The Use of Biochemical Markers of Cardiac and Liver Function for Monitoring of Patients with Severe Covid -19[1]

***Enaam Ahmed Hamza AL-Dagestani, **Mohammad Ahmad Hamza, *Mahmoud A. M. Fakhri**

** Department of Medical Physics, College of Science, University of Mosul, Iraq*

***Department of Chemistry, Faculty of Science, University of Zakho*

Date of Receiving: 21 September 2022, Date of Acceptance: 23 October 2022, Date of Publication: 06 November 2022

ABSTRACT

Coronavirus (COVID-19) is the name given by the World Health Organization to the virus that causes acute pneumonia, a worldwide pandemic caused by SARS-CoV-2 infection, ending with serious complications for patients and creating a global health emergency, the virus is transmitted by droplets from the infected patient during talking, sneezing, coughing, and breathe so crowded areas should be avoided. Most COVID-19 patients have slight to mild signs and get better without treatment. However, a few turns severely unwell and require scientific attention. The clinical condition of patients varies from simple asymptomatic to complicated cases suffering from severe pneumonia which may lead to death. This study aimed to evaluate the biochemical markers of heart and liver function in COVID-19 patients having severe symptoms. Therefore, the clinical laboratory can contribute to the creation of biomarkers to classify the risk of patients developing more severe and dangerous conditions, thus accelerating the clinical decision-making process.

Keywords: *COVID-19, severe condition, biochemical markers, coronavirus.*

INTRODUCTION

COVID-19 was first reported in Wuhan city / China in 2019[1]. It is an emerging infectious disease [2]. The pandemic takes variable forms in how it affects communities in different countries[3,4]. These pathogens consist of single positive RNA chains, that infect mammals and animals[5]. Human coronaviruses are divided based on their ability to cause disease, the most important and pathogenic types include SARS-CoV, MERS-CoV, and SARS-CoV2[6].

Severe COVID-19 virus infection was a companion with overall changes in clinical biochemistry variables, such as elevated markers of tissue damage, C reactive protein (CRP), lactate dehydrogenase(LDH), creatine kinase enzyme (KN), myoglobin, and inflammatory marker, ferritin, liver and kidney dysfunction[7,8].

The biochemical parameter may be predictive analytics in COVID-19 disease. Parameters associated with a high incidence of mortality include an increase in LDH, CRP, Aspartate Aminotransferase (AST), Creatinine, low albumin and Troponin I[9-11]. The

[1] *How to cite the article:* Al-Dagestani E. A. H., Hamza M. A., Fakhri M. A. M., The Use of Biochemical Markers of Cardiac and Liver Function for Monitoring of Patients with Severe Covid -19, *IJPPS*, Oct-Dec 2022, Vol 6, Issue 4, 36-41

evaluation of clinical situational awareness depends on these biochemical parameters to discriminate between those at high or low risk of mortality and severe cases[12].

Clinical laboratories have an important role in the disclosure of the virus and follow-up of patients[13]. Coronavirus is diagnosed by using laboratory tests in patients with clinical symptoms and epidemiological history with the result of x-ray examinations[14,15].

COVID-19 clinical conditions cases varied Symptoms from symptomatic to mild, moderate and severe, with the presence of pneumonia, or not[16]. The most common symptoms were cough and high temperature[17].

In most articles published about COVID-19, The main organ affected by the disease was the lung, while other reports have mentioned that other organs can also be affected including the cardiac and liver which can interfere with the metabolism and excretion of the medicine that uses for treatment.

METHODS

The search was done, to review the studies that report the abnormalities of laboratory markers in patients with severe COVID-19. Table 1 shows the biochemical markers that are related to cardiac and liver function and may potentially aid in identifying and predicting severe COVID-19.

