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Fibrinogen level in coronary artery disease people with COVID-19 patients in Iraq

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***Abstract*---**Background: Since the outbreak of the coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in December 2019, it has affected >200 countries, areas, or territories in 6 continents. At present, whether COVID-19 has an effect on cardiovascular system is unclear. The aim of this study was to evaluate Fibrinogen level in iraqi patients with COVID-19 with Coronary artery disease. Methods: Clinical features, laboratory results, and real time PCR were reviewed for 30 patients with laboratory-confirmed COVID-19 without a history of Coronary artery disease and 30 patients with laboratory-confirmed COVID-19 with Coronary artery disease. They were admitted to the Al-amal Hospital for participating; Iraq between October 2021-April 2022. Healthy participants who underwent routine physical checkups and non-COVID-19 patients the study as the control group. Fibrinogen and Apolipoprotein B levels were determine and compared between the Coronary artery disease COVID-19 and control groups. Results: Fibrinogen higher than the normal range of the patients with Coronary artery disease COVID-19 Compared to the control group. The levels of D.dimer and Ferretin of the patients with Coronary artery disease COVID-19 were significantly higher than those of the healthy control group. The higher of Dimer and Ferretin levels were, with statistical significance ($p < 0.001$). The degree of the increasing in D.dimer and Ferretin levels was positively correlated with the severity of the disease. The Glucose level of the patients with COVID-19 was not significantly different from the control group. A relationship between Homocysteine and Coronary artery disease COVID-19 severity is well known. Conclusions: The Changing Fibrinogen and Homocysteine in the blood of people with Coronavirus may have a role in the infection of Coronary artery disease

***Keywords*---**COVID-19, SARS-CoV-2, Homocysteine, Fibrinogen, Coronary artery disease.

Introduction

At the end of 2019The Chinese city of Wuhan experienced the emergence of the coronavirus illness, which has a wide range of symptoms, the most significant of which are fever and shortness of breath. (Kwok et al. 2020) Over 500 million cases were identified in 188 countries and territories, with over 6.26 million deaths as of May 14, 2022. (CSSE, 2022). The SARS-CoV-2-induced COVID-19 has become one of the most urgent issues of our time as a result of the novel extreme severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spreading throughout the world and the World Health Organization (WHO) declaring a pandemic on March 11, 2020. (Azkur etal., 2020).

Coronaviruses are non-sense positive RNA viruses that cause gastrointestinal and respiratory diseases in animals and humans. (J. Liu et al. 2020) The Nidovirales order's Coronavirinae subfamily of the Coronavirdiae class of viruses, which are enclosed, single-stranded, positive-sense RNA viruses, is what is known as a coronavirus (CoV).(Y. C. Liu, Kuo, and Shih 2020).

Coronaviruses are encapsulated by favorable circumstances RNA viruses have spike-like projections on their surface and range in diameter from 60 nm to 134 nm, giving them a crown-like appearance then the time coronavirus, behind the electron microscope (Singhal, 2020). Humans and other mammals are frequently infected with coronaviruses, which are mammals and members of the Nidovirales order and the Coronaviridae family. (Huang et al. 2020)

Fibrinogen is a procoagulant protein molecule that consists of two outer D domains (Huang et al., 2022), the primary synthesized of Fibrinogen is start in liver hepatic parenchymal cells as a response to IL-1 and IL-6 derived stimulation and in the intracellular of endoplasmic reticulum (ER) assembled the final form of Fibrinogen (İlker Hayıroğlu et al., 2020), The increasing of Fibrinogen level in the blood is a serious matter and pathological indication, Fibrinogen is a vital protein plays a main role in blood clotting for survival as a result of fibrinogen catabolize fraction in (I-6–I-9) process causes reduced turbidity, prolonged thrombin times and generate thinner fibers these thin fibers collect to form Fibrin clots (Sulimai et al., 2022).
It has been demonstrated the value of fibrinogen as one of parameters in disseminated intravascular coagulation (DIC) and because the close relationship between COVID-19 and DIC the dynamic changes in fibrinogen levels are remarkable in COVID-19 patients when compared between COVID-19 patients with healthy controls it showed that the level of fibrinogen and it's degradation products is higher in COVID-19 patients (İlker Hayıroğlu et al., 2020).

There are two types of genetic factors of rare congenital fibrinogen disorders. Type I disorders (a fibrinogenemia and hypofibrinogenemia) reflect levels of fibrinogen in the blood (amount of fibrinogen < 1.8 g/L), and type II (dysfibrinogenemia and hypodysfibrinogenemia) (Clark, R. D., et al .2009). Patients with fibrinogenemia

(hypofibrinogenemia) dysfibrinogenemic face the risk of bleeding events and face in a paradoxically risk developing of thrombosis. Managing thrombosis in these patients is very challenging to prevent the underlying risks of bleeding and clotting (Sulimai et al., 2022).

Plasma fibrinogen levels are effected by environmental and genetic factors it is also regulated by complex interactions of it. It is estimated that only 30–50% of the plasma fibrinogen level is a moderately heritable blood protein that is influenced by gene, environment, and disease status, Studies have shown that there is a close correlation between high levels of fibrinogen and coronary artery disease risks, and that fibrinogen has a relationship with obesity, weight gain and age, where the relationship is positive, that it was found to be high in obese people and old male (Clark, R. D., et al .2009).

