluated based on recovered or non-recovered patients during admission.

Results:
According to our results, 135 COVID-19 patients (21.7%) expired, while 488 patients recovered through hospitalization. The frequency of acute kidney injury was significantly higher in unrecovered COVID-19 patients (71.1%) compared to the recovered group (27.3%) ($p<0.001$). Significant differences were found in terms of AST, direct and total bilirubin, creatinine, BUN, albumin, LDH, and CRP, as well as potassium, phosphorus, calcium, pH, HCO3, and INR serum levels between groups at both baseline and endpoint admission. The non-recovered patients demonstrated significantly higher counts of WBC, MCV, RDW, and neutrophil, as well as significantly lower amounts of RBC, hemoglobin, platelet, lymphocyte, and MXD than the recovered group during admission.

Conclusion:
Our findings revealed that AKI, CRP, LDH, WBC, RDW, neutrophil, and PLT were the significant risk factors in the incidence of mortality due to COVID-19 infection in the present study. These results could be helpful in screening and managing hospitalized patients during the respiratory viral pandemic.

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Nasrin Milani and Mohammad Reza Rouhbakhsh Zahmatkesh contributed equally to the present work.

**** Corresponding author:***
Nanotechnology Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran. E-mail: Kabirimn@mums.ac.ir; mona.kabiri@gmail.com

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Introduction

Coronavirus disease 2019 (COVID-19) emerged in 2019 and spread worldwide rapidly. This has made COVID-19 a top research topic around the world, with scientists looking to find patterns of transmission and symptoms of infected patients. Studies have strongly asserted that the most likely transmission route is via droplets. Patient's clinical characteristics vary, from asymptomatic patients or even simple clue-like symptoms to severe organ failure and death (1).

The majority of patients remained to have minute clinical features for the first week of infection including fever, sore throat, myalgia, fatigue, and shortness of breath that may develop into respiratory involvement such as pneumonia in the following weeks. Notwithstanding, a small proportion of patients could progress to organ failure and death, reviews and analyses have suggested that the severity of symptoms relies on various elements such as the patient's age, health status including the history of diseases namely diabetes and hypertension, and body mass index (BMI) (2). Additionally, there was a growing consensus regarding the possibility of an association between the progression of COVID-19 and a drastic rise in inflammatory cytokines such as IL-2, IL-7, IL-10, GCSF, and tumor necrosis factor-α (TNF-α) (3).

Likewise, recently there have been studies that uncover the correlation between components such as platelet, bilirubin, and creatinine in infected patients and factors such as D-dimer, lactate dehydrogenase (LDH), ferritin, C- reactive protein (CRP), TNF-α and erythrocyte sedimentation rate (ESR) in patients with much more severe conditions in the Intensive care unit (ICU) (4-6). This has brought the idea of utilizing these components as criteria predictive criteria for severe patients. In this study, we intend to ascertain the predictive factors among Iranian COVID-19 patients.

Materials and Methods

Study design and participants

The study population includes the group of patients initially diagnosed based on clinical symptoms or radiological evidence alongside the confirmed polymerase chain reaction (PCR) test. During hospitalization, patients were examined for various blood tests and parameters, such as renal and liver function tests, inflammatory factors, and variables such as oxygen, carbon dioxide, bicarbonate, and pH. Moreover, patients were also evaluated for the possible correlation with variables such as patient age, patient gender, and mortality or improvement.

All patients over 16 years of age with definite confirmation of COVID-19 infection (positive PCR) on the first day of admission in the COVID-19 wards of Imam Reza Hospital affiliated with Mashhad University of Medical Science from February 2020 to January 2022 were included in the study (Ethical approval code: IR.MUMS. REC.1398.308). During several months of the epidemic of this disease, it was tried to evaluate all the patients hospitalized in the COVID-19 wards, according to the inclusion criteria. In all cases, sampling was done only in the examination department and based on the daily request of the attending physician. Markers were checked daily or at longer intervals as needed. For all patients, sampling tests were performed at the beginning of admission, and also, for the following times, only the elements that were determinant of the severity of the disease with intervals between three to a maximum of five days were examined.

