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Association of Changes in Liver Enzymes, Serum Albumin and Renal Function Tests with COVID-19 Disease Severity: A Retrospective Single-Center Study from Hamadan

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Abstract

Background: The outbreak of the COVID-19 pandemic started in Wuhan, China, in December 2019 and spread rapidly around the world. Effective indicators to evaluate the severity and clinical progress of the disease need to be further investigated so that they can be used to reduce mortality. We sought to analyze the laboratory findings of some cases of coronavirus pneumonia in Iran.

Methods: This was a retrospective study of patients hospitalized with confirmed COVID-19 at Sina Hospital, affiliated with Hamadan University of Medical Sciences, between March 20, 2020, and June 21, 2021.

Results: The mean age of the 1400 patients was 57.2 ± 16.18 years, of which 64.2% (896 patients) were over 50, 52.6% were men, and 85.95% were in the critical group. A total of 508 patients (78.0%) had hypoalbuminemia. Creatinine and blood urea nitrogen (BUN) levels increased in 16.2% and 12.5% of patients, respectively. Regarding liver enzymes, 27.7% of patients had an increase in the alanine aminotransferase (ALT) enzyme, and 46.3% also showed an increase in the aspartate aminotransferase (AST) enzyme.

Conclusion: A decrease in serum albumin, increased liver enzymes, and changes in kidney function tests were observed in patients with coronavirus. Moreover, it was found that these changes were associated with inflammatory markers. Screening and daily monitoring of patients lead to early identification of risk factors in patients.

Keywords: COVID-19 disease, Albumin, Liver, Renal function test, Iran

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Introduction

Although more than two years have passed since the emergence of the coronavirus, this virus is still unpredictable (1). In December 2019, an unknown and strange virus was identified among people in Wuhan, China. This virus was initially named coronavirus – severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Then, on February 11, 2020, the International Committee on the Classification of Viruses named the new virus COVID-19 (2). Considering that this virus can be transmitted from person to person through respiratory droplets and close contact, it has become a major challenge for public health (3). Since the appearance of this virus in December 2019 (August 2022), more than 560 million cases of infection with this virus and more than 6 million deaths have been recorded worldwide. On February 19, 2020, the health authorities reported the first coronavirus case in Iran, and the virus spread quickly in the following months (4). According to the official statistics of the Ministry of Health, Treatment, and Medical Education, until March 6, 2020, the number of infected people had reached 137724 people, of whom 7451 had died and 107713 had recovered (5). More than 7 million infections and 142 thousand deaths have been reported in Iran since the observation of the coronavirus until now (August 2022). Also, the number of coronavirus infections in Hamadan city was about 146 thousand people, and the number of deaths was more than 3 thousand.

Coronavirus is one of the pathogenic agents of the coronavirus family, of which 40 species have been identified so far, seven of which are pathogenic to humans. This group of viruses attacks the human respiratory system (6). From the family of coronaviruses that have already caused disease since 2019, we can name SARS, which caused severe respiratory syndrome in China in 2003, and the Middle East respiratory syndrome (MERS), which was reported in Saudi Arabia in 2012 (3).

COVID-19 has relatively heterogeneous clinical manifestations and manifests as a spectrum of symptoms, from asymptomatic/pre-symptomatic to severe pneumonia and acute respiratory distress syndrome (ARDS) (7). It is noted that the symptoms are not fixed, and the patient may enter the next stage at any time (7). The most common symptoms of respiratory infection of COVID-19 are fever, cough, fatigue, and diarrhea. ARDS occurs approximately nine days after the onset of the disease (8). Other symptoms, such as muscle and bone pain, chills, headache, nausea, and vomiting, have also been reported. In addition to the lungs, this virus damages other tissues such as the heart, kidneys, liver, eyes, and nervous system (8).

Studies have shown that SARS-CoV-2 can infect alveolar cells of the lungs through the angiotensin-converting enzyme 2 (ACE2) receptor, which is also expressed in other tissues such as the liver and kidneys (9). After the lungs, the heart and liver are the organs most affected by this disease. Several studies have reported the clinical features and laboratory findings associated with varying degrees of liver and kidney damage in patients with COVID-19. Studies have shown that the incidence of liver damage in patients with severe forms of COVID-19 ranges from 58% to 78% (10). Liver damage is mainly caused by increased levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin, along with a slight decrease in albumin levels (11). There are also significant changes in the laboratory results of corona patients, such as an increase in blood urea nitrogen (BUN) and an increase in serum creatinine, which indicate kidney damage (12).

Effective indicators to assess severity and clinical progression need further investigation and will undoubtedly be useful for reducing mortality from COVID-19. Although many risk factors, such as advanced age, underlying chronic disease, and performance, have been shown to cause weak immune systems, leading to worse prognoses in patients with COVID-19, risk factors for disease severity are not yet known (13).