DISCUSSION

Many studies had been shown that biochemical markers changed in Corona virus-infected patients, and this had been associated with the prognosis of the disease, the alteration in laboratory parameters related to a clinical condition, could allow the categorization of patients with severe stages to improve their clinical care. However, these methods must be reassessed based on new evidence published worldwide, associated with introducing new technologies into the laboratory tests to further refine the search for biochemical markers[25]

Severe Corona virus-infected patients usually had changes in clinical biochemistry variables. Such as elevated LDH, CK, troponin and myoglobin, CRP, increases of bilirubin and aminotransferases and decreases of albumin[7,8].

Table 1: Parameters related to cardiac and liver function in patients diagnosed with severe COVID-19

Parameters	**No. of cases**	**Normal range** **mean**	**Severity of COVID-19 mean**		**P value**	**Reference**
			Total cases	**Serious cases**		
LDH (U/ L)	138	125-243	261	435	S	[18]
	41	≤ 245	286	400	s	[1]
	174	M: 135-225 F: 135-214	267	336	--	[19]
Myoglobin (ng/mL)	65	0-106	58.6	63.4	--	[19]
Troponin I (pg/mL)	138	<26.2	6.4	11	s	[18]
	41	<28	3.4	3.3	---	[1]
CK-MB (U/L)	138	<25	14	18	s	[19]
	40	----	38.1	62	--	[20]

C-reactive protein(mg/L)	136	0-5	34.2	46.6	s	[21]
Alanine aminotransferase (U/L)	138	9-50	24	35	s	[18]
	41	---	32	49	s	[22]
	193	M: 0– 41 F: 0–33	20	21		[23]
Aspartate aminotransferase (U/L)	41	≤40	34	44	NS	[1]
	40	----	34.1	51.2	--	[20]
	138	15-40	31	52	s	[1,20]
Albumin(g/L)	49	40-55	41.6	37.2	s	[24]
	193	35-52	34.2	32.6	--	[19]
	41	-----	31.4	27.9	s	[22]
TB (mmol/L)	138	5-21	9.8	11.5	s	[18]
	41	----	11.7	14	s	[1]

LDH; Lactate dehydrogenase, CK; Creatine kinase, TB; Total bilirubin
M: Male , F: Female, S: significant .

CARDIAC MARKERS

There are several mechanisms of cardiac tissue damage, through studies conducted during the epidemic of SARS and COVID-19. One of the most important explanations for this case is the systemic inflammatory response in case of severe COVID-19 infection, which leads to the release of high levels of cytokines that can infect multiple tissues of the human body, such as the cells of the heart muscle and vascular endothelium[26].

SARS-CoV-2 was detected in endothelial cardiac, smooth muscle, and also in cardiomyocytes[27], indicating that the virus can enter host cells by spatial protein binding to ACE2, resulting in myocardial injury and affecting cardiovascular homeostasis. The presence of SARS-CoV-1 was detected in cardiac tissue biopsy in 35% of subjects[28].

There is an increase in biochemical markers of cardiac function, including elevated cardiac troponin levels in severe cases of patients with coronavirus, which increases the likelihood of developing viral myocarditis, and thus heart infection may lead to other multi-organ failures (MOF), caused by liver failure or kidney failure with elevated levels of liver enzymes[7]. The results of analyzes of severe cases of patients showed a significant increase of troponin, myoglobin and creatine kinase-MB, the slight increase in high sensitivity troponin 1 was caused by direct and indirect cardiac damage[29].

AST enzyme appeared in varying concentrations, as its concentration increased by 62% in ICU patients compared to patients outside the ICU [23]. The study explained by *Zhou et* al, that the death in patient's analysis was associated with elevated cardiac troponin I, ALT, and creatine kinase. [30]. In the cases of mild conditions, the elevation of troponin was less frequent in comparison to patients with severe conditions[31], and the risk factors associated with coronary heart disease include age, previous heart disease, vascular injury, and acute pneumonia[32].

Patients with chronic kidney disease CKD who contract coronavirus have an increased risk of death and vascular disease, and risk factor of the complications of cardiovascular disease than those who have no CKD infection[33].

