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Original Research Article

Evaluation of Fibronectin, C-Reactive Protein and Lipid Profile in Patients with COVID-19

Nagham I. Abdul Hameed[1], Zina A. A. Aldoori[2*]

[1]Department of–Biology, Education Directorate Open Educational College of Science, Ministry of Education- Kirkuk, Iraq
[2]Department of Biology, College of Education for Women, University of Kirkuk, Kirkuk, Iraq

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***Corresponding author:** Zina A. A. Aldoori
Department of Biology, College of Education for Women, University of Kirkuk, Kirkuk, Iraq

Abstract

The SARS-CoV-2 coronavirus was the initial cause of the worldwide epidemic of coronavirus disease 2019 (COVID-19), which started in March of 2020. Patients with coronavirus disease (COVID-19) may have elevated C-reactive protein (CRP) and fibronectin levels owing to the inflammatory response caused by the virus. Nonetheless, the available data imply that infection with COVID-19 affects lipid profile and leads to dyslipidemia. Seventy samples were collected from the Sanitary Isolation Unit of Medical City Hospital in Kirkuk Governorate for this study. Forty of them were taken from SARS-COV2 patients, whereas the other thirty were from healthy individuals. The ages of the two groups ranged between (30-65) years. When a real-time polymerase chain reaction (PCR) tested positive, patients had blood collected to check for other biochemical and inflammatory markers. Fibronectin, C-reactive protein, and d-dimer were some of the indicators checked. The patients' blood was also analyzed for lipids such as total cholesterol (T.C), triacylglyceride (TG), Low-Density Lipoprotein Cholesterol, and High-Density Lipoprotein Cholesterol (HDL-C). In this study, researchers discovered abnormally high concentrations of CRP, D-dimer, fibronectin, triglycerides, LDL-C, and VLDL. The patients also had considerably lower levels of T.C and HDL-C compared to the controls.

Keywords: COVID-19, Fibronectin, lipid profile.

INTRODUCTION

The outbreak of the new coronavirus pandemic was the tipping point that had a significant impact on the whole planet. Corona virus is not only a respiratory virus, but also an acute lung illness that may impact other bodily systems since the early onset of the pandemic (Cheong *et al*., 2020).

In December of 2019, the first known instance of the sickness was discovered in Wuhan, which is located in China. In the weeks that followed, the ailment was discovered in different regions of the globe. The majority of COVID-19 patients mostly suffer from respiratory infections. In addition, clinical worsening to a more severe and lethal form of the illness, including acute respiratory distress syndrome and sepsis, has been documented in some individuals who were infected with MERS-CoV (Bhatraju *et al*., 2020, Kilis-Pstrusinska *et al*., 2021).

The corona virus causes a wide variety of clinical symptoms, some of which are mild while others are severe and can result in death within a short period of time. These symptoms may vary from mild to severe. It is a fact that the coronavirus causes a severe kind of respiratory distress syndrome (SARS), is responsible for severe acute respiratory illness. In addition to causing a respiratory infection, it also produces a more complicated condition that may lead to infection of organs including the liver. This can occur because of the virus's ability to mutate (Kayaaslan and Guner, 2021). Corona virus was detected by using sensitive and specific biomarkers linked to the processes of pathogenesis of the virus. C-reactive protein is a homopentameric acute-phase inflammatory protein, named native CRP (nCRP), is characterized by a dislike arranging of five conforming non-covalently bound. CRP is produced firstly in the liver hepatocytes, but also by smooth muscle cells, macrophages, lymphocytes, endothelial cells, and adipocytes (Hassan and Abbas, 2022).

Increased level of CRP protein might indicate acute inflammation and increased risk of suffering from a heart attack (Abbas *et al*., 2020). Serum C-reactive protein was shown to be a crucial diagnostic marker that changes and rises dramatically in patients with SARAS-COV-2 (Wang *et al*., 2020). In addition to the D-dimer, which is an important diagnostic marker and as a biomarker for predicting the prognosis of infection with the Corona virus upon admission to hospitals, as it is more specific and effective, we can significantly reduce the death rate that is caused by infection with the Corona virus by using the D-dimer, which is a complex protein molecule.

