

COVID-19 and Obesity: The Collision of the Two Great's

Abstract

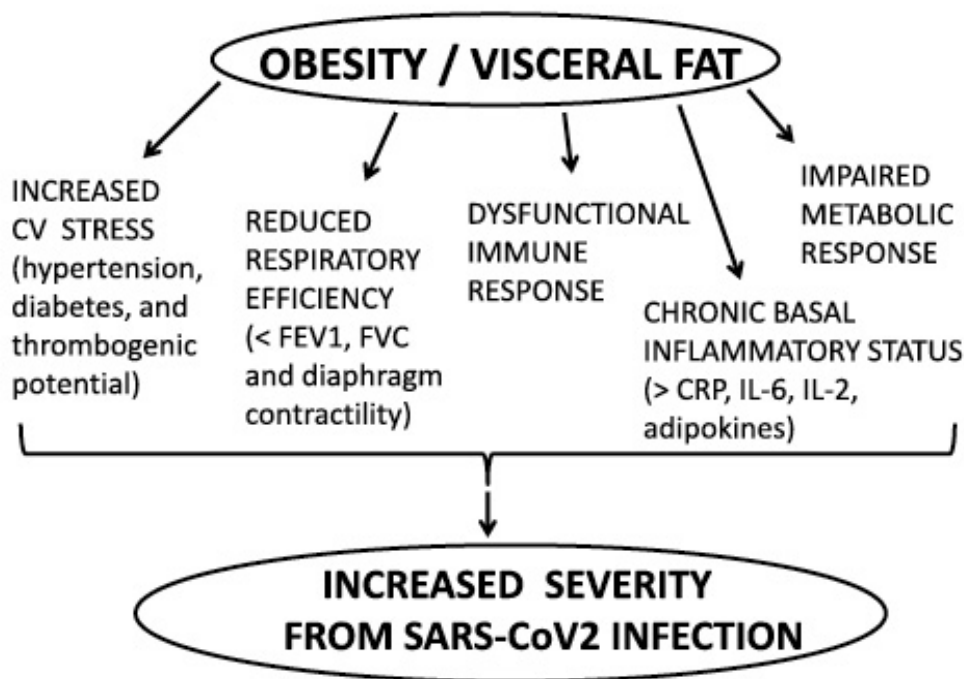
The first instances of COVID-19 were reported in late December in Wuhan, Hubei region, China. This virus is most commonly seen in mammals, most notably bats, camels, cows, and some kinds of pigs. Despite this, it is well recognised that viral transfer from animals to humans is extremely infrequent. It is believed that this new mutated variant of the virus originated because of bats Pangolin and have been demonstrated in study to be the culprit. Although it is currently unknown how the virus spreads to humans. According to sources, the first case's evidence was discovered in an animal market in Wuhan. This is the most likely explanation why SARS-CoV-2 began to transmit. Close contact with an infected individual within 6 feet of each other is the most typical way for this virus to spread. When an individual's symptoms are at their climax, the virus is most contagious. Furthermore, because they do not exhibit any symptoms, carriers are a key contributor to the spread of this condition. Lately the coronavirus disease of 2019 pandemic has motivated global research efforts to find those who are at higher risk of developing more illness. General obesity has been proven to have a significant relationship to seriousness of major COVID infection symptom presentations. Obesity epidemic provides a serious complication to chronic disease avoidance and good health all over the Globe.

Key words: COVID-19, OBESITY, PANDEMIC, RESPIRATORY SYNDROMES;

Introduction

Obesity is a pandemic life long disease with a universal occurrence of 42 percent with a complicated pathophysiology and has a key feature of increased adipose tissue hypertrophy and hyperplasia. Corona virus disease of 2019 has infected over 500 million individuals and 10 million fatalities and counting. COVID-19 is linked to higher hospitalization and mortality rates, which are linked to older age and associated illnesses [1]. Obesity appears to raise the chance of Corona virus disease of 2019 problems as well as death [2]. Multiple probable reasons (Fig.a) can be blamed for the higher chance of grave Corona virus disease of 2019 symptoms in obese

