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Dyslipidaemia and Its Underlying Mechanisms in Coronavirus Disease 2019 (COVID-19) Infection

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Abstract: Dyslipidaemia is a biochemical alteration connected to the pathology accompanying COVID-19 infection. Dyslipidaemia has been recognized as a common complication in COVID-19 infection exerting a significant effect on severity and mortality in COVID-19 infected patients. Disturbance of lipid profile in COVID-19 infection is diverse and shown to have various presentations. Inflammatory markers and acute phase reactants found to have a relation with the disrupted lipid profile during COVID-19 infection. The objective of this short review is to outline the altered lipid profile in COVID-19 infected patient, and to highlight the relationship between dyslipidaemia, inflammatory markers, severity and morbidity of COVID infection. The implemented methodology in this comprehensive short review is based on analysis of the recent published literature pertaining dyslipidaemia in COVID-19 infection. The core literature for this review is the published clinical studies and the case reports that studied the effects of COVID-19 infection on lipid profile. This review showed that low total cholesterol and high-density lipoprotein cholesterol (HDL-C) in addition to elevated low-density lipoprotein cholesterol (LDL-C) constitute the commonest altered lipid profile in COVID-19 infected patients. Lipid peroxidation, oxidative stress and inflammation are the postulated pathogenic mechanisms for dyslipidaemia during COVID-19 infection. However, the results about status of triglycerides (TG) in COVID-19 infection was non-conclusive. Further studies may be required to suite the lipidomic status of triglycerides in COVID-19 infected patients.

Keywords: COVID-19, Dyslipidaemia, Infection, Mechanism

1. Introduction

Dyslipidaemia is a common metabolic pandemic characterized by altered levels of cholesterol, triglycerides (TG), or both, in association with disturbed levels of related lipoproteins [1] The characteristic lipid profile of the clinically encountered dyslipidaemia is elevated TG and free fatty acids (FFA) levels, in addition to reduced high-density lipoprotein cholesterol (HDL-C) and elevated low-density lipoprotein cholesterol (LDL-C), small-dense LDL, and plasma apolipoproteins [2]. However, dyslipidaemia not necessarily to be in the former reported biochemical derangement. Dyslipidaemia refers to an abnormal lipid profile which may be an elevated or reduced plasma lipid parameters [1]. Dyslipidaemia is categorized as primary which is uncommon and secondary dyslipidaemia due to other conditions [3]. Dyslipidaemia is a well-known cause of mortality and morbidity having a negative impact on cardiovascular system and on other vital organs [4, 2]. Coronavirus disease 2019 (COVID-19) has been announced as a public health emergency and occupied an international concern due to the global disruption induced by its pandemic impact. Infection induced by COVID-19 is a multisystemic, involving biochemical, histological, and molecular pathology [5]. Dyslipidaemia is a biochemical alteration connected to the pathology accompanying COVID-19 infection. Dyslipidaemia has been recognized as a common

complication in COVID-19 infection exerting a significant effect on severity and mortality in COVID-19 infected patients [6]. This review aims to discuss the alteration of lipid profile and its underlying mechanisms in patients infected with COVID-19. Moreover, this review may add to the understanding of the link between dyslipidaemia, inflammatory markers and the severity of COVID-19 infection.

2. Alteration of Lipid Profile in COVID-19 Infection

Disturbance of lipid profile in cases of COVID-19 infection is diverse and shown to have various presentations. Early in the pandemic, some cohort studies analysed plasma lipidomic profile and reported high TG, VLDL (very low-density lipoprotein), TG-intermediate-density lipoproteins (TG-IDL), TG-LDL and TG-HDL [7]. Conversely to the former lipid profile presentation, total cholesterol reported to be low [8]. Various researches reported controversial results about TG level in COVID-19 infection. The author [9] reported a very extreme elevation of TG following an episode of COVID-19 infection and they attributed it to a transient reduction of lipoprotein lipase activity. The variable TG profile during COVID-19 infection may be explained by the disturbed physiology of TG metabolism due to dietary habit and loss of appetite that is encountered during COVID-19 infection. Moreover, TG commonly affected by treatment with certain medicines that are frequently used during severe acute respiratory distress induced by COVID-19 infection. A single-centre prospective observational cohort study, recruited 50 patients, 54% of them experienced COVID-19 induced acute respiratory syndrome, and received a continuous propofol administration, they showed elevated TG level [10]. Similarly, COVID-19 infected patients who received a high dose of glucocorticoids may experience hypertriglyceridemia due to the well-known metabolic effect of glucocorticoids on TG metabolism [11]. Tocilizumab, a drug prescribed for COVID-19 infected patient reported to induced hypertriglyceridemia [12].

