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ALTERATION OF LIPID PROFILE IN COVID-19 SAUDI PATIENTS AT AL-MADINAH AL-MUNAWARAH

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ABSTRACT

Background: According to a recent literature review, the most frequent laboratory abnormalities found in Covid-19 patients are fluctuating levels of different organ biomarkers, however, reducing the complications of viral infection and understanding its impact on other body systems is still unknown. **Objectives:** The current study aims to evaluate the effects of viral infection on the lipid profile and the prevalence of dyslipidemia by analyzing the levels of lipid parameters in Covid-19 Saudi patients. **Methods:** A retrospective study was done to study serum levels of LDL-C, HDL-C, TC and TG on 80 patients with Covid-19 infection who were hospitalized in Ohud Hospital and King Fahd Hospital, Al-Madinah Al-Munawarah, Saudi Arabia between March 2020 to May 2020. Age- and gender-matched normal subjects (n= 80) who had routine laboratory lipid tests were also recruited. Data were evaluated using the GraphPad Prism Software (version 5.01). For comparison of lipid profile parameters, unpaired t-test, one-way Anova test was used and the data were represented as mean (SD). **Results:** In the current study, it was found that all lipid parameters were significantly altered through infection. The common lipid changing include a reduce in total cholesterol (TC) levels and a raise in the concentration of triglyceride (P<.001). Also, low- and high-density lipoprotein cholesterol (LDL-C, HDL-C) levels were decreased. Additionally, severely infected patients are at higher risk of developing CVD. **Main Outcome Measures:** Severely Covid-19 infected patients are at high risk for developing CVD due to alterations in lipids profile. **Conclusion:** Covid-19 patients were found to have hypocholesterolemia and hypertriglyceridemia, moreover the low levels of high-density lipoprotein cholesterol (HDL-C) in patients with severe infection were also found. Therefore, it can be concluded that the severely Covid-19 infected patients are at high risk for developing CVD correspondingly.

KEYWORDS: COVID-19, Cholesterol, HDL, LDL, CVD and Triglycerides.

Abbreviations: AIP (Atherogenic Index of Plasma), COVID-19 (Novel Coronavirus Disease), Cholesterol (TC), HDL (high- density lipoprotein), LDL (low-density lipoprotein), CVD (Cardiovascular Diseases) and Triglycerides (TG).

INTRODUCTION

Coronaviruses are a group of viruses that frequently lead to mild or moderate respiratory tract illnesses in mammal and birds. Nevertheless, coronavirus epidemics have appeared three times in the 21st century from animal reservoirs to cause severe disease and global transmission worries. There are seven types of coronaviruses identified to cause human disease.[1,2] hree of them may have more serious outcomes in people, whereas another four types are mild, like viruses 229E, OC43, NL63 and HKU1.[2] The serious types are SARS (severe acute respiratory syndrome) that appeared in late 2002 and disappeared by 2004; MERS (Middle East respiratory syndrome), that came out in 2012 and remains in circulation in camels; and Covid-19, that emerged in December 2019 from China and a global attempt is in progress to contain its spread.[2] In the 20th June 2020, more than 216 countries have Covid-19 infection with more than eight million confirmed cases, some of them leading to more than 400,000 deaths.[2] In Saudi Arabia, the Health Ministry reported that 154,233 people have now contracted the virus, 54,086 are active cases and 1,955 of them are in critical conditions.[3] Patients having Covid-19 may have any of the symptoms; fever, high temperature (> 37.3 °C), cough, myalgia, sputum production, headache or may have diarrhea, dyspnea and acute respiratory distress syndrome (ARDS).[2,3,4] Recently, United States Centers for Disease Control and Prevention (CDC) includes immunocompromised individuals or conditions such as

dyslipidemia, liver or cardiovascular disease as possible risk factors for developing a severe complication of Covid-19 infection,[5] however specific data regarding risks related to these conditions are limited.

Lipids play a vital role in viral infection. The change in serum lipid levels, particularly cholesterol level, has also been reported to happen during viral infections, for example human immunodeficiency virus (HIV) and hepatitis C virus (HCV).[6,7] Moreover, membrane cholesterol has been indicated to be a vital component for the entry of pathogenic viruses into host cells.[8,9] Dyslipidemia has also been reported to be associated with SARS. The studies showed that a lower level of total cholesterol (TC) and higher levels of triglycerides (TG) were indicated in SARS patients as compared with healthy subjects, suggesting the lipid changes may have a prognostic and diagnostic role in certain infections.[10,11] Little is known about the influence of viral infection on the lipid metabolism, and the full information is far missing with the changes of lipid roles during the COVID-19 infection. Some studies reported that the prevalence of hyperlipidemia appears to be largely present in patients diagnosed with Covid-19 and hypercholesterolemia was the third most common (18%) comorbidity in these patients.[12,13] Uncontrolled cholesterol or Triglycerides levels in patients may be considered as risk factors that may lead to major adverse cardiovascular events.

