






## COMMENTARY

# Tackling obesity during the COVID-19 pandemic

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## KEYWORDS

COVID-19, diabetes, obesity, pre-diabetes

## 1 | INTRODUCTION

Most people contracting coronavirus disease 2019 (COVID-19) develop a non-serious disease with some remaining entirely asymptomatic. However, the disease may manifest severely and lead to mortality secondary to the development of respiratory failure and disseminated organ failure.<sup>1</sup> Potential risk factors for severe illness include advanced age and underlying medical conditions, such as diabetes mellitus and cardiovascular disease.<sup>1,2</sup> Furthermore, studies have consistently shown that obesity is an important risk factor for severe COVID-19 (Table 1).<sup>3-10</sup>

The prevalence of obesity has been rising steadily, globally, with a recent report in the United States revealing that 42% of adults are obese, while 9% fulfil the criteria for severe obesity.<sup>11</sup> The current COVID-19 pandemic mandated lockdown in many countries with closure of schools and non-essential businesses. While clearly effective in curbing the epidemic spread, a further increase in the prevalence of obesity is a predictable untoward outcome,<sup>12</sup> as

people eat more and exercise less.<sup>13</sup> A study to assess the effects of lockdown during COVID-19 epidemic on lifestyle in patients with type 2 diabetes in North India reported carbohydrate consumption and frequency of snacking increased in 21% and 23% of study participants, respectively, while exercise duration decreased in 42% and weight gain was documented in 23% of patients.<sup>14</sup> A survey in China showed that during semi-lockdown, normal-weight individuals had less awareness of weight gain, the average steps per day and the average moderate or vigorous-intensity exercise declined significantly for both genders.<sup>15</sup> Increased caloric consumption during the lockdown, as well as poor food choices, increased intake of fast-foods and pre-ordered meals which are frequently high in salt, saturated fat and sugar are possible contributors to weight gain. Moreover, the reduced availability of indoor gyms or outdoor physical activities markedly reduced the opportunity for regular exercise. These restrictions, combined with the sedentary lifestyle imposed by the lockdown, will inevitably lead to further weight gain.

Amit Akirov and Avivit Cahn contributed equally to this paper.

TABLE 1 Risks associated with obesity and recommendations during COVID-19 pandemic

Risk associated with Obesity	Recommendation
Obesity shifts the prevalence of severe COVID-19 disease to a younger age <sup>18</sup>	Encourage obese individuals, at any age, to pay special care to social distancing recommendations Increase awareness of health care teams to the risks associated with obesity In infected young obese patients provide care and monitoring similar to that provided to elderly patients <sup>18</sup>
Obesity is associated with increased risk of venous thromboembolism in patients with COVID-19 <sup>22,23</sup>	Have a low threshold of initiating anti-coagulants in obese patients with COVID-19, as a correlation between heparin use and lower mortality rates has been observed <sup>32</sup> Initiate statins in obese patients with dyslipidaemia poorly controlled by diet alone, as this has been noted to be associated with lower risk for pulmonary embolism <sup>23</sup>
Vitamin D deficiency, more prevalent in the obese, may increase the risk for complications of COVID-19 <sup>30</sup>	Vitamin D supplementation may protect against acute respiratory infections, <sup>33</sup> however, this is still under discussion
Concomitant hypertension and hyperglycaemia increase the risk for severe COVID-19 disease <sup>34-36</sup>	Strive for better control of blood pressure <sup>36</sup> and glucose during the pandemic <sup>34,35</sup> Maintain telehealth contact with primary care to ensure continuous supply of medications and access to medical advice where needed
Periods of quarantine and lockdown lead to further exacerbation of the obesity pandemic <sup>12</sup>	Telehealth services may prevent marked weight gain during lockdown periods <sup>37</sup> Utilize the media to deliver health-promoting messages encouraging physical activity and balanced diet Prioritize opening indoor and outdoor exercise facilities when possible Maintain outdoor activity (such as jogging, biking, power-walking or hiking) or indoor activity (such as indoor gyms, online fitness classes or home exercise), when possible, while maintaining social distancing and using a face mask where mandated

Abbreviation: COVID-19, corona virus 2019.