Materials and Methods

One hundred Iraqi patients with COVID19 participated in the present study. Only 65 patients satisfied all biochemical analysis tests. Their ages ranged between 35-65 years old and the mean of BMI to patients 25.55 ± 3.06. The random blood glucose and HbA1c were 130.12 ± 20.14 mg/dl and 6.08 ± 0.8% respectively. These patients were registered as COVID19 at Al-Amal Specialized Hospital "in Najaf city-Iraq and Al-Sadr Teaching Hospital" in Najaf city-Iraq within October to April period. The patients diagnosis was established by clinical symptoms, PCR and biochemical test. The present study excluded the patients with hypertension, those with endocrinitis infection and inflammation, heart diseases and also the patients from non-Arabic ethnic group, patients with a history of thyroid.

Thirty people were selected as a control group. Their age were comparable to that of patients and the mean of BMI equal 22.94 ± 3.15. The means of random blood glucose and HbA1c were 101.9 ± 11.18 mg/dl, 5.03 ± 0.63% respectively. The people with anemic or having an obvious systemic diseases were excluded.

Body Mass Index (BMI) was classified by the World Health Organization. Weight and height were measured according to WHO guidelines. Using WHO guidelines, BMI was calculated as weight/height^2 (Kg/m^2). Obese individuals were defined as having BMI more than 30 kg/m^2, whereas normal individuals had a BMI of 18-25. Five milliliters of venous blood samples were drown using a disposable needle and plastic syringes from each patient and control subject. Blood divided into two anticoagulant tubes and gel tubes. The blood in gel tube was left at room temperature for 15 minutes for clotting, centrifuged 3000 Xg for 5 minutes, and then serum was separated and transported into new disposable tubes.

The student T-test was employed to assess differences in scale variables between diagnostic categories and analysis of contingency tables (x2-test) was used to check associations between nominal variables. Associations among variables were computed using Pearson's product-moment and Spearman's rank-order correlation coefficients. All tests were 2-tailed and a p-value of 0.05 was used for statistical significance. All statistical analyses were performed using IBM SPSS windows version 25, 2017.

Results and Discussion

The COVID-19 patients had a mean age of 58.3 ± 11.5 years old male and they did not differ statistically from COVID-19 or healthy subjects in age or gender We found that levels of fibrinogen µg/ml and Homocysteine µg / ml were higher in COVID-19 patients than healthy group ($p < 0.001$).

Parameters	Mean±STD Patients	Mean±STD Controls	P-Value
D.dimer ng/mL	3474.6±211.63	280.44±84.96	<0.001*
Ferretin ng/mL	990.42±192.81	105.5±43.73	0.005*
Fibrinogen µg / ml	607±58	350±30.5	<0.001*
Homocysteine µg / ml	922.2±15.5	655.2±24.6	<0.001*

The COVID-19 is an infectious illness that has caused a pandemic worldwide. As a novel type of disease with high infectivity and mortality, the pathophysiology of COVID-19 has not been fully studied. A number of studies have reported severe and complex effects of COVID-19 in several human organs and systems including respiratory, immune, digestive, circulatory, hepatic, renal, and hematological systems. However, whether COVID-19 affects human circulatory system remains unknown. Here, we report the influence of COVID-19 on circulatory system. where the patient are COVID-19 infection and COVID-19 is an inflammation case we can observe an increasing in fibrinogen level, Fibrinogen is a positive acute-phase reactant associated with excessive inflammation in COVID-19 patients. It has been found the levels of fibrinogen and its degradation products increasing in patients with COVID-19 compared to healthy patients and increasing elevation of fibrinogen level as increase the severity of COVID-19 infection (Ulloque-Badaracco et al., 2022).

Furthermore, even though the disease severity was matched, we still found the fibrinogen level of COVID-19 patients was significantly higher than that in non-COVID-19 pneumonia patients. This suggests coronary artery disease in COVID-19 patients, possibly because of the attack of SARS CoV-2 virus. The wide distribution of COVID-19 nucleic acid in respiratory tract, saliva, feces, and breastmilk indicates that direct viral attack to the target cells may be an alternative reason (Lymperopoulos et al., 2021). Angiotensin-converting enzyme 2 (ACE2) is a receptor providing the main entry site for SARS-CoV to invade human cells, and this in turn facilitates direct damage of virus through the course of infection (Bhat et al., 2022.). recently reported that ACE2 was highly expressed in the heart (Vineis et al., 2019), ACE2 is more than a critical gateway for SARS-COV2 entry, it's also the functional disruption of it and can cause the loss of cardiopulmonary homeostasis during COVID-19 (Al-Kindi & Zidar, 2022). Our study showed that circulatory system tended to be associated with viral infection, indicating virus infection and replication may account for the abnormal Thrombosis. However, our study also showed that disease severity, which may influence the viral infection, was associated with circulatory system, thus the true relationship of circulatory system and Thrombosis need to be further studied.

With an exponential increase in COVID-19 infection rate and mortality in an ongoing global pandemic, researchers, clinicians, and government agencies are focusing on repurposing drugs with known safety profiles (Zhang L, Liu Y (2020)). Previously known beneficial outcomes following high doses of vitamin C therapy in clinical studies have made this vitamin a frontline candidate for possible COVID-19 treatment. Also, there are very limited side effects and patients have high tolerability to ascorbic acid high doses (Padayatty SJ, et al. (2004)).

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