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Hyperlipidemia in post-COVID patients; a unique observational follow-up study on lipid levels in post-COVID patients

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ABSTRACT

Aim: Alterations in plasma lipid levels have been shown to be correlated with the severity of infections due to various pathogens such as bacteria, viruses. In this study, we aimed to evaluate the lipid metabolism changes associated with disease severity and prognosis in hospitalized COVID-19 patients during and after (post-COVID) the disease.

Material and Method: Patients who were hospitalized in the COVID-19 wards between April 02, 2020, and November 20, 2020 and were then evaluated in the follow-up outpatient clinic were retrospectively searched.

Results: Lipid levels were present at the admission and follow-up for 95 patients. The mean (S.D) age was 48.49 (16.4), and 49(51.6%) were male. The mean (S.D) day between the admission and the first visit in the COVID-19 follow-up outpatient clinic was 27.8 (12.8). LDL-C (p=0.044), and HDL-C (p=0.004) levels were significantly lower in the severely ill group at the admission. Total cholesterol, LDL-C, HDL-C, and triglyceride levels on follow-up were significantly higher than those levels on the admission day (p<0.001). Delta (Follow up-Admission) levels LDL-C, total cholesterol and triglyceride levels were significantly high in patients who have received steroid therapy. Only delta LDL-C was significantly high in patients who require Intensive Care Unit.

Conclusions: Dyslipidemia is observed in COVID-19 patients both during the disease and in the post-COVID period. Our findings also support the evidence demonstrating that low LDL-C and/or HDL-C levels can increase the risk of developing severe infections, also in COVID-19. The dynamics of lipid profiles before/during and after the entire disease course should be monitorized.

Keywords: COVID-19, dyslipidemia, hyperlipidemia, post-COVID, long-COVID

INTRODUCTION

Although almost two years have been since the start of the Coronavirus Disease 2019 (COVID-19) pandemic, data on the pathophysiology, predictors of severity, and treatment of the disease are still incomplete. To date, thousands of reports have emerged on almost every aspect of COVID-19 and the literature is still growing with new pieces of evidence. However, we still have limited information regarding lipoproteins and COVID-19.

Acute infections have been shown to lead to significant alterations in metabolic regulation, including lipids and lipoproteins, which play a central role in the host immune response (1). The common lipid alterations include a decrease in total cholesterol (TC) and an increase in the concentration of triglyceride (TG) -rich lipoproteins. Additionally, low- and high-density lipoprotein - cholesterol (LDL-C and HDL-C, respectively), apolipoprotein-A1, and apolipoprotein-B levels decrease (1-3). The role of lipid levels as a marker of infection severity and prognosis has been investigated and HDL-C, apo-A1 and LDL-C have been shown as prognostic markers in patients with sepsis, pneumonia and other infections (4,5).

Alterations in lipid and lipoproteins in COVID-19 patients have been observed and dyslipidemia has been associated with the inflammatory response, disease severity and poor prognosis. LDL-C, TC and HDL-C concentrations significantly decreased in COVID-19 patients (6-10). Although most of the studies were in

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hospitalized patients, literature on lipid profiles during follow-up in discharged COVID-19 (post-COVID) patients is rare (11-12).

In this real life, observational follow-up study, we aimed to evaluate the association of lipid metabolism changes with disease severity and prognosis in hospitalized COVID-19 patients during and after the disease.

MATERIAL AND METHOD

The study was carried out with the permission of Hacettepe University Non-Interventional Clinical Researchs Ethics Committee (Date: 31.03.2020, Decision No: 20/353). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study Design and Population

This study was conducted in an accredited tertiary care hospital. A "COVID-19 follow-up outpatient clinic" was established in the initial stages of the pandemic to address and manage the clinical needs of non-critical COVID-19 adult patients after discharge (post-COVID). Patients who were hospitalized in the COVID-19 wards were scheduled a follow-up visit in the 2-4 weeks at the time of discharge.