Although several studies have reported the clinical manifestations, incidence, and prognosis of complications of this disease, most of these studies originated in Wuhan. Nevertheless, these studies provided important evidence that the clinical characteristics of patients in different countries may differ. This study retrospectively examined the relationship between COVID-19 severity and changes in liver enzymes, albumin, and kidney function in patients with COVID-19.

Materials and Methods

Study design and participants

This retrospective study collected data on patients with laboratory-confirmed COVID-19 who died at or were discharged from Sina hospital, Hamadan, Iran, between March 20, 2020 and June 21, 2021. Laboratory confirmation was defined as a positive result for SARS-CoV-2 RNA using a real-time reverse transcription polymerase chain reaction (RT-PCR) assay of pharyngeal swab specimens.

Participants' characteristics data collection

This retrospective study included 1400 patients who died or were discharged from March 20, 2020, to June 21, 2021. Patient information was acquired from the patient's file in the hospital. Data on demographics, comorbidities, clinical symptoms, laboratory examinations, including complete blood count, serum biochemical test, coagulation profile, renal and liver function, C-reactive protein (CRP) and lactate dehydrogenase (LDH) levels, complications, and mechanical ventilation, were collected. The inclusion criteria were as follows: the files of patients with a final diagnosis of COVID-19 with a positive RT-PCR test who were referred and admitted to Sina Hospital from 2020 to 2021 were reviewed. The exclusion criteria were incomplete patient files and lack of access to the patient to complete the file.

Statistical analysis

Data were analyzed using SPSS software version 26, and descriptive statistics were used to express the mean and standard deviation for quantitative variables and ratio and percentage for qualitative variables. The independent t-test and Mann-Whitney test were used to compare quantitative variables between the two groups. After testing the normality of data distribution, ANOVA and Kruskal-Wallis tests (depending on the type of distribution) were used for comparison between several groups. The chi-square test was used to check the relationship between qualitative variables. A significance level of 95% was considered statistically significant.

Results

This study examined 1400 patients infected with coronavirus, but the number of patients was lower due to missing information.

In this retrospective study, the data of 1400 patients with coronavirus were examined, and the average age of these patients was 57.2 ± 16.18 years, ranging from 16 to 97 years. A total of 499 (35.8%) patients aged < 50 years and 896 (64.2%) patients aged > 50 years were included

in the study. In this study, the most common age group involved in coronavirus was 60–69 (21. 9%). It is possible to get infected with the coronavirus at any age. However, due to the weakness of the immune system and perhaps due to underlying diseases, the possibility of infection was severely increased with age. Of the patients, 662 (47.4%) were women and 734 (52.6%) were men. Based on the severity of COVID-19, most patients were in the critical group (85.95). The CRP level was positive in 79.5% of the patients, and elevated CRP levels can occur during inflammation and infections. The average albumin level in patients was 4.13 ± 0.16 g/L, and most of the subjects had hypoalbuminemia (78.0%). In various diseases and critical conditions of the body, the amount of synthesis and distribution of albumin in the body changes, causing it to decrease. Two parameters, ALT and AST levels, were used to evaluate liver function tests. Based on the normal range of parameters and articles, each parameter is divided into two groups, normal and non-normal. For both parameters, values above 40 IU were considered abnormal. In patients, the average levels of the liver enzymes SGPT, SGOT, and alkaline phosphatase (ALP) were 38.33 ± 1.07 U/L, 47.53 ± 1.06 U/L, and 190.53 ± 2.53 U/L, respectively. Two parameters, creatinine and BUN, were used in kidney function tests. Based on the normal range of parameters and articles, each parameter was divided into two groups: normal and non-normal. For BUN, values above 21 mg/dL, and for creatinine, values above 1.3 mg/dL were considered non-normal. This study's average BUN and creatinine levels were 1.64 ± 0.26 and 1.03 ± 0.01, respectively. The exact mechanism of change in BUN and creatinine levels is not known, but considering that ACE2 is the primary cell receptor of SARS-CoV-2 and is strongly expressed in kidney epithelial cells, viral infection may cause this change. Among the 1400 patients, there was a significant difference in some parameters between men and women. In some parameters, such as age group ($P=0.013$), albumin ($P=0.024$), ALP ($P=0.014$), total bilirubin ($P=0.003$), and direct bilirubin ($P=0.007$), a significant difference was observed between the sexes. In addition, a significant difference was also observed in cholesterol ($P=0.029$) and creatine phosphokinase ($P<0.001$) levels. A significant difference was also observed in some hematological factors, such as mean corpuscular volume (MCV) ($P=0.005$), mean corpuscular hemoglobin (MCH) ($P=0.004$), and red cell distribution width (RDW) ($P=0.013$) (Table 1).

In Table 2, we compared the laboratory and clinical parameters of patients with coronavirus based on the severity of the disease. Some parameters such as O2 saturation ($P<0.001$), bicarbonate ($P = 0.005$), partial pressure of oxygen ($P<0.001$), partial pressure of carbon dioxide ($P<0.001$), basophils ($P=0.002$), and blood pH ($P<0.001$) were significantly different between the groups.