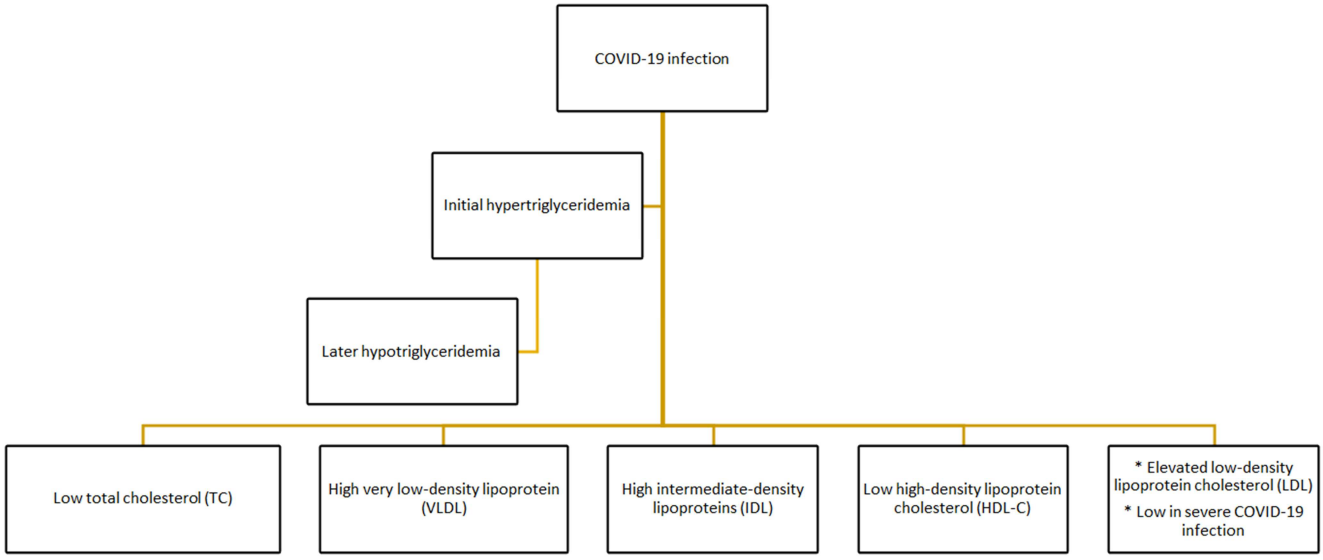

Figure 1. *Summarises the Lipid Alteration in COVID-19 Infection.*

3. Dyslipidaemia Is a Predictor for Risk and Severity in COVID-19 Infection

Abnormal reduction of lipid profile during COVID-19 has been recognised as a pathological hallmark for severity of COVID-19 infection. Dyslipidaemia reported as a mortality cause in cases of severe COVID-19 infection as well as a morbidity factor if it preceded COVID-19 insult [13]. Moreover, the severity of lipid alteration has been linked to the severity of COVID-19 infection [14]. Furthermore, dyslipidaemia detected at hospital admission found to be associated with adverse outcomes and high risk of mortality [15]. Risk of infection shown to have a link with the HDL-C and LDL-C. Subjects with a high HDL-C and low LDL-C reported to have a lower risk for acquiring COVID-19 infection [16]. The severity of cholesterol, LDL-C and HDL-C reduction, has been recognised as a predictive biological mark for the mortality in patients having COVID-19 with concurrent sepsis [17]. Twenty-two studies were analysed for lipid profile of COVID-19 infected patients they demonstrated lower blood cholesterol, LDL-C and HDL-C in patients admitted with severe COVID-19 infection and in those patients who died due to severe infection in comparison to patients had mild disease or recovered from the infection, but TG was not conclusive [18]. On the other hand, apolipoprotein A1 (ApoA1) has been recognised as an independent risk factor for severity of COVID-19 infection and may be used as a risk predictor [19]. Irreversible continuous reduction of LDL-C during course of COVID-19 infection may be considered as a poor prognostic sign and pending death [20].

