RESEARCH ARTICLE

Evaluation of the Vitamin D Level and Cardiac Parameters in the Blood Serum of Patients with COVID-19

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ABSTRACT

The study was carried out to evaluate the vitamin D, Troponin (Tn) and Cardiac Parameters (LDH, CK) for patients with COVID-19. 90 serum samples were conducted in the study with ages ranging between (35–70) years, 55 samples for patients infected with COVID-19 collected from Tikrit General Teaching Hospital in Salah Alden, and 35 samples for healthy individuals a control group. The study includes the determination of serum plasma D-dimer and serum C-reactive protein (CRP), vitamin D, troponin, lactate dehydrogenase-LDH and creatine kinase-CK.

The results of this study showed a significant increase in the level of D-dimer in the blood plasma who infected with COVID-19 compared to the healthy group, and the results also showed that a significant increase in the level of CRP and Troponin, LDH, and CK in the blood serum of people infected with the emerging coronavirus compared to healthy people. As well as a result also showed that a significant decrease in the level of vitamin D in the blood sera of people infected with the emerging coronavirus compared to healthy people.

Keywords: Cardiac Parameters, COVID-19, Vitamin D.

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INTRODUCTION

The emerging coronavirus is considered an infectious disease, which was recently classified as a pandemic at present. The spread of the virus infection is through direct contact with the infected person or by touching surfaces that carry the virus because of an infected person spitting or sneezing.[1] the virus belongs to the so-called coronavirus, which were called by this name for taking shape similar to a crown (crown) or with pointed ends. Corona is a Latin word meaning "crown" in English, as the name refers to the distinctive appearance of the virus of virions that bear large superficial protrusions (fluff) in the form of a crown or a solar halo formed by viral spike capsomeres (S-type proteins) to fill the virus's surface and cause cell infection.[2]

The COVID-19 virus spread rapidly to most countries in the world as of June 28, 2020, as many cases of infection were reported and the death rate, as it was found that patients suffering from heart disease, diabetes, and blood pressure are more likely to die than others.[3,4]

Symptoms this include fatigue, Aches, Headache, runny nose, sore throat, vomiting, diarrhea, fever, coughing, shortness of breath or difficulty breathing.[5-7]

There are many diagnostic methods for COVID-19 virus, like by reverse transcription-polymerase chain reaction (RT-PCR), as main method or tool, by taking a swab from mouth or the nose. Infection can be diagnosed through a set of symptoms and risk factors as well as a computed tomography (CT) scan for pneumonia.[8] It was also found that several immunological analyses are used as a diagnostic function of virus infection, including CRP and high levels of D-dimer.[9,10] It was found that increased D-dimer levels may contribute to the mortality rate associated with immune dysfunction and lead to many diseases. The immune system is mainly sensitive to the rise in D-dimer, which is considered a predictive biological indicator of infection with the Coronavirus.[11-13] It is one of the tests as it can help rule out the presence of a dangerous blood clot, so monitoring its elevation will be an important approach to the clinical diagnosis of COVID-19 infection.[14] Also, some studies confirmed a significant association between CRP concentrations and exacerbation of COVID-19 patients.[15,16] CRP is a non-specific acute-phase inflammatory protein that is increasingly flanked to complete the withdrawal form and the occurrence of infections.[17,18] It is one of the proteins produced by the liver. Its normal concentration in the blood is less than (10 mg/liter), as the peak of this ratio is rapid within hours and gives the highest peak in 48 hours from the onset of the disease.[19]

Some biomarkers were used to predict severe disease in patients with COVID-19, such as ferritin, lactate dehydrogenase,

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interleukin 6.[20-22] In addition, there are many biochemical signs that COVID-19 can be diagnosed, including elevated levels of LDH-lactate dehydrogenase and ferritin levels.[23-25] It was found that the COVID-19 virus may be associated with high levels of troponin,[26-28] as the irregular heartbeat may be accompanied by changes in the level of troponin, which leads to heart damage and thus exposure to the virus.[25,29] Troponin (Tn) is a group of contractile regulatory proteins that regulate muscle contraction and is found in skeletal and cardiac muscle but not in smooth muscle.[30] The Tn complex consists of 3 subunits, namely troponin C (a ligand), troponin I (an inhibitory component), and troponin T (a ligand of tropomyosin). However, type I is considered the most important because it is released faster and rises in a short time ranging between 6–3 hours of morbidity after it is released into the bloodstream as a result of damage to the heart muscle cells, which reveals the formation of a clot or the failure of the work of the heart muscle.[31] High levels of troponin indicate the presence of the injury, not the mechanism of its occurrence. When changes occur in the muscle cell membrane, it is released into its cell juice. Whereas in necrosis, the source of released troponin is due to structural damage to the cardiomyocytes.[32]