Table 3 shows the results of logistic regression to investigate the effect of laboratory variables in predicting the intensity of COVID-19. One level is considered a reference (moderate), and the other two are compared with this reference level. Based on these results, none of the laboratory variables has been effective in predicting the intensity of COVID-19 at both severe and critical levels.

The correlation between inflammatory factors and liver and kidney function tests was analyzed. As shown in Table 4 there was a positive correlation between CRP levels in patients with ALT, AST, and LDH ($r=0.059$, $P=0.046$; $r=0.082$, $P=0.006$; $r=0.192$, $P<0.001$, respectively) and a positive correlation between erythrocyte sedimentation rate (ESR) levels in patients with AST, ALP, LDH, and BUN ($r=0.063$, $P=0.029$; $r=0.176$, $P<0.001$; $r=0.196$, $P<0.001$; $r=0.114$, $P<0.001$, respectively). In addition, there was a positive correlation between ferritin levels and ALT, AST, LDH, and BUN ($r=0.21$, $P=0.020$; $r=0.307$, $P=0.001$; $r=0.415$, $P<0.001$; $r=0.194$, $P=0.027$, respectively). However, there was a negative correlation between albumin and ferritin levels ($r=$ -0.235, $P=0.036$) (Table 4). There was a positive correlation between inflammatory indices and liver and kidney parameters, which may indicate an immune response caused by viral replication.

Discussion

COVID-19 is one of the worst pandemics of our time. This viral disease causes systemic involvement in the body that can cause serious complications such as multiple organ failure and death, which are difficult to predict (7). Since the end of 2019, COVID-19 has been the focus of many studies. In the present study, we described the clinical characteristics of 1400 patients admitted to Sina Hospital of Hamadan University of Medical Sciences with COVID-19 symptoms and tested positive for COVID-19. We retrospectively examined the relationship between COVID-19 severity and changes in liver enzymes, albumin, and kidney function in patients.

The results of this study showed that the average age of the patients was 57.2, and 64.2% of patients were over 50 years old. Additionally, the age range of the participants in this study was reported to be 16–97 years. The results of Lee and colleagues' study said that the average age of their subjects was 61.8 and that most of the patients in their study were in the age group of 50 to 79 years (14). There is a difference of about four years between the average age of our group and that of Lee's group. The highest infection rate in our group was in the age range of 60–69 years. In a study by Huang et al, the average age was 44 (15). The average age of infected people varies according to the country and city under study, and our study showed that adults of any age can be infected with coronavirus (16–97 years). In this study, 52.6% of the patients were men, and