Patients who were hospitalized in the COVID-19 wards between April 02, 2020, and November 20, 2020 and were then evaluated in the follow-up outpatient clinic were retrospectively searched from a prospectively formed database. Patients who had polymerase chain reaction (PCR) confirmed COVID-19 were screened. Those who had plasma lipid levels measured at the time of admission in the COVID-19 wards and in the COVID-19 follow-up outpatient clinic thereafter were included. As this was a retrospective study, there was no intervention to the management of the patients. Patients on statin treatment continued to take their drug while those who were not on statins were not initiated statin treatment during the study period.

The clinical severity of the patients was graded as mild, moderate or severe according to the World Health Organization (WHO) classification (13). Patients who were graded as critical at the time of admission and hospitalized directly to intensive care units (ICU) were not included.

Statistical Analysis

Statistical analysis was performed with IBM SPSS for Windows version 23 package. Normally distributed continuous data were summarized by mean±standard deviation (SD), while non-normally distributed continuous data were summarized by median [25-75th percentiles]. The Chi-square test or Fisher exact test were applied to detect the relation between categorical variables. Independent sample t-test or Mann Whitney U test was used to compare independent two groups in terms of numerical data. Within group differences were shown by Wilcoxon test. A 2-tailed p value of 0.05 was considered significant.

RESULTS

A total of 1105 adult patients with laboratory confirmed COVID-19 were hospitalized in COVID-19 wards. Plasma lipid levels of 108 patients were available at the time of admission, among whom 95 had been evaluated in the follow-up clinic and plasma lipid levels were available (**Figure 1**).

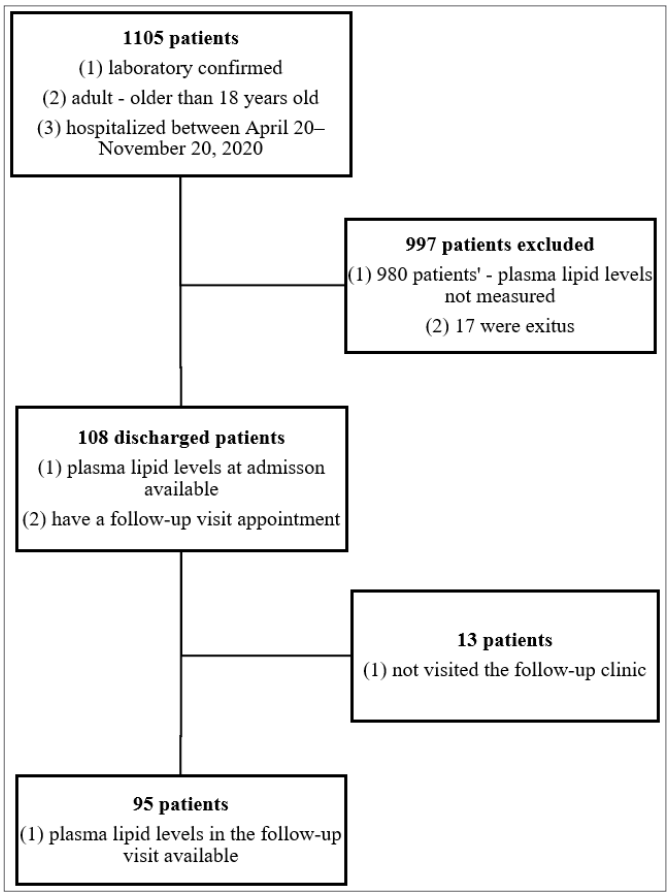

Figure 1. Flowchart of the patient selection

Baseline Characteristics and Plasm Lipid Values at the Time of Admission

The mean (SD) age of the patients was 48.5 (16.4) years, and 49 (51.6%) were male. The median length of stay (LoS) was 6 (IQR=5) days. Baseline characteristics of patients and plasma lipid levels at admission are given in **Table 1**.

The median time from symptom onset to hospital admission (on the day of venous sampling for lipid parameters) was 3 (IQR=4) days. The median (IQR) HDL-C, LDL-C, TC and TG levels were 38.1 (15.1), 106.8 (52), 168.2 (62.1) and 119.5 (89) mg/dL, respectively.

