EXPERT REVIEW OF ENDOCRINOLOGY & METABOLISM
https://doi.org/10.1080/17446651.2021.1979392

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EDITORIAL

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Does abdominal obesity influence immunological response to SARS-CoV-2 infection?

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ARTICLE HISTORY Received 29 July 2021; Accepted 24 August 2021

KEYWORDS Obesity; immune function; prognosis; severity; COVID-19

Several hundred studies, 40 systematic reviews, and nearly 20 meta-analyses had been published by early 2021, confirming an increased need for medical services for people living with overweight or with obesity/super-obesity who develop coronavirus disease 2019 (COVID-19). Higher body mass index (BMI) is associated with increased risk of hospitalization, admission to intensive or critical care, and the need for mechanically assisted ventilation [1–4]. Higher BMI also raises the risk of dying of this infectious disease [5]. These increased risks have been found after adjusting for age, ethnicity, income, and other demographic and socio-economic factors [6]. Notably, individuals with central obesity had lower antibody titers than those without, after two COVID-19 mRNA vaccine inoculations (Pfizer/BioNTech) separated by 3 weeks, which would unfavorably affect their prognosis in the case of vaccine breakthrough [7].

The risk for cardiovascular heart disease (CVD) is higher in people with 'central' or 'visceral-abdominal' obesity [8]; CVD, especially heart failure, is a significant risk factor for worse outcomes in COVID-19 [9]. The innate immune response is also altered in diseases, such as obesity and type 2 diabetes mellitus (T2DM), thus making people more susceptible to SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) infection [10]. However, a higher BMI is also frequently associated with a worse prognosis and higher mortality in COVID-19 patients [11,12]. Obesity-induced adipose tissue inflammation and its effects on the immune system play a crucial role in the pathogenesis of SARS-CoV-2 infection [11]. Not only general obesity but also specifically abdominal obesity, more so than metabolic syndrome, seem to be associated with clinical deterioration, especially respiratory distress, in COVID-19 [13]. Increased abdominal visceral adiposity compromises pulmonary function in supine patients by decreased diaphragmatic excursion, while the base of the lung ventilation is also impaired, resulting in reduced oxygen saturated blood levels [14]. A dysfunctional adipose tissue with a low adiponectin/leptin ratio may cause increased oxidative stress and inflammation [15]. Thus, it has been reported that abdominal visceral adiposity predicts respiratory distress in COVID-19 patients [13]. Likewise, obesity impairs immune function and provokes chronic inflammation by increasing the number of B cells in visceral adipose tissue and producing autoreactive immunoglobulins [16].

Enhanced abdominal visceral adipose tissue deposition in the obese represents the "soil" for chronic low-grade systemic inflammation by activated immune cells in response to overnutrition [17]. Abnormal secretion of cytokines and other immune mediators, such as interferon, tumor necrosis factor-alpha from abdominal adipocytes, is partly responsible for a chronic low-grade inflammation, thus reducing immune system activity and adversely affecting lung function [18]. Visceral obesity also causes fat accumulation in lymphoid tissue, disturbing leukocyte homeostasis, and lymphocyte function [19]. Enlarged adipocytes are more likely to cause endoplasmic reticulum and mitochondrial stress, leading to inflammatory leukocyte infiltration and enhanced cytokine secretion [20]. SARS-CoV-2 also has adipose tissue tropism, leading to intrapulmonary and systemic inflammation [21]. Moreover, the angiotensin-converting enzyme type 2, the SARS-CoV-2 receptor on host cells is expressed at higher levels in abdominal visceral fat than in subcutaneous fat, which may contribute to an amplified 'cytokine storm' in patients with abdominal obesity and high visceral adiposity [3].

The distribution of mortality rates across more than 160 countries appears to be strongly associated with overweight, with a dramatic risk increase at higher levels of overweight prevalence, which is probably particularly noted with abdominal obesity. At the end of 2020, COVID-19 mortality rates were more than 10-fold higher in countries where overweight prevalence exceeds 50% of the adults (weighted average 66.8 deaths per 100,000 adults) compared with countries where overweight prevalence is below 50% (weighted average of 4.5 deaths per 100,000 adults) [6]. Equally, COVID-19 mortality rates appear to be significantly higher in countries where the average adult BMI exceeds 25 kg/m^2. It may be speculated that if all countries had an overweight prevalence below 50%,

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hundreds of thousands of COVID-19-related deaths and countless millions of hospital admissions or quarantine might have been avoided [6]. T2DM is a frequent comorbidity in patients with obesity, implying that most of these patients need concomitant treatment [22].

Evolving evidence on the association between COVID-19 and overweight/obesity/abdominal obesity requires a new urgency for action [23]. The existence of many 'obesity phenotypes' has recently emerged, with different grades of association with CVD risk, according to physical and lifestyle aspects [24]. This may also reflect the existence of different phenotypes and grades of COVID-19 severity among obese individuals. Obesity, which is much more 'pandemic' than COVID-19, has not received prioritization, which is rising fastest in emerging economies. It is a gateway to many other noncommunicable diseases and mental-health illnesses, and is now a major factor in COVID-19 severity, risk of complications and mortality. There is a window of opportunity to advocate for fund and implement these actions in all countries to ensure better, more resilient, and sustainable health for all now and in our post-COVID-19 future.

Declaration of interest

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership, or options, expert testimony, grants or patents received or pending, or royalties.

Reviewer disclosures

Peer reviewers in this manuscript have no relevant financial or other relationships to disclose.

Funding

This paper was not funded.

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