It is generated nevertheless, prior research results have shown that the protein fibronectin is an essential diagnostic marker for the progression of viral infection. Corona one Fibronectin is a glycoprotein that is found in high quantities in the blood and is linked to many different kinds of inflammatory illnesses through the destruction of the fibrin network that is controlled by plasmin and acts as a sign of blood clotting activity. Blood clotting leads to acute trouble breathing and poor lung function (Nasif *et al*., 2022). In addition, other research results have shown that fibronectin protein is one of the important diagnostic markers for virus exacerbation.

The extracellular matrix contains fibronectin, a major protein component. Endothelial and epithelial cells get colonized by bacteria because FN is a target of several bacterial proteins (Lemaska-Perek *et al*., 2015, Lemaska-Perek *et al*., 2016, Lemaska-Perek *et al*., 2020) Extracellular matrix (ECM) remodeling, wound healing, and vascular formation are just a few of the many functions of fibronectin (Shinji et al., 2011, Schroder *et al*., 2006).

Fats play an important part in biology; for instance, fats are required for the backbone of the cell membrane, as well as for components such as cellular communication, membrane transport, energy storage, and heat regulation. Since viral infections modify fat metabolism in favor of proliferation, fats are also necessary for viruses to breach the membrane of the host cell. Inside the host cell is where the virus is located (Abu-Farha *et al*., 2020). Lipids are of fundamental importance in viral infection, they provide structural resources and energy for the creation of viral cell membranes and organelles, as they target RNA viruses for lipid synthesis and for modulating signaling between and within cells to favor the processes required in particle formation required for entry into a host cell, infection, and hiding from the immune system (Tanner and Alfieri, 2021, Cnop *et al*., 2010).

The role of lipids in viral infection cannot be overstated. Lipids are a source of both structural materials and fuel for the creation of viral cell membranes and organelles. Different lipids serve distinct purposes in the body's metabolic processes, including the formation of structural components and the provision of energy. Lipids also play important roles in the transmission of infectious diseases (Fan *et al*., 2020). Lipids are necessary for the control of several immunological pathways as well as macrophages, and a function for the metabolism of lipids has been seen to play in pulmonary infections as well as inflammatory diseases (Beilstein *et al*., 2017). It has been noted that coronaviruses have an impact on the metabolism of lipids in the blood, and various studies have shown substantial changes in the lipid levels of individuals who were infected with viruses (Radenkovic *et al*., 2020, Shen *et al*., 2020). The fact that the virus enters the human body via proteins and certain lipids means that it poses a risk to the immune system and, as a result, increases the likelihood of being exposed to many viruses.

Our study largely evaluated the correlation between COVID-19 infection and levels of C-reactive protein, D-dimer, fibronectin, and lipid profile.

MATERIAL AND METHODS

This study was carried out from November 2020 to March 2021 at Medical City Hospital / Sanitary Isolation Unit in Kirkuk Governorate on 70 people who were aged 30-65 years. Thirty of them were healthy people, while 40 people were patients who had SARS-COV2 diagnosed using PCR that had been recognized with re spiratory symptoms such as fever, fatigue, dry cough, or tough breathing. Five ml of blood were taken from the patient, deposited in test tubes, and left for ten minutes before being put into a centrifuge and spun at 3,000 revolutions per minute in order to collect the serum.

Standard Kits for fibronectin, C-reactive protein, d-dimer, and Lipid profile were purchased from Biomaghreb, tunisie. Serum fibronectin concentration was evaluated by enzyme-linked immunosorbent assay (ELISA)) (Abbas and Alsamarai) produced by ELISA Genie Company, which take the number HUDL01098, C-reactive protein was estimated using the VEDA.LAB device and according to the method (Ridker, 2003); d-dimer; serum total cholesterol (TC) (Lakatos and Hárságyi, 1988); triglyceride (TG)(Fossati and Prencipe, 1982) ; and high-density lipoprotein cholesterol (HDL-C) (Gotto Jr, 1988) were evaluated by previously reported methods. The LDL-C and VLDL-C level were estemated according to the special equation (Steele *et al*., 1976)

Statistical Analysis

The statistical program (SPSS) was used to analyze Mean ±SD was used for the data under study, the T-test was used to simile the parameters among the two groups at the level of probability $P \leq 0.05$.