## 2 | OBESITY AND COVID-19

An early report based on UK Biobank data suggested a dose-response association between body mass index (BMI), waist circumference and positive testing for COVID-19.<sup>16</sup>

Obesity was associated with an approximately threefold increased risk for severe COVID-19 (33.3% vs. 14.7%, respectively), and longer hospital stay (median 23 vs. 18 days, respectively) was noted in obese versus non-obese patients.<sup>4</sup> Obesity has also been associated with a significantly higher rate of Intensive Care Unit (ICU) admission or death.<sup>8</sup> Furthermore, obesity class I (BMI > 30 kg/m<sup>2</sup>) and obesity class II (BMI > 35 kg/m<sup>2</sup>) have been associated with an increased risk for need of invasive mechanical ventilation in patients hospitalized for COVID-19, independent of age, sex, diabetes mellitus and hypertension.<sup>9,13</sup>

Lighter et al. reported that among those under 60 years of age, obesity (BMI > 30 kg/m<sup>2</sup>) was twice as likely to result in hospitalization for COVID-19 and in the need for critical care.<sup>17</sup> A study from France also supported the association between obesity and severe COVID-19, including increased risk for ICU admission in obese individuals.<sup>5</sup>

Kass and colleagues investigated the association of BMI and age in patients admitted to ICUs in the United States due to COVID-19. Their study demonstrated a shift in the age threshold of developing severe COVID-19 disease in obese patients, such that severe obesity places young patients in their 30s at a similar risk category as elderly normal-weight patients.<sup>18</sup> Similarly, Busetto et al. from Italy reported that overweight or obese patients hospitalized due to COVID-19 were more than 10 years younger compared to those with normal weight, yet despite their younger age, these patients required invasive mechanical ventilation and ICU admission more frequently.<sup>6</sup> A study from China reported similar findings, noting the association of obesity with high mortality risk in young patients with COVID-19.<sup>3</sup>

The French Coronavirus SARS-CoV-2 and Diabetes Outcomes study included 1317 patients with diabetes and confirmed COVID-19, and revealed a significant and positive association between BMI and death or mechanical ventilation within a week of admission.<sup>19</sup> Data from England reported that patients with type 1 or type 2 diabetes were at increased risk for COVID-19 associated mortality, and there was a U-shaped relationship with BMI. In patients with type 1 diabetes and BMI  $\geq 40$  kg/m<sup>2</sup> mortality was more than double that of those with BMI 25–29.9 kg/m<sup>2</sup>, and in those with type 2

diabetes and BMI of  $\geq 40$  kg/m<sup>2</sup> mortality risk was almost 1.5-fold higher.<sup>20</sup>

The OpenSAFELY collaborative reviewed electronic medical records from over 17 million UK adults, aiming to identify risk factors for mortality from COVID-19. The study noted that both diabetes and obesity were associated with increased risk for death from COVID-19. The fully adjusted model showed a dose-response association between BMI and mortality, with an increase of 27%, 56%, and 127% in mortality risk for those with BMI 30–34.9, 35–39.9, and  $\geq 40$  kg/m<sup>2</sup>, respectively.<sup>21</sup>

### 3 | PATHOPHYSIOLOGICAL MECHANISMS

Obesity has been observed to be associated with severe COVID-19 disease, independent of diabetes, hypertension and cardiovascular disease—concomitant disorders also known to contribute to severe disease.<sup>18</sup> Several potential underlying mechanisms have been proposed. Disruption of lung function in patients with obesity secondary to excess pressure on the diaphragm while lying supine was suggested to limit ventilation and reduce mucous and probably viral clearance.<sup>18</sup> Obesity is associated with an increase in pro-inflammatory cytokines, and it has been proposed that the pro-inflammatory state, hypoxia, immobilization and diffuse intravascular coagulation triggered by SARS-CoV-2 infection increase the risk for thromboembolism in these more susceptible individuals.<sup>22</sup> Poyiadji et al. reported that in patients with COVID-19 BMI  $>30$  kg/m<sup>2</sup> was associated with a 2.7-fold increased risk for pulmonary embolism. Interestingly, the researchers also reported that statin therapy prior to admission may reduce the risk for thromboembolism in both obese and non-obese patients.<sup>23</sup> Endothelial dysfunction which is a known characteristic of obesity, hypertension and diabetes mellitus may also contribute to the excess morbidity. The acute endothelial damage induced by SARS-CoV-2 may promote lung microvascular dysfunction, vascular leakage, alveolar oedema and hypoxia with those having pre-existing alterations at greater risk.<sup>24</sup> Varga et al. identified the presence of SARS-CoV-2 infectious components within endothelial cells, resulting in endothelial inflammation, apoptosis and pyroptosis in patients with COVID-19.<sup>25</sup>

