



Evaluation of Heart and Liver Enzymes with Oxidative Stress in Covid-19 Patients

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Abstract

Coronavirus disease (COVID-19) is an infectious disease caused by the SARS-CoV-2 virus. Respiratory symptoms ranging from mild to moderate appear on most of those infected with the virus and recover without the need for special therapeutic intervention. However, some of those who become infected develop severe symptoms and require medical attention. People who are most likely to develop severe symptoms of the disease are those with underlying diseases, such as cardiovascular disease. The study was conducted in the public laboratories on the outskirts of Baghdad after collecting 100 samples, (60) of people infected with Covid - 19 and (40) of healthy people and the ages of the people ranged from 18-80 years and the ages of the healthy ones from 18-70 years old. The study was conducted to investigate some biochemical indicators which includes creatine kinase, lactate dehydrogenase, glutathione and malonaldehyde, liver functions (AST, ALT and ALP). The results showed a significant increase in creatine kinase, lactate dehydrogenase, AST, ALT, ALP, and a significant increase in Malonaldehyde in all covid-19 patients and a decrease in glutathione in covid-19 patients

Keywords: covid-19, Creatine kinase, lactate dehydrogenase, malondialdehyde, glutathione, AST, ALT, and ALP.

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The infection is transmitted from one person to another through respiratory droplets resulting from coughing or sneezing, and the time period between exposure to the virus and the appearance of symptoms ranges from two to fourteen days, with an average of five days. chain reaction) on a pharyngeal swab, and the diagnosis can also be made through a CT scan that shows the factors of pneumonia (2) The liver is an important vital organ in the human body, and it is not homogeneous in structural and functional terms. It is the second organ after the brain in terms of complexity (3). The liver is the only organ that has two sources of blood flow and there are 12 different types of cells, as it has a major role in making hydrophobic molecules dissolve in water, defending against foreign particles, and regulating blood volume (4). The liver plays an important role in the

Introduction

Coronavirus disease 2019 (abbreviated for Covid-19), also known as SARS-CoV-2, is a zoonotic respiratory disease caused by SARS-CoV-2 associated with severe acute respiratory distress syndrome (SARS-COV-2). The virus was first discovered in the Chinese city of Wuhan in 2019 and has since spread all over the world, causing the global pandemic of the Corona virus (1). Common symptoms include fever, cough, shortness of breath, muscle aches, spots, and sore throats, while most infections follow a benign course with few symptoms, some progressing to more serious forms such as acute pneumonia and multiple organ dysfunction Deaths and the number of diagnosed injuries 3.4%, but they differ according to age and the presence of other diseases (1).



The ages of the infected people ranged from 18-80 years old, and healthy subjects ranged in age from 18-70 years, 3-5 ml of blood were collected from healthy and patients people by drawing blood from a vein in the arm or elbow using a medical syringe,

Measuring the lactate dehydrogenase activity

Lactate dehydrogenase activity was measured using a colorimetric method and absorption measurements at specific wavelengths for each assay according to the instructions supplied with the kit (Bio System, Spain).

Estimation the creatine kinase

Creatine kinase activity was measured using a colorimetric method and absorption measurements at specific wavelengths for each assay according to the instructions supplied with the kit (Bio System, Spain).

Estimation the liver function

Liver enzyme activity (AST, ALT, ALP) was measured based on a colorimetric method and absorbance measurements at specific wavelengths of each assay according to the instructions supplied with the kit (agappe, India).

statistical analysis

The statistical program SPSS Statistical Package for the Social Sciences version 20 was used to analyze the results obtained, and the arithmetic mean and standard deviation $SD \pm$ for all measurements were used, and the T-test was used to compare the biochemical variables between the two groups of patients and healthy people at the probability level of $P < 0.05$

Results and Discussion

The results shown in Table (1) displayed the activity of cardiac enzymes represented by lactate dehydrogenase and creatine kinase.

metabolism, regulation of red blood cells, glucose synthesis and storage (5), as well as a role in the manufacture of plasma proteins present in the body, such as albumin, as well as important proteins (4), in the metabolism of carbohydrates and fats, and in the removal of toxins from harmful substances. It also has an important role in controlling the metabolic pathways in the body (6), and also in the production of various enzymes, the production and secretion of bile, and in the storage of proteins, glycogen, vitamins and minerals (7). It contributes to the process of manufacturing and secreting some hormones, such as growth hormone and activating vitamin D, and I called it the main gateway to the body, because it has the ability to remove some of the various toxins that are harmful to the body, such as ammonia, drugs and bilirubin (8). Oxidation plays an important role in complications, but there is a possibility to reduce these complications through treatment with antioxidants, as studies have proven that reactive oxygen species (ROS) and free radicals are the main causes of neuronal death in patients infected with the Corona virus (9). It is a highly reactive molecule due to the presence of one or more electrons in its outer shell, which enables it to react quickly with any free radical or other molecule (10). Free radicals consist of two sources, the first is internal as a result of stress, psychological and physical exhaustion, various pathological conditions and aging (11), and the second source is external, such as exposure to ultraviolet rays, X-rays and the use of medical drugs (12, 13).