Materials and laboratory procedure

Demographic variables (age, gender), laboratory parameters (urea, creatinine), elements such as sodium, potassium, and calcium, and other variables such as albumin, LDH, PH, oxygen pressure, carbon dioxide pressure, HCO_3, hemoglobin, hematocrit, ESR, CRP, WBC, liver function test (ALP, ALT, AST), bilirubin and INR were among the subjects being evaluated in this study.

The inclusion criteria were hospitalized patients over 16 years of age with the diagnosis of COVID-19 and the presence of documented clinical and laboratory information of the patients to compare the results. Also, the exclusion criteria were lack of sufficient laboratory data and being hospitalized in other medical centers.

Data collection

This study was conducted in the form of a registration of patients hospitalized in the COVID-19 wards of Imam Reza Hospital. The process initially started with collecting the population with COVID-19 that was admitted to the hospital's emergency department based on imaging, PCR, and the symptoms of the disease. The patients having inclusion criteria were transferred to the COVID-19 departments, and the tests of the first day and the final test results were imported into our database.

The evaluation of patients included checking demographic characteristics, physical examination, assessment of vital signs, and evaluating basic laboratory tests. Subsequently, the hospitalized patients were followed for the duration of admission and evidence of organ failures such as a rise in laboratory elements or even the occurrence of organ failure. Hence, the prognosis of these people was examined according to the available evidence.

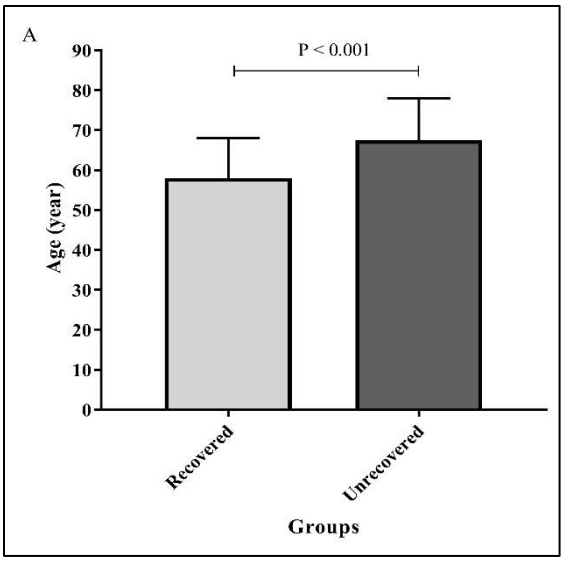
Statistical analysis

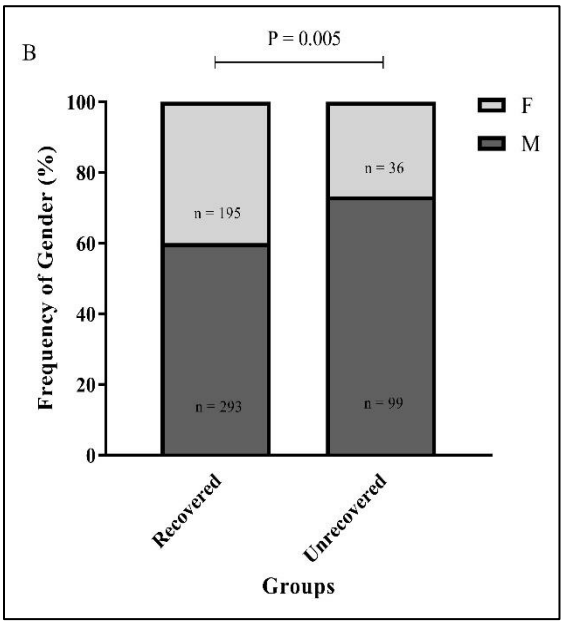
Data were collected, and analyzed by SPSS software (version 20). Continuous variables were evaluated using the Kolmogorov-Smirnov test to check normality and described as the mean ± standard deviation (SD) or median (percentile 25-75) for normal and non-normal distribution, respectively. The Independent sample T-test or Mann-Whitney test was performed to compare quantitative data between the recovered and non-recovered groups. The qualitative variables were described as the frequency (percentage) and compared by the Chi-square or Fisher's exact tests. The logistic regression model was applied to determine the significant risk factors on the incidence of mortality. *P*-values less than 0.05 are considered significant.

