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ORIGINAL ARTICLE

Lipid Profile Variations and Their Associations with Kidney Injury in Patients with COVID-19

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ABSTRACT

Background: COVID effects different people in different ways. Acute kidney injury and variations in lipid profile are frequent complications among patients hospitalized for Covid-19. Severely infected patients with Covid-19 have higher frequency of kidney injury and hypolipidemia, resulting in higher mortality rate.

Objectives: The current study was designed to explore variations in lipid profile and estimated Glomerular Filtration Rate (eGFR) in Covid-19 patients, and to evaluate the association of eGFR with lipid parameters in Covid-19 patients (confirmed cases) and healthy controls.

Methodology: This comparative cross sectional study was carried out at pathology lab of MACCA Diagnostic, Multan from Oct 2020 to Jan 2021. We enrolled 225 Covid-19 patients as test group and 225 healthy subjects (negative for Covid-19) as control group. Fasting blood samples of Covid-19 and control group were collected to test lipid profile and eGFR. Estimated GFR was calculated from the value of serum creatinine, age, gender and ethnicity of all participants by applying Modification of Diet in Renal Disease (MDRD) equation.

Results: All parameters of lipid profile and eGFR were significantly lower in Covid-19 patients group than healthy control group, with p-value <0.0001. We found strong positive association between eGfR and serum High density lipoproteins (HDL) levels (r^2= 0.57) in Covid-19 patients.

Conclusion: Hypolipidemia and decreased in eGFR were observed in Covid-19 patients, and extent of kidney injury (decrease in eGfR) was positively associated with serum HDL.

Keywords	*Address of Correspondence	Article info.
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INTRODUCTION

According to reports, pneumonia caused by Coronavirus (2019-nCoV)- a virus reported for the first time in Wuhan, China in December 2019, is a major symptom of the severity of this viral attack[1]. This virus can spread from person to person at very high rate. WHO declared this fast spreading virus as a global health emergency on 30th

January 2019. Later on, WHO named this disease as Coronavirus disease 2019 (Covid-19)[2]. Covid-19 effects the respiratory system; the reason that it was also named as severe acute respiratory syndrome (SARS-CoV-2)[3]. Currently, SARS-CoV-2 is spreading all around the world, causing a massive social and financial burden to different countries. Almost 85.9 million peoples have been affected with the virus already, among them 48.3 million have been recovered and 1.86 million have been died[4]. In Pakistan 490,476 confirmed cases of Covid-19 have been testified so far, with 10,409 reported deaths. Cases of Covid-19 were highly reported in Sindh and Punjab, respectively, than other provinces of Pakistan[4].

The symptoms of Covid-19 may be mild like flu, dry cough, fever and headache or severe such as Acute lung injury (ALI), respiratory failure, or multiple organ failure[5]. Currently, the effects of this virus on metabolism of humans are quite unknown[6]. For instance, Covid-19 affects lipid metabolism, and appearances of hypolipidemia have been observed in patients with mild to severe symptoms[7]. Ever since, the changes in lipid profile due to other viral infections have already been reported, and it is a metabolic marker to distinguish between viral and bacterial infections[8]. Acute renal dysfunction have been observed in large numbers of Covid-19 patients, some of them may develop renal failure and require dialysis[9]. Some Covid-19 infected patients' exhibit rapid clinical deterioration towards severity of disease and death. In such condition, early assessment of the risk is priority, to prevent the development of severe disease and to minimize the death rate in these patients. Frequency of Acute kidney injury (AKI) in Severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) viral infections was 5-15%, with the mortality rate as 60-90%. The prevalence and prediction of AKI in Covid-19 is unknown yet, and information about the clinical effect remains sparse[10]. We found it exciting to explore alterations in serum lipid profile and its correlation with estimated eGFR to describe the association of lipids variations, and risk of kidney injury in Covid-19 confirmed positive cases.

MATERIAL AND METHODS

This comparative cross-sectional study was carried out at pathology lab of MACCA Diagnostic, Multan from Oct 2020 to Jan 2021. Data and contact numbers of confirmed positive and confirmed negative cases were obtained from Nishtar Hospital, Multan. About 350 confirmed positive cases were approached through their contact details, among them 225 patients agreed to participate in this study, while 225 healthy subjects negative for Covid-19 were included as control group. After getting their informed consent, blood samples were collected in fasting state by following standard operating procedure of sample collection for Covid-19, to test lipid profile and estimated GFR. Lipid profile parameters like: Total Cholesterol (T-Chol), Triglyceride (Trig), High density lipoproteins (HDL), Low density lipoproteins (LDL) and serum creatinine were measured by Mindray 240pro (chemistry analyzer) after applying quality controls of Bio-Rad level 1 and level 2 for all the parameters. eGFR was calculated from the value of serum creatinine, age, gender and ethnicity of all participants by applying Modification of diet in renal Disease (MDRD) equation[11].

eGFR = 186 x (Creatinine/88.4)-1.154 x (Age)-0.203 x (0.742 if female) x (1.210 if black)[11].