Sample and Blood Collection

The study included 100 samples, (60) from people infected with COVID-19 and (40) from healthy people (control group) from public laboratories on the outskirts of Baghdad city for the period from 25/8/2021 to 10/1/2021.



Parameters	Control	Patients
	Mean ± SD	
LDH (U/L)	258.88±56.521	386.12±140.348 *
CK (U/L)	28.43±7.107	36.03±9.134 *

* This sing means different significant at P≤0.05.

The activity of aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase activity were measured for patients infected with the emerging coronavirus (Covid-19) compared to healthy controls, as shown in Table (2).

Parameters	Control	Patients
	Mean ± SD	
AST(U/L)	20.18 ±6.417	28.37±8.696 *
ALT (U/L)	22.73 ±6.528	30.33 ±8.572 *
ALP (U/L)	153.98 ±38.280	214.20±70.293 *

* This sing means different significant at P≤0.05.

Also, the study included measuring the concentration of Glutathione and Malonealdehyde, the results of which are shown in Table (3).

Parameters	Control	Patients
	Mean ± SD	
GSH(μmol/l)	15.60±2.70	6.50±1.90 *
MDA(μmol/l)	1.49±0.80	2.87±0.84 *

* This sing means different significant at P≤0.05.

Table (1) shows that the mean ± standard deviation of LDH was 386.12 ± 140.348 compared to 258.88±56.521 in the healthy group, as shown in Figure (1)

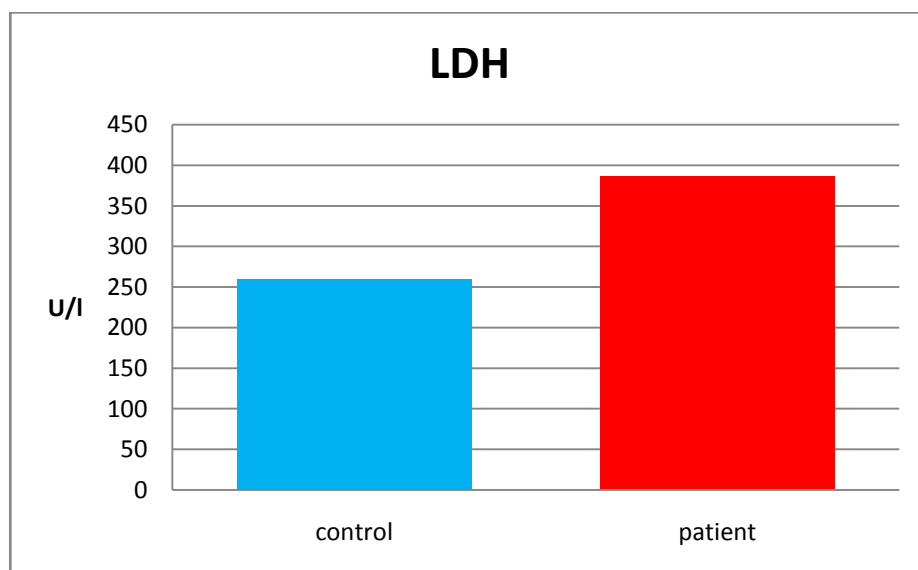


Figure (1) The effectiveness of LDH in the two groups

viral infection or lung damage (16), such as pneumonia caused by SARS-CoV-2., among Yan et al (17). It was done that the level of lactate dehydrogenase in the blood, and can be considered a significant indicator with the mortality rate of Covid-19 patients.

Therefore, serum LDH may represent a rapidly and effectively widely measured biomarker that may predict which patients are most at risk, allowing them to be prioritized and potentially reducing mortality. The results in Table (1) showed that the mean \pm standard deviation of creatine kinase enzyme was 36.03 ± 9.134 in patients, compared to 28.43 ± 7.107 in the healthy group, as shown in Figure (2).

The current study is in agreement with the study by Zhu et al at MedicinaClínica (14), which evaluated organ function in 102 patients with severe COVID-19, which drew attention to a specific test likely to be used as disease prognostic factors: lactate dehydrogenase. (LDH), this enzyme is involved in energy production and is present in nearly all cells of the body (15).

