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Obesity as a Risk Factor for COVID-19

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Title:

Obesity as a Risk Factor for Coronavirus Infectious Disease 2019

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Abstract

The coronavirus pandemic has presented a wide range of challenges for healthcare systems in the world. Coronavirus Infectious Disease 2019 has infected millions of people, with approximately 90% of the population showing mild or no symptoms. The disease has some risk factors that increase its severity, such as obesity, age, diabetes, cardiovascular diseases, suppressed immune system, and pulmonary disorders. Obese individuals have higher chances of having symptomatic COVID-19 infection with excessive rates of hospitalization and ICU admission. Understanding the mechanisms defining the link between COVID-19 and obesity is necessary to develop preventive measures and therapeutic interventions for people with obesity. Patients with obesity suffer from a variety of nutritional deficiencies, which assist in development of low-grade chronic inflammation. This may result in inappropriate immune response against viral infections such as COVID-19. This review article proposes that changes in immune response, nutrition, and respiratory function, are some of the multiple mechanisms of obesity that increase the risks of developing COVID-19 complications. Patients should make changes to their lifestyles, focusing on nutrition modification, exercise, and calorie restriction as well as proper protection from the virus using latest scientific recommendations.

Keywords: *Covid-19, obesity, inflammation, immune dysfunction, respiratory function*

Introduction

In November 2019, Coronavirus Infectious Disease 2019 (COVID-19) began infecting people in Hubei, China, causing increased rates of respiratory dysfunction and death. Since then, the disease has disrupted people's lives and how businesses and governments are operated. (Parasher, 2021)

It is caused by a coronavirus with similar charactersitics as the SARS-CoV, which led to Severe Acute Respiratory Syndrome or SARS in 2003 (Petrakis et al., 2020). The virus responsible for COVID-19 illness is known as the Severe Acute Respiratory Syndrome Coronavirus 2 or SARS-COV2 (Parasher, 2021). Transmission is caused by contact of respiratory droplets coming from an infected individual with another susceptible individual.

Another way of viral transmission is through indirect contact with surfaces or objects used by an infected individual (Karia et al. 2020). The body cells are infected when the virus binds to the angiogensin-converting enzyme 2 (ACE2) and to transmembrane serine protease 2 (TMPRSS2) (Hoffmann et al. 2020; Wrapp et al. 2020). One of the primary organs that are targeted by Covid-19 virus is lungs. The type 2 alveolar cells are specially affected (Zhou et al., 2020). An infected individual may be asymptomatic or will develop fever, dry cough, sore throat, nausea, diarrhea, loss of taste and smell, and respiratory illnesses including acute respiratory distress syndrome (ARDS) and pneumonia (Karia et al., 2020).

The possibility of severe disease and death is increased in patients older than 65 years of age, and associated comorbidities including obesity, hypertension, diabetes mellitus and immune deficiency (Poly et al. 2021). Factors related to the disease severity are closely linked to heart diseases, obesity, and respiratory dysfunction—disorders that increase the risk of COVID-19 complications (Gasmi et al., 2021). Clinical studies indicate a higher number of hospitalized patients due to Covid-19 were obese. A greater percentage of these individuals were admitted to ICU and required mechanical ventilation (Simonnet et al., 2020; Qingxian et al., 2020).

Covid-19 and Obesity

Obesity is due to excessive consumption of ultra-processed diets with low nutritional value, thus causing nutrient deficiencies. Processed foods contain high levels of sodium which increases the rate of hypertension and cardiovascular conditions. Individuals with obesity have several micronutrients deficiencies and long-term deficiencies of these nutrients impact the severity of COVID-19 (Alberca et al. 2020). Obesity causes chronic inflammation, alters immunity, and vitamin deficiency (Gasmi et al., 2021).

The overall mortality rate of obese patients is 20% higher than general population and the morbidity rate is twice as high as a person with normal body weight (Lenz et al., 2009). Although, obesity is a risk factor for severe Covid-19 disease, only a few studies have investigated the specific contribution of being overweight to the severity of Covid-19 (Kwok et al., 2020). Higher body mass index has mainly been a critical contributor to the severity of Covid-19 for patients younger than 65 years of age (Poly et al., 2021). Results showed that COVID-19 patients with obesity have higher mortality rates as compared to those with average weights. COVID-19 patients with increased BMI face the risks of intensive care unit, invasive

mechanical ventilation, and even death. A study in the United States shows that 30% of patients admitted due to COVID-19 were attributed to obesity (Wadman, 2020). Individuals with high BMI have higher odds of hospitalization compared with normal-weight individuals. According to two studies, when obese patients were infected with Covid-19 virus, they were at increased risk of hospitalization and admission to intensive care (Petrakis et al., 2020; Mohammad et al., 2021).

