

LIPID PROFILE FOR PATIENTS WITH ACUTE COVID-19 ILLNESS AND ITS RELATION TO THE SEVERITY OF THE DISEASE. A SINGLE CENTER STUDY

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ABSTRACT

Background: Coronavirus disease-19 (COVID-19) is an acute respiratory illness caused by SARS-CoV-2, with a global impact since its emergence in Wuhan, China, in late 2019. The disease affects multiple organ systems and is transmitted primarily through respiratory droplets, with asymptomatic individuals contributing significantly to its spread. Dyslipidemia, inflammation, and immune responses have been linked to COVID-19 severity, highlighting the potential of lipid profiling as a prognostic tool. The study aims to assess the relationship between COVID-19 severity and lipid metrics in study subjects, including inflammatory markers. **Method:** This cross-sectional study at Al-Shifaa Isolation Center (January–June 2021) included 100 COVID-19 patients categorized into mild, moderate, and severe cases based on WHO criteria. Data on lipid profiles, inflammatory markers, and clinical severity were collected through questionnaires, CT scans, and blood analysis. **Results:** This study revealed statistically significant associations between COVID-19 severity and lipid profiles (TC, LDL, HDL, TG), inflammatory markers (CRP, S. Ferritin, D-dimer), CT scan severity, and BMI (p-values < 0.05). Severe cases exhibited lower lipid levels, higher inflammatory markers, and greater CT involvement. Gender also showed a significant association with disease severity (p = 0.045). **Conclusion:** In COVID-19, lower TC, LDL, and HDL values predict disease severity, according to this study. As S. Ferritin, D-dimer, and CRP levels rise, systemic inflammation may explain this connection. Severity associated substantially with CT scan results, and all patients had a mean BMI >25, suggesting ACE2 expression in adipose tissue increases infection risk. Severe illness was more common in women.

KEYWORDS: Lipid profile, acute COVID-19, severity.

INTRODUCTION

Coronavirus disease-19 (COVID-19) is an acute infectious respiratory illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Accurate diagnosis is crucial, as COVID-19 affects not only the respiratory system but also the gastrointestinal, nervous, and cardiovascular systems. Less typical manifestations, such as dermatologic or ophthalmic symptoms, can complicate diagnosis.^[1] At the end of December 2019, a cluster of pneumonia cases of unknown etiology was reported in Wuhan, China. Genetic studies identified the causative agent as a novel virus of the Coronaviridae family. Coronaviruses, which primarily infect birds and mammals, have previously caused zoonotic outbreaks like SARS-CoV in 2003 and MERS-CoV in 2012. Initially termed 2019-nCoV, the virus was later named SARS-CoV-2, with its associated disease named COVID-19. On March 12, 2020, the World Health Organization (WHO) declared COVID-19

a global pandemic.^[2,3] In Iraq, the first case was reported on February 24, 2020, in a student from Iran. Subsequent cases emerged among individuals with travel history to Iran, with local transmission increasing as testing capacities expanded. To control the outbreak, the Iraqi government implemented measures such as curfews, closure of public venues, and restrictions on inter-governorate travel.^[4] Globally, as of April 2, 2023, over 762 million confirmed cases and 6.8 million deaths have been reported, with Iraq contributing over 2.4 million cases. However, seroprevalence studies indicate that reported cases significantly underestimate the actual burden, suggesting a much higher rate of prior exposure.^[5,6] The COVID-19 outbreak shares characteristics with previous coronavirus outbreaks like SARS-CoV and MERS-CoV, particularly in zoonotic transmission and clinical features. However, phylogenetic analysis shows that SARS-CoV-2 has closer similarity to bat-derived coronaviruses (88–89%)