Result

Participants in this study included 623 hospitalized patients with positive SARS-CoV-2 PCR tests who fulfilled our inclusion and exclusion criteria. Overall, 231 (37.1%) women and 392 (62.9%) men were recruited for the present study. The mean age of patients was 59.10±16.64 years with a range of 16 to 91 years. Of these, 135 COVID-19 patients (21.7%) were expired, while 488 patients (78.3%) recovered during hospital admission.

Figure 1A demonstrated that patients in the non-recovered group were significantly older (67.31±14.64) compared to COVID-19 patients who recovered (56.84±16.46) (p<0.001). As shown in Figure 1B, the frequency of male and female patients was 293 (60.0%) and 195 (40%) in the recovered group versus 99 (73.3%) and 36 (26.7%) in the unrecovered patients, respectively, with the significant difference between groups (p=0.005). Figure 1C depicted that the frequency of acute kidney injury (AKI) was significantly higher in unrecovered COVID-19 patients (71.1%) relative to the recovered group (27.3%) (p<0.001).





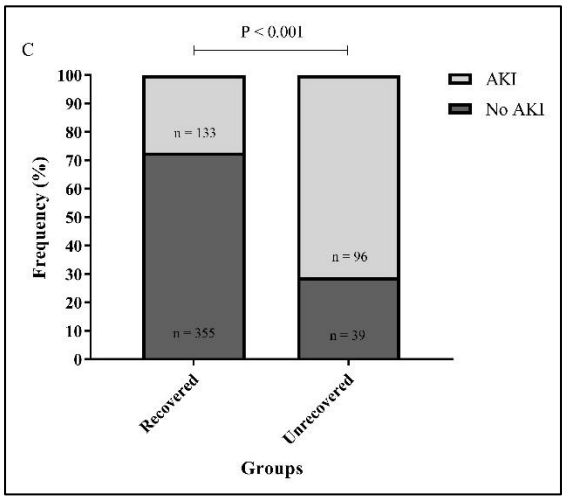


Fig 1: Comparison of hospitalized COVID-19 patients in terms of age (A), gender (B), and AKI (C) based on recovered and unrecovered groups.

The comparison of vital signs and laboratory features based on recovered and non-recovered COVID-19 patients is shown in Table 1. Significant differences were found in terms of AST, direct and total bilirubin, creatinine, BUN, albumin, LDH, and CRP, as well as potassium, phosphorus, calcium, pH, HCO_3, and INR serum levels between groups at both baseline and endpoint admission. The levels of FBG ($p<0.001$), ALT ($p=0.018$), and PO_2 ($p=0.028$) were significantly higher in the unrecovered patients compared to the recovered group at the baseline. Moreover, statistical significance was observed regarding the amounts of sodium ($p<0.001$), PaO_2 ($p=0.040$), PCO_2 ($p<0.001$), and ISI ($p<0.001$) between the mentioned groups at the endpoint of admission. According to Table 1, the levels of ALP, ESR, Fe, TIBC, and SpO_2 had no significant differences between the recovered and unrecovered patients during admission.

Table 1. Comparison of biochemical laboratory findings based on recovered and non-recovered COVID-19 patients during hospitalization. Quantitative variables were reported as the mean ± standard deviation (SD), or median (percentile 25-75).

Variables	Total (n = 623)	Recovered (n = 488)	Unrecovered (n = 135)	P*
FBG, mg/dL				
Baseline	144.18±82.15	136.60±76.45	166.57±93.91	< 0.001
Endpoint	169.11±100.74	156.49±100.06	181.09±100.77	0.196
ALT, U/L				
Baseline	62.78±253.24	40.023±64.17	106.53±404.70	0.018
Endpoint	78.75±168.84	51.092±47.37	123.70±262.67	0.091
AST, U/L				
Baseline	60.49±164.64	41.13±44.56	107.79±293.29	< 0.001
Endpoint	89.44±277.49	37.22±33.49	177.39±442.30	0.001
ALP, U/L				
Baseline	242.97±195.01	226.83±161.92	282.86±256.13	0.064
Endpoint	251.81±162.22	229.74±139.48	290.91±192.18	0.104
Direct Bilirubin, mg/dL				
Baseline	0.36±0.34	0.30±0.21	0.51±0.50	0.001
Endpoint	0.52±0.62	0.33±0.24	0.90±0.92	< 0.001
Total Bilirubin, mg/dL				
Baseline	0.83±0.69	0.73±0.47	1.05±0.99	0.015
Endpoint	1.15±1.37	0.75±0.48	1.83±2.02	< 0.001
BUN, mg/dL				
Baseline	34 (24,49.7)	30 (23,42.7)	53.5 (35,83)	< 0.001
Endpoint	38 (27,86)	32 (24,41)	90 (64.2,132.7)	< 0.001
Creatinine, mg/dL				
Baseline	1.0 (0.8,1.2)	1.0 (0.8,1.1)	1.1 (0.9,1.9)	< 0.001
Endpoint	1.2 (0.9,2.3)	1.0 (0.7,1.2)	1.9 (1.1,2.4)	0.011
Albumin, g/dL				
Baseline	3.45±0.57	3.70±0.61	3.29±0.47	0.005
Endpoint	3.11±0.59	3.48±0.63	2.81±0.37	0.001
LDH, U/L				
Baseline	613 (483,797)	593 (467,752.5)	805 (599,948)	< 0.001
Endpoint	590 (363,918.5)	478.5 (346,618.5)	1148 (700,1867.5)	0.001