Effects of obesity in respiratory system

Obesity features like impaired pulmonary function and coexisting disorders such as diabetes increase the chances of severe COVID-19 complications. In the COVID-19 context, obesity may increase the risk of virus infection since there is a likelihood for the condition to cause respiratory dysfunction. This dysfunction is caused by impaired air exchange, reduced lung volume, low respiratory muscle strength, and increased airway resistance. In addition, people with obesity are vulnerable to pulmonary hypertension, cardiac arrest, and pneumonia (Mohammad et al., 2021).

Obesity-related clinical features such as reduced lung capacity, tachypnea, aberrant respiratory muscle adaption, and reduced chest wall compliance make ventilation in obese patients more difficult (Alberca et al., 2020). Obesity affects respiratory functions through several mechanisms, including ventilation-perfusion mismatch, pulmonary restriction, and muscle fatigue. It adversely affects lung compliance due to the large accumulation of fat within the thorax cavity. Excess fat in the abdomen pushes on the diaphragm causing decreased chest cavity and thus restricted airflow. Movement of the chest wall and diaphragm is therefore limited, resulting in reduced functional residual capacity. These fat deposits in the mediastinum reduce the compliance of the entire respiratory system by reducing the lung capacity resulting in the collapse of airways (Alberca et al., 2020). Consecutively this leads to reduced ventilatory capacity and increased load of the respiratory system. Thus, the respiratory muscle strength for obese patients is poor because of the increased airway resistance. The stress of a respiratory infection puts the patients at increased risk for respiratory failure and causes wheeze and dyspnea, which worsens the prognosis of COVID-19. Moreover, the necessity for invasive mechanical ventilation increases with the rising levels of obesity. Thus, during the COVID-19 pandemic, obese patients have reduced survival advantage when they come in contract with the virus (Alberca et al., 2020).

Obesity and Immune System

Obesity is linked with impairing immune function, thus resulting in significant changes in the adaptive immune response. The immune system has a crucial responsibility in responding to disturbances in homeostasis. Obesity alters leucocyte counts, which impairs immunocompetence, and makes the body more vulnerable to infections. The immune response of obese people weakens partly because fat cells infiltrate the organs where immune cells are produced and stored, i.e., bone marrow, spleen, and thymus (Wadman, 2020). In particular, the adipose tissue invades the organs where immune cells are produced, reducing the immune response's effectiveness. Changes in the lymphoid tissues adversely impair T-cells activity and cause diminished immune defense. Fewer immune cells such as T cells do not function well, and they produce fewer molecules to help destroy virus-infected cells. The overall consequence is reduced immune response to infectious viruses like the coronavirus. (Wadman, 2020). On the other hand, the level of CD8+ T cells is increased and the level of CD4+ helper and regulatory T cells is decreased in adipose tissue. These changes increase the risk of immune activation (Nishimura et al. 2009).

Obesity is closely related to chronic systemic inflammation. Beyond the condition impairing the immune response, obese people also suffer from chronic low-grade inflammation. The adipose tissue is an essential endocrine organ that secretes cytokines and chemokines, profoundly impacting metabolism and the immune system (Wadman, 2020). It is a vital organ that is necessary to maintain a balance in the anti-inflammatory and pro-inflammatory environment. Obesity is closely related to endothelial infection, which is a contributor to pro-inflammation. Excess calorie consumption leads to expansion of the adipose tissue to store the excess fat. The excess body fat activates inflammatory reactions, which change the architecture and function of the tissue. Dysregulated fatty acid metabolism and mitochondrial dysfunction due to excess fats result in substantial alteration of the cellular structure of the adipose tissues. Excess adiposity disrupts the balance between pro-inflammatory and anti-inflammatory immune regulatory cells. Obesity impairs immune response by reducing anti-inflammatory Th-2 cells and T-cells. The fat cells secrete cytokines that come from macrophages to clean the dead fat cells. The arrangement thus perpetuates a pro-inflammatory environment. It leads to a state of chronic low-grade inflammation in obese patients, which is responsible for initiating cytokine storms in

COVID-19 patients (Wadman, 2020). Chronic inflammation is a severe complication of COVID-19 infection. A recent study shows that COVID-19 amplifies acute inflammation resulting in poorer outcomes. Obesity causes a pro-inflammatory state in the lungs, which compromises respiratory activity. This leads to increased pro-inflammatory cytokines, thus resulting in chronic inflammation, a significant complication of COVID-19 infection (Wadman, 2020).