On the other hand, a retrospective study was performed to investigate the lipid profiles in patients with Covid-19, suggesting that Covid-19 patients had hypolipidemia, that positively correlated with the severity of infection.[14,15]

Therefore, in our current study, we work to analyze serum lipid profile of the patients with Covid-19 infection to find whether the viral infection cause alterations in serum lipid and indicate if its alteration is a risk factor for CVD.

METHODS

This is a retrospective study, a data of 80 cases of Covid-19 patients were randomly collected from the Ohud Hospital and King Fahd Hospital, Al-Madinah Al-Munawarah, Saudi Arabia. All cases were reviewed according to the inclusion and exclusion criteria; the inclusion criteria were patients diagnosed with Covid-19 infection. However, patients were excluded if they had a history of endocrine diseases or history of major renal, liver, heart or neurological disease. Laboratory data collected included all lipid profile parameters for each participant. The Atherogenic Index of Plasma (AIP) = log (TG/HDL-C) was further calculated as an Atherogenic dyslipidemia index. An AIP value of <0·11 depicts the low risk of CVD, 0·11-0·21 is indicative of intermediate-risk whereas >0·21 was associated with high-risk CVD. Patients with confirmed Covid-19 infection were categorized to severe, moderate, mild, and asymptomatic according to the results from clinical characteristics, chest radiography, and all symptoms, based on the Saudi Health Ministry protocol.[3]

Ethical authorization was permitted from the Ethical clearance committee at the Faculty of Applied Medical Sciences at Taibah University and Saudi Arabia Ministry of Health, General Administration for Researches & Studies (SREC/AMS 2020/63/CLD, IRB 452).

Statistical analysis: Data were analyzed using the GraphPad Prism Software (version 5.01). Quantitative data were presented as percentages, mean, standard deviation and range. T-test was used for two variables and one-way Anova test for comparing between different categories of Covid-19 infected patients. Spearman's coefficient test was used to investigate the association between different variables and the severity of the infection. Statistical significance is set at P <.05and <.001.

RESULTS

Serum lipid levels generally altered in infected patients

In this study, 80 patients were diagnosed with Covid-19 with a mean age of 55.5 (13.6) years (extremes: 30–80 years). The study subjects included 43 males and 37 females, 10% of them were smokers and 5% had diabetes. Compared with the healthy controls, the infected patients have low levels of serum TC, and LDL-C, which were 1.05 (1.07) mmol/L and 1.1(0.87) mmol/L respectively, decreased sharply (P＜.001), also the lower serum levels of HDL-C (1.05 mmol/L) was indicated in Covid-19 patients. Whereas, TG 3.9 (1.80) was higher than 1.4 (1.01) healthy control (Table 1).

More significant rise in TG levels and decline in TC levels in severe cases

The patients were classified into three groups, the asymptomatic infection cases (23.7%), mild to moderate infection cases (23.2%) and severe infection cases (53.1%). The TG results indicated that the significantly higher levels 4.99 (1.23), in the severe infection cases than that, (1.83(0.88), 2.8(1.11)), in the asymptomatic and mild infection cases respectively (P＜.001). Whereas, the patients with severe infection had a slightly lower level of TC than those with asymptomatic and mild infection cases (P=.002 and P=.001 respectively). Moreover, a significant decrease in the level of HDL-C was detected in the severe infection cases compared to asymptomatic infection cases (P=.03). Therefore, the higher TG/HDL-C ratio (4.57(0.82)) was found in the severe infection cases, compared with the asymptomatic and mild infection groups (P=.001 and P=.01 respectively, Table 2).

The patients were grouped by gender. Among the patients, the levels of TC and LDL-C in the male patients were significantly lower than that in the female patients, (0.85(0.34), 1.18(0. 4)) vs (1.20 (0.54), 1.80 (1.3) respectively). Comparing with the female patients, the

male patients had a higher level of TG (4.80(1.1)) and the ratio of TG/HDL-C (3.5 (0.57), Table 3).

Atherogenic Index of Plasma (AIP=Log TG/HDL) predicts cardiovascular risk. An AIP less than 0.11 denotes low risk while that between 0.11 – 0.21 denotes intermediate risk. An AIP greater than 0.21 denotes high cardiovascular risk. In this current study, the severe infection patients had high risk (AIP=0.66) while asymptomatic and mild infection patients had low risk (AIP= 0.081 and AIP=0.11 respectively).

Tables

Table 1: Serum lipid level in patients and healthy controls

Parameters	Covid-19 patients (n=80)	Control (n=80)	*P*-Value
Age	55 (12.6)	51 ± 11.2	
Sex (Number)	Male= 43	Male= 40	
	Female = 37	Female = 40	
TC	1.05 (1.07)	3.8 (1.6)	**0.001****
LDL-C	1.1 (0.87)	2.7 (0.84)	**0.002****
HDL-C	1.05 (1.20)	2.9 (1.50)	**0.04***
TG	3.9 (1.80)	1.4 (1.01)	**0.003****
TG/HDL-C ratio	3.7 (1.35)	0.48 (0.67)	**0.002****

TC= Total Cholesterol, TG= Triglycerides. Data presents as Mean (SD), *P*<.05* or <.001**

Table 2: Lipid level in asymptomatic infection cases, mild cases and severe infection cases

