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COVID 19 and Obesity, a deadly duo? A short commentary

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Abstract
The number of COVID 19 cases worldwide has been increasing steadily in the past few months. Due to the novelty of the virus, we are grappling with uncertainty as our proficiency in severe acute respiratory syndrome coronavirus 2 (SARS CoV 2) and the disease which ensues is in its infancy. The proportion COVID 19 cases with severe disease varies significantly between countries and regions depending on the demographics of those infected. Although most people have mild illness, studies show 12-19% of patients experience severe disease which can lead to mortality. Until the advent of definitive treatment or a vaccine, we must be able to identify the patients at high risk accurately in order to provide closer monitoring and treatment to this cohort of patients. This will allow streamlining of services and resources which are already stretched at this time of a global pandemic.

Studies have shown older age, cardiovascular disease, diabetes, chronic respiratory disease, inflammatory diseases hypertension, smoking, and cancer were all associated with an increased risk of death in COVID 19.

Although obesity has also been implicated in numerous studies from Asia, Europe and America to cause increased risk of severe disease in COVID 19 patients, it remains understated.

This does not come as a surprise as obesity has been linked to worse prognosis in previous flu pandemics (1917 Spanish Flu, 1957 Asian Flu, 1968 Hong Kong Flu and 2009 H1N1 pandemic).

Keywords: COVID19, Obesity

Introduction

The number of COVID 19 cases worldwide has been increasing steadily in the past few months. Due to the novelty of the virus, we are grappling with uncertainty as our proficiency in severe acute respiratory syndrome coronavirus 2 (SARS CoV 2) and the disease which ensues is in its infancy. The proportion COVID 19 cases with severe disease varies significantly between countries and regions depending on the demographics of those infected. Although most people have mild illness, studies show 12-19% of patients experience severe disease which can lead to mortality [1, 2]. Until the advent of definitive treatment or a vaccine, we must be able to identify the patients at high risk accurately in order to provide closer monitoring and treatment to this cohort of patients. This will allow streamlining of services and resources which are already stretched at this time of a global pandemic.

Studies have shown older age, cardiovascular disease, diabetes, chronic respiratory disease, inflammatory diseases hypertension, smoking, and cancer were all associated with an increased risk of death in COVID 19 [3].

Although obesity has also been implicated in numerous studies from Asia [4, 5], Europe [9, 8] and America [6, 7] to cause increased risk of severe disease in COVID 19 patients, it remains understated.

This does not come as a surprise as obesity has been linked to worse prognosis in previous flu pandemics (1917 Spanish Flu, 1957 Asian Flu, 1968 Hong Kong Flu and 2009 H1N1 pandemic) [10].

The Obesity Dilemma

With obesity now being perceived as an epidemic in its own accord, the association of obesity with a global pandemic presents a bothersome proposition. WHO data shows in 2016, 15.1 % of women and 13.1% of men aged 18 and over were obese with the numbers steadily increasing year on year [11]. Obesity catalyses an intricate constellation of systemic syndromes ranging from psychiatric illnesses to defective immunological functions.

Worryingly, research indicates that obesity is more prevalent in lower socioeconomic status groups [12], leaving them in vulnerable populations where a myriad of factors such as poor access to primary care, low education levels, poor economy and cultural barriers may thwart the delivery of appropriate care to this group of individuals [13].

Defining and Assessing Obesity

Despite studies being in concurrence on obesity being a nexus between SARS-CoV-2 infection and severe COVID 19, it has been noted that the mortality rate does not correspond to the prevalence of obesity between countries and regions [14]. This may be due to numerous aspects including the bandwidth and resilience of healthcare systems in respective countries to endure the pandemic. But there also may be an issue with the current methods of defining obesity.

Anthropometric assessments such as body mass index (BMI), abdominal circumference and skinfold measurements are often used as the index of obesity, a surrogate for total body fat measurement with BMI being the most widely used modality. However, there are inherent problems with BMI which should be acknowledged such as the inability to precisely distinguish body composition and the variability across phenotypes, gender, race, ethnicity, and age group [15].

Due to the challenges to implement BMI as the sole criteria to define obesity, the annexation of Edmonton Obesity Staging System (EOSS) scale to BMI may augment the accuracy of obesity assessment. Although EOSS scale has its own challenges to implement given its subjectivity and the possibility of patients having undiagnosed complications of obesity, it provides a more holistic assessment of the possible presence of underlying obesity syndromes. Another mechanism which can be used to gauge obesity is the waist – hip ratio (WHR). Studies have shown that WHR is a better predictor of all-cause mortality [16] and impaired immune response [17] compared to BMI.

