

# Association of serum lipid profile ratios with disease severity and in-hospital outcome of patients with COVID-19

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## ABSTRACT

**Background:** The association of lipid ratios with the severity and hospital outcome of COVID-19 patients has been a topic of interest in the medical community. Lipids, particularly cholesterol and triglycerides, play a significant role in the human body, including cell membrane formation, energy storage and the regulation of various biological processes. The aim of this study was to assess the association of lipid ratio with the severity and hospital outcome of COVID-19 patients.

**Methods:** This observational study was carried out in COVID unit of Bangabandhu Sheikh Mujib Medical University (BSMMU) among hospital admitted COVID patients from March 2021 to February 2022.

**Results:** Total patients were 138 including 65.9% males. Majority (27.5%) were in the 41-50 age group. One third (31.2%) were clinically severe COVID-19. There was overall significant difference of lipid ratio in different severity except LDL/HDL group ( $p > 0.05$ ). The correlation coefficients of disease severity with TC/HDL ( $r_s = .338$ ), LDL/HDL ( $r_s = .289$ ) and TG/HDL ( $r_s = .444$ ). There was significant correlation between disease severity and lipid ratio having moderate correlation with TG/HDL and weak correlation with TC/HDL and LDL/HDL. The correlation coefficients between TC/HDL and hospital outcomes of use/development of rebreather ( $r_s = .217$ ), HFNC ( $r_s = .282$ ), ARDS ( $r_s = .307$ ), arrhythmia ( $r_s = .201$ ), HDU/ICU ( $r_s = .200$ ) and ventilator ( $r_s = .072$ ). There was significant correlation between TC/HDL and development of ARDS, use of rebreather and HFNC and no other significant correlation with other outcomes. The correlation coefficients between LDL/HDL and hospital outcomes of use/development of rebreather ( $r_s = .211$ ), HFNC ( $r_s = .132$ ), ARDS ( $r_s = .286$ ), arrhythmia ( $r_s = .106$ ), HDU/ICU ( $r_s = .064$ ) and ventilator ( $r_s = .028$ ). There was no significant correlation between LDL/HDL and hospital outcomes. The correlation coefficients between TG/HDL and hospital outcomes of use/development of rebreather ( $r_s = .427$ ), HFNC ( $r_s = .271$ ), ARDS ( $r_s = .502$ ), arrhythmia ( $r_s = .088$ ), HDU/ICU ( $r_s = .158$ ) and ventilator ( $r_s = .041$ ). There was significant correlation between TG/HDL and development of ARDS, also with use of rebreather and HFNC. No other significant correlation found with other outcomes.

**Conclusion:** From the findings of this current study, it can be concluded that lipid ratios are associated with disease severity and hospital outcome of COVID-19 patients. There was moderate association between disease severity and TG/HDL and weak association with TC/HDL and LDL/HDL. There was also association between TC/HDL and the development of ARDS and the use of HFNC and between TG/HDL and the development of ARDS, the use of rebreather, and HFNC.

**Key words:** lipid ratio, hospital outcome, COVID-19.

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## INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has significantly impacted global public health and the economy since its emergence in December 2019.<sup>1</sup> As of September 2021, over 200 million confirmed cases and more than 4 million deaths have been reported worldwide and these numbers continue to grow.<sup>2</sup> Identifying factors that influence the severity and hospital outcomes of COVID-19 patients is crucial for optimizing patient care and allocating medical resources efficiently. One such factor that has recently gained attention is the lipid ratio, which refers to the relative concentrations of different lipids in