Biomarkers	Asymptotic cases (23.7%) Vs. Sever cases (53.1%)		Mild to Moderate cases (23.2%) Vs. Sever cases (53.1%)		Sever cases (53.1%)
	Mean (SD)	*P*	Mean (SD)	*P*	Mean (SD)
TC	3.05 (1.21)	**0.002****	2.05 (1.29)	**0.001****	1.05 (0.35)
LDL-C	2.75 (1.51)	**0.003****	1.55 (1.25)	**0.05***	1.02 (0.71)
HDL-C	2.20 (1.10)	**0.03***	2.13 (1.60)	>0.05	1.09 (1.50)
TG	1.83 (0.88)	**0.03***	2.8 (1.11)	**0.002****	4.99 (1.23)
TG/HDL-C ratio	0.83 (0.8)	**0.001****	1.32 (0.7)	**0.01***	4.57 (0.82)

One-way Anova test was used to compare between different categories of Covid-19 infected patients in lipid markers levels. Data presents as Mean (SD), *P*<.05* or <.001**

Table 3: The Mean (SD) for the Lipid levels in Covid -19 patients based on the gender

Parameters	Female (n=37)	Male (n=43)	*P*-Value
TC	1.20 (0.54)	0.85 (0.34)	**0.05***
LDL-cholesterol	1.80 (1.3)	1.18 (0.4)	**0.04***
HDL-cholesterol	1.11 (0.94)	1.37 (1.9)	**>0.05**
TG	2.90 (1.64)	4.80 (1.1)	**0.03***
TG/HDL-C ratio	2.61 (1.7)	3.5(0.57)	**0.05***

Data was analyzed by T-test to compare between two genders patients with Covid-19 and a statistical significance differences was considered as *P*<.05*

DISCUSSION AND CONCLUSION

A recent viral outbreak that started in Wuhan, China is now distribution all around the world. This new viral epidemic has been known as Coronavirus Disease 2019, (COVID-19), and is sustained by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).[2,16] However, a lot of information about this virus is unknown and the whole world is working on this Covid-19 infection and associated complications. Therefore, in the current study, researchers investigated the pathological modifications of low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c), and total cholesterol (TC) and their associations with Covid-19 severity and the risk of CVD. The serum lipid changes in a critically infected case and it's a major risk factor that is associated with CVD.

Lipid metabolism has an important key role in viral infection cycle. Genetic alterations or other secondary factors may influence on hypolipidemia or dyslipidemia.[17] Our study demonstrates the possible association of abnormal lipid profile with the patients suffering from Covid-19. In current study, the decreased serum level of TC, LDL-C and HDL-C and increased level of TG have already been highly co-related with CVD in severe infected cases with Covid-19. We used the mean of all lipid markers from the normal control as reference value to compare it in COVID-19 patients. Based on these findings it may be concluded that the

alteration in the lipid levels frequently develops during Covid-19 infection and is associated with the severity or the stage of infection. This in agreements with studies showed that hypercholesterolemia was indicated in 18% of Covid-19 patients with developing chronic diseases such as CVD and Hypertension,[18] also hyperlipidaemia was occurred in 25% of hospitalized patients.[12] Moreover, the observational database from 169 hospitals in Asia, North America and Europe, revealing that the prevalence of hyperlipidaemia was indicated in 30.2% of survivors from Covid-19 infection and 35% in non-survivors.[13] Interestingly, in current study, it was illustrated that serum levels of HDL-C were lower in patients with the severe as compared to those with the milder Covid-19 infected patients. These results may possibly support the idea that HDL particles may have some protection against Covid-19 virus as a result of their anti-microbial and anti-inflammatory actions.[19]

In this study, we also observed and speculated that the decreased levels of serum TC, LDL-C and HDLC are most likely outcome of viral infection, while increased levels of triglycerides raises the severity of Covid-19, including the risk of increasing cardiac complications, particularly acute cardiac injury and arrhythmias, acute coronary syndrome, venous thromboembolism; acute myocardial injury that are most common in patients with preexisting cardiovascular disease with high mortality rate. It is verified from different studies that there is significant correlation between AIP and CVD risk factors. In this current study, the severe infection patients had high risk (AIP=0.66) while asymptomatic and mild infection patients had low risk (AIP= 0.081 and AIP=0.11 respectively). In agreement with research has done by Chinese Center for Disease Control and Prevention (CCDC), indicating that the death rate for Covid-19 patients with heart disease was 10.5%.[20]

Findings of this study may help to reflect the abnormal lipid profile in Covid-19 patients having mild to severe symptoms. This may clarify some clinical manifestations and provide important information for future researches regarding Covid-19 infection complications. Therefore, a prospective study with a large sample size recommended to describe the lipid metabolism status and gives the awareness to clinician and general public.

Limitations: A potential limitation of this study were the limited numbers of samples. Therefore, a prospective study with a large sample size recommended to describe the lipid metabolism status and gives the awareness to clinician and general public. More broadly, research is also needed to determine the causes or the exact mechanisms that lead to change the lipid levels in Covid -19 patients.

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