LIVER FUNCTION MARKERS

In seriously ill patients, who suffer from liver dysfunction, the markers of liver function enzymes ALT, AST and total bilirubin were elevated compared with those with mild conditions [34]. In one of the studies, 43 of the patients suffer from liver dysfunction, AST or ALT in those cases elevate above the normal range [35]. Another study by Cai, *et al*. [36], established that 90% of moderate COVID-19 patients had abnormal hepatic enzymes, and the elevated of AST and bilirubin to more than three times was moderate. For patients with abnormal hepatocellular and mixed-type hepatic tests, this severe condition is lead to a serious illness. In particular, In one case, a patient was suffering from a serious defect in the functions of hepatocytes with an increase in liver enzymes, ALT reached more than 7000 U/L and A ST elevated more than 1400U/L[35]. The use of lopinavir and ritonavir medicine has a negative effect on Liver damage [36], and hypoxia-related to pneumonia and cytokine storm can also affect liver function, this situation is a severe infection that can produce hepatic insufficiency [34]. Complications in some patients, such as multiple organ failure and respiratory distress syndrome, result in hypoxia and shock, and can also cause hypoxia, reperfusion, and hepatic ischemia[37].

Coronavirus reaches various organs and tissues of the body through the presence on the surfaces of cell membranes by using a receptor for special proteins expressed by the virus[38]. Analytical patterns are useful for categorising COVID-19 patients[39], The differences in normal laboratory parameters, could help to determine the appropriate treatment to eliminate infectious agents[40]. It has been declared by the investigation that the laboratory evaluation of COVID-19 patients showed a different level of liver enzymes, the main and direct cause of liver damage in patients is coronavirus infection[41]. The liver can be damaged in patients with coronavirus, which may lead to difficult reach the therapeutic dose of medicine and elevate the risk of the adverse effect of drug reactions. Careful monitoring of liver functions in patients with the coronavirus can lead to early diagnosis of liver disorders or damage and helps in achieving optimal therapeutic concentrations and reducing the risks of harmful drugs[42].

The current study showed the difference between laboratory biochemical parameters in patients with COVID-19, and this is useful for evaluating disease progression and classifying patients with a severe clinical condition.

CONCLUSION

COVID-19 a pandemic major health problem that affects the general population and results in many complications. The variation in clinical biochemical variables that appeared in patients has an impact and importance in diagnosing patients with COVID-19 through the assessment of patient's metabolic disorders and the development of support tools to make the appropriate clinical decision and modify the treatment given to the patient.

Financial Support and Sponsorship: Nil

Conflict of interest: None

REFERENCES

[1] 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(10223):497–506.

[2] El Zowalaty ME, Järhult JD. From SARS to COVID-19: A previously unknown SARS-related coronavirus (SARS-CoV-2) of pandemic potential infecting humans--Call for a One Health approach. One Heal. 2020;9:100124.

[3] Van Damme W, Dahake R, Delamou A, Ingelbeen B, Wouters E, Vanham G, et al. The COVID-19 pandemic: diverse contexts; different epidemics—how and why? BMJ Glob Heal. 2020;5(7):e003098.

[4] COVID WHO. coding in ICD-10 2020 [https://www. who. int/classifications/icd. COVID-19-coding-icd10 pdf. 19AD.

[5] Darweesh O, Abdulrazzaq GM, Al-Zidan RN, Bebane P, Merkhan M, Aldabbagh R, AlOmari N. Evaluation of the Pharmacologic Treatment of COVID-19 Pandemic in Iraq. Current Pharmacology Reports. 2021 Sep;7(4):171-8.

[6] Magadum A, Kishore R. cells Cardiovascular Manifestations of COVID-19 Infection. Available from: www.mdpi.com/journal/cells

[7] Henry BM, De Oliveira MHS, Benoit S, Plebani M, Lippi G. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis. Clin Chem Lab Med. 2020;58(7):1021–8.