than to SARS-CoV (79%) or MERS-CoV (50%).^[7] The primary transmission route for SARS-CoV-2 is human-to-human via respiratory droplets and aerosols. Asymptomatic and pre-symptomatic individuals play a significant role in transmission, necessitating isolation and preventive measures to limit spread. Studies have demonstrated that the virus can survive on surfaces for varying durations, highlighting the importance of disinfection protocols.^[8,9] The clinical spectrum of SARS-CoV-2 infection ranges from asymptomatic cases to critical illness, with manifestations including fever, cough, and dyspnea. Severe cases are often associated with advanced age or comorbidities. Laboratory findings such as lymphopenia and elevated inflammatory markers, along with imaging studies, aid in diagnosis and severity assessment.^[10,11] Lipids play a pivotal role in viral pathogenesis and immune responses. Cholesterol in host cell membranes facilitates viral entry, while dyslipidemia has been linked to COVID-19 severity. Mechanisms include liver dysfunction, cytokine storms, and inflammation-induced alterations in lipid metabolism. Studies suggest that low levels of total cholesterol, LDL-C, and triglycerides are associated with severe COVID-19, making lipid profiling a potential tool for risk assessment.^[12,13]

Aim of the study to Evaluate the association of COVID-19 severity with changes in the lipid parameters in patients of the study including its association with different markers of inflammation.

Method

This single-center cross-sectional study was conducted at Al-Shifaa Isolation Center from January to June 2021, involving 100 COVID-19 patients who met the inclusion criteria and provided consent. Patients were classified into mild (n=25), moderate (n=43), and severe (n=32) categories based on the WHO COVID-19 clinical management protocol. Disease severity was correlated with serum lipid profiles and inflammatory markers.

Severity Classification

- Mild: Clinical symptoms without lung imaging abnormalities.

- Moderate: Fever and respiratory symptoms with lung imaging showing pneumonia; oxygen saturation $\geq 94\%$.
- Severe/Critical: Shortness of breath (RR $\geq 30/\text{min}$), oxygen saturation $\leq 93\%$, PaO₂/FiO₂ ≤ 300 mmHg, or requiring ICU care due to respiratory failure, shock, or multi-organ failure.

Inclusion Criteria: Adults diagnosed with COVID-19 pneumonia via RT-PCR from nasopharyngeal swabs or CT scan criteria were included.

Exclusion Criteria: Pregnancy and chronic medical conditions causing fatal acute organ injuries (e.g., stroke, acute coronary syndrome) were excluded.

Data Collection: Data were collected using a pre-prepared questionnaire covering socio-demographics, oxygen saturation, respiratory rate, lipid profile (TC, LDL, HDL, TG), BMI, and CT scan severity. A 5 mL fasting venous blood sample was taken for laboratory analysis.

Ethical Considerations: Oral informed consent was obtained from all participants.

Statistical Analysis: Data analysis was performed using SPSS-24. Results were expressed as frequencies, percentages, means, standard deviations, and ranges. ANOVA tested differences among quantitative variables, while Chi-square or Fisher's exact test was used for qualitative variables. Statistical significance was set at $p \leq 0.05$.

RESULTS

This study included 100 PCR-positive COVID-19 patients, 25 (25%) of whom had mild illness, 43 (43%) intermediate illness, and 32 (32%) seriously or critically sick. The average age was 38 ± 8 for light sickness, 61 ± 15 for intermediate illness, and 70 ± 8 for severe illness. Table (1) shows that the male-to-female ratio was 1.5:1, 3:2 in light sickness, 2:3.375 in moderate illness, and 1:2.55 in severe illness.

Table 1: The age and gender of patients with COVID-19 with all severity levels.

		Severity category					
		Mild		Moderate		Severe	
		Fr	%	Fr	%	Fr	%
Age group	30-39 YO	15	15%	5	5%	0	0%
	40-49 YO	6	6%	7	7%	0	0%
	50-59 YO	4	4%	7	7%	5	5%
	60-69 YO	0	0%	10	10%	9	9%
	70-79 YO	0	0%	9	9%	14	14%
	80-89 YO	0	0%	5	5%	4	4%
Age mean \pm SD (range)		38 \pm 8 (30-54)		61 \pm 15 (32-85)		70 \pm 8 (54-85)	
Sex	Male	15	15%	16	16%	9	9%
	Female	10	10%	27	27%	23	23%
Total		25	25%	43	43%	32	32%

Table 2 analyzed CT scan severity, lipid profiles, BMI, and inflammatory markers among COVID-19 patients with varying illness severities.

