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# A Review Article on the Assessment of Role of Obesity in Determining the Severity of COVID-19 Disease

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#### **ABSTRACT**

Obesity, for the most part alludes to overabundance of muscle versus fat. It has turned into a medical problem of public worry as its predominance is expanding consistently all around the world and doesn't have all the earmarks of being diminishing in the front coming occasions. On the other hand, toward the beginning of December 2019, in Wuhan City of China, an episode of COVID illness 2019 (COVID-19), brought about by a novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The World Health Organization announced the flare-up as a Public Health Emergency of International Concern on January 30, 2020. It has made medical services framework breakdown everywhere. Most people infected with COVID-19 are asymptomatic yet some foster complications and few of them show serious side effects causing a high death rate. Having excess body fat puts individuals in danger for some other genuine chronic sicknesses and directly or by indirectly, builds the chances of extreme ailment from COVID-19. Subsequently, it is of vital value to investigate the connection of stoutness with the disease severity of this pandemic. In spite of partaking partially similar aetiologies with other non-communicable diseases like malignancies, hypertension, diabetes mellitus, etc., obesity gets little consideration and care under typical conditions and its administration could be especially in danger during the COVID-19 flare-up. Many studies have been conducted and are still going on. We have conducted a literature review of the freely accessible data to sum up information about the role of obesity in deciding the seriousness of COVID-19 illness.

Key words: Obesity, COVID-19, Immune system, Disease severity, Chronic diseases

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#### INTRODUCTION

The COVID-19 pandemic began in the Wuhan city on China. It is caused by the new coronavirus (SARS-CoV-2). Coronaviruses belong to RNA group of viruses. The first case was reported in December 2020 following which its incidence rose continuously and turned out to be one of the greatest burdens on the healthcare system globally. Many interventions have been tried all over the world but little has proven effective in limiting the progress of this disease. Higher rates of mortality have been observed in the persons living with co-morbidities like diseases of cardiovascular system, diabetes mellitus, hypertension, and cancer. There are many studies which suggest obesity is a strong factor in causing severe disease in COVID-19. Lesser prevalence of obesity was seen in people who were not infected with SARS-CoV-2 when compared to those who were infected [1].

Obesity can be called as a whole pandemic on its own. It is a complicated, multifactorial condition but is mostly preventable. According to the current scenario, it can be said that 38% of the global adult population will become overweight and 20% will turn obese. Obesity significantly amplifies the risk of chronic non-communicable diseases like-stress, depression, cardiovascular diseases, type 2 diabetes mellitus, and several malignancies. Thus, obesity increases the economic and psychological cost of the already morbid chronic diseases [2].

COVID-19 has been classified into four clinical subtypes on the basis of severity of illness during hospitalization (*i.e.*, mild, moderate, severe, or critically ill depending on managing strategies [3]. The worldwide pandemic of COVID-19 has brought about the faults in the healthcare system. As there is no conventional management to combat COVID-19 infection and supervision is restricted, it has caused quite a chaos. Individuals having COVID-19 display very varied symptoms ranging from symptomless forms to severe acute respiratory distress. Ailing individuals have a higher probability of having raised levels of inflammatory markers, and persons who develop extreme forms of the disease necessitate mechanical ventilation in most cases. Elderly and those with much

comorbidity are the most susceptible to severe disease. Precisely, obesity (generally quantified by Body Mass Index, BMI) is recurrently stated as a chief risk factor for severe complications of COVID-19 including respiratory failure, the necessity for invasive mechanical ventilation, and deaths [1].

Obesity is typically defined as surplus body weight for height [2]. Although there is not a lot of evidence, many reports have displayed a contribution of adiposity in the COVID-19 vulnerability as well as severity. As of late, Watanabe et al. observed that individuals with COVID-19 disease requiring Intensive Care Unit (ICU) support had a higher percentage of instinctive fat along with age, aggravation markers, and severity of interstitial pneumonia. Also, Battisti, et al. stated that COVID-19 seriousness is related with distribution of adipose tissue in abdomen. In another new review, creators found a positive relationship between visceral fat tissue and upper stomach periphery with COVID-19 seriousness. In addition, Yang, et al. Report that, in COVID-19 patients, instinctive adiposity or high intramuscular fat statement builds threat for undeveloped sickness [4]. Obesity was defined as BMI  $\geq 25 \text{ kg/m}^2$  in this Asian population [5].