[8] Bloom PP, Meyerowitz EA, Reinus Z, Daidone M, Gustafson J, Kim AY, et al. Liver Biochemistries in Hospitalized Patients With COVID-19. Hepatology. 2021;73(3):890–900.

[9] Galloway JB, Norton S, Barker RD, Brookes A, Carey I, Clarke BD, et al. A clinical risk score to identify patients with COVID-19 at high risk of critical care admission or death: An observational cohort study. J Infect. 2020;81(2):282–8.

[10] Lei F, Liu Y-M, Zhou F, Qin J-J, Zhang P, Zhu L, et al. Longitudinal Association Between Markers of Liver Injury and Mortality in COVID-19 in China. Hepatology. 2020;72(2).

[11] Du R-H, Liang L-R, Yang C-QC, Wang W, Cao T-Z, Li M, et al. Predictors of mortality for patients with COVID-19 pneumonia caused by SARS-CoV-2: a prospective cohort study. Hepatology [Internet]. 2020;72(2). Available from: https://doi.org/10.1183/13993003.00524-2020

[12] Kubina R, Dziedzic A. Molecular and serological tests for COVID-19. A comparative review of SARS-CoV-2 coronavirus laboratory and point-of-care diagnostics. Diagnostics. 2020;10(6):434.

[13] Lippi G, Plebani M. Laboratory abnormalities in patients with COVID-2019 infection. Clin Chem Lab Med. 2020;58(7):1131–4.

[14] Ahn D-G, Shin H-J, Kim M-H, Lee S, Kim H-S, Myoung J, et al. Current status of epidemiology, diagnosis, therapeutics, and vaccines for novel coronavirus disease 2019 (COVID-19). 2020.

[15] Chan JF-W, Yip CC-Y, To KK-W, Tang TH-C, Wong SC-Y, Leung K-H, et al. Improved molecular diagnosis of COVID-19 by the novel, highly sensitive and specific COVID-19-RdRp/Hel real-time reverse transcription-PCR assay validated in vitro and with clinical specimens. J Clin Microbiol. 2020;58(5):e00310--20.

[16] Dong X, Cao Y, Lu X, Zhang J, Du H, Yan Y, et al. Eleven faces of coronavirus disease 2019. Allergy. 2020;75(7):1699–709.

[17] Jin X, Lian J-S, Hu J-H, Gao J, Zheng L, Zhang Y-M, et al. Epidemiological, clinical and virological characteristics of 74 cases of coronavirus-infected disease 2019 (COVID-19) with gastrointestinal symptoms. Gut. 2020;69(6):1002–9.

[18] Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus--infected pneumonia in Wuhan, China. Jama. 2020;323(11):1061–9.

[19] Li Z, Wu M, Yao J, Guo J, Liao X, Song S, et al. Caution on kidney dysfunctions of COVID-19 patients. MedRxiv. 2020.

[20] Liu J, Li S, Liu J, Liang B, Wang X, Wang H, et al. Longitudinal characteristics of lymphocyte responses and cytokine profiles in the peripheral blood of SARS-CoV-2 infected patients. EBioMedicine. 2020;55:102763.

[21] Zhang J-J, Dong | Xiang, Cao | Yi-Yuan, Yuan Y-D, Yang Y-B, Yan Y-Q, et al. O R I G I N A L A R T I C L E Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. 2020.

[22] Gong J, Dong H, Xia Q-S, Huang Z, Wang D, Zhao Y, et al. Correlation analysis between disease severity and inflammation-related parameters in patients with COVID-19: a retrospective study. BMC Infect Dis. 2020;20(1):1–7.

[23] Liu W, Tao Z-W, Wang L, Yuan M-L, Liu K, Zhou L, et al. Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease. Chin Med J (Engl). 2020;133(09):1032–8.

[24] Wang Q, Zhao H, Liu L-G, Wang Y-B, Zhang T, Li M-H, et al. Pattern of liver injury in adult patients with COVID-19: a retrospective analysis of 105 patients. Mil Med Res. 2020;7(1):1–8.

