

# Evaluation of Hepatic, Renal and Cardiac Diagnostic Markers in Patients With Severe COVID-19

Sara Mobarak<sup>1,2</sup>, Asma Mohammadi<sup>3</sup>, Atefeh Zahedi<sup>4</sup>, Saeed Jelvay<sup>3,5</sup>, Fatemeh Maghsoudi<sup>6</sup>, Mohammad Hosein Assareh Zadegan Dezfuli<sup>7</sup>, Ali Reza Balizadeh Karami<sup>7</sup>, Esmat Radmanesh<sup>7,8</sup>

<sup>1</sup> Clinical Research Development Unit, Taleghani Educational Hospital, Abadan University of Medical Sciences, Abadan, Iran

<sup>2</sup> Department of Infectious Disease, School of Medicine, Abadan University of Medical Sciences, Abadan, Iran

<sup>3</sup> Clinical Research Development Unit, Valiasr Educational Hospital, Abadan University of Medical Sciences, Abadan, Iran

<sup>4</sup> Department of Public Health, Asadabad School of Medical Sciences, Asadabad, Iran

<sup>5</sup> Department of Health Information Technology, Abadan University of Medical Sciences, Abadan, Iran

<sup>6</sup> Department of Public Health, School of Health, Abadan University of Medical Sciences, Abadan, Iran

<sup>7</sup> Student Research Committee, Abadan University of Medical Sciences, Abadan, Iran

<sup>8</sup> Department of Physiology, School of Medicine, Abadan University of Medical Sciences, Abadan, Iran

Received: 18 Apr. 2021; Accepted: 24 Sep. 2021

**Abstract-** SARS-CoV-2 that causes Coronavirus disease 2019 (COVID-19) was first known in Wuhan, China, in December 2019. The aim of this study was to evaluate the level of common hepatic, renal, and cardiac diagnostic markers in hospitals in patients with severe COVID 19. In this study, 259 patients with symptoms of severe COVID-19 and a positive RT-PCR assay of nasopharyngeal samples were enrolled. Inclusion criteria are positive for COVID-19 patients at the diagnosis of an infectious disease physician. Diagnostic markers of liver, kidney, and heart were evaluated by age and gender. In this study, 48.3% of patients severe with COVID-19 were male, and 51.7% were female. The mean of markers such as LDH, Direct Bilirubin, SGOT, SGPT, D-dimer was higher than normal, which was observed in men more than women. The mean of CK-MB also was higher than normal, which was observed in women more than men. The highest mean of markers was seen in the older ages. The mean of BUN was observed in the age range of 55-64 years and above 65 years above normal. But the mean of CPK, creatinine, potassium and alkaline phosphatase were normal. The results of the present study showed an increase in the level of some of the most important diagnostic markers of hepatic, renal, and cardiac in patients with COVID 19. This increase was greater in some markers, including SGOT, SGPT, Direct bilirubin, LDH, D-dimer, in men than in women, and more in older patients.

© 2021 Tehran University of Medical Sciences. All rights reserved.

*Acta Med Iran* 2021; 59(11):656-661.

**Keywords:** Diagnostic markers; Coronavirus disease 2019 (COVID-19); Abadan

## Introduction

SARS-CoV-2 which causes Coronavirus disease 2019 (COVID-19) was first known in Wuhan, China, in December 2019. An asymptomatic COVID-19 case is someone who has developed signs and symptoms of COVID-19 (1) and transmitted through respiratory droplets and person-to-person contact routes. Transmission can also occur by touching objects or

carriers of the infection occur close to an infected person (2). The possibility of viruses and pathogens of common z-human origin in the future remains. Therefore, extensive efforts must be made to prevent the spread of the common origin between humans and animals in the future (3). If COVID-19 to become a threat to global health, yet to be studied further. Quick and fast testing of pathogens and possible differential diagnoses based on clinical descriptions for doctors at first contact with

**Corresponding Author:** E. Radmanesh

Department of Physiology, School of Medicine, Abadan University of Medical Sciences, Abadan, Iran

Tel: +98 9171438307, Fax: +98 6153262617, E-mail address: esmatradmanesh33@gmail.com, e.radmanesh@abadanums.ac.ir

Copyright © 2021 Tehran University of Medical Sciences. Published by Tehran University of Medical Sciences

This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International license (<https://creativecommons.org/licenses/by-nc/4.0/>). Non-commercial uses of the work are permitted, provided the original work is properly cited

suspected patients is very important (4).