CRP, mg/L				
Baseline	90.4 (41.3,164.0)	78 (31.1,148.1)	143.2 (99.3,207.2)	< 0.001
Endpoint	31.5 (20.0,108.3)	22.3 (14.6,30.2)	154.6 (90.3,294.2)	0.001
ESR, mm/hr				
Baseline	56.56±31.09	55.24±30.31	60.94±33.29	0.134
Endpoint	56.57±34.02	54.07±32.99	65.00±37.17	0.301
Sodium, mg/dL				
Baseline	136.00 (134,139)	137.00 (134,139)	136.00 (133,138)	0.775
Endpoint	137.00 (134,139)	136.00 (134,138)	138.00 (133-144)	< 0.001
Potassium, mg/dL				
Baseline	4.10 (3.80,4.50)	4.10 (3.80,4.50)	4.30 (3.90,4.70)	0.006
Endpoint	4.20 (3.80,4.52)	4.10 (3.80,4.50)	4.40 (3.85,5.10)	< 0.001
Phosphorous, mg/dL				
Baseline	3.80±1.51	3.36±1.12	4.09±1.59	0.017
Endpoint	4.84±2.78	3.71±1.59	5.29±3.03	0.014
Calcium, mg/dL				
Baseline	8.20 (7.80,8.80)	8.450 (8.20,8.80)	8.00 (7.40,8.80)	0.004
Endpoint	7.90 (7.40,8.40)	8.350 (7.975,9.125)	7.70 (7.25,8.15)	< 0.001
Fe, mg/dL				
Baseline	41.15±37.58	45.58±38.95	27.10±31.69	0.266
Endpoint	34.07±15.18	34.63±15.99	29.00±15.95	0.600
TIBC, µg/dL				
Baseline	308.46±62.55	306.74±51.90	313.14±90.48	0.864
Endpoint	291.00±46.97	280.50±33.22	396.01±167.62	0.182
pH				
Baseline	7.41 (7.36,7.45)	7.41 (7.37,7.45)	7.39 (7.34,7.44)	0.002
Endpoint	7.37 (7.27,7.44)	7.42 (7.37,7.47)	7.29 (7.18,7.38)	< 0.001
HCO3, mg/L				
Baseline	25 (21.9,28.5)	25.5 (22.7,28.9)	23.15 (19.62,26.97)	< 0.001
Endpoint	23.3 (20.2,27.5)	25.1 (22.7,28.9)	21.1 (17.5,25.4)	< 0.001
SpO_2, %				
Baseline	71.40±19.06	70.53±19.10	73.68±18.86	0.135
Endpoint	78.16±15.90	79.71±15.74	76.92±16.00	0.286
PaO_2, mmHg				
Baseline	32.95±17.62	33.27±16.61	32.16±19.88	0.617
Endpoint	24.10±15.01	26.75±14.80	21.72±14.89	0.040
PO_2, mmHg				
Baseline	43.43±23.01	41.50±20.43	48.89±28.54	0.028
Endpoint	54.07±26.51	51.16±19.53	56.69±31.38	0.162
PCO_2, mmHg				
Baseline	40.82±10.43	41.31±9.61	39.49±12.35	0.149
Endpoint	45.14±14.95	40.09±8.45	49.49±17.77	< 0.001
INR				
Baseline	1.11 (1.02,1.24)	1.08 (1.01,1.16)	1.24 (1.12,1.40)	< 0.001
Endpoint	1.23 (1.12,1.48)	1.12 (1.07,1.23)	1.39 (1.22,1.53)	< 0.001
ISI				
Baseline	1.22 (1.20,1.22)	1.22 (1.20,1.22)	1.22 (1.20,1.22)	0.825
Endpoint	1.21 (1.20,1.22)	1.20 (1.20,1.22)	1.22 (1.20,1.22)	< 0.001