Table 1. Clinical and biological characteristics of COVID-19 patients

Variable	Patients Number (N%)
Age	57.28 (16–97)
Age groups	
>50	896 (64.2)
<50	499 (35.8)
Gender	
Female	662 (47.4)
Male	734 (52.6)
Blood in urine	
Negative	525 (71.3)
Positive	128 (17.4)
Trace	83 (11.3)
CRP (mg/L)	
Negative	250 (20.5)
Positive	969 (79.5)
Ketones	
Negative	719 (98.5)
Positive	11 (1.5)
Bilirubin	
Negative	736 (52.3)
Positive	0 (0.0)
Urobilinogen	
Negative	715 (97.1)
Positive	21 (2.9)
Protein	
Negative	578 (78.5)
Positive	88 (12)
Trace	70 (9.5)
Nitrite	
Negative	723 (98.2)
Positive	13 (1.8)
Glucose	
Negative	669 (90.9)
Positive	67 (9.1)
Troponin I (pg/mL)	
Negative	993 (99.3)
Positive	3 (0.3)
Weakly	4 (0.4)
Intensity of COVID-19	
Moderate	73 (10.7)
Sever	23 (3.4)
Critical	585 (85.9)
Potassium (mmol/L)	4.16±0.01 (2.40–8.60)
Sodium (mmol/L)	136.40±0.09 (109–156)
Magnesium (mmol/L)	2.33±0.17 (0.07–189)
Calcium (mmol/L)	8.39±0.02 (6.30–22)
Phosphorus (mmol/L)	2.93±0.029 (0.80–9.20)
Albumin (g/L)	4.13±0.16 (2–92)
ESR (mm/h)	44.39±0.76 (1–144)
SGPT (U/L)	38.33±1.07 (3–548)
SGOT (U/L)	47.53±1.06 (4.30–535)
ALP (U/L)	190.53±2.53 (24–1706)
Blood sugar (mmol/L)	148.87±2.41 (67–747)
PTT (s)	36.30±0.29 (22–139)
PT (s)	13.43±0.06 (4–57)
INR	1.09±0.01 (1–14)
Bilirubin direct (µmol/L)	0.30±0.02 (0.04–11.44)
Bilirubin total (µmol/L)	0.75±0.03 (0.1–20.03)
Creatinine (µmol/L)	1.03±0.01 (0.1–15)
BUN (mmol/L)	16.64±0.26 (1.01–121)
O2 saturation (%)	73.30±0.57 (37–99.80)
Bicarbonate (mmol/L)	24.70±0.15 (10.50–49.80)
Partial pressure of oxygen (80–100 mm Hg)	42.19±0.70 (16–160)
Partial pressure of carbon dioxide (35–45 mm Hg)	37.37±0.27 (4.27–68.70)
FBS (mmol/L)	177.62±10.18 (71–643)
HbA1C (%)	9.29±0.25 (6.40–14.60)
LDH (U/L)	631.13±7.96 (24–3867)
TG (mmol/L)	153.35±7.51 (130–783)
HDL (mmol/L)	30.41±1.72 (4–212)
LDL (mmol/L)	96.54±6.95 (10–634)
Cholesterol (mmol/L)	131.51±3.35 (28–302)
Creatine Phosphokinase (U/L)	206.28±10.16 (12.69–6290)
CKMB (U/L)	34.56±1.05 (20–237)
Ferritin (ng/ml)	499.59±30.57 (7–1463)
WBC ($\times 10^9$/L)	6.25±0.08 (1.10–31)
Neutrophils ($\times 10^9$/L)	73.02±0.31 (2.00–95.00)
Lymphocyte ($\times 10^9$/L)	22.79±0.37 (2.00–336.00)
Monocytes ($\times 10^9$/L)	2.93±0.04 (1.00–12.00)
Eosinophils ($\times 10^9$/L)	2.00±0.07 (1.00–45.00)
Basophils ($\times 10^9$/L)	1.14±0.06 (1.00–3.00)
Band cells ($\times 10^9$/L)	3.07±0.09 (1.00–19.00)
RBC ($\times 10^9$/L)	4.87±0.01 (2.37–7.65)
MCV (FL)	87.72±0.17 (57.20–122.70)
MCHC (%)	32.79±0.04 (2.00–45.30)
MCH (pg)	28.82±0.07 (14.10–40.60)
Hemoglobin (g/L)	14.10±0.07 (1.40–54.40)
Hematocrit (%)	42.51±0.14 (11.90–65.50)
Mean platelet volume ($\times 10^9$/L)	10.10±0.03 (7.50–33.30)
Platelets ($\times 10^9$/L)	191.81±2.12 (11–792)
RDW	13.49±0.04 (11.20–33.00)

Table 1. Continued.

Abbreviations: PT, prothrombin time; PTT, partial thromboplastin time; ALP, Alkaline phosphatase; AST, aspartate transaminase; ALT, alanine transaminase; SGPT, serum glutamate pyruvate transaminase; SGOT, serum glutamate oxaloacetate transaminase; BUN, blood urea nitrogen; FBS, fasting blood sugar; MCV, Mean corpuscular volume; MCH, mean corpuscular hemoglobin; RDW, red cell distribution width; ESR, erythrocyte sedimentation rate; TG, triglycerides; LDL, low-density lipoprotein; HDL, high-density lipoprotein; WBC, white blood cells; RBC, red blood cells; CKMB, Creatine Kinase-MB.