4. Inter-Relation Between Lipid Profile and Inflammatory Markers in COVID-19 Infection

Inflammatory cytokine storm that is associated with COVID-19 infection involves production of a considerable number of inflammatory markers such as: Interleukins 1 (IL-1), 6 (IL-6), and 10 (IL-10), tumour necrosis factor alpha (TNF-α), and monocyte chemoattractant protein 1 (MCP1) [21]. Over production of proinflammatory cytokines linked to aggravation of acute respiratory distress syndrome (ARDS) and multiple organ failure [22]. Inflammatory markers and acute phase reactants found to have a relation with the disrupted lipid profile during COVID-19 infection. High TG level in COVID-19 patients was positively associated with high levels of inflammatory markers such as: CRP, procalcitonin, and D-dimer [15]. The COVID-19 positive patients, who had high HDL-C and low LDL-C, expressed low CRP [16, 23]. These findings are supported by the research [24], who reported a negative correlation between HDL-C and CRP. On the other hand, high serum level of LDL-C found to be associated with elevated levels of inflammatory cytokines [21]. Considering gender differences pertaining inflammatory markers, a study of 781 cases of both genders showed that men have a higher inflammatory marker response during COVID-19 infection in comparison to women. Men had a high CRP and IL-6 with associated poor outcome in comparison to women [25]. Inflammatory markers peaked a high level in dyslipidemic obese patients who had COVID-19 infection. Level of CRP and ESR as well as d-dimer found to be very high and linked to worse clinical outcomes [26].

5. Mechanisms of Dyslipidaemia in COVID-19 Infection

Coronavirus disease 2019 is the third discovered corona virus that infected human and caused severe acute respiratory syndrome hence the name is SARS-CoV-2 [27]. It is a single stranded virus with an envelope mainly of lipid structure [6]. All human cells are having a lipid bi-layer cell membrane, this facilitated the transportation of COVID-19 virus across the cells either by endocytosis or through membrane fusion [27].

Cell membrane cholesterol deficiency solely found to retard the viral efficiency [28]. Viral life cycle and the infected host response are markedly influenced by lipid metabolism [8]. Interestingly, experimentation demonstrated a significant reduction of entry of SARS-CoV-2 mimic particles into the cells when the cell membrane cholesterol was extracted [21]. Furthermore, drugs targeting cholesterol metabolism such as statins, have been hypothesized to have anti-COVID-19 effects. These drugs are able to reduce the synthesis of cholesterol, hence may exhibit direct antiviral activity by altering the target cell membrane cholesterol [29].

According to the research [24], serum HDL-C is an anti-inflammatory as well as a protective lipoprotein against lipid peroxidation, and is functioning as an immune modulator during COVID-19 infection. This is based on their study that showed dropped TC, LDL-C and HDL-C [24].

Lipid peroxidation, oxidative stress and inflammation are postulated as a pathogenic mechanism for dyslipidaemia during COVID-19 infection [30]. Studies reported a significant reduction of lipoprotein concentration as a consequence to acute inflammation and infection [31]. Recently, lipid peroxides, oxidized LDL (ox-LDL) and antibodies IgG against oxidized LDL (Ab-ox-LDL) reported to be in an altered status during active COVID-19 infection and linked to the disrupted lipid profile due to oxidative damage. Furthermore, the study showed suppressed endogenous antioxidants during acute severe COVID-19 infection [32].