Based on liver and renal function tests, amounts of AST (p≤0.001), total (p≤0.015) and direct (p≤0.001) bilirubin, and INR (p<0.001) as well as BUN (p<0.001), and creatinine (p≤0.011) were significantly higher in non-recovered patients than others recovered at baseline and endpoint. Regarding electrolyte and gasometers, unrecovered patients had significantly higher potassium (p≤0.006), and phosphorus (p≤0.017), as well as significantly lower calcium (p≤0.004), PH (p≤0.002), and HCO_3 (p<0.001) in comparison with the recovered group during admission. Furthermore, the amounts of PaO_2 (p=0.040) were significantly lower in non-recovered patients, and higher levels of sodium (p<0.001) and PCO_2 (p<0.001) were found relative to the recovered group at the

endpoint. According to inflammatory factors, unrecovered patients had significantly higher LDH (p≤0.001), and CRP (p≤0.001) levels compared to others recovered during hospitalization, whereas there was no significant difference in ESR levels between groups.

As shown in Table 2, hematological parameters including WBC, RBC, HGB, MCV, PLT, RDW, Lymph, Neut, and MXD were statistically significant between the two groups at both baseline and endpoint measured values. Moreover, significant between-group differences were observed in terms of HCT (p=0.001) and EOS (p=0.011) levels at the endpoint or baseline admission, respectively. The non-recovered patients demonstrated significantly higher counts of WBC (p<0.001), MCV (p≤0.005), RDW (p<0.001), and neutrophil (p<0.001), as well as significantly lower amounts of RBC (p≤0.020), hemoglobin (p≤0.023), platelet (p≤0.017), lymphocyte (p<0.001), and MXD (p≤0.029) than the recovered group during admission.

Table 2. Assessment of hematological parameters in recovered and non-recovered COVID-19 patients during hospitalization. Quantitative variables were reported as the mean ± standard deviation (SD), or median (percentile 25-75).

Variables	Total (n = 623)	Recovered (n = 488)	Unrecovered (n = 135)	P*
WBC, $10^3/\mu L$				
Baseline	7 (5.2,9.3)	6.65 (4.9,8.7)	8.8 (5.9,11.7)	< 0.001
Endpoint	7.6 (5.8,10.5)	7 (5.3,8.6)	12.7 (8.9,17.9)	< 0.001
RBC, $10^6/\mu L$				
Baseline	4.59±0.76	4.63±0.72	4.43±0.88	0.020
Endpoint	4.32±0.72	4.42±0.67	4.04±0.79	< 0.001
HGB, g/dL				
Baseline	13.20±2.33	13.34±2.19	12.73±2.72	0.023
Endpoint	12.31±2.12	12.55±1.94	11.62±2.46	< 0.001
HCT, %				
Baseline	37.81±6.21	38.07±5.83	36.91±7.27	0.102
Endpoint	36.30±5.67	36.83±5.12	34.72±6.84	0.001
MCV, fL				
Baseline	82.8 (80.1,85.9)	82.5 (80.0,85.4)	84.3 (80.6,86.8)	0.005
Endpoint	84.3 (81.5,87.7)	84.0 (81.4,86.9)	86 (81.9,89.7)	0.001
PLT, $10^3/\mu L$				
Baseline	209.34±103.97	214.93±107.55	191.13±89.34	0.017
Endpoint	239.74±116.35	266.58±113.80	178.58±98.02	< 0.001
RDW, %				
Baseline	13.4 (12.8,14.4)	13.3 (12.7,14.1)	14.0 (13.1,15.7)	< 0.001
Endpoint	13.7 (12.9,14.9)	13.4 (12.7,14.2)	15.1 (13.9, 16.9)	< 0.001
Lymph, %				
Baseline	16.2 (10.1,22.8)	17.5 (11.5,24.8)	10.1 (6.5,17.8)	< 0.001
Endpoint	16.4 (9.2,24.4)	20.0 (13.1,26.8)	6.1 (3.4,11.0)	< 0.001
Neutrophil, %				
Baseline	78.4 (70.4,85.3)	77.0 (68.9,83.4)	84.1 (76.9,89.4)	< 0.001
Endpoint	76.3 (66.2,86.3)	71.6 (64.0,80.5)	90.3 (84.1,93.2)	< 0.001
Eosinophil, %				
Baseline	1.07±2.95	1.32±3.39	0.341±0.62	0.011
Endpoint	1.51±2.17	1.57±2.18	1.23±2.21	0.643
MXD, %				
Baseline	5.32±3.23	5.47±3.34	4.81±2.77	0.029
Endpoint	6.44±3.79	7.36±3.84	3.72±1.82	< 0.001