Table 1. Baseline characteristics of the patients and plasma lipid levels at the time of admission

	Total, n=95 (%)	HDL-C median (IQR), mg/dL	P	LDL-C median (IQR), mg/dL	P	Triglycerides median (IQR), mg/dL	P	Total cholesterol median (IQR), mg/dL	P
Age, years, mean (S.D.)	48.49 (16.4)								
Plasma lipid level, median (IQR)		38.1 (15.1)		106.8 (53)		119.5 (89)		168.2 (62.1)	
Sex, n (%)			<0.001		0.771		0.474		0.760
Female	46 (48.4)	45.2 (14.6)		112.85 (47.5)		126 (87)		167.8 (67.9)	
Male	49 (51.6)	34.2 (13.3)		98.9 (65.1)		114 (83)		168.6 (60)	
Smoking, n (%)			0.031		0.066		0.619		0.204
Never smokers	68 (71.6)	40.5 (16.8)		113.35 (51.9)		116 (87)		185.6 (64.3)	
Active smoker	15 (15.8)	34.5 (14.2)		91.7 (39.3)		112 (100)		149.3 (61.4)	
Ex-smoker	11 (11.6)	30.7 (14.0)		121.0 (56.0)		148.0 (65.0)		177.3 (66.7)	
Chronic diseases, n (%)									
Type 2 diabetes mellitus	29 (30.5)	34.95 (12.7)	0.011	111 (54.8)	0.599	151 (76)	0.001	184.6 (78.7)	0.357
Hypertension	35 (36.8)	37.0 (13.8)	0.108	111 (53)	0.666	137 (80)	0.026	166 (68.75)	0.693
Coronary artery disease	13 (13.7)	32.5 (11.8)	0.036	93.0 (34.0)	0.324	162 (77)	0.019	167.6 (54.18)	0.884
COPD	8 (8.4)	39.55 (17.8)	0.850	106.35 (65.3)	0.880	102.0 (79)	0.750	160 (92.73)	0.637
Medications, n (%)									
ACE/ARB	26 (27.4)	38.65 (14.2)	0.550	109 (48.4)	0.920	130.5 (58)	0.160	165.9 (66.9)	0.830
Metformin	18 (18.9)	34.5 (12.5)	0.018	103.95 (43.3)	0.595	148.0 (57)	0.029	169.2 (74.7)	0.800
Statin	8 (8.4)	27.3 (11.0)	0.006	89.5 (25.4)	0.142	158.0 (197)	0.198	147.6 (72.4)	0.232
Asetil salicylic acid	13 (13.4)	31 (22)	0.382	95.6 (38.5)	0.420	151 (92.0)	0.484	164.8 (61.9)	0.549
Beta-blocker	17 (17.9)	34.0 (14.0)	0.022	121.4 (66.5)	0.273	158 (113)	0.085	172.2 (83.35)	0.576
Calcium channel blockers	6 (6.3)	32.4 (10.1)	0.185	100.45 (78.7)	0.387	96.5 (153)	0.862	164.1 (108.3)	0.477
Disease severity, n (%)			0.004		0.044		0.161		0.091
Mild	55 (62.1)	40.0 (12.7)		106.6 (46.4)		112 (97)		161.7 (55.7)	
Moderate	26 (27.4)	38.65 (19.2)		130.3 (59.7)		128 (74)		203.2 (103.3)	
Severe	10 (10.5)	27.1 (5.9)		89.25 (39.8)		148 (86)		139.6 (57.7)	
Treatment, n (%)			0.351		0.110	85 (90)	0.352		0.062
No treatment	5 (5.3)	31.3 (13.4)		73.1 (60.1)				130.5 (62.1)	
Hydroxychloroquine	11 (11.6)	44.6 (7.9)		84.5 (62.5)		112 (73)		152.5 (69.5)	
Hydroxychloroquine + AZ	11 (11.6)	40.7 (15.1)		98.1 (39.0)		86 (52)		151.4 (51.6)	
Hydroxychloroquine + AZ + FAV	10 (10.5)	30.5 (22.5)		116.9 (66.3)		105 (61)		194.1 (81.5)	
Hydroxychloroquine + FAV	4 (4.2)	39.2 (33.8)		90.6 (41.1)		137 (112)		138.4 (78.7)	
Favipiravir (FAV)	54 (56.8)	38.1 (16.4)		113.3 (52.3)		74.5 (64)		186.5 (62.85)	
Corticosteroids add-on, n (%)	8 (8.4)	28.5 (28.8)	0.081	93 (77)	0.328	96 (100)	0.254	137.5 (89.2)	0.040
Intensive Care Unit requirement	10 (10.5)	29.2 (13.8)	0.010	93.6 (66.4)	0.524	126 (65)	0.746	155.2 (89.2)	0.389