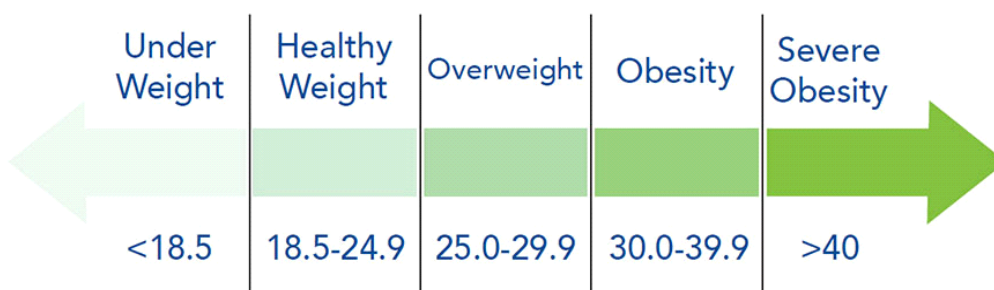
Fig.1. Relation of obesity with COVID 19



SARS-CoV-2 infection mostly disrupts the ACE2 regulatory axis, resulting in an increase in angiotensin type 1 receptor activation, which promotes Multiple mediators and hormones of inflammation are found in adipose tissue. Increased adipose tissue collection and lean muscle loss does have an adverse impact on overall body function. The above mentioned changes will not only impair immune reaction of the body but they will increase inflammatory responses, respiratory and metabolic distress; on long run, they may affect improvement duration and the risk of chronic disabilities, all of which increase the risk of grave morbidities and fatality

Figure 2 : Weight Categories Based On BMI

Weight Categories Based on BMI



DISCUSSION

- Adipokine Dysregulation and Cellular Crosstalk as Instrument of Obesity Associated Fat Inflammation

Recent scientific study has uncovered a complex pathological framework involving adipocyte dysregulation, which is not only a diet-related illness [3]. The group of fat cells are a self-contained endocrine organ capable to save energy from food. It produces a significant count of bioactive peptides which have a function in immunological & vascular control.

Fat tissue is associated with production of a large variant of adipokines that are indulged in cardiovascular homeostasis, appetite control, glucose & lipid metabolism, and more biological functions, as we now know. Adipokines are involved in the control of energy storage and use, as well as several cell metabolisms [4]. These molecules can have pro-inflammatory (leptin) or anti-inflammatory (adiponectin) actions and travel to various organs, affecting a different functions ranging from appetite curb to inflammatory control [5].