Inflammatory process in COVID-19 has been linked with abnormal lipid profile through a correlational study, even though the underlying molecular mechanism not yet clarified [30]. Recent intensive work showed that during COVID-19 infection; lipid peroxidation may be responsible for hyperinflammatory status activation through NLRP3 (NOD-, LRR- and pyrin domain-containing protein 3) inflammasome signaling pathway [23]. Likewise, low cholesterol level during COVID-19 infection could be explained by the oxidative modification of lipoproteins [30].

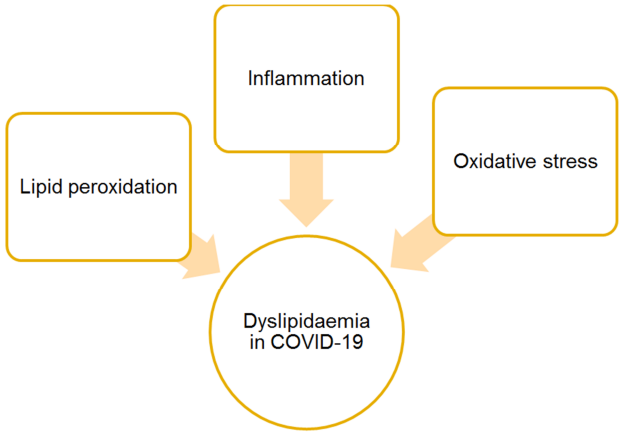

Figure 2. *Summarises the Underlying Pathogenic Mechanisms of Dyslipidaemia in COVID-19 Infection.*

6. Conclusion

Altered lipid profile has been recognized as one of the commonest biochemical complications of COVID-19 infection. Low total cholesterol and HDL-C in addition to elevated LDL-C constitute the commonest altered lipid profile in COVID-19 infected patients. Serum TG is controversial may be hyper- or hypo-triglyceridemia. The underlying pathological mechanism of dyslipidaemia in COVID-19 infection is an interplay between oxidative stress, lipid peroxidation and inflammation. Severity of lipid profile alteration is interconnected with the severity of COVID-19 infection and is a predictor for the clinical outcomes. Further studies may be required to suite the status of TG in COVID-19 infection.

References

[1] Berberich, A. J., & Hegele, R. A. (2022). A Modern Approach to Dyslipidemia. *Endocrine Reviews*, *43* (4), 611–653. https://doi.org/10.1210/endrev/bnab037

[2] Klop, B., Elte, J. W. F., & Cabezas, M. C. (2013). Dyslipidemia in Obesity: Mechanisms and Potential Targets. *Nutrients*, *5* (4), 1218–1240. https://doi.org/10.3390/nu5041218

[3] Pirillo, A., Casula, M., Olmastroni, E., Norata, G. D., & Catapano, A. L. (2021). Global epidemiology of dyslipidaemias. *Nature Reviews Cardiology*, *18* (10), 689–700. https://doi.org/10.1038/s41569-021-00541-4

[4] Cho, L. (2020). A practical approach to the cholesterol guidelines and ASCVD prevention. *Cleveland Clinic Journal of Medicine*, *87* (5), 15–20. https://doi.org/10.3949/ccjm.87.s1.02

[5] Patel, P., Decuir, J., Abrams, J., Campbell, A. P., Godfred-Cato, S., & Belay, E. D. (2021). Clinical Characteristics of Multisystem Inflammatory Syndrome in Adults: A Systematic Review. *JAMA Network Open*, *4* (9), 1–15. https://doi.org/10.1001/jamanetworkopen.2021.26456

[6] Forchette, L., Sebastian, W., & Liu, T. (2021). A Comprehensive Review of COVID-19 Virology, Vaccines, Variants, and Therapeutics. *Current Medical Science*, *41* (6), 1037–1051. https://doi.org/10.1007/s11596-021-2395-1

[7] Bruzzone, C., Bizkarguenaga, M., Gil-Redondo, R., Diercks, T., Arana, E., García de Vicuña, A., … Millet, O. (2020). SARS-CoV-2 Infection Dysregulates the Metabolomic and Lipidomic Profiles of Serum. *IScience*, *23* (10). https://doi.org/10.1016/j.isci.2020.101645