S.D.; standard deviation, COPD; Chronic obstructive pulmonary disease, ACE/ARB; Angiotensin-converting enzyme inhibitors/Angiotensin receptor blockers, AZ; Azithromycin

Median HDL-C levels were significantly lower in males than females at admission (20.7 vs 45 mg/dL, respectively; p<0.001) and were higher in never smokers than remains (p=0.031). Among patients who had type 2 diabetes mellitus (T2DM) and coronary artery disease (CAD) median HDL-C levels were significantly lower than those who did not have T2DM (34.95 vs 41.25 mg/dL, p=0.011) and CAD.(32.55 vs 39.45 mg/dL, p=0.036). Median HDL-C levels were significantly lower in patients on metformin (34.5 vs 40.5 mg/dL, p=0.018) and beta-blocker (34.0 vs 40.5 mg/dL, p=0.022) therapy than those who did not take these medications.

Median TG levels were higher in patients with T2DM (151 vs 105 mg/dL, p=0.001), hypertension (HT) (139 vs 137 mg/dL, p=0.026) and CAD (162 vs 114 mg/dL, p=0.019) than those who did not have these diseases. In addition, also patients on metformin therapy had significantly higher median TG levels than those who did not use metformin (148 mg/dL vs 112 mg/dL, p=0.029).

There was no significant difference in median LDL-C and TC levels with regards to age, sex, smoking status, existing diseases and medications used.

Eight (8.4%) of the patients were on statin treatment and no new statin therapy was initiated in any patient during hospitalization. While there was no significant difference in median LDL-C, TG, and TC levels in patients on statin treatment, HDL-C (27.3 vs mg/dL vs 39.1, p=0.006) was significantly lower compared to non-users.

Severe patients had significantly lower HDL-C (28.7 mg/dL, p=0.004) and LDL-C (93 mg/dL, p=0.044) levels in comparison with mild and moderate patients. The patients who require ICU during hospitalization had also lower HDL-C (29.2 vs 39.9 mg/dL, p=0.010) than those who do not require ICU.

Plasma Lipid Values at the Time of Follow-up Visit

The mean (SD) time period between the admission and the first visit in the COVID-19 follow-up outpatient clinic was 27.8 (12.8) days.

The median (IQR) HDL-C, LDL-C, TC and TG levels were 45.5 (15.1), 125 (43.6), 207 (67.5) and 148 (153) mg/dL, respectively. Plasma HDL-C, LDL-C, TC and TG levels on follow-up were significantly higher than those on the admission (p<0.001) (**Figure 2**).

There was no significant difference in the increment in plasma lipid levels with regards to age, sex, existing diseases and medications used (**Table 2**). Delta (Follow up-Admission) TG (26.9 mg/dL, p= 0.030) and delta TC (25.5 mg/dL, p= 0.026) levels were significantly lower in never smokers than remains.