In this review we will discuss, how obesity affects the severity of disease in persons with COVID-19 disease, why the obese host is so susceptible to COVID-19 and what can be done to improve the survival in obese patients.

#### LITERATURE REVIEW

# Effect of obesity on course of disease in COVID-19 patients

A few reports have shown that weight is a solid component for turning out to be truly sick with Coronavirus 19. A report from the assembled realm assessed the destiny of 16,750 hospitalized patients of COVID-19 in the UK. The creators presumed that there was a higher likelihood of deaths in obese individuals. A solitary community study Italian study on a group of 485 patients viewed stoutness as a solid, free danger factor for extreme disease and death because of coronavirus. While persons having a BMI  $\geq 30 \text{ kg/m}^2$  had an increased probability for serious sickness with COVID-19, a BMI ≥ 35 kg/m<sup>2</sup> drastically expanded the chances of demise. Zhang, et al. revealed that due to obesity, young individuals with COVID-19 (14-45 Years old) were inclined to the danger of essentially increased mortality. Cai, et al. Inspected relationship of weight with seriousness of coronavirus in an assigned medical clinic in Shenzhen. China and reasoned that fat persons have more chances of advancing to extreme illness because of Coronavirus. Reports from different nations seriously impacted by the pandemic including Spain, Germany and Mexico have additionally tracked down a huge relationship among BMI and the expanding seriousness of the illness and mortality because of coronavirus [1].

As of late, likewise it was observed by Klang, et al. excess weight appears to have a harmful influence for the

movement of COVID-19 independent of cardiovascular illness and diabetes. This recommends a critical pathophysiological connect between increased adiposity and extreme COVID-19 disease [6].

Critically, the requirement for IMV (Intermittent Mandatory Ventilation) expanded in fat patients. Aspiratory work studies have presumed that underlying changes in the thoracic-stomach area in obese patients decrease diaphragm's flexibility, which is fundamental for satisfactory pneumonic capacity [7]. Frequent need of IMV (Intermittent Mandatory Ventilation) can be partly explained by obesity related impeded lung capacity. Individuals having coronavirus along with extreme weight present apparent administration challenges as to ventilation support [8].

#### What makes the host vulnerable?

Obese individuals suffer from common illnesses like renal deficiency, cardiovascular illnesses, Type 2 diabetes mellitus, and a critical level of endothelial weakness. The mentioned chronic diseases serve as significant dangerous factors for severity of disease and deaths related with COVID-19. Thus, obesity has been thought to be especially unfavourable in COVID-19. In any case, there is sufficient evidence which recommends that weight is an extra risk factor related with more unfortunate results in persons with COVID-19. Caussy, et al. explicitly checked out if weight was related with more terrible results in individuals with COVID-19 with added danger factors (Figure 1) [1].

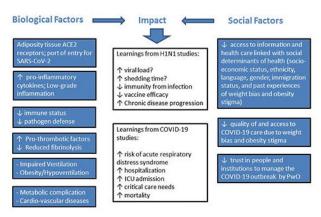


Figure 1: Significant of dangerous factors for severity of disease and deaths related with COVID-19.

### Inflammation due to obesity and its effect on SARS-CoV-2 infection

Overabundant calorie consumption or potentially decreased energy use prompts a fast extension of fat tissue to lodge and store abundance supplements. In any case, obesity incited extension adjusts the capacity and design of fat tissue and enlarged adipocytes undergo apoptosis and draw in macrophages and different cells to form inflamed fat. Aggravation is at the front line of COVID-19 examination and significant confusion of COVID-19 disease is straightforwardly connected with

fundamental irritation. Hamer, et al. explicitly took a look at how low grade inflammation affects the seriousness of COVID-19 illness. The researchers witnessed low grade inflammation can partly explain the high rate admissions in hospitals in obese subjects [1].

#### Impaired cellular function in obesity

A few lines of proof have emphatically shown that weight causes both innate and adaptive immune response to undergo critical changes. People with heftiness are in a condition of low-grade inflammation constantly. The general outcome is a diminished resistant reaction to irresistible specialists, bringing about less fortunate results post-disease [1].