the blood, such as total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and triglycerides (TG).<sup>3</sup> The lipid ratio is often used to assess an individual's risk of developing cardiovascular diseases (CVD).<sup>4</sup> For example, the TC/HDL-C, LDL-C/HDL-C and TG/HDL-C ratios are considered predictors of atherosclerosis, coronary heart disease and metabolic syndrome, respectively.<sup>5</sup> Emerging evidence suggests that dyslipidemia, may play a role in the pathogenesis of COVID-19.<sup>6</sup> In particular, SARS-CoV-2 has been shown to interact with lipid metabolism and signaling pathways, leading to alterations in lipid homeostasis that might contribute to the host immune response and viral replication.<sup>7</sup> Additionally, an imbalance in lipid metabolism has been associated with the overproduction of inflammatory cytokines, which may contribute to the cytokine storm observed in severe COVID-19 cases.<sup>8</sup> Cholesterol has been demonstrated to have a significant role in the entrance of the SARS-CoV-2 virus into cells and is a crucial component of the membranes of host cells and enveloped viruses.<sup>9</sup> The lipid rafts in the host cell membranes are constantly in contact with serum lipids, particularly low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C), which can affect how well a virus interacts with host cells and the severity of the ensuing illness. Nevertheless, the magnitudes of the associations between COVID-19 and TC, LDL-C and triglycerides (TG) are contradictory. Many investigations have found a link between COVID-19 severity and low blood levels of HDL-C.<sup>10,11</sup> Multiple studies have reported that COVID-19 patients with comorbidities like hypertension, diabetes and obesity, which are often accompanied by dyslipidemia, are more likely to experience severe outcomes, including intensive care unit (ICU) admission, mechanical ventilation or death.<sup>12-14</sup> This study aimed to explore the association of lipid ratios with the severity and in-hospital outcomes of COVID-19 patients.

## METHODS

This observational study was carried out in COVID unit of Bangabandhu Sheikh Mujib Medical University (BSMMU) among hospital admitted COVID patients from March 2021 to February 2022. Total 138 COVID-19

patients were enrolled in this study. All admitted patients were classified into mild, moderate, severe, critical illness as per national guideline.<sup>15</sup> Lipid ratios was calculated. Radiological assessment was also done in necessary cases. Then these patients were followed up during admission period to see any disease progression and hospital outcomes. Socio-demographic data (age, sex, BMI), clinical data (symptoms and signs) and data on chronic medical illness were collected in structured pre-designed data collection sheet. Data were analyzed with the help of SPSS, Microsoft excel and Graph pad prism software.

Inclusion criteria were age  $\geq 18$  with informed written consent, COVID-19 confirmed case by RT-PCR and/or radiological evidence suggestive of COVID-19. Exclusion criteria were patients with malignancy receiving chemo or radio therapy, patients with poorly controlled COPD, DPLD, bronchial asthma, pregnancy, high BMI ( $\geq 40$  kg/m<sup>2</sup>), ESRD and decompensate CLD.

## RESULTS

Total 138 patients were enrolled in this study with age from 21 to over 70 years and 27.5% were in the 41-50 years age group. There is a higher proportion of males (65.9%). The most common comorbidities were diabetes mellitus (DM) (52.2%), hypertension (HTN) (44.7%) and smoking (44.9%). Others are shown in Table I. There were 31 (22.5%) patients in mild group, 35 (25.4%) in moderate, 43 (31.2%) in severe and 29 (21.0%) in critical group.

Among them median (IQR) of TC/HDL in mild patients 3.96 (3.36-4.64), in moderate 4.79 (3.44-5.23), in severe 4.95 (4.07- 5.67) and in critical 5.77 (4.73-6.76); LDL/HDL in mild 1.93 (1.43-2.38), in moderate 2.17 (1.50-2.71), in severe 2.48 (1.97-2.79), and in critical 2.60 (2.10- 3.05); TG/HDL in mild 4.77 (3.21-6.06), in moderate 5.65 (4.23-7.00), in severe 9.33 (6.61-11.63), and in critical 9.15 (7.73-10.15). There was overall significant difference of lipid ratio in different severity except LDL/HDL group ( $p > 0.05$ ) (Table II).

The correlation coefficients of disease severity with TC/HDL ( $r_s$ )=.338, LDL/HDL ( $r_s$ )=.289 and TG/HDL ( $r_s$ )=.444. There was significant correlation between disease severity and lipid ratio having moderate correlation with

TG/HDL and weak correlation with TC/HDL and LDL/HDL (Table III).