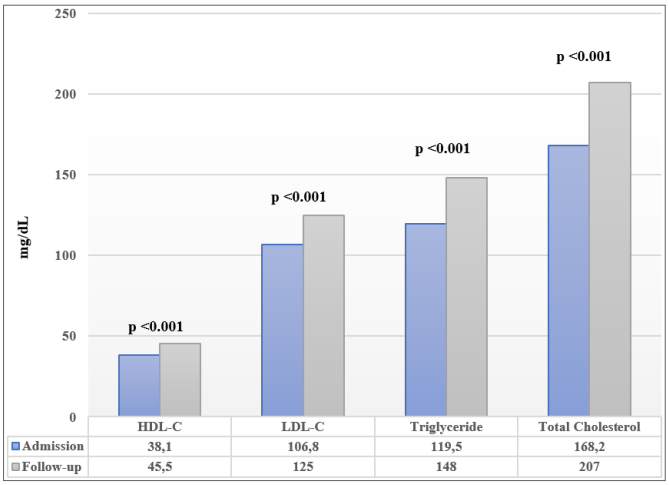

Figure 2. Plasma lipid levels of the study patients at the time of admission and in the follow-up visit

Table 2. Delta (the difference between the values in the follow up clinic and at the time admission) plasma lipid levels

	Total, n=95	Delta HDL-C median (IQR), mg/dL	P	Delta LDL-C median (IQR), mg/dL	P	Delta triglycerides median (IQR), mg/dL	P	Total cholesterol median (IQR), mg/dL	P
Age, years, mean (S.D.)	48.4 (16.4)								
Delta lipid levels, median (IQR)		5.9 (9.5)		16.3 (24.8)		59.3 (68.2)		35.1 (48.7)	
Sex, n (%)			0.821		0.540		0.203		0.24
Female	46 (48.4)	6.3 (11.5)		14.8 (26.5)		34.6 (100.2)		28.4 (40.2)	
Male	49 (51.6)	6.8 (7.5)		18 (23.2)		79.4 (213.2)		40.7 (54.6)	
Smoking, n (%)			0.690		0.372		0.030		0.026
Never smokers	68 (71.6)	6.1 (10.7)		14.1 (26.4)		26.9 (82.8)		25.5 (42)	
Active smokers	15 (15.8)	6.6 (5.4)		21.1 (16.1)		134.1 (343.1)		54.5 (67.2)	
Ex-smokers	11 (11.6)	8.8 (7.2)		23.4 (24)		132.1 (165.3)		58.7 (42.9)	
Chronic diseases, n (%)									
Type 2 diabetes mellitus	29 (30.5)	6.8 (6)	0.913	12.5 (24.9)	0.300	104.5 (288.3)	0.285	38.8 (64.1)	0.654
Hypertension	35 (36.8)	7.8 (6.6)	0.413	15.1 (23.5)	0.670	43.9 (116.9)	0.580	30.3 (38.1)	0.371
Coronary artery disease	13 (13.7)	12 (7.6)	0.685	14.9 (30.6)	0.840	53.9 (177.3)	0.915	3.1 (52.5)	0.873
COPD	8 (8.4)	6.6 (9.8)	0.889	0.2 (25)	0.098	193.7 (503.8)	0.029	42.5 (106.2)	0.682
Medications, n (%)									
ACE/ARB	26 (27.4)	7.2 (6.9)	0.698	14.9 (25.9)	0.708	61 (118.6)	0.942	34.1 (40.7)	0.899
Metformin	18 (18.9)	5.5 (5.6)	0.642	18.2 (12.5)	0.744	60.8 (115.2)	0.961	37.1 (40.1)	0.866
Statin	8 (8.4)	10.4 (5.4)	0.274	27.2 (33.2)	0.201	33 (164.3)	0.687	45.5 (59.9)	0.562
Asetil salicylic acid	13 (13.4)	8.7 (7.7)	0.443	22.9 (28.5)	0.350	59 (133.5)	0.998	45.2 (53.7)	0.490
Beta-blocker	17 (17.9)	7.3 (5.6)	0.784	15.1 (28.5)	0.802	98.2 (172)	0.373	41.8 (54.1)	0.580
Calcium channel blockers	6 (6.3)	7.8 (3.1)	0.470	20.3 (17.8)	0.696	159.8 (210.6)	0.136	60.1 (45.5)	0.195
Disease severity, n (%)			0.045		0.100		0.196		0.112
Mild	55 (62.1)	5.8 (8.8)		14.4 (21.7)		37.3 (47)		27.9 (37.3)	
Moderate	26 (27.4)	6.2 (11.7)		12.6 (31.4)		113.6 (282.5)		41.6 (68.9)	
Severe	10 (10.5)	14.1 (13.6)		37.5 (23.8)		52.5 (159.5)		62.2 (40.7)	
Treatment, n (%)			0.077		0.117		1.710		0.072
No treatment		14.7 (20.6)		26.6 (35.3)		78.2 (190.3)		128.8 (33.8)	
Hydroxychloroquine		2.4 (3.9)		2.50 (18.0)		24.7 (36.2)		169.7 (39.1)	
Hydroxychloroquine + AZ		5.9 (3.9)		15 (21)		28.5 (28.5)		162.1 (36.4)	
Hydroxychloroquine + AZ + FAV		12.3 (9.1)		28.3 (27)		202.7 (439.2)		190.9 (46.1)	
Hydroxychloroquine + FAV		11.5 (7.3)		33.8 (10.9)		14.7 (36.8)		154.7 (45)	
Favipiravir (FAV)		5.5 (9.7)		15.2 (24.9)		50.1 (115.5)		189 (50.2)	
Corticosteroids add-on, n (%)	8 (8.4)	6.2 (8.1)	0.912*	42.4 (16.9)	0.004*	173.4 (127)	0.042*	83.3 (37.2)	0.004*
Intensive Care Unit requirement	10 (10.5)	12.1 (14.2)	0.242*	29.6 (26.1)	0.045*	191 (435.7)	0.341*	79.9 (78.9)	0.096*