[8] Casari, I., Manfredi, M., Metharom, P., & Falasca, M. (2021). Dissecting lipid metabolism alterations in SARS-CoV-2. *Progress in Lipid Research*, *82* (January), 101092. https://doi.org/10.1016/j.plipres.2021.101092

[9] Fijen, L. M., Grefhorst, A., Levels, J. H. M., & Cohn, D. M. (2021). Severe acquired hypertriglyceridemia following COVID-19. *BMJ*, *14* (11), 2–5. https://doi.org/10.1136/bcr-2021-246698

[10] Kenes, M. T., McSparron, J. I., Marshall, V. D., Renius, K., & Hyzy, R. C. (2020). Propofol-Associated Hypertriglyceridemia in Coronavirus Disease 2019 Versus Noncoronavirus Disease 2019 Acute Respiratory Distress Syndrome. *Critical Care Explorations*, *2* (12), e0303. https://doi.org/10.1097/cce.0000000000000303

[11] Dunford, E. C., & Riddell, M. C. (2016). The metabolic implications of glucocorticoids in a high-fat diet setting and the counter-effects of exercise. *Metabolites*, *6* (4). https://doi.org/10.3390/metabo6040044

[12] Giles, J. T., Sattar, N., Gabriel, S., Ridker, P. M., Gay, S., Warne, C., … Fleming, T. R. (2020). Cardiovascular Safety of Tocilizumab Versus Etanercept in Rheumatoid Arthritis: A Randomized Controlled Trial. *Arthritis and Rheumatology*, *72* (1), 31–40. https://doi.org/10.1002/art.41095

[13] Zuin, M., Rigatelli, G., Bilato, C., Cervellati, C., Zuliani, G., & Roncon, L. (2021). Dyslipidaemia and mortality in COVID-19 patients: a meta-analysis. *Oxford University Press*, *114* (6), 390–397. https://doi.org/10.1093/qjmed/hcab071

[14] Feingold, K. R., & Grunfeld, C. (2022). *The Effect of Inflammation and Infection on Lipids and Lipoproteins*. *Endotext*. South Dartmouth: MDText.com, Inc. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/26561701

[15] Bellia, A., Andreadi, A., Giudice, L., De Taddeo, S., Maiorino, A., D'ippolito, I., … Lauro, D. (2021). Atherogenic dyslipidemia on admission is associated with poorer outcome in people with and without diabetes hospitalized for covid-19. *Diabetes Care*, *44* (9), 2149–2157. https://doi.org/10.2337/dc20-2838

[16] Chidambaram, V., Kumar, A., Majella, M. G., Seth, B., Sivakumar, R. K., Voruganti, D., … Mehta, J. L. (2022). HDL cholesterol levels and susceptibility to COVID-19. *EBioMedicine*, *82*, 104166. https://doi.org/10.1016/j.ebiom.2022.104166

[17] Guirgis, F. W., Black, L. P., Henson, M., Labilloy, G., Smotherman, C., Hopson, C., … Reddy, S. T. (2021). A hypolipoprotein sepsis phenotype indicates reduced lipoprotein antioxidant capacity, increased endothelial dysfunction and organ failure, and worse clinical outcomes. *Critical Care*, *25* (1), 1–13. https://doi.org/10.1186/s13054-021-03757-5

[18] Zinellu, A., Paliogiannis, P., Fois, A. G., Solidoro, P., Carru, C., & Mangoni, A. A. (2021). Cholesterol and Triglyceride Concentrations, COVID-19 Severity, and Mortality: A Systematic Review and Meta-Analysis With Meta-Regression. *Frontiers in Public Health*, *9* (August), 1–14. https://doi.org/10.3389/fpubh.2021.705916

[19] Zhu, Z., Yang, Y., Fan, L., Ye, S., Lou, K., Hua, X., … Gao, G. (2020). A Preliminary Study on Blood Lipid Profile in Patients with COVID-19, *14 August*, 1–18.