- CT Scan Severity: All patients with mild illness showed no lung involvement. Moderate cases mostly had moderate lung involvement (22%), while severe cases had predominantly severe lung involvement (20%).
- Lipid Profiles:
 - Total Cholesterol (TC): Highest in mild cases (254.9 ± 9.3), lower in moderate cases (196.3 ± 9.2), and lowest in severe cases (129.4 ± 7.52).
 - LDL: Highest in mild cases (175.8 ± 9.2), decreasing in moderate cases (117 ± 7.7), and lowest in severe cases (74 ± 6.3).
 - HDL: Highest in mild cases (44.4 ± 2.2), moderate cases (36.7 ± 2.7), and lowest in severe cases (29.6 ± 3.3).

- Triglycerides (TG): Highest in moderate cases (212.7 ± 64.3), followed by mild cases (173.7 ± 16.3), and lowest in severe cases (128.9 ± 29).
- BMI: Mild cases had the highest mean BMI (28.6 ± 3.5), followed by severe cases (27.6 ± 3.2) and moderate cases (26.2 ± 3.8).
- Inflammatory Markers:
 - CRP: Highest in severe cases (35.7 ± 8.6), moderate cases (12.3 ± 7.3), and lowest in mild cases (7.4 ± 5.3).
 - S. Ferritin: Highest in severe cases (1318.8 ± 442.9), moderate cases (1165 ± 475.5), and mild cases (981.6 ± 413.6).
 - D-dimer: Highest in severe cases (648.8 ± 172.2), with similar levels in mild (435.7 ± 130.6) and moderate cases (442.2 ± 114.9).

Table 2: COVID-19 Patient Characteristics by Severity.

Parameter	Mild	Moderate	Severe
CT Scan Severity	No lung involvement (25%)	Moderate (22%), Mild (16%)	Severe (20%), Moderate (12%)
Total Cholesterol (TC)	254.9 ± 9.3	196.3 ± 9.2	129.4 ± 7.52
LDL	175.8 ± 9.2	117 ± 7.7	74 ± 6.3
HDL	44.4 ± 2.2	36.7 ± 2.7	29.6 ± 3.3
Triglycerides (TG)	173.7 ± 16.3	212.7 ± 64.3	128.9 ± 29
BMI	28.6 ± 3.5	26.2 ± 3.8	27.6 ± 3.2
CRP	7.4 ± 5.3	12.3 ± 7.3	35.7 ± 8.6
S. Ferritin	981.6 ± 413.6	1165 ± 475.5	1318.8 ± 442.9
D-dimer	435.7 ± 130.6	442.2 ± 114.9	648.8 ± 172.2

Gender showed a statistically significant association with severity categories among patients of the study with p-value of 0.04 as shown in table number (3) below.

Table 3: The association of gender among all severity categories.

			Severity category			Total	Pearson chi-square	P-value
			Mild	Moderate	Severe			
Sex	Male	Fr	15	16	9	40	6.186	0.045*
		%	15.0%	16.0%	9.0%	40.0%		
	Female	Fr	10	27	23	60		
		%	10.0%	27.0%	23.0%	60.0%		
Total		Fr	25	43	32	100		
		%	25.0%	43.0%	32.0%	100.0%		
Significant p-value at 0.05 using a Chi-square test.								

Significant p-value at 0.05 using a Chi-square test.

Testing for the association of lipid profile tests among severity categories, using one-way ANOVA test showed a high statistically significant association between the

patients' severities with p-value of 0.001 among all for lipid profile test (TC, LDL, HDL and TG) as shown in table (4) below.

Table 4: The lipid profile test including testing for TC, LDL, HDL and TG levels of patients with COVID-19 association with all severity levels.

		Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum	F- test	P-value
					Lower Bound	Upper Bound				
TC	Mild	254.9	9.33	1.86	251.11	258.81	241	271	1466	0.001
	Moderate	196.3	9.24	1.40	193.51	199.19	182	212		

	Severe	129.4	7.52	1.30	126.69	132.12	117	145		
	Total	189.5	48.4	4.84	179.97	199.19	117	271		
LDL	Mild	175.8	9.24	1.85	172.06	179.70	161	191	1210	0.001
	Moderate	117.0	7.77	1.18	114.68	119.46	96	133		
	Severe	74.06	6.32	1.11	71.78	76.34	65	88		
	Total	118.0	39.1	3.91	110.25	125.77	65	191		
HDL	Mild	44.44	2.27	.455	43.50	45.38	40	48	194.1	0.001
	Moderate	36.74	2.70	.413	35.91	37.58	31	43		
	Severe	29.63	3.30	.585	28.43	30.82	25	38		
	Total	36.39	6.24	.625	35.15	37.63	25	48		
TG	Mild	173.7	16.3	3.27	166.95	180.49	140	210	39.5	0.001
	Moderate	212.7	64.3	9.81	192.92	232.52	110	390		
	Severe	128.9	29.0	5.14	118.49	139.45	100	210		
	Total	176.1	58.2	5.82	164.62	187.72	100	390		

For association of lipid profile with CT scan severity score, there was a high statistically significant association for them with p-value of 0.001 as shown in table (5) below.

Table 5: The association of lipid profile with CT scan severity score.

		Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum	F test	P-value
					Lower Bound	Upper Bound				
TC	Mild	233.32	28.697	4.48	224.26	242.37	186	271	132.3	0.001
	Moderate	190.71	18.881	3.85	182.74	198.68	136	211		
	Severe	137.57	22.920	3.87	129.70	145.44	117	210		
	Total	189.58	48.423	4.84	179.97	199.19	117	271		
LDL	Mild	153.22	30.161	4.71	143.70	162.74	96	191	102.7	0.001
	Moderate	114.21	10.384	2.12	109.82	118.59	86	130		
	Severe	79.37	16.362	2.76	73.75	84.99	65	125		
	Total	118.01	39.106	3.91	110.25	125.77	65	191		
HDL	Mild	41.32	4.725	.738	39.83	42.81	31	48	44.7	0.001
	Moderate	35.71	3.183	.650	34.36	37.05	27	42		
	Severe	31.09	4.680	.791	29.48	32.69	25	42		
	Total	36.39	6.246	.625	35.15	37.63	25	48		

For assessment of the inflammatory markers, there was a statistically significant association for CRP test levels with all severity categories with p-value of 0.001 as shown in table (6).

Table 6: The association between CRP test levels with all severity categories.

	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum	F test	P-value
				Lower Bound	Upper Bound				
Mild	7.455	5.37710	1.0754	5.2354	9.6745	.28	20.06	129.95	0.001
Moderate	12.37	7.36406	1.1230	10.1129	14.6455	1.06	30.90		
Severe	35.72	8.63467	1.5264	32.6128	38.8390	19.97	53.62		
Total	18.61	14.0121	1.4012	15.8388	21.3994	.28	53.62		

Similarly, there was a statistically significant association between S. Ferritin levels and severity of COVID-19 patients with p-value of 0.023 as shown in table (7) below.

Table 7: The association between S. Ferritin levels and severity of COVID-19 patients of the study.

	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum	F test	P-value
				Lower Bound	Upper Bound				
Mild	981.661	413.6	82.733	810.907	1152.41	334.71	1832.57	3.933	0.023

Moderate	1165.94	475.5	72.517	1019.59	1312.28	347.99	2277.33		
Severe	1318.88	442.9	78.305	1159.17	1478.58	537.14	2289.36		
Total	1168.81	463.6	46.366	1076.81	1260.81	334.71	2289.36		

Likewise, there was a statistically significant association between D. dimer levels and severity of COVID-19

patients with p-value of 0.001 as shown in table (8) below.