S.D.; standard deviation, COPD; Chronic obstructive pulmonary disease, ACE/ARB; Angiotensin-converting enzyme inhibitors/Angiotensin receptor blockers, AZ; Azithromycin, * T-test

There was no statistically significant increase in lipid profiles in terms of disease severity, except HDL-C. HDL-C increased more in the severely ill patient group (delta HDL-C; 14.1, p=0.045) which was lower on the admission in comparison with mild and moderate patients.

Antiviral treatment protocols for SARS-CoV-2 infection had no effects on the incremental values. Delta LDL-C (42.4 mg/dL, p=0.004), TG (173.4 mg/dL, p=0.042), and TC (83.3 mg/dL, p=0.004) levels were significantly higher in patients who have received corticosteroid therapy. Only delta LDL-C (29.6 mg/dL, p=0.045) was significantly higher in patients who require ICU during hospitalization.

Since the trend of increase in lipid levels was observed especially in patients with low lipid levels on admission, subgroups were created as above and below average lipids in the cohort, and lipid increment was re-examined according to the subgroups. In the patient group presenting with low LDL-C (<100 mg/dL) on admission, the increase in LDL was significantly higher than the rest of the cohort (Delta LDL (mean/SD); 25.5/22.3 mg/dL, p=0.001). In patients with low TG (<150 mg/dL), a similar pattern is observed only in TG levels, but it is not statistically significant (Delta Triglyceride (mean/SD); 91.14/222.151 mg/dL, p=0.075). Individuals presenting with low HDL-C (<40 mg/dL) showed an increase in all parameters during the post-COVID and it was statistically significant (Delta HDL-C (mean/S.D); 9.87/8.401 mg/dL, p=<0.001), (Delta LDL-C (mean/S.D); 25.49/21.06 mg/d, p=<0.001), (Delta TG (mean/S.D); 86.83/218.27 mg/dL, p=0.069), Delta TC (mean/S.D); 53.29/49.95 mg/dL, p=<0.001).