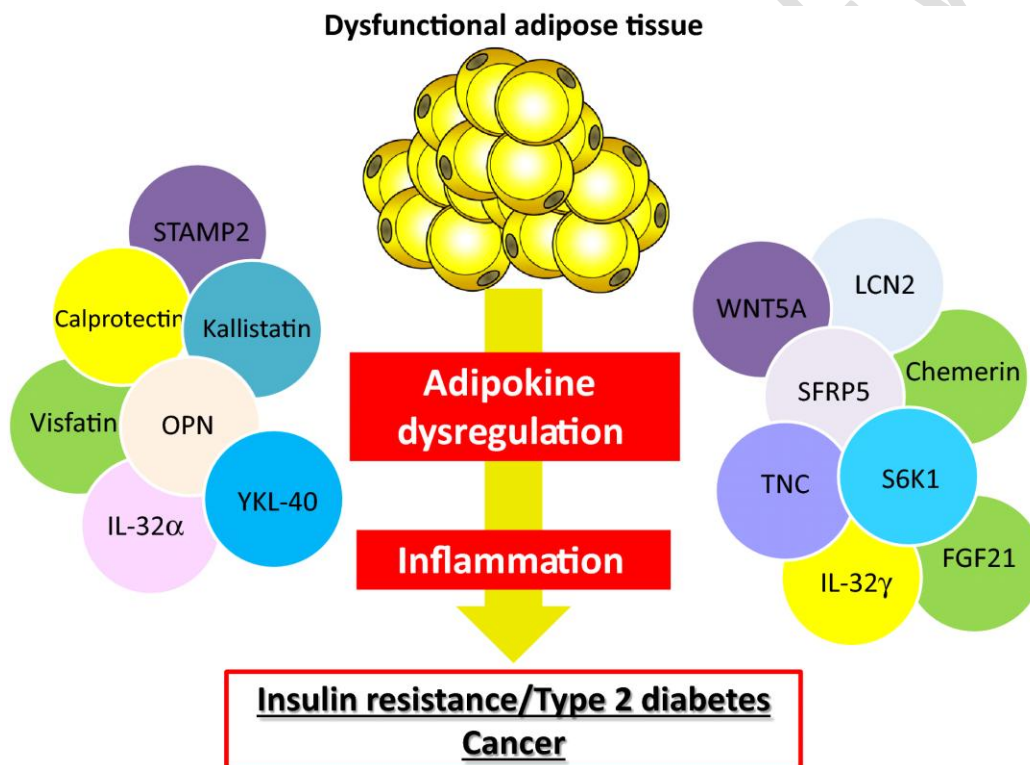


Figure 3 : Insulin resistance/Type 2 diabetes cancer

Leptin's anorexigenic activity influences repletion and food consumption, and the blood work's are related to white fat tissue and Body Mass Index. Leptin is a hormone that controls energy levels having a number of neuroendocrine functions [6] which includes unbalancing lymphocyte Th profiles through decreasing regulatory T cells and promoting Th17 polarization, as well as enhancing resident macrophage migration and supporting their change to a pro-inflammatory stage in WAT [7]. The new trend of diet-related obesity is exhibited by hyper-leptinemia and refusal to leptin's fat-decreasing effects [8].

Endothelial leptin signaling is disrupted by leptin resistance, which predisposes overweight persons to atherogenesis and creates a pro-inflammatory environment that can lead to cardiovascular issues [9].

Another adipokine, adiponectin, has a negative relationship with the quantity of adipose tissue in the blood [9]. Low adiponectin levels linked to a variety of obesity-related metabolic disorders [10]; low adiponectin is regarded to high inflammatory mediators. Lymphocyte Th1 polarization and antiviral inflammation are aided by adiponectin. Lipocalin-2, for example, suppresses inflammatory Th polarization and regulatory lymphocytes. Clinical investigations have shown that obese people's levels of adiponectin, CRP, and IL-6 are significantly reduced once losing weight . . In the obese pro-inflammatory milieu, other functions like oxidative stress and hypoxia play key function[11]. Hypoperfusion of the quickly growing mass of fat, where partial pressure of O₂ and blood flow reduced, appears to be the cause of adipose tissue hypoxia [12]. Local hypoxia reduces adiponectin mRNA levels while increasing pro-inflammatory genes and hypoxia response genes : these increase the inflammatory reaction of fat cells & adds contribution to complications associated to obesity. subcutaneous fat expands at a hyperplastic rate and is not associated with reduced inflammation levels [13] whereas visceral fat accumulation is characterized by an altered adipokine profile and increased pro-inflammatory signals. With increased adiposity, most pro-inflammatory adipokines are produced in excess, wherein insulin-sensitizing adipokines are diminished.

-Prothrombotic Substrate and Endothelial Activation

COVID-19 is linked to increased coagulation and thrombotic events, which have been identified in a large number of infected individuals [14]. Exudative diffuse alveolar destruction, pulmonary embolism, and lung infarction were the most prevalent histological changes detected in individuals with lung micro thrombosis. These findings reveal that microthrombi can be identified in several organs in COVID-19 corpses (particularly in the context of comorbidities). These postmortem findings imply that in COVID-19, severe endothelial hyperactivation can lead to thrombotic episodes, with fibrin and activated leukocyte deposits in the alveoli causing respiratory failure [15]. Endothelial cell damage/hyperactivation activates intracellular signaling pathways, resulting in production of cell adhesion molecules, adipokines, and pro-inflammatory cytokines, that direct inflamed cells in the direction of the endothelium[16].