Tests that measure the effectiveness of LDH in the blood are used to monitor tissue damage associated with a wide range of disorders, including liver disease and lung disease. Increased LDH reflects tissue destruction. Cells are a common marker of tissue damage, indicating the presence of

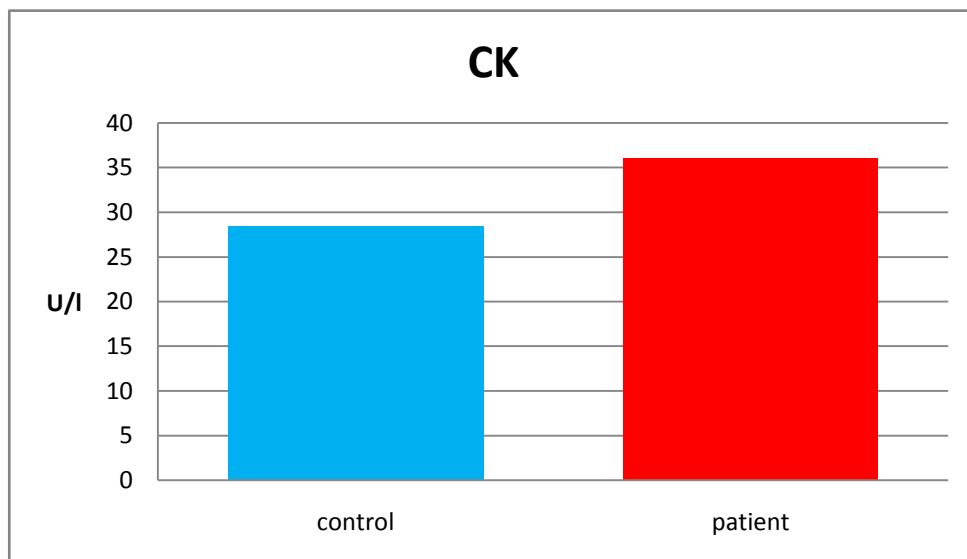


Figure (2) The CK level of the two groups

Xinghuan et al. (18) note, higher CK levels were significantly associated with higher overall mortality risk among COVID-19 patients. The overall risk of death in COVID-19 patients with elevated CK levels was more than 7 times that of patients with normal CK levels. Furthermore, CK level was also an important predictive factor for COVID-19 severity. The study of Li and his group (19) also showed that more than 70% of patients showed symptoms of fever or fatigue and respiratory symptoms, these symptoms were characteristic of the virus and may be related to the ACE2 receptor of the angiotensin-converting enzyme 2 (20) ACE2 reported that ACE2 has been identified as a receptor responsible for SARS-CoV-2-induced acute lung injury and that ACE2-regulated expression is protective against infection.

The results showed that the mean \pm standard deviation of AST enzyme activity was 28.37 ± 8.696 for patients infected with COVID-19 compared with 20.18 ± 6.417 for healthy people, while the mean \pm standard deviation of ALT was 30.33 ± 8.572 for the infected group compared with 22.73 ± 6.528 for healthy subjects, while the mean \pm standard deviation of ALP was 214.20 ± 70.293 for the affected group compared with 153.98 ± 38.280 for the healthy group, as shown in Figure (3)

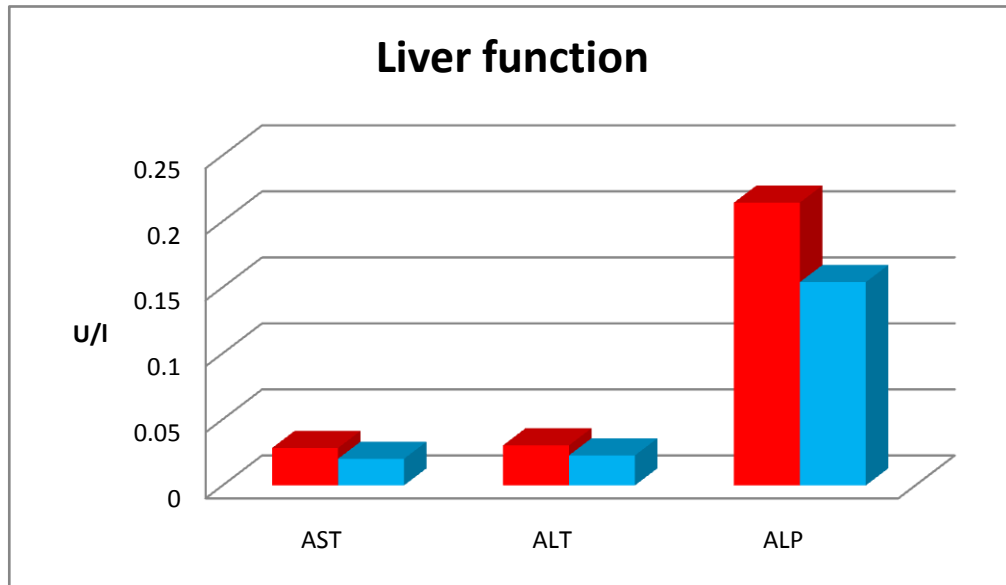


Figure (3) The activity of liver enzymes in the two groups

severity. In addition, the control group in their study had pneumonia, which may affect the level of the two enzymes in the blood, and thus cannot be considered as a useful way to differentiate between people with Covid-19 and pneumonia patients who do not have infection with Covid-19 virus. As for Hachimet al (24) They found that the effectiveness of the enzyme ALT and AST was higher in patients who needed to stay in the intensive care ward, compared to those who did not need to.