DISCUSSION

In this real-life study, we evaluated the lipid metabolism changes in 95 hospitalized COVID-19 patients during and after the disease and the association of lipid levels with disease severity and prognosis. Alterations in lipid levels have been seen both at admission (in acute phase) and after discharge (post-COVID). While lipid levels were generally lower at admission in patients with some existing diseases (T2DM, HT, CAD), taking drugs (metformin, beta-blockers, statins) and the severity of the disease, all lipid levels were found to increase significantly after COVID.

Lipids have a valuable function in the pathophysiology of viral pneumonia. Native surfactant lipids have been recognized recently as key regulators of lung inflammation that occupy a common ground at the intersection of tissue homeostasis, host defense, and biophysics (14). It has recently been shown that diet-induced dyslipidemia alters trafficking of immune cells to the lung in a manner that may have important implications for the pathogenesis of acute lung injury, asthma, pneumonia, and other lung disorders (15). Acute inflammation caused by viruses may result in dyslipidemia in patients, and lipid metabolism is known to play an important role in the host immune response. Studies showed alterations in lipid levels in acute Epstein-Barr virus (EBV) infection (lower concentrations of apoA-I, HDL-C, TC, LDL-C), cytomegalovirus (CMV) infection (lower HDL-C) and in dengue-positive patients (lower HDL-C and LDL-C) (16-18). Remarkably, while SARS patients had lower concentrations of apoA-I in the acute phase, altered lipid metabolism has been shown in recovered SARS-CoV-1 patients even 12 years after the infection (19-20).

Detailed information on the changes in lipid profiles during COVID-19 infection is lacking. Wang et al. (21) showed that loading cells with cholesterol from blood serum using the cholesterol transport protein apolipoprotein E (apoE) enhances the entry of pseudotyped SARS-CoV-2 and the infectivity of the virion. Wang et al. (21) suggest that cholesterol concomitantly traffics ACE2 to viral entry sites, where SARS-CoV-2 docks in order to properly exploit entry into cells. Therefore, decreased cholesterol levels in the blood may indicate severe loading of cholesterol in peripheral tissue and escalated SARS-CoV-2 infectivity. In a recent study, abnormal lipid metabolism has been demonstrated in cured COVID-19 patients when they were about to be discharged from the hospital, indicating that viral infection and drug treatment affected the patients' systemic metabolism (11). In the related study a high-resolution mass spectrometry-based lipidomic strategy was used to characterize the endogenous plasma lipids and most of the significantly changed lipids were up-regulated in cured patients. A positive correlation existed between the alteration of lipids and deterioration of the disease (11). In addition, several different hypotheses related to dyslipidemia in COVID-19 have been stated such as reduction of LDL-C biosynthesis with damage of liver function caused by SARS-CoV-2, dyslipidemia due to acute inflammation (inflammatory cytokines, such as TNF-alfa, IL-6, and IL-1 beta, have been shown to modify lipid composition), increased vascular permeability, degradation of lipids due to generally elevated free radical signals in infected host cells, leakage of LDL-C into alveolar spaces to form exudates and suppress the levels of many proteins related to cholesterol metabolism (22,23).

Recent studies have reported that hypolipidemia in hospitalized COVID-19 patients at the admission and the decrease in lipid levels were associated with the severity of the symptoms (6-10,12,14,15). In one of the first studies

early in the pandemic, patients with COVID-19 develop hypolipidemia as early as when they have mild symptoms and a reduction of lipid levels in patients with COVID-19 has an association with the severity of the symptoms (23).

In our study, median HDL-C was 38.1 (15.1) mg/dL and lower in males, and lower HDL-C was correlated with the severity of COVID-19 consistent with the literature. Severe patients and the patients who required intensive care during hospitalization had lower HDL-C at the time of admission. In a study from China, HDL-C was negatively correlated with c-reactive protein (CRP) and positively correlated with lymphocytes and found and independent association with the severity of COVID-19 as a predictor (8). In another study, low concentrations of HDL-C and apoA-I at admission were significantly associated with high concentrations of CRP, prolonged hospital stay and increased disease severity (6). In an observational study, low HDL-C in COVID-19 patients was correlated with a higher risk of developing severe events (9). In a cross-sectional study including 1411 hospitalized patients with COVID-19 and an available standard lipid profile prior (n:1305) or during hospitalization (n:297), patients with severe COVID-19 progression had lower HDL-C and higher TG levels before the infection (10). Median HDL-C levels were also significantly lower in patients with T2DM and CAD, which are poor prognostic factors for COVID-19 (24). On the other hand, while HDL-C and LDL-C levels upon ICU admission were low in severe COVID-19 patients, they were not found to be associated with poor outcomes (9).