Adipose tissue secretes some hormone such as adipokines and leptin, which affect the immune system (Francisco et a. 2018). Higher amounts of adipokines and cytokines (TNF-α and IFNs) are produced in obese individuals. In addition, the level of short chain saturated fatty acids is higher in these patients. The combined effects of these abnormalities result in low grade inflammation and reduced response against viral infections (Huttunen et al. 2013). Leptin influences migration leukocytes and regulates release of oxygen radicals from neutrophils. It also reduces chemotaxis and increases TNF-α production (Montecucco et al. 2006). Obese patients have higher level of leptin, which may cause severe lung inflammation in viral infections (Ubags et al. 2014).

Obesity and Nutritional Imbalance

Obesity and nutrient imbalance affect immune deficiency in a bidirectional way. Some diets taken by people with obesity contain high amounts of carbohydrates and saturated fat, but not enough amount of vitamins, minerals, and antioxidants (Martinez et al. 2017). This is the main reason behind immunodeficiency today since nutrient deficiency impairs immune response against COVID-19. High-fructose and high-salt diets reduces ACE2 expression in the heart and in the kidneys. This reduction is associated with higher severity of Covid-19 cases (Bundalo et al. 2016; Alghatrif et al. 2020). Lack of enough protein intake in obese patients is also associated with impaired immune response (Hashimoto et al. 2012).

Vitamins and trace elements play a significant role in regulating COVID-19 immune response. Vitamin deficiency is associated with increased inflammatory cytokines, which significantly increases respiratory tract infections. T regulatory lymphocytes have been reported to be low among many obese COVID-19 patients. However, it can be increased by taking vitamin D supplements. Nutrients have anti-inflammatory and antioxidant properties, which help the proper functioning of the immune system. Vitamin D deficiency is prevalent among people with obesity. The deficiency worsens obesity by enhancing lipogenesis and increases infection

risk. Vitamin D plays a vital role in supporting innate and adaptive immune systems. Research shows that Vitamins such as A, D play a complementary role in the immune system (Alberca et al., 2020). Vitamin D is a vital nutritional component that induces antiviral responses. It influences the secretion of antimicrobial peptides that block viral cellular entry, thus diminishing the spread of the virus. Individuals with severe obesity have high rates of vitamin D deficiency. The deficiency of vitamin D has been reported to be a potential factor in susceptibility to COVID-19. (Margarucci et al., 2021).

Vitamin A is important in the maintenance and regulation of the immune system as well as normal function of respiratory and intestinal epithelia (Oliveira et al., 2018). When obese patients who are commonly vitamin A deficient are infected with Covid-19 virus, they may have cytokine storm and severe viral disease (Huang et al., 2020)

Trace elements such as zinc is important for normal function of immune system. Long-term micronutrient deficiencies such as iron and zinc increase the severity of COVID-19 (Alberca et al., 2020). Iron deficiency is common in obese patients and it reduce T cell and natural killer cell activation, and impairs immune response against Covid-19 (Bonaccorsi-Riani et al., 2015; Dao et al., 2013)

Discussion and Conclusion

Global health is challenged by obesity and coronavirus. With the worldwide prevalence of obesity, it is necessary to explore its relationship with the viral infection. Establishing risk factors associated with COVID-19 is essential to optimize patient treatment and immunization distribution. The mechanisms linking obesity and COVID-19 include the state of low-grade inflammation, nutritional deficiency, and damage to the respiratory system. Obesity makes the patient vulnerable to COVID-19 by weakening their immune system. Individuals with severe obesity are deemed more vulnerable to the disease, and therefore, they require special treatment during the pandemic to avoid further complications and health burdens. Clinical trials and vaccinations should prioritize the inclusion of people with obesity.

An important lesson from the COVID-19 pandemic is the significance of maintaining a healthy lifestyle. Some of the healthy promotion measures in preventing obesity can include eating a non-processed nutrient-rich diet, doing sufficient exercises, and getting adequate sleep. When the underlying mechanisms are established, proper intervention can be emphasized to

counter the complications of the disease for the vulnerable groups. What can be done is to eat healthy foods as well as the appropriate number of calories. Consecutively, this will help with weight loss and support optimal immune function. Regular physical exercise also helps boost immune function. Weight loss intervention can have significant benefits during the COVID-19 pandemic. People should follow health advice from experts of getting vitamin supplementation to prevent deficiency and maintain muscle health during the pandemic.

The limitation of the study is that the current knowledge about obesity increasing the mortality rates among COVID-19 patients is based on a few observational studies. Further research should be necessary to establish molecular and cellular mechanisms that cause this increased risk. More studies should explore the link between these mechanisms and COVID-19 before any conclusions are made.

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