What about Obesity Paradox?

The results of current studies on obesity and COVID 19 certainly challenges the obesity paradox.

Obesity paradox is a controversial concept popularized early this century which describes better clinical outcomes in patients who are obese by virtue of 'favourable' biochemical, physiological and body composition alteration [18]. However, there are numerous authors who have challenged this. Most studies supporting obesity paradox have been retrospective analyses and did not consider confounding variables such as underlying comorbidities [19]. Further, many studies did not have obesity paradox as their primary outcome increasing the risk of false positive errors from inadequately powered sample sizes [20]. Also as discussed earlier BMI may not be an appropriate gauge to diagnose and stratify obesity. Large studies have shown obese patients have higher rates of all-cause mortality [21]. This brings forth the argument that obesity paradox may be a fallacy.

Why Are Obese Patients at Higher Risk of Severe COVID 19?

A complex variation of physiology is seen in patients with obesity which predisposes them to severe disease.

Alteration of the immune system due to increased secretion of proinflammatory cytokines and impaired B and T cell functions can result in increased susceptibility to severe infections[10].

The high prevalence of other elements which are associated with obesity such as diabetes/insulin resistance, reduced physical activity and chronic kidney disease debilitates the immune response further.

It is well established that pulmonary functioning is significantly altered in obese patients with reduced lung volumes, decreased compliance, respiratory muscle inefficiency leading to abnormal ventilation and perfusion relationship causing impaired gas exchange. This predisposes the patients to increased risk of severe COVID 19 [22].

Obese patients are also at a higher risk of microvascular inflammation and thrombosis due to exaggerated response to stimuli such as sepsis compared to lean patients as proven in animal models [23]. With COVID 19 causing coagulation abnormalities on its own accord, the amalgamation of these factors is associated with increased risk of death [24].

In addition, obese patients are known to have increases incidence of gastroesophageal reflux disease (GERD), swallowing impairment and weak cough reflex, all of which can lead to development or worsening of pulmonary infections [25].

Whilst some of the concepts of obesity is well established, studies have proposed new mechanisms by which obesity can have detrimental effects in COVID 19.

Studies have implicated the increased expression of angiotensin converting enzyme 2(ACE2) in adipose tissue potentially enhances the propensity of SARS CoV-2 entry into cells [26]. This notion is however controversial and is yet to be proven in clinical or experimental studies. Lei Zhio hypothesized that the higher volume of epicardial adipose tissue (EAT) in those with high BMI confers a negative inotropic effect could explain the myocardial complications experienced by some patients with COVID 19; though it will be difficult to substantiate this proposition [27].

Why are obese patients infected with COVID19 are at higher risk of thrombosis?

Obesity is associated with chronic inflammation which puts at higher risk of thrombosis. There is impairment of fibrinolysis which also poses an additional risk for thrombosis. COVID19 has a thromboembolic phenomenon. In a meta-analysis by Guru *et al* [28] the pooled rate of major VTE was 12.5% in hospitalized patients and 17.2% in intensive care unit patients. Many societies and experts recommend routine prophylactic anticoagulation with heparin for VTE prevention in hospitalized COVID-19 patients.

COVID19 and metabolic syndrome

Metabolic associated fatty liver disease is associated with increased risk of severe COVID-19 disease [29].

Given the metabolic associations of MAFLD and obesity as the primary aetiology, it is still plausible that the association between COVID-19 severity and MAFLD could have been a coincidence.

Conclusion

With the current evidence available, we can deduce that there is no variation in the management of obese patients with COVID 19 compared to the non-obese population. Nevertheless, it is clear that obesity presents significant risk of developing severe disease and mortality. With the possibility of COVID 19 becoming an endemic disease and most patients being treated in the community, we should be cognizant of the fact that obesity is a risk factor which should not be overlooked. The cohort of obese patients with COVID 19 must be afforded more attention and resources. Countries should attempt to define obesity based on local demographics and identify this population using more accurate modalities such WHR. With obesity being more common lower socioeconomic groups, it is essential that this population is

actively engaged in the crusade against COVID 19 with better awareness and access to healthcare.

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