Also, a lack of vitamins may contribute to exposure to the virus, including vitamin D, which may lead to a lack of response to immune cells and, therefore, their weakness. Hence, the virus may have the ability to attack those cells, leading to exposure to the emerging virus,[33] vitamin D is one of the most important vitamins necessary for the body and is one of the fat-soluble vitamins. It is also called the sunshine vitamin because ultraviolet rays from the sun's rays are necessary for its formation under the skin in the case of vitamin D3, so sunlight is the main source for generating this vitamin in the body Humans, but there are natural food sources that include fish oil (especially salmon and mackerel), liver, eggs, butter and margarine. There are foods fortified with vitamin D such as milk and other derivatives, orange juice, some breakfast cereals such as oats, and nutritional supplements and drugs.[34] Vitamin D is a steroid hormone that affects many metabolic pathways, and its deficiency is associated with an increased risk of many chronic diseases, including autoimmune diseases, some types of cancer and cardiovascular diseases. Therefore, we find that Italy is the country most affected by COVID-19 in Europe. The reason for the prevalence of this disease is associated with the very high prevalence of vitamin D deficiency.[35]

So, this study aimed to evaluate the levels of Vitamin D and Cardiac parameters in sera of patients infected with COVID-19.

MATERIAL AND METHODS

Study Design: A total of 90 serum samples were conducted in the study, 55 samples (30 males and 25 females) for patients infected with COVID-19 collected from Tiktit General Teaching Hospital in Salah Alden and 35 samples (20 males and 15 females) for healthy individuals as a control group, The age range for patients and control between 35 to 70 years.

Methods

The study includes determination of Serum CRP by using CRP-latex test kit provided from Specterum-Spanish.[36]

Estimation of D-dimer

The d-dimer level was estimated according to the fast Test kit (Immunofluorescence Assay).[37]

Estimation of Vitamin D Level in Blood Sera

The level of vitamin D was estimated according to the kits prepared by the German Human Company.[38]

Estimation of Troponin in Blood Sera

The level of troponin was estimated according to the kits prepared from the company Boditech Med Inc., Korea

Estimation of Lactate Dehydrogenase in Blood Sera

The level of LDH was estimated according to the kits prepared from the company Spectrum – Egypt.[39]

Estimation of Creatine Kinase –CK in Blood Sera

The level of CK was estimated according to the kits prepared from the company Shenzhen Mindray Bio-Medical Electronics Co., China.[40]

Statistical Analysis

The SPSS statistical program was used to analyze the result between patients and control using the F test and at a probability level $p \leq 0.001$ (Table 1).

RESULTS AND DISCUSSION

Measurement of the D-dimer level and CRP and some biochemical includes Vit. D, Tn and LDH.CK levels in the samples under study.

C-reactive Protein in Blood Sera

Table 1 showed that the mean ± SD of the CRP level was (65.072 ± 15.879) mg/L in patients with COVID-19 and (4.420 ± 0.884) mg/L in the healthy group. The results showed a significant increase ($p \leq 0.001$) in CRP level in the sera of patients with Corona-virus as compared with control group, Figure 1.

The results agreed with previous researches[41,42] that an increase in the level of CRP in patients with COVID-19.

Since coronavirus virus is one of the acute respiratory syndrome diseases, it was found that the level of CRP reflects the resulting changes in the intensity of the inflammatory

Table 1: The mean ± SD of the D-dimer and some biochemical samples under study

Groups / *Parameter*	*Mean ± SD*	
	Control	*Patients*
CRP (mg/L)	4.420 ± 0.884	65.072 ± 15.879
D-dimer (ng/mL)	201.56 ± 55.584	670.17 ± 72.552
Vitamin D (ng/mL)	29.10 ± 1.57	9.77 ± 1.24
Troponin (ng/mL)	0.320 ± 0.137	0.8200 ± 0.0407
CK U/L	45.32 ± 7.35	95.23 ± 2.10
LDH U/L	110.26 ± 8.45	331.1 ± 43.4

response when strong inflammation appears[43,44] and that CRP is an independent variable related to the severity of the disease and in various cases, including acute and critical.[43]