### Lymphoid tissue architecture and integrity affected by excess fat deposition

A few examinations have detailed that obesity prompts more lipid to deposit in primary lymphoid organs (thymus and bone marrow). Abundant accumulation of lipid in their tissues affects the appropriation of the number of leucocytes, the movement of lymphocytes bringing about a checked change in the immune defence [1]. Lipid collections of lymphoid organs are more commonly seen in elderly individuals antagonistically influence their insusceptibility. Thus, obesity is expected to advance untimely "maturing" of the immune system [9]. It is also seen that obesity leads to reduced size of inguinal lymph nodes, disturbs the transport of lymphatic fluid, reduced quantity of T lymphocytes in lymph nodes and movement of dendritic cells. Altogether, obesity causes commotion in integrity of immune system and changes the mobility, growth and diversity of leucocytes significantly.

## Negative impact of insulin resistance on immune system

Obesity regularly prompts fundamental "insulin resistance" a peculiarity which is portrayed by decreased insulin motioning in peripheral tissues bringing about a few metabolic irregularities. No study has explicitly taken a glance at the relationship between insulin resistance and the seriousness of CoVID-19 illness on the grounds that clinical and biochemical markers of insulin obstruction are not regularly estimated in individuals with CoVID-19. More examinations are expected to use more satisfactory insulin opposition models like Quantitative Insulin Sensitivity Check Index (QUICKI) or Homeostatic Model Assessment (HOMA) to explore the commitment of insulin obstruction on infection seriousness and deaths in individuals with CoVID-19 [1].

### Impaired immune function due to resistance to leptin in obesity

Other than insulin, adipocytes discharge a chemical named leptin which applies significant consequences for both intrinsic and versatile invulnerability. Leptin has been found to control both intrinsic and versatile invulnerable reactions by the balance of resistant cell

digestion, expansion, and movement. Stout subjects have notably raised degrees of flowing leptin yet protection from leptin seriously compromises the reaction of target tissues to leptin. Consequently, leptin obstruction would significantly affect the appropriate turn of events and action of insusceptible cells in hefty cases, debilitate the host guard, and increment the odds of serious infection and helpless result in patients of COVID-19 [1]. A study conducted recently provided a thorough scrutiny of the leptin's role in dictating severity of COVID-19 disease in obese subjects. It states that although, early investigations show that starvation and other leptin deficient states are related with diminished immune reactivity, hyperleptinemia has likewise been displayed to effectively affect the invulnerable reaction. These investigations plainly show that leptin is an important connection interfacing nutritional status and immune reactions [10].

### Role of thrombosis/coagulopathy in pathogenesis of SARS-CoV-2

A few examinations have portrayed that being obese is related with a hypercoagulable state and there are raised degrees of prothrombin factors in obese subjects and diminished degrees of anti-thrombin molecules. In the meantime, seriously sick COVID-19 patients are frequently connected with coagulopathy/apoplexy and heftiness might actually aggravate it [1]. Gazzaruso, et al. conducted a research on a group of 50 patients who were admitted to hospitals with COVID-19 disease. They concluded that higher number of deaths was unequivocally connected with decreased Antithrombin (AT) levels. They discovered that troponin levels were altogether higher in non-survivors, regardless of whether they keep up with the measurable importance in multivariate examination. This might be expected to the generally little review populace. Be that as it may, raised troponin levels are articulation of cardiovascular weakness and consequently they might be dependable indicators of more regrettable results of COVID-19, as of late recorded. This might suggest that troponin ought to be considered as an indicator of endurance in extreme COVID-19 along with other natural boundaries, including AT (Figure 2) [11].

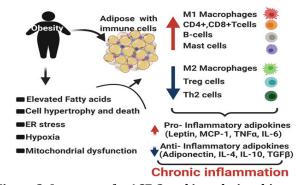


Figure 2: Impact on fat ACE-2 and its relationship with obesity in persons with COVID-19.

### Impact of change in ACE2 expression in obese subjects on course of COVID-19

Angiotensinogen Converting Enzyme (ACE-2) helps the COVID-19 virus to enter the cells. ACE2 receptors are expressed on cells present of mucus membrane of the lungs, nose, kidneys, pancreas and stomach fat, and in covering of veins, in the cardiac muscle, and cells circulating in the blood. It is accepted that increased ACE2 would help the passage of infection inside the cells and hence, result in serious illness with more regrettable clinical results. Arising proof demonstrates that ACE2 articulation is expanded in fat and overweight people. Higham, et al. exhibited augmented expression of ACE2 in the epithelium of bronchus of Chronic Obstructive Pulmonary Disease (COPD) patients who are overweight or obese contrasted with lean subjects [12]. According to the writers, expanded expression of ACE2 might be identified with augmented severity of disease in overweight or obese patients of COVID-19. Remarkably, even though lung is the primary target of COVID-19, higher expression of ACE-2 is seen in adipose tissue when compared to lung tissue [13]. This enhances the possibility of fat tissue being a significant objective and a potential supply for COVID-19. Fat tissue has been displayed to go about as a supply for other microbes infecting humans. All the more significantly, lipid beads which are available in fat tissue have been exhibited to assume a vital part in the development of the Hepatitis C infection. In this manner, it is sensible to accept that fat tissues may go about as a supply for COVID-19 and lipid drops may work with viral creation and spread. Thus, abundance fat as found in obesity would make it an obvious objective for the infection passage and spread and hence, result in extreme illness with terrible clinical results. More examination is expected to comprehend the useful meaning of fat ACE-2 and its relationship with obesity in persons with COVID-19 [1].