Table 3 illustrates the effect of significant risk factors on the incidence of mortality based on the logistic regression model with an odds ratio (OR) at a %95 confidence interval (CI). Accordingly, AKI (OR=4.588, CI=1.405-14.977), CRP (OR=1.009, CI=1.001-1.017), LDH (OR=1.002, CI=1.001-1.004), WBC (OR=1.114, CI=1.059-1.172), RDW (OR=1.264, CI=1.118-1.430), neutrophil (OR=1.060, CI=1.032-1.089), and PLT (OR=0.996, CI=0.993-0.999) were defined as the significant risk factors on the mortality due to COVID-19 infection in the present study.

Table 3. Evaluation of significant risk factors on the incidence of mortality using a logistic regression model

Variables	Odds ratio	95% CI		P value
		Lower	Upper	
AKI	4.588	1.405	14.977	0.012
CRP	1.009	1.001	1.017	0.024
LDH	1.002	1.001	1.004	0.009
WBC	1.114	1.059	1.172	<0.001
RDW	1.264	1.118	1.430	<0.001
Neutrophil	1.060	1.032	1.089	<0.001
PLT	0.996	0.993	0.999	0.006

Discussion

The COVID-19 pandemic which emerged in China in 2019 has put the world in an emergent circumstance and caused detrimental health damage. The unpredictable nature of the disease rendered the management and treatment of the disease very difficult so there were many mortalities and morbidities at the start of the pandemic. As the scientific evaluation of the diseases developed, the strategies regarding the management of COVID-19 have ripened and hence the number of mortalities has dwindled. In this regard, one of the major steps was to predict the probability of severe disease and ICU admission by utilizing certain laboratory factors. Studies have widely recommended elements including inflammatory, liver function tests, gasometrical elements, kidney functional tests, electrolytes, and complete blood count (CBC) as noteworthy factors for the prediction of COVID-19 severity (7, 8).

In the current study, which was conducted on 623 patients with COVID-19 hospitalized in the COVID-19 wards we aimed to evaluate laboratory elements concerning liver and kidney status, inflammatory factors, hematologic elements such as CBC, electrolytes, gasometrical elements at the beginning of admission, and during the admission to elucidate the probable connection between the elements and disease severity and to recommend some of the elements as predictive factors. This study found that patients who developed severe COVID were significantly older with a majority of males compared to females.

Liver function tests: There have been several heated controversies regarding the repercussions of COVID-19 on the liver and the disturbance of liver function tests (9). In the present study, we aimed to investigate the COVID-19 patient's laboratory data and in this regard, our study showed significant differences in AST, direct and total bilirubin, albumin, and INR between groups at both baseline and endpoint admission. Based on liver function tests, the amounts of AST, total and direct bilirubin, and INR were significantly higher in non-recovered patients than in others recovered at baseline and endpoint. Our finding was consistent with the previous studies. In a retrospective cohort study, liver function tests were assessed in COVID-19 patients with different severity. Aspartate aminotransferase (10), alanine aminotransferase (11), alkaline phosphatase (12), total bilirubin (TBIL), and albumin were evaluated in 1,827 COVID-19 patients in three-time In points (pre-infection baseline, admission, and peak hospitalization) and patients were categorized as severe COVID-19, intensive care unit (13) admission, mechanical ventilation, and death. The study revealed that abnormal liver tests were frequently observed in hospitalized patients with COVID-19, mutually at admission and hospitalization. In the conclusion the study