The findings highlight the high mortality of people with underlying and severe COVID-19 kidney disease and emphasize the importance of identifying safe and effective COVID-19 treatments for this vulnerable population (5). AKI in patients with severe infection and the COVID-19 mortality rate is higher. Clinicians should pay more attention to the monitoring and treatment of patients with AKI who have COVID-19 (6).

Liver function abnormalities, especially elevated AST and ALT levels, are not only common in COVID-19 but also have poor results. Therefore, future studies should carefully investigate the cause of liver damage during COVID-19 infection (7).

High blood pressure, diabetes, and CVD are the most common diseases in COVID-19 patients, and these factors are associated with the progression and severity of COVID-19. However, in the aging population, the effects are more intense COVID-19, naturally prone to the disease are common (8).

Risk factors for cardiovascular disease, its manifestations, and laboratory biomarkers are powerful predictors of death in COVID-19 patients and instability of the cardiovascular system in mortality in COVID-19 patients (9). The aim of this study was to evaluate the level of common hepatic, renal and cardiac diagnostic markers in hospital in patients with severe COVID 19.

## Materials and Methods

This is a cross-sectional descriptive study. The information of 259 patients with COVID-19 disease hospitalized from March 2020 to May 2020 in the HIS system of Taleghani Educational Hospital in Abadan, Iran, was received. In this study, 259 patients with symptoms of severe COVID-19 (decreased level of consciousness or respiratory rate above 24 or oxygen saturation less than 94%) and a positive RT-PCR assay of nasopharyngeal samples were enrolled. Inclusion criteria are positive for COVID-19 patients at the diagnosis of an infectious disease physician. Diagnostic markers of liver, kidney and heart, such as sodium, potassium, creatinine, urea, and bilirubin, ALK Ph, SGOT, SGPT, CPK, LDH, CK-MB and D-dimer were evaluated by age and gender.

To describe the data, mean and standard deviation in quantitative variables and frequency and percentage in qualitative variables were used. The normality of quantitative variables was assessed using the

Kolmogorov-Smirnov test. Chi-square test and t-test were used to analyze the data. Data analysis was performed by SPSS software version 22 and  $P < 0.05$  was considered statistically significant.

## Results

In this study, 259 patients severe with COVID-19 were studied with mean age  $51.27 \pm 16.896$ , of which 48.3% were male and 51.7% were female. The mean age was  $52.5 \pm 16.08$  for men and  $50.12 \pm 17.6$  for women.

The mean of LDH was higher than normal, which was observed in men more than women, which was not significant. Also, the highest mean was seen in the age range of 64-55 years, which was not significantly related to other age groups.

The mean of direct bilirubin in total patients was higher than normal. The mean was higher in men than normal and higher than women, which was not significant, but in women, the amount was normal. And in the age range of 55-64 years, it was higher than normal and had the highest average compared to other age groups. The mean of total Bilirubin was observed in the age range of 55-64 years above normal.

The mean of SGOT was higher than normal in all patients, which is higher in men than women. This relationship was not significant. And in the age range under 34 years is normal and in other periods was observed more than normal, and the highest rate was observed above 65 years. The mean of SGPT is generally higher than normal, which is higher than normal in men and higher than women, and this rate is normal in women. This connection was not significant. It was higher than the average in all age groups, and the highest average was observed above 65 years.

The mean of BUN was observed in the age range of 55-64 years and above 65 years above normal, with the highest mean observed above 65 years, which was a significant relationship.

The Mean of D-dimer was observed above normal and was observed in men more than normal and more than women. This connection was not significant. It was higher than the average in all age groups, and the highest value was observed in more than 65 years.

The mean of CK-MB in total was higher than normal in all patients, which was higher in women than men. And this connection was not significant. Based on age, it was seen in the age range of 44-35 years and 54-45 years above normal, with the highest mean observed in

## Evaluation of diagnostic markers in patients with COVID-19

54-45 years. And this relationship between ages was not significant. Mean sodium ions were also observed to be higher than normal. But the mean of CPK, BUN,

creatinine, potassium and alkaline phosphatase were normal.