Higher levels of angiotensin-converting enzyme-2 (ACE-2), the receptor enabling the penetration of SARS-CoV-2, have been noted in obese patients, due to higher volume of adipose tissue. This increased number of ACE-2 expressing cells potentially promote increased viral shedding, immune activation and cytokine disturbances.<sup>26</sup>

Visceral adipose tissue may play an important role in the pre-disposition to worse COVID-19 outcomes. Interleukin-6, which can be secreted from visceral adipose tissue, was found to be increased in patients who died of COVID-19. Furthermore, ectopic visceral fat is also important, as studies have shown that patients with obesity present accumulation of adipose tissue within the lung parenchyma, which correlated with inflammatory infiltrate and pulmonary injury.<sup>27</sup> Visceral deposition of fat within the abdomen was also reported to be

independently associated with worse clinical outcomes in patients with COVID-19 and visceral adipose tissue accumulation was strongly associated with the need of intensive care and intubation.<sup>28</sup>

Scherer et al. suggested lipofibroblasts in the lung can dedifferentiate into myofibroblasts that can contribute to lung fibrosis that potentially can increase the severity of the lung response to SARS-CoV-2.<sup>29</sup> Tyemoori-Rad et al. suggested that vitamin D deficiency, which is more commonly observed in obese patients, may increase the risk for complications secondary to viral infections, including COVID-19, as it has been suggested that vitamin D may inhibit viral replication and had important effects on the immune system and inflammatory response.<sup>30</sup> However, the association between vitamin D deficiency and severe COVID-19 disease is still debated.

The prognostic role of diabetes independently from obesity and vice-versa have not always been addressed appropriately in all the studies reported.

### 4 | RECOMMENDATIONS

The COVID-19 pandemic has resurfaced human vulnerability to communicable diseases, yet, non-communicable disorders have emerged as no less important at these times as well. Obesity is clearly a pivotal risk factor associated with severe disease—including greater rate of hospital admission, ICU admission, need for ventilation and excess mortality. In fact, obesity has been the underlying cause of the severe form of the disease seen in many young patients. Thus, greater attention to protective measures against contracting the disease and heightened vigilance to complications in this population is mandated.

It is yet unclear how to prevent risk of complications in the obese patient contacting COVID-19, yet, close follow up, early use of anti-coagulants, statins, in appropriate cases, and maintenance of a balanced nutrition alongside vitamin and mineral supplementations or repletion as needed are sound recommendations. Control of additional comorbidities if present including hyperglycemia and blood pressure cannot be overstated. While limited data are available to support the use of aspirin for the treatment of SARS-CoV-2, it is frequently used off-label to treat viral infections as previous studies have supported its antiviral effects, including inhibition of viral replication and reduction of lung injury secondary to neutrophil and platelet aggregation.<sup>31</sup>

Furthermore, periods of quarantine and lockdown lead to further exacerbation of the *obesity pandemic*, one for which no 'vaccine' is available for in the foreseeable future. Thus, special care should be taken to mitigate progression of obesity secondary to quarantine, including increasing availability of healthy food choices aiming to maintain adequate supply of fruits, vegetables and low caloric nutrients, while limiting advertisement of fast-foods and emphasizing the importance of wise food choices in the media. Consideration should be taken to encouraging physical activity either outdoor activity (such as jogging, biking, power-walking or hiking) or indoor activity (such as indoor gyms, online fitness classes OR home exercise) when possible while maintaining social distancing.

## 5 | CONCLUSION

While the present data support the increased tendency of obese people to develop severe COVID-19 disease once contracted, an increased risk of infection with increasing BMI has not been clearly demonstrated. There is need for additional studies to explore the benefits of various interventions in reducing the morbidity and mortality of obese patients, and a holistic approach addressing the infected individuals as well as the overall obese population must be adopted.

### CONFLICT OF INTEREST

All authors have no conflict of interest relevant to this paper to declare.

### ETHICAL STATEMENT

This is a review and not a study involving human or animal studies, therefore ethics approval was not required.

### AUTHOR CONTRIBUTION

Amit Akirov and Avivit Cahn drafted the manuscript. All authors reviewed the manuscript, provided comments and expanded discussion and all authors approve the final submitted version.

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