asserted that a significant proportion of severe patients had abnormal liver tests in prehospitalization suggesting an association between abnormal liver tests and severe COVID-19, including ICU admission, mechanical ventilation, and death; The result of this assessment was in contrast to our findings so that alkaline phosphatase was associated with the severity of the patients (9). In another study, which was a systematic review of Sixty-four studies with 11 245 patients with COVID-19, parameters such as the liver enzymes, bilirubin, gamma-glutamyl transferase (GGT), and alkaline phosphatase were evaluated. The study reported abnormal amounts of factors such as aminotransferase (AST), alanine aminotransferase (ALT) levels, total bilirubin, gamma-glutamyl transferase (GGT), and alkaline phosphatase in the patients, and stated that the prevalence of elevated AST was substantially higher among those with severe cases compared to non-severe cases and concluded that elevated liver enzymes and associated with disease severity. In line with this study, the importance of AST was also mentioned in our study, however, we did not assess GGT in severe patients (14).

Renal function tests: In COVID-19 patients with a severe condition, much attention has been paid to acute kidney injury and its consequences. Acute kidney injury is the second cause of mortality and morbidity after acute respiratory syndrome in COVID-19 patients (15,16).

In the current study, the results of laboratory analysis of the participants showed a significant increase of blood urea and creatinine in the patients with a severe form of the disease, therefore, we have concluded that there is a significant correlation between blood urea and creatinine. The investigation among these patients showed that COVID-19 could cause different degrees of acute kidney failure so the patients with a more severe degree of acute kidney failure showed much higher amounts of urea and creatinine than the patients with a milder state of disease. One systematic and meta-analysis study reported 17 articles with 3396 patients and reported that there was a significant increase in blood urea nitrogen (BUN), and creatinine (Cr) in the patients with severe state of disease compared with the non-severe group. The study concluded that there was a significant correlation between abnormal renal function tests and the severe state of COVID-19 (16).

In our study, elements such as sodium, potassium, and calcium were also investigated to evaluate renal function. The results showed that sodium and potassium were also significantly abnormal among the studied population. Hence, we conclude that there is a significant relationship between the investigated elements (higher amount of sodium, potassium, and lower amount of calcium) among the patients with more severe patients and patients admitted to ICU recovery and death. Our study showed that patients with more severe degrees of acute kidney failure had much higher amounts of potassium than patients without acute kidney failure. Finally, the results showed that the significant decrease in the amount of calcium during the measurement was more evident among patients with acute kidney failure than uncomplicated patients. Studies regarding the sodium and potassium imbalance as a result of a kidney injury are limited, however, one study reported cases of severe COVID-19 and argued patients' electrolyte levels. The study asserted that in the patients with more severe COVID-19, there was an increase in sodium concentration. Moreover, it was mentioned that critically ill patients developed hypernatremia which was therapy-resistant (17).

However, in contrast with our study, one study described several reports with an evaluation of electrolytes in 1415 COVID-19 patients and suggested that sodium and potassium were significantly lower in patients with severe COVID-19. Moreover, calcium level was also significantly lower in the patients with more severe COVID-19 compared to uncomplicated patients therefore it was concluded that patients with more severe COVID-19 have a lower percentage of sodium, potassium, and calcium (18).

Gasometrical evaluation: One of the pivotal parameters among severe COVID-19 patients was VBG and ABG. Studies reported that patients with abnormal Gasometrical

evaluations have a higher risk of developing severe diseases (19). In this regard, our study found that patients with the more severe condition showed an abnormal state of PCO2, HCO3, and pH. It was found that the lower state of pH and HCO3 was significantly associated with the severity of the disease. However, PaO2 showed no correlation with the disease severity. Regarding PCO2, there is no significant relationship between its level and mortality in the early stages of hospitalization, but it occurs in more advanced stages, still, it should be mentioned that severe COVID-19 patients may initially have a low PCO2 due to tachypnea. In this regard, one study evaluated a total of 309 patients admitted with confirmed COVID-19 and assessed a multiple linear regression to predict blood gas findings by clinical/laboratory data. The study reported that the survival status of patients' PCO_2 and HCO_3 levels were found to be higher in the uncomplicated patients, whereas pH and lactate levels were significantly higher in patients who were severely ill. The study also reported that the effect of pH and lactate results was found to have a positive effect on the total tomography score of the patients. Therefore, it concluded that there was a correlation between venous blood gas indices and radiologic scores in COVID-19 patients (20).