The correlation coefficients between TC/HDL and hospital outcomes of use/development of rebreather ( $r_s$ )=.217, HFNC ( $r_s$ )=.282, ARDS ( $r_s$ )=.307, arrhythmia ( $r_s$ )=.201, HDU/ICU ( $r_s$ )=.200 and ventilator ( $r_s$ )=.072. There was significant correlation between TC/HDL and development of ARDS, use of rebreather and HFNC and no other significant correlation with other outcomes. The correlation coefficients between LDL/HDL and hospital outcomes of use/development of rebreather ( $r_s$ )=.211, HFNC ( $r_s$ )=.132, ARDS ( $r_s$ )=.286, arrhythmia ( $r_s$ )=.106, HDU/ICU ( $r_s$ )=.064 and ventilator ( $r_s$ )=.028. There was no significant correlation between LDL/HDL and hospital outcomes. The correlation coefficients between TG/HDL and hospital outcomes of use/development of rebreather ( $r_s$ )=.427, HFNC ( $r_s$ )=.271, ARDS ( $r_s$ )=.502, arrhythmia ( $r_s$ )=.088, HDU/ICU ( $r_s$ )=.158 and ventilator ( $r_s$ )=.041. There was significant correlation between TG/HDL and development of ARDS, also with use of rebreather and HFNC (Table IV).

**Table I.** Baseline characteristics of the study people (N=138)

Characteristics	Total	Percentage	
Age (year)	21-30	8	5.8
	31-40	24	17.4
	41-50	38	27.5
	51-60	29	21
	61-70	30	21.8
	>70	9	6.5
Gender	Male	91	65.9
	Female	47	34.1
BMI (Kg/m <sup>2</sup> )	Under weight	1	0.7
	Normal	80	58
	Over weight	45	32.6
	Obese	12	8.7
Comorbidities	Smoking	62	44.9
	DM	72	52.2
	HTN	63	44.7
	Asthma	10	7.2
	COPD	8	5.8
	IHD	21	15.2
	CKD	7	5.1
	CVD	11	8
	Malignancy	1	0.7
	Others	10	7.2

**Table II.** Frequencies (Median+ IQR) and comparison lipid ratio with different severity (N=138)

Metabolic markers	Mild	Moderate	Severe	Critical	P-value
TC/HDL	3.96(3.36-4.64)	4.79(3.44-5.23)	4.95(4.07-5.67)	5.77(4.73-6.76)	<0.05
LDL/HDL	1.93(1.43-2.38)	2.17(1.50-2.71)	2.48(1.97-2.97)	2.60(2.10-3.05)	<0.05>0.05
TG/HDL	4.77(3.21-6.06)	5.65(4.23-7.00)	9.33(6.61-11.63)	9.15(7.73-10.17)	<0.05

**Table III.** Correlation between disease severity and lipid ratio (N=138)

N=138	Pearson co-relation	TC/HDL	LDL/HDL	TG/HDL
Disease severity	Correlation Coefficient ( $r_s$ )	.338	.289	.444
	Sig. (2-tailed)	.000	.001	.000

Correlation is significant at the 0.01 level (2-tailed)

**Table IV.** Correlation between lipid ratio and hospital outcomes (N=138)

N=138	Pearson correlation	Rebreather	HFNC	ARDS	Arrhythmia	HDU/ICU	Ventilator
TC/HDL	Correlation Coefficient ( $r_s$ )	.217	.282	.307	.201	.200	.072
	Sig. (2-tailed)	.010	.001	.000	.018	.019	.402
LDL/HDL	Correlation Coefficient ( $r_s$ )	.211	.132	.286	.106	.064	.028
	Sig. (2-tailed)	.013	.122	.001	.218	.453	.748
TG/HDL	Correlation Coefficient ( $r_s$ )	.427	.271	.502	.088	.158	.041
	Sig. (2-tailed)	.000	.001	.000	.303	.065	.633