RESULTS

Demographic data and test results of Covid-19 patients and control group were entered and analyzed by SPSS 20.0 software (platform of advanced statistical analysis). P-value <0.05 was considered significant for pair-wise comparisons of the parameters between two groups.

Demographic characteristics of Covid-19 patients and the control group are given in Table **1**. The prevalence of Covid-19 was high in males (61.3%) than the females (38.66%) and the 40-50 years age group (24.4%) was more affected. Middle socioeconomic status patients were also higher in number (39%). While according to the smoking rate, the prevalence rate in smokers (81.8%) is high as compared to non-smokers or ex-smokers (18.6%).

Comparison of Lipid profile parameters and eGFR were performed by using two sample t-tests, shown in Table **2**. Almost all parameters of lipid profile were low in Covid-19 patients group as compared to control group. eGFR was also low in Covid-19 patients group.

Decrease in all lipid parameters have been observed in Covid-19 patients group. All lipids parameters of Covid-19 patients are significantly low with p-value <0.00001 than control group. Estimated GFR also have been decreased

significantly in Covid-19 patient group with p-value <0.00001. Correlation between lipid parameters and eGFR is shown in Table **3**. HDL has significant positive correlation with eGFR in covid-19 patients.

Table 1. Demographic Data of Covid-19 Patients and Healthy Controls.

Variables	Group	Covid-19 Patients (n = 225)	Healthy Controls (n = 225)
Gender	Males	138 (61.33%)	130 (57.77%)
	Females	87 (38.66%)	95 (42.23%)
Age (Years)	10-20	14 (6.2%)	23 (10.2%)
	20-30	37 (16.4%)	33 (14.6%)
	30-40	33 (14.6%)	35 (15.5%)
	40-50	55 (24.4%)	52 (24.4%)
	50-60	49 (21.77%)	47 (23.1%)
	>60	37 (16.44%)	35 (15.5%)
Smoking Status	Non-Smokers	177 (81.4%)	169 (75.1%)
	Smokers or Ex-Smokers	42 (18.6%)	56 (24.8%)
Socioeconomic Status	Rich	66 (30%)	70 (31%)
	Medium	88 (39%)	92 (41%)
	Low	71 (31%)	63 (28%)

Table 2. Comparison of Lipid Profile and Estimated Glomerular Filtration Rate between of Covid-19 Patients and Healthy Controls by Two Samples t-test.

Test	Covid-19 patients	Healthy Controls	p-value
Cholesterol	164 ± 16	178 ± 18	<0.00001
Triglyceride	127 ± 14	148 ±18	<0.00001
HDL	37 ± 6	48 ± 7	<0.00001
LDL	85 ± 12	119 ± 16	<0.00001
eGRF/ml	75 ± 8	106 ± 4	<0.00001

Table 3. Correlation of Estimated Glomerular Filtration Rate with Lipid Profile Parameters in Covid-19 Patients by Pearson Correlation Coefficient.

Parameter	Correlation(r^2) with eGRF
Cholesterol	0.28
Triglyceride	0.34
HDL	0.57
LDL	0.25

DISCUSSION

Demographic data of our study demonstrated that the prevalence of Covid-19 is higher in males than females, middle aged group 40-50 years are the high-risk group, and middle standard people according to socioeconomic status have higher prevalence of Covid-19. In present study, among total participant of Covid-19 patients, 18.6% were smokers (Table **1**).

The differences in the immune system of males and females may affect the capacity to fight against infection including Covid-19. Generally, females are more resistant to get infected as compared to males, and this may be due to several factors like sex hormones (estrogen) in females and relatively high expression of receptors for coronavirus (ACE2) in males[12]. The life style of males, such as higher levels of tobacco smoking may be another risk factor of higher prevalence of Covid-19 in males than females. Furthermore, females are more responsible to follow preventive measures for Covid-19 pandemic than males, like regular hand washing, applying face mask, and remains at home[12].