Studies have confirmed a significant correlation between CRP concentrations and the worsening of patients infected with coronavirus.[45] It was also found that patients with low blood oxygen levels (less than 90%) have higher CRP levels than patients with Increasing the oxygen level in their blood (more than 90%). As high CRP levels led to lung damage in people infected with the COVID-19 virus, this is a clear sign in evaluating the cases of patients infected with the virus.[46]

D-dimer in Plasma Sample

Table 1 showed that the mean ± SD of the D-dimer level was (670.17 ± 72.552) ng/mL in patients with COVID-19 and (201.56 ± 55.584) ng/mL in control group. The results showed a significant increase ($p \leq 0.001$) in the level of d-dimer in the sera of patients with Corona-virus as compared with control group, Figure 2.

Our results agreed with some other researches[47,48] showing an increase in the level of D-dimer in patients with COVID-19, and confirmed that high D-dimer values were common and associated with an increase in disease severity and mortality in the hospital and an increase in D-dimer levels.

D-dimer is a protein resulting from the breakdown of fibrin, which is part of the small proteins in the blood, and that the occurrence of blood clots is a result of its high levels resulting from the dissolution of fibrin, as determining its concentrations is considered a clinical test that helps in diagnosing thrombotic conditions, including pulmonary embolism.[49] The Studied showed that high levels of D-Dimer higher than 1360 ng/mL on the fifth day of infection may help doctors diagnose the virus in the early stages of COVID-19 patients.[50]

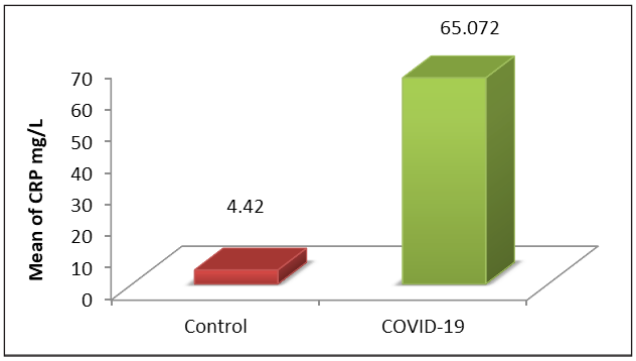

Figure 1: Mean of Sera CRP level in groups under investigation

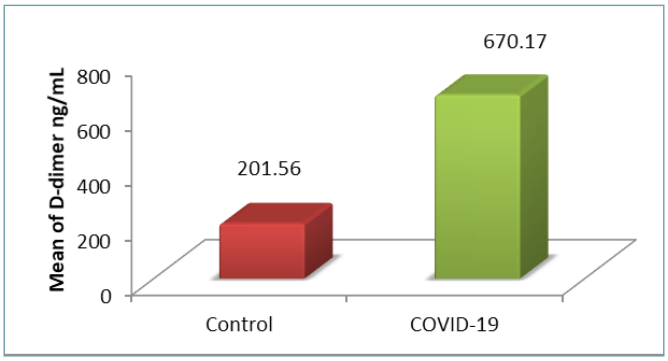

Figure 2: Mean of plasma D-dimer level in groups under investigation

Vitamin D in Blood Sera

Table 1 showed that the mean ± SD of the Vitamin D was (9.77 ± 1.24) ng/mL in patients with COVID-19 and (29.10 ± 1.57) ng/mL in control group. The results show a significant decrease ($p \leq 0.001$) in the level of vitamin D in the sera of patients with corona-virus as compared with control group (Figure 3).

The results agreed with other researches[51] who showed a decrease in the level of Vitamin D in patients with COVID-19. Also, other researches[52] indicated that vitamin D supplementation might boost the immune system, and thus, taking the vitamin leads to a reduction in exposure to the COVID-19 virus.

