Review Article

Obesity and Metabolic Associated Fatty Liver Disease (MAFLD) as Risk Factors for COVID-19 Severity

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ABSTRACT

In December 2019 Coronavirus disease 2019 (COVID-19) emerged in Wuhan, China and rapidly spread to other areas and has been declared a pandemic in 2020. Until now there are about half million deaths. Of note the highest fatality rate was found for cardiovascular disease, diabetes mellitus followed by chronic respiratory diseases, hypertension and cancer. Remarkably early data have reported higher BMI is associated with a higher risk of developing severe symptoms and complications of COVID-19 disease. Patients with metabolic associated fatty liver disease (MAFLD) are often obese and have additional metabolic risk factors which may increase risk of respiratory diseases. Identification of risk factors of COVID-19 severity is crucial to provide additional medical care; in this review we shed light on the association between MAFLD and COVID-19 severity.

In December 2019 Coronavirus disease 2019 (COVID-19) emerged in Wuhan, China and rapidly spread to other areas and has been declared a pandemic in 2020 [1]. Up to date 8th of August 2020 there are 20,040,805 Coronavirus cases, with 734,247 deaths while 12,911,199 has been recovered. Of note the highest number of deaths belonged to USA 5,199,444 deaths followed by Brazil 3,035,582, India 2,217,645 and Russia 892,654 [2]. Among the comorbid conditions, reports from china showed that the highest fatality rate was found for cardiovascular disease (CVD) (10.5%) and diabetes mellitus (7.3%), followed by chronic respiratory diseases (6.3%), hypertension (6.0%) and cancer (5.6%) [3].

Higher BMI is a main risk factor for these comorbidities and more generally for impaired metabolic health. Early data have reported higher BMI is associated with a higher risk of developing severe symptoms and complications of COVID-19 disease [4]. Increasing number of reports explored the link between obesity and COVID-19 disease severity; A descriptive analysis of only 24 patients (63% men) with confirmed

COVID-19 admitted to the intensive care unit (ICU) of nine hospitals in Seattle region was among the first to report the data of BMI; (3 patients had normal BMI, 7 patients had BMI > 25 kg/m2, 13 had BMI > 30 kg/m2 and 1 with missing data) whereas 85% of the patients with obesity required mechanical ventilation and 62% died [5].

In china, data of 383 patients with confirmed COVID-19 showed that overweight was associated with an 86% higher risk of developing severe pneumonia compared with patients of normal weight in statistical models that controlled for potential confounders. Also, obesity was associated with 2.42 folds higher for developing disease severity [6]. A larger study including 4,103 patients in New York City reported hospitalized patients were more likely to have considerable co-morbidities than non-hospitalized patients especially with respect to cardiovascular disease (44.6 vs. 16.4%), diabetes (31.8% vs. 5.4%) and obesity (39.8% vs. 14.5%). The authors concluded that BMI >40 kg/m2 was the second strongest independent predictor of hospitalization, after age > 75 years [7].

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Additionally, in a single center retrospective cohort study in France included 124 patients with COVID-19, where the patients were classified according to their BMI into four categories as lean (from 18.5 to < 25 kg/m2), overweight (from 25 to < 30kg/m2), moderate obesity (from 30 to < 35 kg/m2) and severe obesity (≥ 35 kg/m2). Obesity (BMI > 30 kg/m2) and severe obesity (BMI > 35 kg/m2) were significantly more frequent among COVID-19 patients (p < 0.0001) and the need for invasive mechanical ventilation was associated with a BMI of ≥ 35 kg/m2, independently of other comorbidities [8].

Another retrospective study in New York City was the first to analyse the data of BMI stratified by age in 3615 COVID-19 patients; 775 (21%) had a body mass index (BMI; kg/m2) 30-34, and 595 (16%) had a BMI ≥ 35 kg/m2. Interestingly the authors concluded that there was significant differences in admission and ICU care only in patients < 60 years of age with varying BMIs; Patients aged < 60 years who had BMI 30 -34 kg/m2 were 2.0 and 1.8 times more likely to be admitted to acute and critical care, respectively, compared to individuals with a BMI < 30 (P < 0.0001). Similarly, patients aged < 60 years and had BMI ≥ 35 were 2.2 and 3.3 (P < 0.0001) times more likely to be admitted to acute and critical care than patients of the same age and BMI < 30. These data highlighted the importance of obesity as a risk factor for disease severity in younger ages [9].

Moreover, Gao *et al.*, reported that obesity is associated with a nearly 3-fold increased risk for severe COVID-19 with a dose-effect relationship between increasing BMI and the proportion of patients with severe illness [10]. Patients with metabolic associated fatty liver disease (MAFLD) that was previously identified as non-alcoholic fatty liver disease (NAFLD) are often obese and have additional metabolic risk factors which may increase risk of respiratory diseases [11].

In a multi-center study in Wenzhou, China, including sixty six patients with laboratory confirmed COVID-19 were divided into two groups; those with obesity (n = 45) and those without (n = 21) showed that MALFD patients that were obese had more severe COVID-19 disease (37.5% vs. 9.5%, p = 0.021), independent of other metabolic risk factors. The authors stated that patients were of Asian ethnicity and thus the applicability of the results to other ethnic groups is uncertain [12].

In a retrospective analysis of 76 lab confirmed COVID-19 patients and NAFLD by hepatic steatosis score in china showed that patients with NAFLD had a higher risk of disease progression (87 % vs. 25% p <0.0001) [13]. The association of metabolic associated fatty liver disease (MAFLD) to COVID-19 severity in non-diabetic patients was investigated by Gao freng *et al.*, aiming to recognize whether non-diabetic patients with metabolic dysfunction are more prone to COVID-19 disease severity or no. They concluded in non-diabetic patients with COVID-19, the presence of MAFLD was associated with a 4-fold increased risk of severe COVID-19; the risk increased with increasing numbers of metabolic risk factors. The association with COVID-19 severity persisted after adjusting for age, sex and coexisting morbid conditions [14].

Remarkably, in patients aged younger than 60 years, a more than two-fold higher prevalence of severe COVID-19 was observed in MAFLD patients compared to those without; this association remained significant after adjusting for age, sex, smoking status, overweight, diabetes, and hypertension. Similar results were also observed by the authors by using 55 and 65-years cut-offs. However, they pointed a notable limitation of their study to the smaller sample size of the older cohort of patients, which might influence the validity of the results [15]. Moreover, in a letter to the editor replying to the authors, Ji *et al.*, stated if multivariate analysis had been performed with the whole cohort, there was a high likelihood that MAFLD would be an independent factor for severe COVID-19 [16].

Furthermore, patients with MAFLD with increased fibrosis scores, such as FIB-4 or NFS were at higher risk of having severe COVID-19 illness, regardless of other metabolic comorbidities [17]. There are significant differences between China, Europe and the US in population demographics, prevalence of comorbidities and outcome. There is also limited data worldwide about patients with MAFLD requiring hospitalization with COVID-19. Further studies are needed to understand the clinical features of disease presentation, management and outcomes.

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Conflicts of Interest

None.

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