Socioeconomic status also had a prominent impact on Covid-19 prevalence; people who belongs to high or moderate socio-income groups followed Covid-19 preventive measures strictly, they tried to limit their activities and were more focused on nutritious diet, that's why they were at low risk. While, people who lives at poverty or below poverty line could not afford hospitalization or Covid-19 testing due to financial issues or lack of awareness. This group reported low prevalence that is possibly under reported. Group belonged to moderate socio-economic background was highly prevailed group because they not only they didn't follow Covid-19 precautionary measures but also are in majority among all population groups, they were tested more and that is why reported as high prevalent group[13, 14].

Nicotine has defensive potential against Covid-19, current smokers were at low risk of morbidity and mortality with Covid-19, but ex-smokers had higher severity of disease[15].

Moreover, analysis supports that severe Covid-19 patients showed deregulated lipid metabolism[16]. We observed more hypolipidemia, with all parameters of lipid profile in the patients with Covid-19 infection than the control group (Table **2**). We found that the High density lipid profile (HDL) levels were significantly low in patients with Covid-19 infection and our findings were in line with previous study conducted in China in 2020[17]. Several studies observed the decrease in all parameters of lipid, whereas strong association of low HDL level has been described with disease severity, hospitalization, duration and morbidity rate. Disparities in lipid profile are due to proteome deregularization in synthesis of Apo-lipoprotein[18-20].

We found that the Estimated glomerular filtration rate (eGFR) was significantly lower in Covid-19 patients than the healthy controls (Table **2**), which indicated that the Covid-19 infected causes kidney injury. Renal failure may be a key factor in the evolution of Covid-19 patients. Progression of acute disease is divided into three phases which include, early infection phase, pulmonary phase, and severe hyper-inflammatory phase[21, 22]. In early phase of Covid-19, the virus enters lung parenchyma and starts to multiply. During this phase, Renin-angiotensin-aldosterone system (RAAS) seems to play a significant role. Covid-19 virus interacts with RAAS via Angiotensin-converting enzyme 2 (ACE2). This enzyme physiologically causes RAAS activation and it also acts as receptor for Covid-19 virus. The ACE2 (Type I membrane protein) is generally expressed in kidneys, lungs, and heart and mostly linked with cardiac diseases[23]. It has been observed from latest research that ACE2 expression in kidneys is almost 100 times higher than lungs or any other organ. Hence, renal disorder may be caused by corona virus that enters the renal cells via ACE2-dependent pathway[24]. As the dyslipidemia and renal injury are serious disorders caused by Covid-19 infection, we linked the variations in parameters of lipid profile with eGFR in Covid-19 infected patients, and we surprisingly found a strong association (r^2= 0.57) between HDL and eGFR (Table **3**). Various studies supports the co-incidence of renal injuries and dyslipidemia in the patients infected with Covid-19[25-27], but first time we explored the link between parameters of lipid and eGFR. More studies are needed on large sample size and with imaging investigations of kidneys to reveal the association between lipids variations and renal injury in Covid-19 infected patients.

CONCLUSION

Hypolipidemia along with low HDL and decreased in eGFR were observed in Covid-19 patients and extent of kidney injury (decrease in eGFR) was positively associated with serum HDL.

LIMITATIONS OF THE STUDY

Sample size was small and gender related variations in lipid and eGFR were not considered separately. Further studies on large sample size and imaging investigations of kidneys are needed to demonstrate the relationship between lipids variations and kidney injury in Covid-19 patients. Physiologic variations of lipid and eGFR for both genders should be addressed clearly.

ETHICAL APPROVAL

Ethical approval was obtained from the Ethical review committee of The Children Hospital & Institute of Child Health, Multan, Pakistan.

CONFLICTS OF INTEREST

None.

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LIST OF ABBREVIATIONS

ACE2	Angiotensin-Converting Enzyme 2
ALI	Acute Lung Injury
AKI	Acute Kidney Injury
COVID	Corona Virus Disease
eGFR	estimated Glomerular Filtration Rate
HDL	High Density Lipoproteins
LDL	Low Density Lipoprotein
MDRD	Modification of Diet in Renal Disease
MERS	Middle East Respiratory Syndrome
nCoV	Novel Coronavirus
SARS-Cov2	Severe Acute Respiratory Syndrome coronavirus 2
RASS	Renin-Angiotensin-Aldosterone System
Trig	Triglyceride
T-Chol	Total Cholesterol
WHO	World Health Organization

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