As for Jinendra et al, it was shown in their study, which included increasing the activity of the ALP enzyme in patients with Covid-19 (25). Increased ALP activity was a prominent feature in two patients with COVID-19. A component of the fatty liver as background, as suggested by imaging studies in the first case, may have contributed to the increased ALP activity but not in the second case.

This increase in the effectiveness of AST and ALT indicates the presence of the effect of the virus COVID-19 on liver function. The results of this study are in agreement with previous studies conducted in other geographical areas (21,22).

The study of Chen et al (23), which included 78 patients with Covid-19 and 26 non-infected people, found that the average percentage of patients who had an increase in the activity of the two enzymes compared to healthy subjects, but without a significant difference. On the contrary, the percentage of patients who had an increase in AST enzyme was a significant difference between patients with high severity compared to patients with mild severity and with a high significant difference. But the ALT enzyme did not show a significant difference in the increase between the two groups, and they mentioned that their results were in this way because the majority of their patients were of slight

Kerksick notes that natural intracellular glutathione is essential for maintaining immunity (lymphocytes and macrophages), optimal lymphocyte function and proliferation (29), as well as in preventing apoptosis. Glutathione deficiency also reduces the formation of anti-inflammatory cytokines (30).

As for oxidative stress, it has a critical function in inflammatory processes. Reactive oxygen species (ROS) and H₂O₂ can activate NF- κ B to stimulate inflammatory cytokine production (31). Cecchini et al (32) studies the relationship between oxidative stress and the pathogenesis of Covid-19. This study provides evidence that Covid-19 patients showed a higher serum level of oxidative stress and inflammatory markers and a lower serum level of antioxidants, compared to the control group, especially in patients admitted to the intensive care unit (33). It indicated an elevated serum level of MDA in the case groups.

MDA is an important indicator of oxidative stress. There is a significant association between markers of oxidative stress and respiratory viral infection especially RNA viruses (34).

Kim and his group point out on in vitro and in vivo studies that some viruses can alter the redox balance in the cell. The onset of oxidative stress by viral infection (eg respiratory syncytial virus) is necessary for activation of innate immunity via the production of cytokines (35). Besides, oxidative stress induced by several viruses is involved in facilitating intracellular virus replication (36).

Conclusions

From the results of the current study, we can conclude. High content of creatine kinase and lactate dehydrogenase for people infected with the emerging coronavirus compared to the control group, indicating that heart cells

Despite the hepatobiliary infection caused by the virus (26).

Liver biopsy samples of patients with COVID-19 showed mild microvascular steatosis. Guan and his group found that expression of ACE2 receptors is very low in hepatocytes and is expressed only in hepatic cholangiocytes, (27) suggesting that cholangiocytes may be a direct target of severe acute respiratory syndrome (SARS)-coronavirus. 2 (CoV-2) invasion of the liver. However, in our study, ALP, an indicator of cholangiocyte injury, remained primarily within the normal range during hospitalization.

Table (3) showed that the mean \pm standard deviation of GSH was 6.50 ± 1.90 in the group of patients with COVID-19 compared with 15.60 ± 2.70 in the healthy people as a control group. And the mean \pm standard deviation MDA was 2.87 ± 0.84 in the group of patients with COVID-19 compared to 1.49 ± 0.80 in the healthy people.

The human body is naturally equipped with enzymatic and non-enzymatic antioxidant systems to prevent damage to cells and vital organs due to free radicals. Glutathione peroxidase, catalase are enzymatic antioxidants Non-enzymatic antioxidants are vitamin E, vitamin C and natural thiol (glutathione) antioxidants (28). In vivo, ROS are mostly purified by glutathione and glutathione peroxidase which is a down-regulating enzyme. When ROS production is uncontrolled, there is depletion of glutathione and as a result the patient becomes susceptible to immune suppression, organ damage, increased vascular permeability, trauma, and thrombotic events.

N-acetyl-cysteine is a byproduct of glutathione and increases glutathione levels in tissues by providing the amino acid cysteine.



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may be damaged by the virus. Also, an increase in the activity levels of liver enzymes such as AST, ALT and ALP in COVID-19 patients compared to the control group. This is evidence of the effect of viral infection on hepatocytes, an increase in oxidative stress and a decrease in antioxidants

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