[20] Fan, J., Wang, H., Ye, G., Cao, X., Xu, X., Tan, W., & Zhang, Y. (2020). Letter to the Editor: Low-density lipoprotein is a potential predictor of poor prognosis in patients with coronavirus disease 2019. *Metabolism: Clinical and Experimental*, *107* (January). https://doi.org/10.1016/j.metabol.2020.154243

[21] Khatchadourian, C., Sisliyan, C., Nguyen, K., Poladian, N., Tian, Q., Tamjidi, F., … Venketaraman, V. (2021). Hyperlipidemia and obesity's role in immune dysregulation underlying the severity of covid-19 infection. *Clinics and Practice*, *11* (4), 694–707. https://doi.org/10.3390/clinpract11040085

[22] Ragab, D., Salah Eldin, H., Taeimah, M., Khattab, R., & Salem, R. (2020). The COVID-19 Cytokine Storm; What We Know So Far. *Frontiers in Immunology*, *11* (June), 1–4. https://doi.org/10.3389/fimmu.2020.01446

[23] Lage, S. L., Amaral, E. P., Hilligan, K. L., Laidlaw, E., Rupert, A., Namasivayan, S., … Sereti, I. (2022). Persistent Oxidative Stress and Inflammasome Activation in CD14highCD16− Monocytes From COVID-19 Patients. *Frontiers in Immunology*, *12* (January), 1–18. https://doi.org/10.3389/fimmu.2021.799558

[24] Hu, X., Chen, D., Wu, L., He, G., & Ye, W. (2020). Declined serum high density lipoprotein cholesterol is associated with the severity of COVID-19 infection. *Clinica Chimica Acta*, *510*, 105–110. https://doi.org/10.1016/j.cca.2020.07.015

[25] Lau, E. S., McNeill, J. N., Paniagua, S. M., Liu, E. E., Wang, J. K., Bassett, I. V., … Ho, J. E. (2021). Sex differences in inflammatory markers in patients hospitalized with COVID-19 infection: Insights from the MGH COVID-19 patient registry. *PLoS ONE*, *16* (4 April), 1–9. https://doi.org/10.1371/journal.pone.0250774

[26] McNeill, J. N., Lau, E. S., Paniagua, S. M., Liu, E. E., Wang, J. K., Bassett, I. V., … Ho, J. E. (2021). The role of obesity in inflammatory markers in COVID-19 patients. *Obesity Research & Clinical Practice*, 96–99.

[27] Liu, Y., Pan, Y., Yin, Y., Chen, W., & Li, X. (2021). Association of dyslipidemia with the severity and mortality of coronavirus disease 2019 (COVID-19): a meta-analysis. *Virology Journal*, *18* (1), 1–11. https://doi.org/10.1186/s12985-021-01604-1

[28] Abu-Farha, M., Thanaraj, T. A., Qaddoumi, M. G., Hashem, A., Abubaker, J., & Al-Mulla, F. (2020). The role of lipid metabolism in COVID-19 virus infection and as a drug target. *International Journal of Molecular Sciences*, *21* (10). https://doi.org/10.3390/ijms21103544

[29] Garg, H., & Khanna, P. (2021). Covid and cholesterol (C & C): Something to worry about or much ado about nothing? *Trends in Anaesthesia and Critical Care Journal*, *36* (2021), 39–40.

[30] Aparisi, Á., Martín-Fernández, M., Ybarra-Falcón, C., Gil, J. F., Carrasco-Moraleja, M., Martínez-Paz, P., … Tamayo-Velasco, Á. (2022). Dyslipidemia and Inflammation as Hallmarks of Oxidative Stress in COVID-19: A Follow-Up Study. *International Journal of Molecular Sciences*, *23* (23). https://doi.org/10.3390/ijms232315350

[31] Feingold, K. R. (2021). Lipid and Lipoprotein Levels in Patients with COVID-19 Infections. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/33237691

[32] Pincemail, J., Cavalier, E., Charlier, C., Cheramy–bien, J. P., Brevers, E., Courtois, A., … Rousseau, A. F. (2021). Oxidative stress status in covid-19 patients hospitalized in intensive care unit for severe pneumonia. A pilot study. *Antioxidants*, *10* (2), 1–12. https://doi.org/10.3390/antiox10020257