**Table 1. Mean and standard deviation of laboratory factors studied in patients based on gender**

Variable	Mean±SD		Mean±SD	P
	Male	Female		
Age	52.5±16.08	50.12±17.6	51.27±16.896	
CPK	236.70±246.03	144.43±135.377	197.15±210.177	0.02*
BUN	18.32±12.682	15.25±13.224	16.73±13.031	0.06
Cr	1.25±0.608	1.16±1.133	1.20±0.921	0.44
Albumin	3.94±0.685	3.68±0.669	3.83±0.661	0.52
Na	137.93±4.058	139.03±4.871	138.50±4.522	0.06
K	4.13±0.624	4.01±0.631	4.07±0.630	0.12
CK MB	23.78±7.804	26.75±18.799	24.99±13.163	0.57
Total Protein	7.20±0.781	5.35±1.626	6.46±1.412	0.17
ALK Ph	211.23±147.809	194.48±94.483	202.38±122.419	0.39
LDH	569.29±271.794	515.23±229.377	541.91±251.845	0.18
Total Bilirubin	1.18±2.303	0.68±0.656	0.91±1.650	0.16
Direct Bilirubin	0.58±1.152	0.27±0.232	0.41±0.813	0.08
SGOT	99.73±501.572	31.51±20.606	64.40±349.146	0.22
SGPT	61.28±202.223	23.68±14.987	41.79±141.562	0.1
D Dimer	1419.83±1383.028	704.90±482.936	1156.44±1171.407	0.2

**Table 2. Mean and standard deviation of laboratory factors studied in patients based on age groups**

variable	≥65	64-55	54-45	44-35	34≥	P
CPK	246.72±314.124	176.64±115.185	140.35±90.128	158.14±83.861	253.625±236.81	0.380
BUN	22.72±14.234	22.91±16.713	15.84±12.605	11.89±9.292	10.19±3.535	0.000*
Cr	1.29±0.551	1.30±0.519	1.24±0.747	1.30±1.832	0.90±0.173	0.149
Albumin	3.45±0.778	4.25±1.061	3.75±0.636	4.05±0.636	3.75±0.705	0.845
Na	138.62±5.609	138.26±4.853	138.67±4.782	137.82±3.135	138.90±3.199	0.820
K	4.17±0.695	4.23±0.624	4.06±0.789	3.91±0.463	3.97±0.384	0.091
CK MB	24.71±13.471	21.67±12.897	30.40±19.932	26.17±7.489	18.00±1.414	0.840
ALK Ph	223.60±157.347	223.50±88.288	183.97±66.852	205.46±168.951	183.25±70.723	0.526
LDH	535.48±193.843	678.44±265.843	532.90±265.693	503.03±181.899	520.64±325.221	0.180
Total Bilirubin	1.36±3.108	0.88±0.752	0.68±0.399	0.69±0.225	0.81±0.828	0.687
Direct Bilirubin	0.80±1.536	0.35±0.324	0.24±0.116	0.31±0.138	0.26±0.179	0.153
SGOT	152.50±712.036	44.70±76.145	32.69±16.286	31.14±11.782	42.63±35.674	0.506
SGPT	72.49±278.952	46.16±105.684	30.94±23.694	25.29±11.711	33.00±24.242	0.623
D Dimer	1822.90±1171.407	726.56±70.088	835.21±467.465	1188.83±609.264	1304.40±1706.879	0.875

## Discussion

Some studies have suggested several biochemical factors as laboratory determinants commonly used to predict the severity of COVID-19 (10). In the present study, it was observed that the mean of SGOT, SGPT, and Direct Bilirubin was higher than normal in patients with COVID-19, which was higher in men than women,

and the highest was in the age group of 55-64 years. But the mean alkaline phosphatase and CPK in this study were normal.

The results showed that while severe cases of COVID-19 showed higher levels of ALT, AST, and total bilirubin compared with non-severe cases, albumin values were significantly lower in severe cases and highlighted that an abnormal amount of liver-related

examinations might reflect disease progression toward adverse outcomes (10). Abnormal liver tests are common in COVID-19 patients. An increase in ALT-AST and AST/ALT ratio >one was related to the more severe course and elevated mortality in COVID-19. COVID-19 patients were associated with increased hepatic aminotransferases at admission with a greater need for intensive care, extensive lung disease, and individual therapy. The presence of liver abnormalities at admission can be used as a predictor of the severity of COVID-19 (11).

Biochemical parameters of liver strongly associated with mortality COVID-19. Non-surviving had greater levels of TBIL, AST, ALT, LDH, GLB, and GGT. Measuring the biochemical parameters of the liver may help clinicians assess the prognosis of COVID-19 (12,13).

In the present study, the mean D-dimer was higher than normal and was higher in men than women, and the highest value was observed in more than 65 years.

D-dimer values in COVID-19 patients with severe disease were significantly higher than in those without, highlighting that the height of this parameter may be associated with disease progression to an adverse clinical outcome (14,15). Dyspnea, age, neutrophilia, increased D-dimer on admission are risk factors for mortality in elderly COVID-19 patients. Early diagnosis and supportive care for elderly patients is of utmost importance COVID-19 (16).

In our study, the mean LDH was higher than normal, which was higher in men than women. Also, the highest mean was seen in the age range of 64-55 years, which was not significantly related to other age groups.