RESULTS

Table 1: Biochemical markers and lipid profile levels of patients with COVID-19 and healthy people

Parameters	Mean ±S. D	
	Health people	SARS COV-2
CRP (mg/L)	7.58±2.79	51.10±18.14
D. dimer (ng/ml)	323.56±68.594	791.17±84.982
Fibronectin (mg/L)	872.35±204.78	1718.23±682.66
Cholesterol mg/dl	256.10±63.03	147.12±61.33
TG mg/dl	112.71±63.32	155.32±59.72
HDL mg/dl	85.59±32.56	63.05±14.13
LDL mg/dl	110.33±36.21	163.71±47.27
VLDL mg/dl	24.56±8.23	49.51±7.52

TG triglyceride, HDL-C high-density lipoprotein cholesterol, LDL-C low-density lipoprotein cholesterol, VLDL very low-density lipoprotein cholesterol, SD standard deviation.

The results in Table 1 displayed significant elevated ($p \leq 0.05$) in the concentrations of C-reactive protein, D-dimer, and fibronectin, triglycerides, LDL, and VLDL in serum of patients with infected of SARS COVID-2 (51.10, 791.17, 1718.23,155.32,163.71 and 49.51), respectively incomparision with healthy people. On the other hand, the levels of cholesterol and HDL-C were significantly decreased ($p \leq 0.05$) in sera of patients with COVID-19 (155.32 and 63.05) as compared to healthy people.

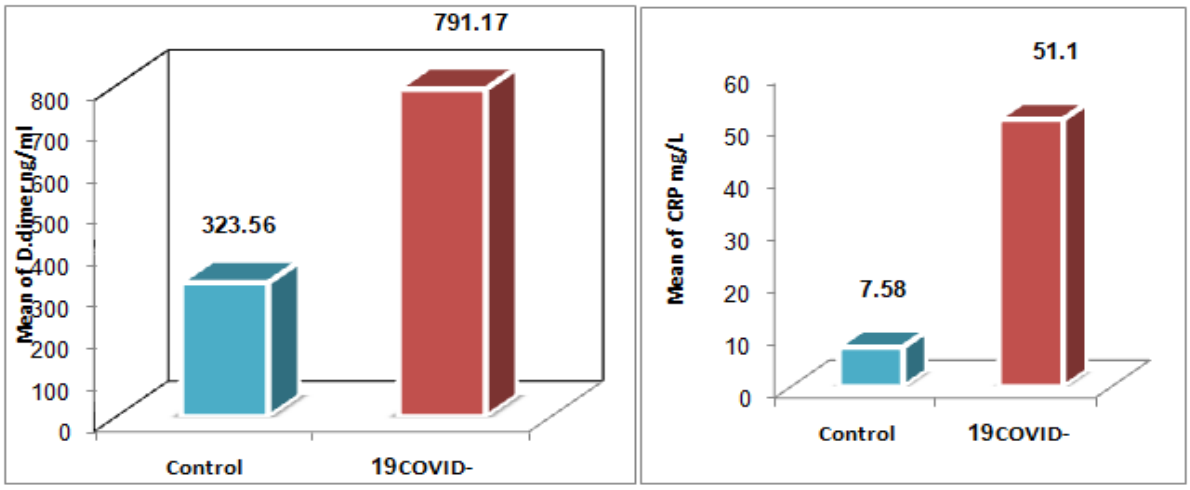

Figure 1: The significant ($p \leq 0.05$) associations between the levels of D-dimer and CRP in patients with COVID-19 and the healthy people