## DISCUSSION

The findings of this study indicate a significant association between lipid ratios and the severity of COVID-19, as well as some in-hospital outcomes. As the severity of the disease increased, so did the median values for TC/HDL, LDL/HDL and TG/HDL lipid ratios. There was overall significant difference of lipid ratio in different severity except LDL/HDL group ( $p > 0.05$ ). The correlation coefficients of disease severity with TC/HDL ( $r_s = .338$ ), LDL/HDL ( $r_s = .289$ ) and TG/HDL ( $r_s = .444$ ). There was significant correlation between disease severity and lipid ratio having moderate correlation with TG/HDL and weak correlation with TC/HDL and LDL/HDL. These findings are consistent with some previous studies that have investigated the relationship between lipid profiles and COVID-19 severity. For instance, Wei et al.<sup>16</sup> reported that dyslipidemia was a risk factor for severe COVID-19 and that lower levels of HDL cholesterol and higher levels of TG were associated with a higher risk of severe disease. Similarly, Hu et al.<sup>17</sup> found that lipid profiles, including reduced HDL cholesterol and elevated TG, were significantly associated with the severity of COVID-19. Furthermore, Fan et al.<sup>18</sup> demonstrated that elevated TC/HDL and TG/HDL ratios were independently associated with a higher risk of developing severe COVID-19. On the other hand, some studies have reported different findings. For example, Rahimibashar F et al.<sup>19</sup> found no significant association between lipid profiles and COVID-19 severity.<sup>4</sup> This discrepancy could be due to differences in study populations, sample sizes, and methods of data analysis. The correlation coefficients between TC/HDL and hospital outcomes of use/development of rebreather ( $r_s = .217$ ), HFNC ( $r_s = .282$ ), ARDS ( $r_s = .307$ ), arrhythmia ( $r_s = .201$ ), HDU/ICU ( $r_s = .200$ ) and ventilator ( $r_s = .072$ ). There was significant correlation between TC/HDL and development of ARDS, use of rebreather and HFNC and no other significant correlation with other outcomes. The correlation coefficients between LDL/HDL and hospital outcomes of use/development of rebreather ( $r_s = .211$ ), HFNC ( $r_s = .132$ ), ARDS ( $r_s = .286$ ), arrhythmia ( $r_s = .106$ ), HDU/ICU ( $r_s = .064$ ) and ventilator ( $r_s = .028$ ). There was no significant correlation between LDL/HDL and hospital outcomes. The correlation coefficients between TG/HDL and hospital outcomes of use/development of rebreather ( $r_s = .427$ ), HFNC ( $r_s = .271$ ), ARDS ( $r_s = .502$ ), arrhythmia ( $r_s = .088$ ), HDU/ICU ( $r_s = .158$

and ventilator ( $r_s = .041$ ). There was also a significant correlation between TC/HDL and the development of ARDS and the use of HFNC and between TG/HDL and the development of ARDS, the use of rebreather and HFNC. No significant correlation was observed between LDL/HDL and hospital outcomes. Alcántara-Alonso E et al.<sup>20</sup> demonstrated the positive association of TG/HDL-C ratio with LDH, the severity of disease, and the necessity of invasive mechanical ventilation in COVID-19 patients. In a study of Rohani-Rasaf M et al.<sup>21</sup>, they found that all lipid ratios and TyG index statistically are correlated with COVID-19 mortality.

## Limitations

This study was conducted in one center which is not representing our whole population. In this study, COVID-19 vaccination status was not validated against disease severity. There is variable gap between symptom onset and hospital admission/consultation, which may influence parameters level and the actual picture of disease progression. Time of lipid tests were also different. Repeated measurement of laboratory parameters were not taken for analysis in this study, which might show more precise results regarding the association of these markers with COVID-19 disease progression. Disease severity may vary along course of time of study with new variant like delta and omicron.

## Conclusion

From the findings of this current study, it can be concluded that lipid ratios are associated with disease severity and hospital outcome of COVID-19 patients. There was moderate association between disease severity and TG/HDL and weak association with TC/HDL and LDL/HDL. There was also association between TC/HDL and the development of ARDS and the use of HFNC, and between TG/HDL and the development of ARDS, the use of rebreather, and HFNC. Further study with larger sample size is recommended to have better understanding.

**Authors' contribution:** MAK, MNA, KMM, AAM planned the research. MNA collected data. KMM and AAM drafted the manuscript. MAK was the overall supervisor. All authors read and approved the final version for publication.