ALB, LYM, LYM (%), LDH, NEU (%) and CRP were strongly associated with acute lung injury. Age, viral load, damage to the lungs, and blood biochemical parameters, albumin (ALB), CRP, LDH, LYM (%), LYM and NEU (%), perhaps predictors of disease severity (17). The results of the COVID-19 mRNA clearance ratio were found to be significantly associated with decreased serum creatine kinase (CK) and lactate dehydrogenase (LDH) levels. Decreased serum LDH or CK may predict a favorable response to treatment for COVID-19 infection (18). By analyzing nine published studies (1532 COVID-19 patients), a correlation was observed between elevated LDH levels in the hospital for the first time and disease outcomes in patients with COVID-19 criteria. LDH levels increase by a 6-fold increase in the risk of severe disease and death in 16% of COVID-19 patients. LDH in patients should be closely monitored for signs of disease progression or

compensation (19).

The results of this study showed that the mean CK-MB in total in patients with COVID-19 was higher than normal in all patients, which was higher in women than men. The highest average was observed in 45-54 years.

In patients with COVID-19, an increase in CK-MB and myoglobin on admission perhaps an effective predictor of adverse outcomes, and combined use of CK-MB and myoglobin performed better for prediction (20).

Studies have shown an increase in BUN and scr levels as well as a decrease in BUA levels in COVID-19 patients within 28 days of admission in deaths (21). Initial levels of BUN and D-dimer were associated with mortality in COVID-19 patients. It seems a combination of BUN  $\geq 4.6$  mmol/L and D-dimer  $\geq 0.845$   $\mu\text{g/ml}$  to identify patients at high risk of dying in the hospital, so there may be a risk assessment tool for patients COVID-19 is severe (22). The results showed that in the non-survival group, varying degrees of damage to the liver, kidneys, blood coagulation, and cardiac function there. PLT, AST, BUN, CR, D-Dimer, PT, FIB, F VIII: C, CK-MB, CK, and LDH were valuable in assessing the prognosis of the disease. The results showed that the performance indicators limb function has the prognostic value of the infections are COVID-19 (23). The incidence of AKI in COVID-19 patients was 10%, which is mainly indicated by increased levels of CR and BUN, which in patients with serious infections was significantly higher than patients without severe, and these factors were significantly associated with mortality in patients COVID-19 had (6).

In this study, the mean BUN was observed in the age range of 55-64 years and above 65 years above normal, with the highest mean observed above 65 years, which was significant in patients with COVID-19. Mean sodium ions were also observed to be higher than normal. But the average creatinine potassium was normal in patients with COVID-19.

The 2019-nCoV infection has started in cluster form, is likely to affect older men with other diseases, and can lead to severe and even fatal respiratory illnesses such as acute respiratory distress syndrome (24). Elderly patients with COVID-19 have a higher mortality rate. Data analysis showed that older patients with comorbidities require more medical care (16).

In the present study, an increase in the level of markers (SGOT, SGPT, and direct bilirubin, LDH, D-dimer) in patients with COVID-19 was observed in men more than women and in the elderly more than other ages. The results of the present study showed an

increase in the level of some of the most important diagnostic markers of hepatic, renal, and cardiac in patients with COVID 19. This increase was greater in some markers, including SGOT, SGPT, direct bilirubin, LDH, D-dimer, in men than in women, and more in older patients. To reach a definitive conclusion, further studies with large sample sizes are needed to confirm the association between the level of diagnostic markers and COVID-19 disease in the future.

### Acknowledgments

This work was a funded research project (99U-766). Ethical Approval was with (IR.ABADANUMS.REC.1399-002) as a reference number. The authors thank the help the financial support of this study of Abadan University of Medical Sciences and the Clinical Research Development Unit of Taleghani Educational Hospital, Abadan University of Medical Sciences, for providing disease data.