Table 8: The association between D. dimer levels and severity of COVID-19 patients of the study.

	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum	F test	P-value
				Lower Bound	Upper Bound				
Mild	435.71	130.601	26.12	381.802	489.620	143.25	694.69	24.491	0.001
Moderate	442.21	114.925	17.52	406.845	477.583	150.85	783.38		
Severe	648.83	172.250	30.44	586.733	710.939	272.62	1180.36		
Total	506.70	169.227	16.92	473.129	540.285	143.25	1180.36		

For association of BMI of the patients with severity level. One-way ANOVA test showed a statistically

significant association between all three groups with p-value of 0.026 as shown in table (9) below.

Table 9: The Body Mass Index of patients with COVID-19 with all severity levels.

		Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum	F test	P-value
					Lower Bound	Upper Bound				
BMI	Mild	28.6	3.535	.707	27.140	30.059	21.0	35.0	3.80	0.026
	Moderate	26.2	3.816	.581	25.058	27.407	20.0	32.0		
	Severe	27.6	3.127	.552	26.528	28.783	21.0	32.0		
	Total	27.2	3.637	.363	26.558	28.001	20.0	35.0		

DISCUSSION

This study found a significant association between lipid profile alterations and COVID-19 severity levels. A consistent trend of declining total cholesterol, LDL, and HDL levels with increasing disease severity was observed, with the lowest levels in severe cases. These findings align with studies from Mexico and Chen Q et al., which showed decreased lipid levels correlate with greater severity and prolonged hospital stays. Improvement in lipid levels during hospitalization was linked to better outcomes.^[14,15] The mechanism is likely multifactorial, including impaired liver function, systemic inflammation, and cytokine storms, similar to mechanisms proposed in HIV patients.^[16,17] The excessive immune response and pro-inflammatory cytokines impair lipid metabolism, exacerbate vascular permeability, and worsen inflammation.^[18,19] For triglycerides (TG), the study found the highest levels in moderately ill patients, with the lowest in severe cases. However, findings on TG levels have varied. Barman H et al. reported no significant difference across severity levels, while Sampedro-Nuñez M. observed increased TG levels in severe cases, suggesting demographic and sample variations may explain discrepancies.^[20,21] Elevated inflammatory markers such as CRP, ferritin, and D-dimer levels were significantly associated with severity, consistent with Sampedro-Nuñez M. and Huang I. et al., which reported their correlation with poor prognosis, increased mortality, and ICU admissions.

Excessive inflammation and a hypercoagulable state during cytokine storms can lead to complications such as microthrombi, sepsis, and multiorgan failure.^[21,22,23] Radiographic imaging further supported the association of lipid profile changes with disease severity. Patients with more severe CT scan involvement had lower lipid levels, echoing findings by Hu X. et al.^[24] BMI showed no significant association with severity in severe cases but was significantly different between mild and moderate cases. This contrasts with Mosaad YO et al., who found BMI correlates with increasing severity, likely due to differences in sample size and characteristics.^[25] However, the overall mean BMI above 25 across severity levels aligns with the proposed role of ACE2 expression in adipose tissue facilitating viral entry.^[26] A significant association between gender and severity was found, with more severe cases in females. This differs from Hu X. et al. and Barman H et al., who found no such association, possibly due to a higher female-to-male ratio in this study.^[20,24] In summary, lipid profile alterations, inflammatory markers, and CT severity are strongly associated with COVID-19 severity, highlighting their potential use in prognostication and management.

CONCLUSION

This study highlights the prognostic significance of lipid parameters in COVID-19, showing that lower TC, LDL, and HDL levels are associated with greater disease

severity. Systemic inflammation, indicated by elevated S. Ferritin, D-dimer, and CRP levels, likely contributes to this association. Increased severity correlated significantly with CT scan findings, and all patients had a mean BMI >25, suggesting a higher infection risk via ACE2 expression in adipose tissue. Female patients were more frequently diagnosed with severe disease than males.

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