Table 2. Baseline characteristics of disease severity in patients with COVID-19

Variable	Moderate	Sever	Critical	*P* value
Age (year, mean, SD)	73 (56.68±16.20)	23 (57.78±14.46)	585 (59.09±16.35)	0.470
Age groups				0.628
0–59	41 (56.2)	12 (52.2)	286 (48.9)	
60–79	24 (32.9)	10 (43.5)	236 (40.3)	
≥80	8 (11)	1 (4.3)	63 (10.8)	
Gender	73 (10.7)	23 (3.4)	585 (85.9)	
Female	31 (42.5)	7 (30.4)	283 (48.4)	0.167
Male	42 (57.5)	16 (96.6)	302 (51.6)	
CRP (mg/L)	68 (11.1)	20 (3.3)	526 (85.7)	0.836
Negative	10 (14.7)	2 (10.0)	78 (14.8)	
Positive	58 (85.3)	18 (90.0)	448 (85.2)	
Blood in urine	41 (9.3)	15 (3.4)	386 (87.3)	0.822
Negative	31 (75.6)	11 (73.3)	261 (67.6)	
Positive	6 (14.6)	3 (20.0)	77 (19.9)	
Trace	4 (9.8)	1 (6.7)	48 (12.4)	
Ketones	40 (9.2)	15 (3.4)	382 (87.4)	0.195
Negative	40 (100)	14 (93.3)	378 (99.0)	
Positive	0 (0.0)	1 (6.7)	4 (1.0)	
Protein	41 (9.3)	15 (3.4)	386 (87.3)	0.917
Negative	30 (73.2)	12 (80.0)	287 (74.4)	
Positive	7 (17.1)	2 (13.3)	52 (13.5)	
Trace	4 (9.8)	1 (6.7)	47 (12.2)	
Nitrite	41 (9.3)	15 (3.4)	386 (87.3)	0.597
Negative	41 (100.0)	15 (100)	379 (98.2)	
Positive	0 (0.0)	0 (0.0)	7 (1.8)	
Glucose	41 (9.3)	15 (3.4)	386 (87.3)	0.216
Negative	39 (95.1)	15 (100)	345 (89.4)	
Positive	2 (4.9)	0 (0.0)	41 (10.6)	
Troponin I (pg/mL)	54 (10.1)	20 (3.7)	464 (86.2)	0.729
Negative	53 (98.1)	20 (100)	461 (99.4)	
Positive	1 (1.9)	0 (0.0)	2 (0.4)	
Weakly	0 (0.0)	0 (0.0)	1 (0.2)	
Potassium (mmol/L)	71 (4.16±0.40)	22 (4.17±0.35)	577 (4.18±0.49)	0.921
Sodium (mmol/L)	71 (135.77±3.67)	22 (135.68±3.56)	577 (136.03±3.88)	0.792
Magnesium (mmol/L)	58 (2.14±0.40)	20 (2.18±0.39)	463 (2.17±0.49)	0.881
Calcium (mmol/L)	55 (8.17±0.48)	19 (8.11±0.39)	437 (8.29±0.62)	0.180
Phosphorus (mmol/L)	44 (2.91±1.01)	17 (3.43±1.61)	395 (2.91±0.81)	0.058
Albumin (g/L)	31 (3.79±0.42)	10 (3.77±0.34)	396 (4.03±0.22)	0.940
ESR (mm/h)	70 (46.95±28.01)	22 (42.18±22.66	551 (46.09±28.02)	0.779
SGPT (U/L)	68 (39.47±27.89)	21 (43.00±22.91)	553 (40.22±1.86)	0.945
SGOT (U/L)	67 (52.85±32.70)	21 (50.80±19.66)	562 (51.81±43.08)	0.974
ALP (U/L)	67 (180.35±66.87)	21 (169.76±52.66)	550 (190.51±78.65)	0.306
Blood sugar (mmol/L)	69 (154.76±96.26)	18 (156.72±105.00)	521 (154.87±86.05)	0.996
PTT (s)	69 (36.05±10.15)	22 (34.70±12.84)	561 (36.91±11.50)	0.584
PT (s)	69 (13.62±2.20)	22 (13.93±2.21)	562 (13.47±2.50)	0.632
INR	69 (1.09±0.20)	22 (1.12±0.27)	562 (1.08±0.34)	0.894

Table 2. Continued.

