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Dyslipidemia is associated with severe coronavirus disease 2019 (COVID-19) infection

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ABSTRACT

Background and aims: The number of positive and death cases from coronavirus disease 2019 (COVID-19) is still increasing. The identification of risk factors for severe outcomes is important. Dyslipidemia has been shown as a long-known risk factor for cardiovascular disease. The aim of this study is to analyze the potential association between dyslipidemia and the severity of COVID-19 infection.

Methods: We systematically searched the PubMed database using specific keywords related to our aims until July 9th, 2020. All articles published on COVID-19 and dyslipidemia were retrieved. Statistical analysis was done using Review Manager 5.4 software.

Results: A total of 7 studies with a total of 6922 patients were included in our analysis. Our meta-analysis showed that dyslipidemia is associated with severe COVID-19 infections [RR 1.39 (95% CI 1.03–1.87), p = 0.03, I² = 57%, random-effect modelling].

Conclusion: Dyslipidemia increases the risk of the development of severe outcomes from COVID-19 infections. Patients with dyslipidemia should be monitored closely to minimize the risk of COVID-19.

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Coronavirus disease 2019 (COVID-19) is a pandemic disease that has been caused a significant burden in all aspects of life, especially health and economics. The number of positive and death cases is still increasing until now. In this meantime, identification of the factors that involve in the development of the severe disease is very important to enable stratification of risk, optimize the reallocation of hospital resources, and guide public health recommendations and interventions. Dyslipidemia has long been established as one of the risk factors for cardiovascular disease. A previous study by Saballs et al. [1] has also shown that one of the components in dyslipidemia, which is high-density lipoprotein (HDL) can predict the presence of respiratory disease and the clinical outcome of community-acquired pneumonia (CAP). However, the association between dyslipidemia and COVID-19 has not yet been established. This study aims to analyze the potential association between dyslipidemia and the severity of COVID-19 infection.

We conducted a systematic search of the literature on PubMed using the keywords “dyslipidemia” OR “hyperlipemia” OR “clinical characteristics” OR “comorbidities” OR “risk factors” AND “coronavirus disease 2019” OR “COVID-19”, until the present time (July 9th, 2020) with language restricted to English only. The title, abstract, and full text of all articles identified that matched the search criteria were assessed, and those reporting the rate of dyslipidemia in COVID-19 patients with a clinically validated definition of “severe disease” were included in this meta-analysis. The references of all identified studies were also analyzed (forward and backward citation tracking) to identify other potentially eligible articles.

A meta-analysis was performed using Review Manager 5.4 (Cochrane Collaboration) software. Dichotomous variables were calculated using the Mantel-Haenszel formula with random-effects models. We used the I² statistic to assess the heterogeneity, value of <25%, 25–50%, and >50% considered as low, moderate, and high degrees of heterogeneity, respectively. The effect estimate was reported as risk ratio (RR) along with its 95% confidence intervals (CIs) for dichotomous variables, respectively. P-value was two-tailed, and the statistical significance set at <0.05.

A total of 950 records were obtained through systematic electronic searches and other ways. After screening titles, abstracts, and full texts, 7 studies [2–8] with a total of 6922 COVID-19 patients...
were included in the meta-analysis. The essential characteristics of included studies are summarized in Table 1, whilst the individual and pooled RRs for dyslipidemia predicting severe COVID-19 is shown in Fig. 1. Our pooled analysis showed a significant association of dyslipidemia with severe COVID-19, with high heterogeneity [RR 1.39 (95% CI 1.03–1.87), p = 0.03, I² = 57%, random-effect modelling].

Based on our meta-analysis of available data, dyslipidemia seems to be associated with an enhanced risk of severe COVID-19 infection. Several reasons can be proposed to explain this result. First, patients with dyslipidemia have high levels of low-density lipoprotein (LDL). This LDL can have interaction with macrophages in atherosclerotic plaques that lead to an increase in inflammatory gene expression. Human atherosclerotic plaques express increased levels of cytokines and chemokines that are dependent on MYD88-mediated signaling via various TLRs, especially TLR2, where one of its most important ligands are modified forms of LDL [9]. Moreover, LDL accumulation will give rise to cholesterol crystal formation in macrophages that lead to inflammation and foam cell formation. Inflammation in macrophages will then promote the secretion of the proinflammatory cytokines such as IL-1B and TNF-α which then enhances inflammation and foam cell formation.

Fig. 1. Forest plot that demonstrates the association of dyslipidemia with severe COVID-19 disease.

Table 1
Characteristics of included studies.

| Study or Subgroup | Dyslipidemia Events | Non-Dyslipidemia Events | Total | Weight | M-H, Random, 95% CI | Risk Ratio M-H, Random, 95% CI |
|-------------------|----------------------|-------------------------|-------|--------|---------------------|--------------------------------|
| Chang M et al. 2020 | 2 6 11 | 205 | 4.8 | 6.21 [1.75, 22.30] |
| Chen Q et al. 2020 | 1 1 42 | 144 | 9.4 | 2.56 [1.11, 5.92] |
| Petrelli C et al. 2020 | 465 1157 525 | 1572 | 36.4 | 1.20 [1.09, 1.33] |
| Simonnet A et al. 2020 | 24 34 61 | 90 | 29.4 | 1.04 [0.80, 1.35] |
| To W et al. 2020 | 2 2 8 | 21 | 11.6 | 2.16 [1.04, 4.48] |
| Zhang C et al. 2020 | 1 3 23 | 77 | 3.0 | 1.12 [0.22, 5.73] |
| Zhang J et al. 2020 | 2 7 56 | 133 | 5.4 | 0.68 [0.21, 2.23] |
| Total (95% CI) | 1210 | 2242 | 100.0% | 1.39 [1.03, 1.87] |

Heterogeneity: Tau² = 0.06, Chi² = 14.09, df = 6 (p = 0.03); I² = 57%

Test for overall effect: Z = 2.15 (p = 0.03)

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Declaration of competing interest

The authors declare no conflict of interest regarding this article.

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