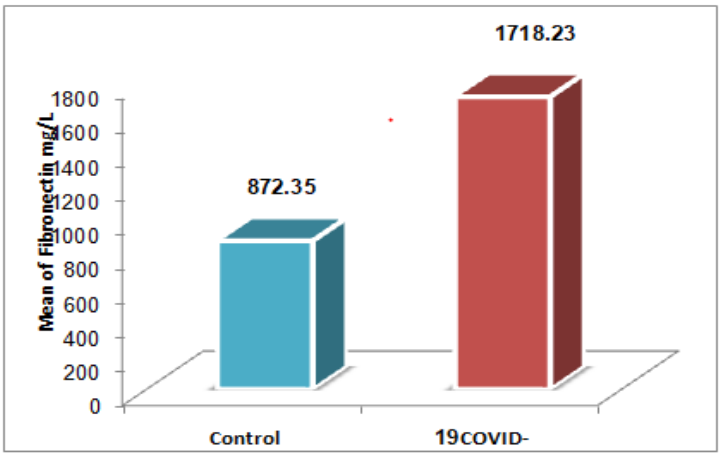

Figure 2: The significant ($p \leq 0.05$) associations between the levels of fibronectin in patients with COVID-19 and the healthy people

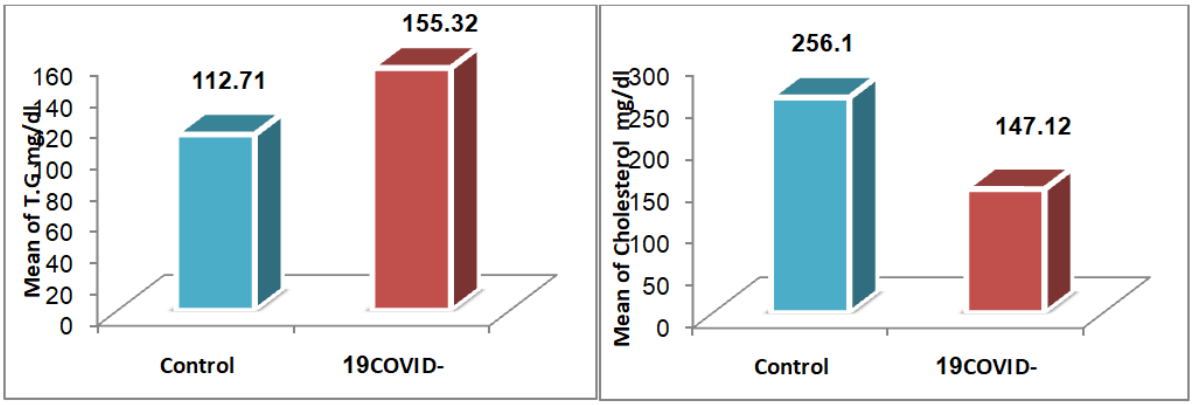

Figure 3: The significant ($p \leq 0.05$) associations between the levels of total cholesterol and triglyceride in patients with COVID-19 and the healthy people