Variable	Moderate	Sever	Critical	*P* value
Bilirubin direct (µmol/L)	41 (0.32 ± 0.05)	14 (0.32 ± 0.07)	352 (0.32 ± 0.04)	0.999
Bilirubin Total (µmol/L)	40 (0.80 ± 0.57)	14 (0.83 ± 0.45)	355 (0.79 ± 0.07)	0.990
Creatinine (µmol/L)	71 (1.03 ± 0.43)	22 (0.96 ± 0.28)	580 (1.05 ± 0.72)	0.815
BUN (mmol/L)	71 (18.54 ± 13.11)	22 (16.25 ± 9.54)	579 (17.70 ± 11.43)	0.700
O2 saturation (%)	73 (91.91 ± 1.26)	23 (88.76 ± 1.80)	585 (68.59 ± 13.82)	**< 0.001**
Bicarbonate (mmol/L)	72 (23.40 ± 4.47)	23 (23.80 ± 3.19)	572 (24.95 ± 4.05)	**0.005**
Partial pressure of oxygen (80–100 mm Hg)	53 (59.47 ± 5.32)	18 (49.27 ± 9.60)	410 (37.54 ± 10.48)	**< 0.001**
Partial pressure of carbon dioxide (35–45 mm Hg)	70 (33.01 ± 6.36)	23 (33.68 ± 5.56)	566 (38.24 ± 7.04)	**< 0.001**
FBS (mmol/L)	73 (7.44 ± 0.04)	23 (7.45 ± 0.03)	583 (7.41 ± 0.04)	**< 0.001**
HbA1C (%)	5 (170.20 ± 85.40)	------	40 (187.85 ± 89.82)	0.679
LDH (U/L)	5 (8.98 ± 1.41)	1 (13.40)	28 (9.32 ± 1.98)	0.116
TG (mmol/L)	62 (687.62 ± 228.42)	21 (613.23 ± 224.13)	506 (681.59 ± 325.04)	0.606
HDL (mmol/L)	7 (157.28 ± 66.06)	2 (124.50 ± 16.26)	87 (166.60 ± 102.43)	0.822
LDL (mmol/L)	7 (23.28 ± 9.30)	2 (19.50 ± 0.70)	80 (30.34 ± 25.28)	0.643
Cholesterol (mmol/L)	7 (88.85 ± 63.47)	2 (69.00 ± 5.65)	83 (87.76 ± 70.75)	0.631
Creatine phosphokinase (U/L)	7 (129.34 ± 60.02	2 (101.50 ± 20.50)	86 (131.63 ± 40.05)	0.596
CKMB (U/L)	57 (202.57 ± 30.26)	19 (175.47 ± 29.33)	476 (230.48 ± 19.05)	0.750
Ferritin (ng/ml)	32 (37.46 ± 34.35)	14 (28.35 ± 9.29)	301 (34.15 ± 23.31)	0.496
WBC ($\times 10^9$/L)	4 (730.00 ± 472.48)	2 (643.35 ± 545.39)	66 (612.89 ± 351.80)	0.817
Neutrophils ($\times 10^9$/L)	72 (6.42 ± 2.91)	22 (6.04 ± 2.37)	571 (6.46 ± 3.35)	0.839
Lymphocyte ($\times 10^9$/L)	72 (77.48 ± 8.48)	22 (74.72 ± 9.40)	570 (74.56 ± 11.38)	0.107
Monocytes ($\times 10^9$/L)	72 (18.50 ± 7.99)	22 (20.36 ± 9.72)	569 (21.16 ± 10.82)	0.126
Eosinophils ($\times 10^9$/L)	70 (2.91 ± 1.79)	19 (2.89 ± 1.82)	524 (2.95 ± 1.58)	0.966
Basophils ($\times 10^9$/L)	29 (1.75 ± 0.26)	13 (1.46 ± 0.21)	282 (1.85 ± 1.10)	0.430
Band cells ($\times 10^9$/L)	2 (1.50 ± 0.70)	1 (1.00)	19 (1.00 ± 0.00)	**0.002**
RBC ($\times 10^9$/L)	41 (3.51 ± 0.44)	12 (3.00 ± 0.56)	334 (3.14 ± 2.49)	0.653
MCV (FL)	72 (4.92 ± 0.59)	22 (4.81 ± 0.51)	571 (4.85 ± 0.63)	0.617
MCHC (%)	72 (88.80 ± 6.75)	22 (87.48 ± 3.49)	566 (87.68 ± 6.31)	0.355
MCH (pg)	72 (32.94 ± 1.46)	22 (33.03 ± 0.93)	567 (32.63 ± 2.21)	0.381
Hemoglobin (g/L)	71 (29.22 ± 2.65)	22 (28.84 ± 1.65)	567 (28.7 ± 2.61)	0.305
Hematocrit (%)	72 (14.33 ± 1.64)	22 (15.03 ± 5.12)	571 (13.96 ± 2.50)	0.090
Mean platelet volume ($\times 10^9$/L)	72 (43.53 ± 4.50)	22 (40.95 ± 7.53)	570 (42.36 ± 5.00)	0.067
Platelets ($\times 10^9$/L)	72 (10.12 ± 0.93)	20 (10.20 ± 1.04)	557 (10.10 ± 0.99)	0.887
RDW	72 (179.73 ± 61.53)	22 (181.77 ± 51.28)	570 (191.22 ± 77.57)	0.420

Abbreviations: PT, prothrombin time; PTT, partial thromboplastin time; ALP, Alkaline phosphatase; AST, aspartate transaminase; ALT, alanine transaminase; SGPT, serum glutamate pyruvate transaminase; SGOT, serum glutamate oxaloacetate transaminase; BUN, blood urea nitrogen; FBS, fasting blood sugar; MCV, Mean corpuscular volume; MCH, mean corpuscular hemoglobin; RDW, red cell distribution width; ESR, erythrocyte sedimentation rate; TG, triglycerides; LDL, low-density lipoprotein; HDL, high-density lipoprotein; WBC, white blood cells; RBC, red blood cells; CKMB, Creatine Kinase-MB.

47.4% were women. Our data are similar to the results of Huang et al and Chen et al, who showed that men are more likely to be infected with coronavirus (15). However, the results of our study were different from those of Wang et al and Fan et al (2,16).

Based on the results of our study, a significant number of COVID-19 patients showed decreased serum levels of albumin, calcium, phosphorus, and high-density lipoproteins cholesterol (HDL-C). In addition, an increase was seen in AST, ALP, total bilirubin, LDH, creatine phosphatase, ferritin, and CRP. This is similar to the results of other studies (15,17).