## Existence of paradox of survival in obese COVID-19 patients

Increased risk of pneumonia is evident in obese individuals yet incidentally, pneumonia in obese accounts for lower mortality when contrasted with non-fat patients. This peculiarity can be termed as "obesity survival paradox" which is the focus of many researches. This irony in COVID-19 patients is as yet an issue of discussion. Biscarini, et al. dissected an accomplice of 330 individuals who conceded to clinic with COVID-19. The creators detailed that obese individuals with COVID-19 have higher chances to be conceded to ICU than leaner subjects yet being obese was not essentially connected with death, death in ICU and extent of medical clinic stay. In any case, greater part of the examinations has announced that fat subjects are at an expanded danger of serious infection and expanded mortality because of COVID-19 [1].

#### DISCUSSION

Obesity is a multifaceted disease with numerous causative variables. A portion of the elements affecting corpulence are design of the individual's surroundings, admittance to solid, reasonable food sources and drinks, and admittance to protected and advantageous spots for actual work. The racial and ethnic aberrations in stoutness feature the need to address social components of wellbeing like destitution, training, and lodging to eliminate boundaries to wellbeing. This will prompt activity designated at the approach and frameworks level to warrant early anticipation and the management of obesity so that great nourishment and safe spots to be actually dynamic are available to all. Local area pioneers and strategy creators should attempt to ensure that their networks, surroundings, and frameworks support a solid, dynamic way of life for everybody [14].

Foundational changes and sustainable weight reduction set aside time and require way of life adjustment. Notwithstanding the previously mentioned steps, people can assist with securing themselves and their families during this pandemic by different measures. One ought to eat a balanced diet with a lot of products of the soil, lean protein, and entire grains just as the fitting number of calories. These outcomes in weight reduction and preventing weight gain [15]. A solid eating routine can help forestall or support self-administration of sicknesses, for example, coronary illness and type 2 diabetes, which additionally increment the danger of serious disease from COVID-19. Standard active work assists one with feeling good, lessens uneasiness and rest better. It can likewise assist with forestalling weight gain and assists with weight reduction when joined with calorie decrease. Actual work can likewise assist with forestalling sicknesses that increment an individual's odds of having serious ailment from COVID-19, for example, coronary illness and type 2 diabetes. Arising research recommends it might likewise assist with helping invulnerable capacity. Lack of rest has been connected to gloom, just as persistent sicknesses that might build the danger of extreme ailment from COVID-19 like coronary illness, type 2 diabetes, and corpulence. Flare-up of an illness can prompt pressure which causes unhinged rest or eating designs, expanded utilization of liquor and tobacco, or deteriorating of persistent medical conditions [14].

Over the long run, these activities can assist people with obesity work on their general wellbeing. Furthermore, assuming they result in even unassuming weight reduction, there are medical advantages, like enhancements in pulse, blood cholesterol, and blood sugars. The danger of serious ailment from COVID-19 is decreased with a solid BMI.

#### CONCLUSION

In this manner, the frequency of CoVID-19 and obesity can be portrayed as the event of two covering pandemics. The low-grade chronic inflammatory state in fat individuals, as demonstrated by raised benchmark serum

levels of CRP, TNF- $\alpha$ , and IL-6 (decidedly corresponded with BMI, midsection circuit, and instinctive fat tissue), is liable for starting the cytokine storm in COVID-19 patients and can decide various basic obsessive circumstances and complexities. In this set up relationship between BMI based heftiness and extreme course of COVID-19, muscle to fat ratio dissemination is by all accounts urgent, with instinctive fat tissue fundamentally raising the chance of a more serious course of COVID-19. Individuals all over the world ought to be urged to work on their way of life to diminish chances both in the current and resulting influxes of COVID-19.

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