In the present study, severe patients had also lower LDL-C at the admission. Lower serum levels of LDL-C and TC at admission were found as an independent predictor of LoS prolongation (2). In a small cohort of 21 patients, lipid profiles were checked before viral infections and during the course of their illness, and demonstrated that the degree of decreased LDL-C was associated with severity and mortality of the disease (25).

The most distinctive feature of this study is the follow-up lipid levels of the patients after discharge (post-COVID). All plasma lipid levels (HDL-C, LDL-C, TG and TC) on follow-up were significantly higher than those levels on the admission. The change in the pattern of increase in lipid levels was most evident in the severity of disease (HDL-C), corticosteroid use (LDL-C, TC, TG), and the need for ICU (LDL-C). Previous studies have demonstrated an increase in lipid levels during the course of the disease (in recovery phase and/or during hospitalization). In a study from China, in 68 severe cases, serum lipids were followed up three times with 5-10 days intervals during hospitalization. The median LoS was 29 days. The average levels of HDL-C, LDL-C, TG and TC, in 68 severe cases gradually and significantly increased during the following in the 2nd (except for LDL-C) and 3rd tests (both $p < 0.05$) (2). In another study, lipid profiles were analyzed on admission (day 1), on days 5–7 and days 15–17 after admission. From day 1 to day 15–17, TC, LDL-C, HDL-C and apoAI showed a slow upward trend in survivors, but maintained lower concentrations or showed a rapid downward trend in non-survivors (6). In a follow up study from China, LDL-C, HDL-C and TC were all significantly higher at follow-up than at the time of admission in severe/critical cases. LDL-C and TC levels were significantly higher at follow-up than at the time of admission in mild patients. The overall follow-up time was 100 days after discharge (12). In our study, HDL-C increased more in the severe patient group, although lower at presentation, confirming that HDL-C is a prognostic marker.

In our study delta (Follow up-Admission) LDL-C, TG and TC levels were significantly higher in patients who have received corticosteroid therapy. All patients were given 6 mg/day p.o dexamethasone totally for 10 days in accordance with the local guidelines (13). Although all of the patients receiving corticosteroids were in the severely ill group, it was remarkable that only LDL-C, TG and TC increased significantly. The increase in HDL-C, which is significant in severe patients, was not significant in patients receiving corticosteroids. This situation may also support that HDL-C may be a predictor associated with the pathogenesis of COVID-19.

The clinical meaning and consequences of low lipid levels on admission (during the disease period) and the increase in the recovery period (post-COVID) are unknown. It is not known whether the surge in lipid levels consists only of a reactive process or that it may be associated with endothelial damage and vascular events during the recovery period. Whether this is a reactive increase or the effect of reverting to the patient's basal lipid profiles is unknown.

Our study has some limitations. This is a single centered study. Although the results are consistent with the literature, the sample size is small. Although the lipid levels of the patients seemed to be low at admission, it would have been better to know the basal lipid levels before the disease.

CONCLUSION

This study is valuable in that it confirms the dyslipidemia seen in previous studies in COVID-19 patients, as well as being one of the first studies in the literature in terms of showing the course of dyslipidemia in the post-COVID period. Dynamics of lipid levels before, during and after the entire disease course in a large cohort of COVID-19 patients should be monitored for better characterization of dyslipidemia.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Hacettepe University Non-Interventional Clinical Researchs Ethics Committee (Date: 31.03.2020, Decision No: 20/353).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The author has no conflicts of interest to declare.

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Author Contributions: The author declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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