Vitamin D has many effects, including regulating the immune system by stimulating macrophages,[53] as it plays an important role in regulating and suppressing the cytokine inflammatory response that causes acute respiratory distress syndrome, which characterizes severe and often fatal forms of COVID-19, as there is a significant correlation between low vitamin D levels and mortality from COVID-19.[54] It is recommended for people over the age of 60 and infected with COVID-19 to undergo clinical tests for the level of vitamin D, as it is recommended to take therapeutic doses of 50,000–100,000 international units in the event of a deficiency in D levels, which can help reduce respiratory complications.[53]

Patients with immunodeficiency and bronchiectasis[55] as well as the elderly[56] have low levels of vitamin D and these levels are mild to severe, as they constitute those groups at risk of developing severe disease from COVID-19 in addition to this vitamin D, which has a key role in cardiovascular disease and diabetes.[57]

It was found that vitamin D deficiency may be a risk factor for respiratory infection,[58] so if there is a link between its deficiency and the development of COVID-19.[59]

Troponin in Blood Sera

Table 1 showed that the mean ± standard deviation of the Troponin level was (0.8200 ± 0.0407) ng/mL in patients with COVID-19 and (0.320 ± 0.137) ng/mL in control group. The results indicate a significant increase ($p \leq 0.001$) in the

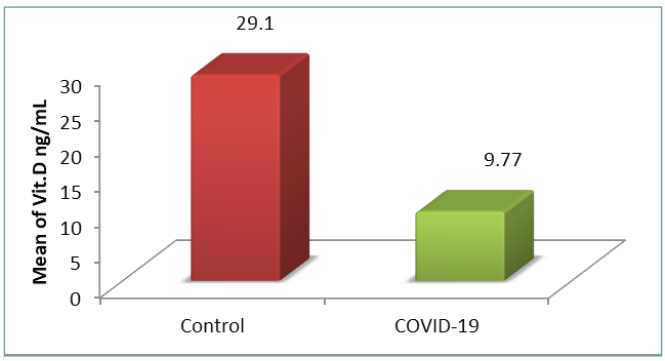

Figure 3: Mean of Sera Vit. D level in groups under investigation

level of Troponin in the sera of patients with Corona-virus as compared with control group (Figure 4).

The results agreed with other previous researches[60] that showed an increase in Troponin level in patients with COVID-19.

It was found that the level of cardiac troponin protein increased at very high levels in patients who have heart diseases with infection with the COVID-19 virus and that the elevated protein troponin indicates an acute heart attack, after which it is difficult for the patient to live.[61]

Studies have indicated the relationship between COVID-19 and heart problems, as people with heart diseases are more vulnerable to the virus and therefore more likely to die.[62]

This is due to their having other heart injuries during infection with the virus. There are two explanations about how the COVID-19 virus affects the heart, as the first proposal is that the virus can spread from the lungs to the body through the blood or the lymphatic system, but what he indicated is that no Coronary heart disease has been diagnosed in the heart until now. However, rheumatic fever causes problems in the valves, which become narrow or reflux, which causes the heart muscle to be exposed to inflammation that affects muscle efficiency and may end in heart failure causing death.[63,64] The other suggestion is that the virus may cause infections in the body, as those with coronary artery problems, suffer from deposition of harmful cholesterol on the artery wall, and this causes exposure to atherosclerosis, which leads to inflammation of the artery wall, in which case the immune system resists that inflammation, which leads The patient's immunity is weak in the face of any other infection. Thus, when infected with the COVID-19 virus, which depends primarily on the immune system's efficiency, the latter is busy fighting inflammation and cannot resist the virus, leading to heart patients' exposure to serious complications.[63,64]

The reason for the increase in troponin in COVID-19 patients is attributed to reasons such as myocarditis, muscle damage caused by elevated cytokines, angiopathy, or the virus's binding to the angiotensin-enzyme receptors to enter the cell.[65] Angiotensin-converting enzyme 2 (ACE2) is highly present in the pericytes of adult human hearts.[66]

However, studies have shown that elevated troponin levels were evident in patients with COVID-19 who had severe symptoms compared to mild ones.[67,68]

The researchers concluded through his study that evaluation of the level of troponin is necessary to know the extent to which it predicts the clinical diagnosis of COVID-19 patients.[69,70]

CK Enzyme in Blood Sera

Table 1 showed that the mean ± standard deviation of the CK level was (95.23 ± 2.10) U/L in patients with COVID-19 and (45.32 ± 7.35) U/L in control group. The results indicate a significant increase ($p \leq 0.001$) in the level of CK in the sera of patients with COVID-19 as compared with control group (Figure 5).

The result of this study agreed with researches[71] that the level of CK was significantly higher in patients with COVID-19 than the control group.