CBC and inflammatory factors: One of the major causes of COVID-19 in critical patients is reported to be cytokine storm and studies have mentioned that prognostic factors in cytokine storm could lead us to predict the prognosis in COVID-19 patients. Studies suggested markers such as ESR CRP, LDH, serum ferritin, and D-dimer could be potential markers for the prediction of infection progress (7). In the current study, we found that unrecovered patients had significantly higher inflammatory factors such as LDH and CRP levels compared to the recovered patients during hospitalization, while, there was no significant difference in ESR level between groups. Also, in terms of hematological parameters, we evaluated parameters such as WBC, RBC, HGB, MCV, PLT, RDW, Lymph, Neut, and MXD. The results showed that there was a statistically significant correlation between the two groups at both baseline and endpoint measured values. Furthermore, a significant correlation was found in terms of HCT and EOS levels at the endpoint or baseline admission, respectively. Our study confirmed that in the non-recovered patients, there were significantly higher counts of WBC, MCV, RDW, and neutrophil, as well as significantly lower amounts of RBC, hemoglobin, platelet, lymphocyte, and MXD than in the recovered group during the admission. In this regard, in a retrospective observational study, 160 COVID-19 patients were observed to designate laboratory parameters to evaluate the possible markers of severe inflammation and the progression to mechanical invasive ventilation (MIV). In this study serum ferritin, lactate dehydrogenase (LDH), platelet count, absolute lymphocyte count (ALC), and C-reactive protein (CRP) were analyzed. The study showed that LDH, ALC, and CRP were positively correlated to the severity of patients (21). In another retrospective study, 101 patients with positive COVID-19 with a range of 17 to 75 years old were evaluated to address the role of hematological parameters in determining COVID-19 disease severity. The study showed that in patients with severe conditions, WBCs, D-dimer level, and LDH were significantly elevated compared with non-severe patients which were in line with our study, however, unlike the results of our study, parameters such as hemoglobin, HCT, MCV, platelet count, prothrombin time, and ALC showed no significant association with severity of the disease (22). In one study, 98 patients with COVID-19 were assessed to determine the value of hematological parameters in the development of patients with severe COVID-19 infection. The study revealed that the people with more severe diseases were older. Additionally, hematological parameters demonstrated that red blood cells (RBC), lymphocyte count, hematocrit (HCT), hemoglobin (HGB), mean corpuscular hemoglobin (MCH), and mean corpuscular volume (MCV) were significantly lower in the patients with severe disease group than in the group with a good outcome. Also, it was shown that the red cell volume distribution width-SD (RDW-SD), and red cell volume distribution width-CV (RDW-CV) were significantly higher in the group with severe

disease. The study confirmed that RDW-SD was the most noteworthy parameter for predicting the prognosis of severe patients (23).

The limitation was that our study was performed in only one center of treatment for COVID-19, and we had no permit to access the data from other medical centers. It is recommended that future studies be accomplished based on the data extracted from multi-centers of COVID-19 treatment applied with a larger sample size in different geographical areas.

Conclusion

In the present study, the respiratory and laboratory findings of hospitalized COVID-19 patients were assessed based on recovered or unrecovered subjects during admission to determine the significant risk factors on mortality rate in mentioned patients. Our results revealed that paraclinical parameters such as liver and renal function tests as well as LDH, CRP inflammatory marker, neutrophils, and white blood cells were significantly higher in the non-recovered groups compared to others at the end-point, which illustrated the severe condition of unrecovered patients. AKI (OR=4.588), CRP (OR=1.009), LDH (OR=1.002), WBC (OR=1.114), RDW (OR=1.264), neutrophil (OR=1.060), and PLT (OR=0.996) were found as the significant risk factors on the incidence of mortality due to COVID-19 disease in this study. Our findings could be helpful in screening and managing hospitalized patients during the respiratory viral pandemic.

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Ethical approval

The present study has been approved by Ethical committee of Mashhad University of Medical Sciences (IR.MUMS.REC.1398.308).

Conflict of Interest

The authors declare no conflict of interest.

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