Innate and acquired immune responses differ between men and women (18). The symptoms and consequences of sex-related diseases are influenced by two factors: steroids and X-chromosome-related genes, both of which modulate the immune system (18). Studies have shown that estradiol protects women against viral infections (19). In this study, we investigated laboratory parameters using sex-specific epidemiological analysis. A significant

Table 3. Multiple logistic regression intensity of COVID-19: moderate, severe, and critical

Intensity of COVID-19	Variables		OR	95% CI	*P* value
Moderate			**Ref**	**Ref**	**Ref**
Severe	Gender	Male	0.29	(-1.07,1.65)	0.681
		Female	Ref	Ref	Ref
	Age groups	0–59	Ref	Ref	Ref
		60–79	0.02	(-1.42, 1.45)	0.982
		≥80	-14.87	(-3252.07, 3222.33)	0.993
	Albumin	Albumin<3.5	Ref	Ref	Ref
		Albumin>3.5	0.02	(-1.64, 1.68)	0.980
	Creatinine	Normal	Ref	Ref	Ref
		Elevated	-7.61	(-1370.57, 1355.35)	0.991
	BUN	Normal	Ref	Ref	Ref
		Elevated	0.57	(-1.72–2.88)	0.625
	SGPT (ALT)	Normal	Ref	Ref	Ref
		Elevated	-0.57	(-1.71, 2.85)	0.625
	SGOT (AST)	Normal	Ref	Ref	Ref
		Elevated	0.23	(-0.52–0.98)	0.550
Critical	Gender	Male	0.24	(-0.53–1.02)	0.539
		Female	Ref	Ref	Ref
	Age groups	0–59	Ref	Ref	Ref
		60–79	-0.56	(-1.45–0.34)	0.224
		≥80	-0.21	(-1.58- 1.16)	0.764
	Albumin	Albumin<3.5	Ref	Ref	Ref
		Albumin>3.5	-0.54	(-1.42–0.33)	0.226
	Creatinine	Normal	Ref	Ref	Ref
		Elevated	-0.44	(-1.23–0.35)	0.278
	BUN	Normal	Ref	Ref	Ref
		Elevated	-0.38	(-2.05, 1.29)	0.652
	SGPT (ALT)	Normal	Ref	Ref	Ref
		Elevated	0.19	(-0.83–1.20)	0.719
	SGOT (AST)	Normal	Ref	Ref	Ref
		Elevated	-0.31	(-0.78–0.15)	0.183

Abbreviations: AST, aspartate transaminase; ALT, alanine transaminase; SGPT, serum glutamate pyruvate transaminase; SGOT, serum glutamate oxaloacetate transaminase; BUN, blood urea nitrogen.

Table 4. Correlation between inflammatory factors with liver and kidney function tests

	ALT (U/L)		AST (U/L)		ALP (U/L)		LDH (U/L)		Albumin (g/L)		Creatinine (μmol/L)		BUN (mmol/L)	
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*
CRP (mg/L)	0.059	0.046	0.082	0.006	0.004	0.896	0.192	<0.001	-0.079	0.057	-0.024	0.411	0.021	0.466
ESR (mm/h)	0.023	0.428	0.063	0.029	0.176	<0.001	0.196	<0.001	0.068	0.100	0.003	0.926	0.114	<0.001
Ferritin (ng/mL)	0.21	0.020	0.307	0.001	-0.110	0.241	0.415	<0.001	-0.235	0.036	0.111	0.209	0.194	0.027

Abbreviations: ALP, Alkaline phosphatase; AST, aspartate transaminase; ALT, alanine transaminase; BUN, blood urea nitrogen; ESR, erythrocyte sedimentation rate; LDH, lactate dehydrogenase; CRP, C-reactive protein.

difference was observed in some specific laboratory parameters such as albumin ($P=0.024$), ALP ($P=0.014$), total bilirubin ($P=0.003$), cholesterol ($P=0.029$), creatine phosphatase ($P<0.001$), monocytes ($P=0.003$), MCV ($P=0.005$), and MCH ($P=0.004$) between men and women. The results of the study by Meng et al showed a significant difference between the two sexes in some laboratory parameters (19). The number of parameters that showed a significant relationship was greater in the study by this group than in our group.

Similar to other proteins, albumin is produced by the liver. This protein plays an important role in regulating

osmotic pressure and the nutritional conditions of the body (20). Various factors, including malnutrition and liver and kidney damage, influence the decrease in albumin concentration. In patients infected with coronavirus, it can occur due to adverse drug reactions and systemic inflammation (21). Studies have shown that reducing albumin levels increases the risk of severe COVID-19 (22). In our study, 78.3% of the patients with COVID-19 had hypoalbuminemia. In a study by Kheir et al, 60.2%, and in the study by Huang et al, 49.6% of patients had hypoalbuminemia (23,24). Our study found a significant relationship between laboratory parameters and decreased albumin concentration. Our findings are consistent with those of previous studies showing a relationship between hypoalbuminemia and laboratory parameters (22-24). However, our findings do not agree with previous studies that show a relationship between hypoalbuminemia and the severity of COVID-19 (25), as our study did not observe a relationship between the two.