International reports indicated that people infected with COVID-19 have elevated levels of cardiac enzymes, including creatine kinase, as well as lactin dehydrogenase.[72]

The increase in creatine kinase may be attributed to the fact that the coronavirus may cause muscle infections, as the virus uses the angiotensin-converting enzyme receptors to enter the cells of the human respiratory system, thus causing infection. Since it is present in different tissues, it is possible for the virus to directly invade the skeletal muscle and nervous system via the same pathway. The immune pathway may also contribute to the pathogenesis of muscle injury in COVID-19 patients, and thus muscle atrophy may occur because of acute myopathy or polyneuropathy and thus cause weakness in critically ill patients.[73]

On the other hand, a study indicated that the cause of the increase in creatine kinase enzyme may be due to muscle damage often, as it was found that creatine kinase is also high in patients with COVID-19 who suffer from severe diseases and thus cause death.[74,75] Therefore, high levels of CK can be used as a prognostic marker to indicate a more severe clinical picture of COVID-19.

LDH Enzyme in Blood Sera

Table 1 showed that the mean ± standard deviation of the LDH level was (331.1 ± 43.4) U/L in patients with COVID-19and (110.26 ± 8.45) U/L in the control group. The results indicate a significant increase ($p \leq 0.001$) in the level of LDH in the sera of patients with COVID-19 as compared with control group (Figure 6).

The result of this study agreed with other researches[76] indicated that the level of LDH was significantly higher in patients with COVID-19 than in the control group.

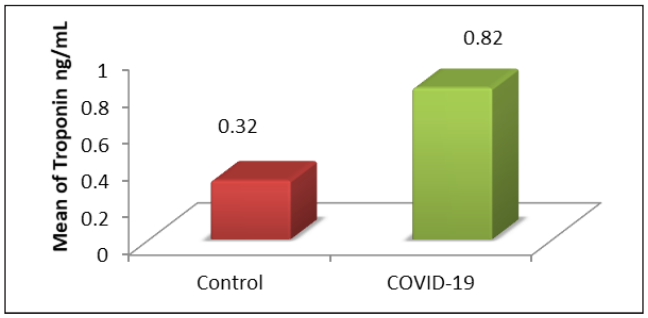

Figure 4: Mean of sera troponin level in groups under investigation

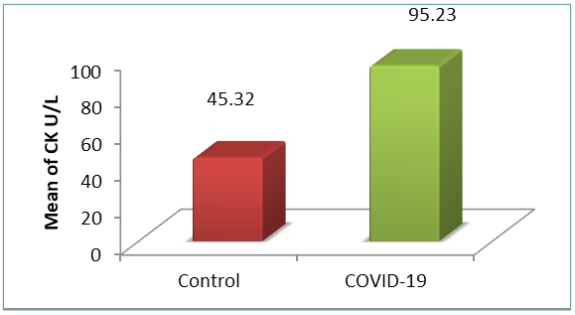

Figure 5: Mean of sera CK level in groups under investigation

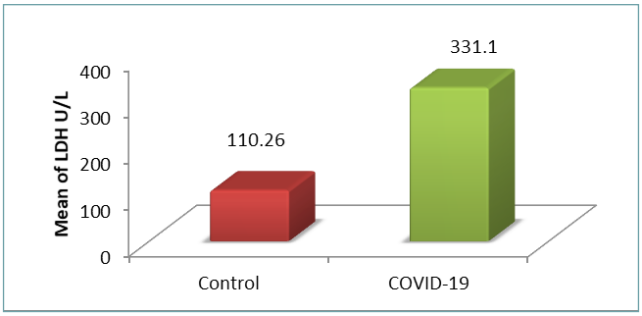

Figure 6: Mean of Sera LDH level in groups under investigation

The reason for the high LDH in patients infected with COVID-19 is attributed to the occurrence of injuries in the lung, and cardiac tissues.[77] as the virus may lead to insufficient maturity of the tissues and consequently to the failure of organs as a result of blood clots, which leads to high levels of cardiac enzymes.[78] LDH is a biological marker as the association between it, and various diseases may increase the severity of COVID-19.[79,80]

CONCLUSION

From all the above results, we can conclude that COVID-19 is a disease that increases the CRP, D-dimer, and Troponin, CK, LDH in patients with diabetes mellitus, so the above parameters may be considered as important biochemical markers in the diagnosis of patients infected with COVID-19. But the level of vitamin D has decreased in the blood of COVID-19 patients, so it is recommended to take nutritional supplements rich in vitamin to enhance the immune system's ability against infection with the virus.

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