**Conflicts of interest:** Nothing to declare.

## REFERENCES

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. *New England Journal of Medicine* 2020 Jan 24; 382(8), pp.727–33.
2. World Health Organization. 2021. WHO Coronavirus (COVID-19) Dashboard. Retrieved from <https://covid19.who.int/>
3. Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation* 2019 Jun 18; 139(25):e1082-143.
4. Durrington P. Dyslipidaemia. *The Lancet* 2003 Aug 30; 362(9385):717-31.
5. Millán J, Pintó X, Muñoz A, Zúñiga M, Rubiés-Prat J, Pallardo LF, et al. Lipoprotein ratios: physiological significance and clinical usefulness in cardiovascular prevention. *Vascular Health and Risk Management* 2009 Sep 18;757-65. *Vasc Health Risk Manag* 2009;5:757-65.
6. Wei X, Zeng W, Su J, Wan H, Yu X, Cao X, et al. Hypolipidemia is associated with the severity of COVID-19. *Journal of Clinical Lipidology* 2020 May 1; 14(3):297-304.
7. Roncato R, Angelini J, Pani A, Talotta R. Lipid rafts as viral entry routes and immune platforms: A double-edged sword in SARS-CoV-2 infection? *Biochimica et Biophysica Acta (BBA)-Molecular and Cell Biology of Lipids* 2022 Mar 4;159140.
8. Delgado-Roche L, Mesta F. Oxidative Stress as Key Player in Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) Infection. *Arch Med Res* 2020; 51(5):384-7.
9. Song J, Ping LY, Duong DM, Gao XY, He CY, Wei L, et al. Native low density lipoprotein promotes lipid raft formation in macrophages. *Molecular Medicine Reports* 2016 Mar 1;13(3):2087-93.
10. Peng Y, Akmentin W, Connelly MA, Lund-Katz S, Phillips MC, Williams DL. Scavenger receptor BI (SR-BI) clustered on microvillar extensions suggests that this plasma membrane domain is a way station for cholesterol trafficking between cells and high-density lipoprotein. *Molecular Biology of The Cell* 2004 Jan;15(1):384-96.
11. Feingold KR. Lipid and lipoprotein levels in patients with COVID-19 infections. NIH, National Library of Medicine <https://www.ncbi.nlm.nih.gov/>.
12. Sun JT, Chen Z, Nie P, Ge H, Shen L, Yang F, et al. Lipid profile features and their associations with disease severity and mortality in patients with COVID-19. *Frontiers in Cardiovascular Medicine* 2020 Dec 4;7:584987.
13. Guan WJ, Liang WH, Zhao Y, Liang HR, Chen ZS, Li YM, et al. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. *European Respiratory Journal* 2020 May 1; 55(5). *Eur Respir J* 2020 May; 55(5): 2000547.
14. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet* 2020 Feb 15; 395(10223):497-506.
15. National Guidelines on Clinical Management of COVID-19. [https://covidlawlab.org/wp-content/uploads/2021/01/Bangladesh\\_2020.11.05\\_Guideline\\_National-Guidelines-on-Clinical-Management-of-COVID-19\\_EN.pdf](https://covidlawlab.org/wp-content/uploads/2021/01/Bangladesh_2020.11.05_Guideline_National-Guidelines-on-Clinical-Management-of-COVID-19_EN.pdf)
16. Wei X, Zeng W, Su J, Wan H, Yu X, Cao X, et al. Hypolipidemia is associated with the severity of COVID-19. *Journal of Clinical Lipidology* 2020 May 1; 14(3):297-304.
17. Hu X, Chen D, Wu L, He G, Ye W. Low serum cholesterol level among patients with COVID-19 infection in Wenzhou, China. China (February 21, 2020). 2020 Feb 21.  
Low Serum Cholesterol Level Among Patients with COVID-19 Infection in Wenzhou, China (February 21, 2020). Available at SSRN: <https://ssrn.com/abstract=3544826> or <http://dx.doi.org/10.2139/ssrn.3544826>
18. Fan J, Wang H, Ye G, Cao X, Xu X, Tan W, et al. Low-density lipoprotein is a potential predictor of poor prognosis in patients with coronavirus disease 2019. *Metabolism* 2020 Jun 1;107:154243.
19. Rahimibashar F, Sedighi L, Shahriary A, Reiner Z, Pourhoseingholi MA, Mirmomeni G, et al. Is there any association between plasma lipid profile and severity of COVID-19? *Clinical Nutrition ESPEN* 2022 Jun 1;49:191-6.
20. Alcántara-Alonso E, Molinar-Ramos F, González-López JA, Alcántara-Alonso V, Muñoz-Pérez MA, Lozano-Nuevo JJ, et al. High triglyceride to HDL-cholesterol ratio as a biochemical marker of severe outcomes in COVID-19 patients. *Clinical Nutrition ESPEN* 2021 Aug 1;44:437-44.
21. Rohani-Rasaf M, Mirjalili K, Vatannejad A, Teimouri M. Are lipid ratios and triglyceride-glucose index associated with critical care outcomes in COVID-19 patients? *PLoS One* 2022 Aug 1;17(8):e0272000.