ACE2 acts as a receptor for SARS-CoV-2 and is expressed in the alveoli of the lung and in the heart and kidney (26). In addition to these tissues, Chia et al showed that it is also expressed in liver and bile duct cells, thus causing damage in these tissues (26). This study observed increased AST, ALP, and LDH. ALT and AST levels increased in 27.7% and 46.13% of the patients, respectively. The results of the study by Benedé-Ubieto et al showed an increase in the liver enzymes ALT, AST, ALP, and gamma glutamine transferase (GGT), which is similar to our results (26). Various independent studies from America (27), Italy, and Australia have reported increased ALT and AST enzymes in corona patients (26). Lactate dehydrogenase is an enzyme upregulated in several disorders, including liver and lung diseases. This study observed an increase in the levels of this enzyme, along with other liver enzymes. An increase in LDH has been observed in several studies, which in some cases was related to the severity of the coronavirus disease.

In some cases, it was related to the death of people (2,26). An increase in ALP is less common than other liver enzymes (28); however, in our study, an increase in ALP was observed, which is similar to the results of Fan et al (2). Serum ferritin levels increase during inflammation and infection (14). This study shows that ferritin levels increase in corona patients. Li et al (14) and Benedé-Ubieto et al (26) confirmed our results. Several studies have reported increased total bilirubin levels in patients with liver disease (29). An increase in bilirubin has also been observed in coronavirus patients, which is consistent with our results (29). One of the complications of COVID-19 is thrombosis. Coagulation factors are produced in the liver, so liver damage affects coagulation (30). The results of a study by Benedé-Ubieto et al showed a positive correlation between LDH and D-dimer, also between fibrinogen and LDH, as well as between AST and elevated fibrinogen (26). The results of our study also showed a significant relationship between coagulation tests and AST ($P=0.001$) and ALT ($P=0.013$) levels. A positive correlation was observed between the inflammatory indices of CRP, ferritin, ESR, and liver enzymes in patients, which indicated an immune response caused by virus replication (29). The results of the studies by Fan et al (28) and Saini et al (29) confirm our results.

This study used creatinine and BUN levels to assess kidney function. In our study, only 12.5% of patients had elevated BUN levels, and 16.2% had elevated creatinine levels. However, the results of Küçükceran et al showed that the rate of BUN increased and was related to the severity of the disease, hospitalization, and death, which is contrary to the results of our study (31). Like our study, Zhang et al (32) showed no obvious difference in creatinine levels between the severe and non-severe groups. Contrary to our results, Cheng et al (33) showed that increased creatinine levels are associated with disease severity, ICU admission, and death. The results of Li et al indicated proteinuria and hematuria in patients with COVID-19, in addition to an increase in BUN levels (34). This study showed that only 17.4% of patients had hematuria and 12% had proteinuria, and increased BUN was observed in only 12%. The results showed that some patients with H1N1 showed increased creatine kinase activity (33). In the results of the studies by Zhang et al and Cheng et al, an increase in creatine kinase activity was seen in patients with COVID-19 (32,33), which was also observed in our study. Creatine kinase is an enzyme that increases for various reasons, including heart disease, muscle damage, and smooth and striated muscle involvement (32). However, we had no direct radiological or histopathological evidence to determine which body part was damaged. Therefore, the effect of the new coronavirus 2019 on body organs needs further study.

In this study, we classified corona patients based on the severity of the disease: 10.7% of patients were in the moderate group, 3.4% in the severe group, and 85.9% in the critical group. We examined the relationship between the laboratory parameters and disease severity. Our study results showed no significant difference between the severity of COVID-19 and most laboratory parameters, which was contrary to the results of previous studies (22,35). The results of our study show a significant relationship between O2 saturation ($P<0.001$), bicarbonate ($P=0.005$), partial pressure of oxygen ($P<0.001$), partial pressure of carbon dioxide ($P<0.001$), and blood pH ($P<0.001$) with the severity of COVID-19.

Our study had several limitations: Data were collected from one center, and the study design was retrospective. Data were extracted from electronic documents, and only the patients' laboratory results were available. The underlying diseases and demographic information of the patients were not available. In addition, patients with

COVID-19 who tested negative for SARS-CoV-2 by NAA were excluded from this study. However, our study results are comparable to those of many similar recent studies.

Conclusion

Our study demonstrated that low serum albumin in patients with COVID-19 has a significant relationship with liver and kidney tests and may lead to liver and kidney damage. Although elevated liver enzymes were also common in patients with COVID-19, in our study, most showed only mild elevations, which may be due to chronic hypoxia and excessive inflammation. Examination of kidney function tests revealed that the prevalence of kidney involvement was not high. Nevertheless, screening, early diagnosis, and effective intervention may help reduce the mortality of patients with COVID-19.

Authors' Contribution

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Competing Interests

The authors declare no conflict of interest.

Ethical Approval

This study was approved by the Ethics Committee of Hamadan University of Medical Sciences (IR.UMSHA.REC.1400.811), and the requirement of written informed consent was waived.

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