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

**Keywords:**

Coronavirus disease 2019  
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Dear Editor,

Coronavirus disease 2019 (COVID-19) has caused significant health burden across the world. Identification of factors contributing to severe disease is important to enable stratification of risk, optimize the reallocation of hospital resources, and guide public health recommendations and interventions. Unfortunately, until now, no study provides clear evidence regarding the link between thyroid disease and COVID-19. This article aims to explore the potential association between thyroid disease and the severity of COVID-19 infection.

A search of the literature was conducted on Google scholar using the keywords “thyroid disease” OR “hyperthyroid” OR “hypothyroid” OR “clinical characteristics” OR “comorbidities” OR “risk factors” AND “coronavirus disease 2019” OR “COVID-19”, between 2019 and present time (July 18th, 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 thyroid disease in COVID-19 patients with a clinically validated definition of “severe disease” were included in this meta-analysis.

A meta-analysis was performed using Review Manager 5.4 (Cochrane Collaboration) software. Dichotomous variables were

calculated using the Mantel-Haenszel formula with fixed-effects models. We used the  $I^2$  statistic to assess the heterogeneity, value of <25%, 26–50%, and >50% considered as low, moderate, and high degrees of heterogeneity, respectively. The effect estimate was reported as odds ratio (OR) along with its 95% confidence intervals (CIs) for dichotomous variables, respectively. *P*-value was two-tailed, and the statistical significance set at  $\leq 0.05$ .

A total of 17,200 records were obtained through systematic electronic searches and other ways. After screening titles, abstracts, and full texts, 8 studies [1–8] with a total of 2169 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 ORs for thyroid disease predicting severe COVID-19 is shown in Fig. 1. Our pooled analysis showed a significant association of thyroid disease with severe COVID-19, with no relevant heterogeneity [OR 2.48 (95% CI 1.32–4.66),  $p = 0.005$ ,  $I^2 = 0\%$ , fixed-effect modelling].

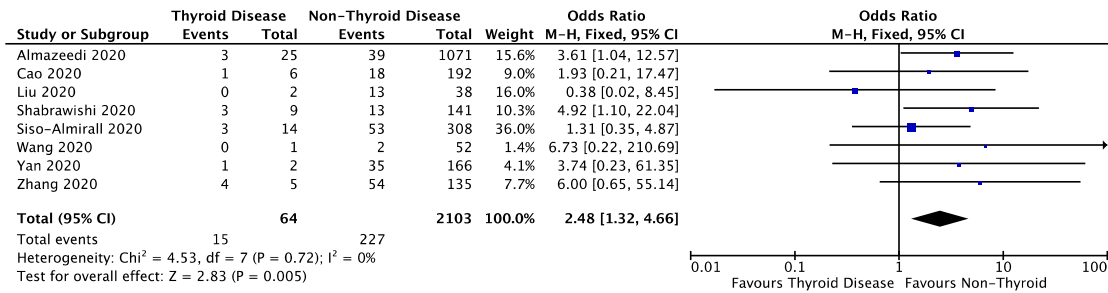
Based on a contrite meta-analysis of available data, thyroid disease seems to be associated with an enhanced risk of severe COVID-19 infection. Several reasons can be proposed to explain this result. First, thyroid hormones were important in the regulation of innate immune response [9]. Therefore, excess or deficiency of thyroid hormones levels observed in thyroid disease will lead to dysregulation of innate immune response. Meanwhile, innate immune response were thought to be contributed the most in the pathogenesis of COVID-19 as it is the front lines of body defense system to fight against SARS-CoV-2, the virus responsible for causing COVID-19 infection. Dysregulation of innate immune response as evidenced by higher levels of neutrophil, increased levels of CD14<sup>+</sup> monocytes and macrophages, decreased levels of NK cells, and increased levels of complement was significantly associated with severe COVID-19 infections [10]. Second, increased levels of proinflammatory cytokines such as TNF- $\alpha$  and IL-6 was observed in patients with thyroid disease [11,12]. Increased levels of these

**Table 1**  
 Characteristics of included studies.

Study	Sample size	Design	Severe patients		Non-severe patients	
			n (%)	Age (years)	n (%)	Age (years)
Almazeedi S et al. [1] 2020	1096	Retrospective cohort	42 (3.8%)	55 (44–66)	1054 (96.2%)	37 (21–53)
Cao M et al. [2] 2020	198	Retrospective cohort	19 (9.6%)	63 (56–80)	179 (90.4%)	48 (33–64)
Liu J et al. [3] 2020	40	Retrospective cohort	13 (32.5%)	59 (49–70)	27 (67.5%)	43 (31–55)
Shabrawishi M et al. [4] 2020	150	Case series	16 (10.6%)	49 (34–65)	134 (89.4%)	46 (30–61)
Siso-Almirall [5], 2020	322	Case series	56 (17.3%)	68 (53–83)	266 (82.7%)	54 (46–71)
Wang Y et al. [6] 2020	55	Retrospective cohort	2 (3.6%)	62 (62–64)	53 (96.4%)	49 (3–69)
Yan S et al. [7] 2020	168	Retrospective cohort	36 (21.4%)	61 (50.3–68)	132 (78.6%)	49 (34–60)
Zhang J et al. [8] 2020	140	Retrospective cohort	58 (41.4%)	64 (25–87)	82 (58.6%)	51.5 (26–78)

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

cytokines were also observed in patients with severe COVID-19 and correlates to the development of severe outcomes [13]. Finally, some thyroid patients, especially subacute thyroiditis were taking corticosteroids as their medications [14]. On the other side, meta-analysis showed that corticosteroid treatment in COVID-19 patients was associated with higher mortality, longer length of hospital stay, and higher rate of bacterial infections [15].

Patients with thyroid disease should hence be advised to take extra precaution to minimize risk exposure to the virus. Physicians should be engaged in close monitoring of thyroid disease patients with suspected COVID-19, for timely detecting signs of disease progression. Finally, the presence of thyroid disease shall be regarded as an important factor in future risk stratification models for COVID-19.

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#### Declaration of competing interest

The authors declare no conflict of interest regarding this article.

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