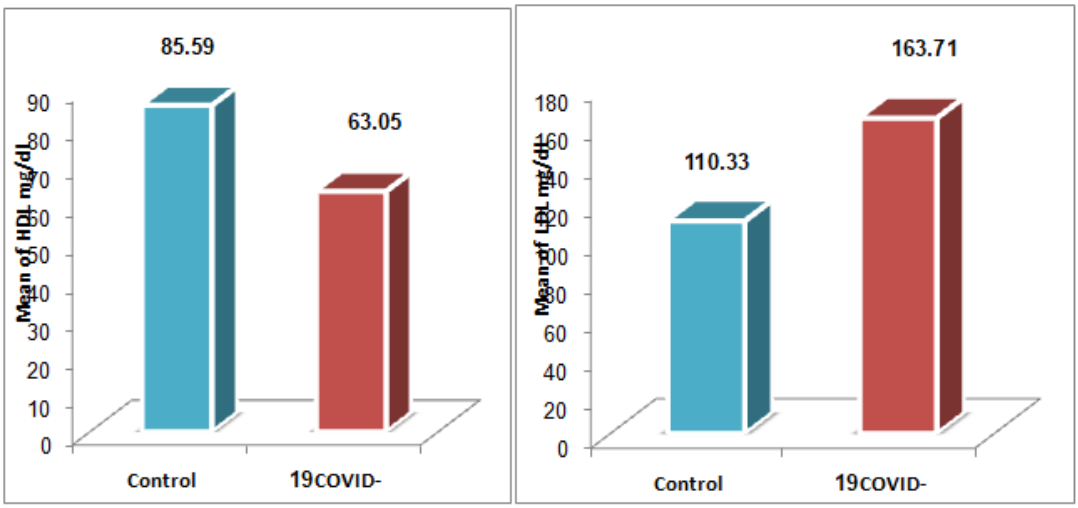

Figure 4: The significant ($p \leq 0.05$) associations between the levels of HDL-C and LDL-C in patients with COVID-19 and the healthy people

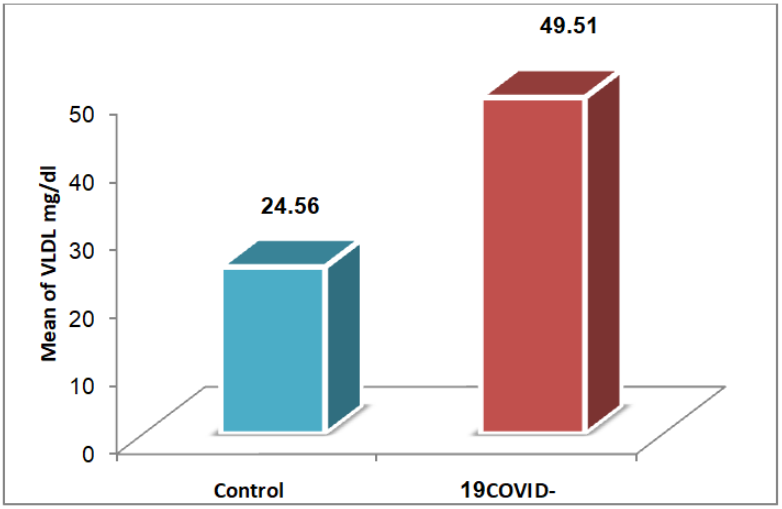

Figure 5: The significant ($p \leq 0.05$) associations between the levels VLDL-C in patients with COVID-19 and the healthy people

DISCUSSION

According to the findings of the research, elevated levels of CRP are consistent with the existence of acute inflammation and a worsening of the viral infection in individuals who are infected with the Corona virus (Sahlah *et al*., 2020, Yitbarek *et al*., 2021,

SeyedAlinaghi *et al.*, 2022).CRP is the most broadly used indicator of acute inflammation and used to calculate the systemic inflammatory response (Abbas *et al*., 2022, Nursan and Sahlah, 2022).

This reactive reaction leads to the stimulation of inflammatory cytokines and tissue destruction, which head rise in CRP in patients with SARS-COV-2, which in turn drove to several serious diseases, including lung damage and a decrease in oxygen in the body. As the reason for the high CRP, this reactive reaction leads to the stimulation of inflammatory cytokines and tissue destruction. It may also be regarded that the high level of CRP may be an early and valuable sign in forecasting the probability of development COVID-19 illness and infection with the virus (Smilowitz *et al*., 2021, Akbari *et al*., 2020, Buttenschøn *et al*., 2022). Moreover, higher levels of pro- SARS-CoV-2 patients' inflammatory cytokines and chemokines have a pathogenic role in MERS-CoV infection, thus solidifying CRP's central importance in corona virus detection (Gao *et al*., 2021).