### References

1. World Health Organization. Clinical management of COVID-19: interim guidance, 27 May 2020. Geneva: World Health Organization; 2020. (Accessed at WHO/2019-nCoV/clinical/2020.5.)
2. World Health Organization. Transmission of SARS-CoV-2: implications for infection prevention precautions: Scientific brief, 09 July 2020. Geneva: World Health Organization; 2020. (Accessed at WHO/2019-nCoV/Sci\_Brief/Transmission\_modes/2020.3.)
3. Singhal T. A Review of Coronavirus Disease-2019 (COVID-19). *Indian J Pediatr* 2020;87:281-6.
4. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395:497-506.
5. Flythe JE, Assimon MM, Tugman MJ, Chang EH, Gupta S, Shah J, et al. Characteristics and Outcomes of Individuals With Pre-existing Kidney Disease and COVID-19 Admitted to Intensive Care Units in the United States. *Am J Kidney Dis* 2021;77:190-203.e1.
6. Shao M, Li X, Liu F, Tian T, Luo J, Yang Y. Acute kidney injury is associated with severe infection and fatality in patients with COVID-19: A systematic review and meta-analysis of 40 studies and 24,527 patients. *Pharmacol Res* 2020;161:105107.
7. Sharma A, Jaiswal P, Kerakhan Y, Saravanan L, Murtaza Z, Zergham A, et al. Liver disease and outcomes among COVID-19 hospitalized patients - A systematic review and meta-analysis. *Ann Hepatol* 2021;21:100273.
8. Levett JY, Raparelli V, Mardigyan V, Eisenberg MJ. Cardiovascular Pathophysiology, Epidemiology, and Treatment Considerations of Coronavirus Disease 2019 (COVID-19): A Review. *CJC Open* 2020;3:28-40.
9. Shoar S, Hosseini F, Naderan M, Mehta JL. Meta-analysis of Cardiovascular Events and Related Biomarkers Comparing Survivors Versus Non-survivors in Patients With COVID-19. *Am J Cardiol.* 2020;135:50-61.
10. Pourbagheri-Sigaroodi A, Bashash D, Fateh F, Abolghasemi H. Laboratory findings in COVID-19 diagnosis and prognosis. *Clin Chim Acta* 2020;510:475-82.
11. Medetalibeyoglu A, Catma Y, Senkal N, Ormeci A, Cavus B, Kose M, et al. The effect of liver test abnormalities on the prognosis of COVID-19. *Ann Hepatol* 2020;19:614-21.
12. Ye L, Chen B, Wang Y, Yang Y, Zeng J, Deng G, et al. Prognostic value of liver biochemical parameters for COVID-19 mortality. *Ann Hepatol* 2021;21:100279.
13. Wang Y, Shi L, Wang Y, Yang H. An updated meta-analysis of AST and ALT levels and the mortality of COVID-19 patients. *Am J Emerg Med* 2021;40:208-9.
14. Bashash D, Abolghasemi H, Salari S, Olfatifar M, Eshghi P, Akbari ME. Elevation of D-Dimer, But Not PT and aPTT, Reflects the Progression of COVID-19 Toward an Unfavorable Outcome: A Meta-Analysis. *Iran J Blood Cancer* 2020;12:47-53.
15. Lippi G, Favaloro EJ. D-dimer is Associated with Severity of Coronavirus Disease 2019: A Pooled Analysis. *Thromb Haemost* 2020;120:876-8.
16. Li P, Chen L, Liu Z, Pan J, Zhou D, Wang H, et al. Clinical Features and Short-term Outcomes of Elderly Patients With COVID-19. *Int J Infect Dis* 2020;97:245-50.
17. Liu Y, Yang Y, Zhang C, Huang F, Wang F, Yuan J, et al. Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury. *Sci China Life Sci* 2020;63:364-74.
18. Yuan J, Zou R, Zeng L, Kou S, Lan J, Li X, et al. The correlation between viral clearance and biochemical outcomes of 94 COVID-19 infected discharged patients. *Inflamm Res* 2020;69:599-606.
19. Henry BM, Aggarwal G, Wong J, Benoit S, Vikse J, Plebani M, et al. Lactate dehydrogenase levels predict coronavirus disease 2019 (COVID-19) severity and mortality: A pooled analysis. *Am J Emerg Med* 2020;38:1722-6.
20. Yang J, Liao X, Yin W, Wang B, Yue J, Bai L, et al. Elevated cardiac biomarkers may be effective prognostic predictors for patients with COVID-19: A multicenter,

- observational study. *Am J Emerg Med* 2021;39:34-41.
21. Liu YM, Xie J, Chen MM, Zhang X, Cheng X, Li H, et al. Kidney function indicators predict adverse outcomes of COVID-19. *Med (N Y)* 2021;2:38-48.e2.
  22. Cheng A, Hu L, Wang Y, Huang L, Zhao L, Zhang C, et al. Diagnostic performance of initial blood urea nitrogen combined with D-dimer levels for predicting in-hospital mortality in COVID-19 patients. *Int J Antimicrob Agents* 2020;56:106110.
  23. Zhu Y, Du Z, Zhu Y, Li W, Miao H, Li Z. Evaluation of organ function in patients with severe COVID-19 infections. *Med Clin (Barc)* 2020;155:191-6.
  24. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020;395:507-13.