[25] Letelier P, Encina N, Morales P, Riffo A, Silva H, Riquelme I, et al. ROLE OF BIOCHEMICAL MARKERS IN THE MONITORING OF COVID-19 PATIENTS ZNA^AJ

BIOHEMIJSKIH MARKERA ZA PRA]ENJE COVID-19 PACIJENATA. J Med Biochem. 2021;40(2):115–28.

[26] Zheng Y-Y, Ma Y-T, Zhang J-Y, Xie X. COVID-19 and the cardiovascular system. Nat Rev Cardiol [Internet]. Available from: https://doi.org/10.1001/jama.2020.1585

[27] Perico L, Benigni A, Remuzzi G. Should COVID-19 concern nephrologists? Why and to what extent? The emerging impasse of angiotensin blockade. Nephron. 2020;144(5):213–21.

[28] Oudit GY, Kassiri Z, Jiang C, Liu PP, Poutanen SM, Penninger JM, et al. SARS-coronavirus modulation of myocardial ACE2 expression and inflammation in patients with SARS. Eur J Clin Invest. 2009;39(7):618–25.

[29] Salbach C, Giannitsis E. Kardiale Biomarker und COVID-19-Phänotypen und Interpretation. DMW-Deutsche Medizinische Wochenschrift. 2020;145(11):755–60.

[30] Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395(10229):1054–62.

[31] Li J-W, Han T-W, Woodward M, Anderson CS, Zhou H, Chen Y-D, et al. The impact of 2019 novel coronavirus on heart injury: a systematic review and meta-analysis. Prog Cardiovasc Dis. 2020;63(4):518–24.

[32] 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(3):364–74.

[33] Lambourg EJ, Gallacher PJ, Hunter RW, Siddiqui M, Miller-Hodges E, Chalmers J, et al. Early View Cardiovascular outcomes in patients with chronic kidney disease and COVID-19: a multi-regional data-linkage study Cardiovascular outcomes in patients with chronic kidney disease and COVID-19: a multi-regional data-linkage study. Available from: https://doi.org/10.1183/13993003.03168-2021

[34] Velavan TP, Meyer CG. Mild versus severe COVID-19: laboratory markers. Int J Infect Dis. 2020;95:304–7.

[35] 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(10223):507–13.

[36] Cai Q, Huang D, Yu H, Zhu Z, Xia Z, Su Y, et al. COVID-19: Abnormal liver function tests. J Hepatol. 2020;73(3):566–74.

[37] Feng G, Zheng KI, Yan Q-Q, Rios RS, Targher G, Byrne CD, et al. COVID-19 and liver dysfunction: current insights and emergent therapeutic strategies. J Clin Transl Hepatol. 2020;8(1):18.

[38] Hamming I, Timens W, Bulthuis MLC, Lely AT, Navis GJ van, van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. J Pathol A J Pathol Soc Gt Britain Irel. 2004;203(2):631–7.

[39] Stanković B, Kotur N, Gašić V, Klaassen K, Ristivojević B, Stojiljković M, et al. Pharmacogenomics landscape of COVID-19 therapy response in Serbian population and comparison with worldwide populations. J Med Biochem. 2020;39(4):488.

[40] Messner CB, Demichev V, Wendisch D, Michalick L, White M, Freiwald A, et al. Ultra-high-throughput clinical proteomics reveals classifiers of COVID-19 infection. Cell Syst. 2020;11(1):11–24.

[41] Zhang Y, Zheng | Liang, Liu | Lan, Zhao M, Xiao J, Zhao Q. Liver impairment in COVID-19 patients: A retrospective analysis of 115 cases from a single centre in Wuhan city, China. 2020.

[42] Rismanbaf A, Zarei S. Liver and Kidney Injuries in COVID-19 and Their Effects on Drug Therapy; a Letter to Editor [Internet]. Vol. 8, Arch Acad Emerg Med. 2020. p. 17. Available from: http://journals.sbmu.ac.ir/aaem.