On the other hand, compared to the control group, the plasma concentration of the dimer appeared to be higher in the Corona patients. The findings of this investigation supported the conclusion of (Luo *et al*., 2020, Yin *et al*., 2021). While D-dimer is a protein molecule that acts as a foundation during fibrin degradation mediated by plasmin, fibrin particles are forming after fibrinogen cleavage that is mediated by thrombin, which is one of the plasma soluble glycoproteins. When D-dimer formation begins, fibrin particles have already begun to form. The location of binding with fibrinogen or other fibrin molecules, which leads to the production of thrombosed clots (Doolittle and Pandi, 2007). The creation of such clots frequently leads to a weakening of the microcirculation in patients with corona virus (Bray *et al*., 2020). In addition, additional research conducted on patients Coronaviruses have been demonstrated to cause endothelium infection and cell membrane breakdown, as was the case with SARS-COV-2. These actions in turn suppress endothelial cell fibrinolytic activity, which encourages clot formation. (Merrill *et al*., 2020). Moreover, proinflammatory cytokines may have a role in both the inflammatory process as well as the thrombotic process (Yao *et al*., 2020).

Also, consistent with previous research, patients with corona virus had higher levels of the fibronectin protein in their plasma than did healthy individuals (Lemanska-Perek *et al*., 2022, Stukalov *et al*., 2021). Microcoagulation seems to be the cause of the elevated fibronectin protein seen in COVID-19 patients, which in turn leads to arterial blockage and organ ischemia. (Lemanska-Perek (Xu *et al*., 2020). On the other hand, cholesterol showed a significant low in the sera of Covid-19 patients in comparison to healthy people, as the results agree with the (Cao *et al*., 2019, Osuna-Ramos *et al*., 2020), that fat metabolism has an important role in the cycle of viral infection, as it may affect genetic changes that predispose to dyslipidemia (Masana *et al*., 2021). As studies have shown that cholesterol concentration were low for Covid-19, and that the reason for the decrease in fats, including cholesterol, may be a result of taking medications or nutritional supplements that were taken during the disease, and loss of appetite that leads to malnutrition, which is one of the early symptoms of some patients with corona virus of the reasons that lead to low cholesterol, as one of the early symptoms of some patients with corona virus of the reasons that lead to low cholesterol, as one of the early symptoms of some patients (Wei *et al*., 2020).

In addition, a research that was only recently published in China shown that T.C levels are noticeably lowers in individuals who had Coronavirus. The pattern of hypolipidemia is progressively linked with infection with SARS-COV-2, and this relationship is inversely connected with acute phase levels, which suggests that SARS-CoV-2 is a causal factor for the change in lipid levels (Cao *et al*., 2019). Also indicated in his study that the level of triglycerides did not show changes in Covid-19 patients when they were approval to the intensive care unit, and this did not agree with the results of the current research (Fan *et al*., 2020, Mohammed saeed *et al*., 2020). On the other hand, T.G show up a significant increase in patients group compared with control group, as the results of our current research agree with (Fan *et al*., 2020, Mohammed.

Also LDL-C appear elevated in sera of SARS-COV2 patients in comparison with healthy people, as the results agree with (Cao *et al*., 2019, Wei *et al*., 2020), and the high level of LDL-C may be attributed to the degradation that occurs in Binding of LDL-C to the receptors present in the liver, which plays role in reducing the transfer of LDL-C to the liver tissues and then increasing its concentration in the blood serum, which (Sun *et al*., 2020). In addition, extremely low-density lipoprotein levels seem to be on the increase in patients compared to healthy people, if the findings of our study are to be believed, and if they are in agreement with the findings of other studies, then (Fan *et al*., 2020).

In addition, HDL-C showed a significant decrease in COVID-19 patients when compared with healthy group, as the results agree with (Osuna-Ramos *et al*., 2020). As COVID-19 patients and those with serious diseases appear low HDL -C levels and apoA-1, which have been closely linked with inflammatory states, therefore Low levels of good cholesterol (HDL-C) and bad cholesterol (apoA-1) may be an excellent predictor of severe illness and hospital death with CO (Thompson *et al*., 2008). Decreased lipoprotein lipase activity leads to higher levels of T.G and lower of HDL-C and altered activity of the esterified cholesterol transporter protein leads to lower HDL concentrations, Despite the fact that some of these routes could help explain Decreased levels

of high-density lipoprotein, but there are other reasons that lead to a decrease as well, including the inhibition of ApoA1, which has been associated with inflammatory conditions, as low levels of it lead to a decrease in HDL concentration (Trinder *et al*., 2019, Malik *et al*., 2021).

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