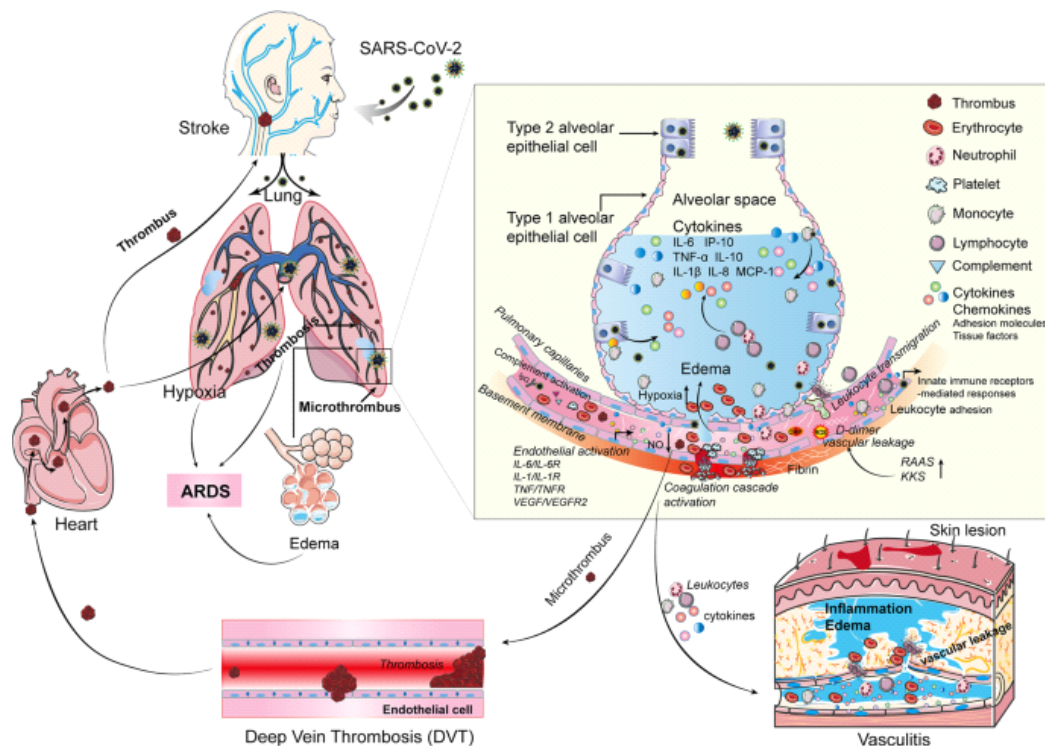


Figure 4-Excess fat accumulation impairs the architecture and integrity of lymphoid tissue.

Blood cells are generated by pluripotent hematopoietic stem cells originating in the marrow. Secondary lymphoid tissues, such as lymph nodes and the spleen, contain mature cells that perform immunological monitoring and wait for pathogen activation. As a result, any change in lymphoid tissue architecture may have a detrimental influence on its function, leading to a shift in immune cell population distribution, decreased T cell activity, and impaired immunological protection. Obesity along with metabolic syndrome, surprisingly, has an effect on group of lymphoid cell function. Ectopic fat accumulation in cell apart from fat tissue is a characteristic feature associated to obesity. Many researches has connected obesity to an increase of fat buildup inside main lymphoid tissues. Excess lipid buildup in these organs has an impact on the location of leukocyte populations as well as lymphocyte activity, casuing a major fall in the boyd's immune response. Fatty tissue accumulation in lymphoids has shown to weaken immunity amongst the elderly. As a result, obesity is considered to hasten the ageing of the immune system. Furthermore, diet-induced obesity in mice has a deleterious impact on secondary lymphoid tissue dynamics, resulting in a shift in the effector/memory T cell ratio and a reduction in T cell receptor diversity overall. As a result, T cells in obese mice can only respond to a limited number of pathogens compared to T cells in chow food eaten mice. Obesity shrinks inguinal lymph nodes, slows lymphatic fluid transfer along with dendritic cell migration, and lowers the amount of T cells in lymph nodes. In general Obesity wreacks havoc on the immune system, limiting leukocyte proliferation, mobility, and diversity. Indeed, a recent study indicated that BMI was inversely related with total lymphocyte count in COVID-19 individuals.

Obesity-related leptin resistance affects immune function.

Aside from insulin, the adipocyte-produced hormone leptin affects both innate and adaptive immunity. Leptin is a major regulator of metabolic balance, and it primarily operates through Leptin receptors

(LEPR), which are numerous in POMC neurons in the hypothalamus, the appetite and energy expenditure control centre. Leptin is also involved in a variety of other physiological processes in the body. LEPRs have been found in immune system cells. research has shown that leptin modulates various aspects of immune cell growth and function. Leptin has been found to impact both innate and adaptive immunological responses by altering immune cell metabolism, proliferation, and activity. Obese people have much higher levels of circulating leptin, but their leptin responsiveness is greatly reduced due to leptin resistance. As a result, leptin resistance would have a significant influence on the correct growth and function of immune cells in obese individuals, jeopardising host defence and raising the probability of severe illness and a poor prognosis in COVID-infected patients..

Insulin resistance wreaks havoc on the immune system.

Many research shows insulin is the main mediator of T-cell metabolism along with its activity. Insulin signalling has essential immunity associated effects on T-cells, regulating its development along with proliferation, glucose metabolism, and cytokine release in a positive way, resulting in a greater host defence against infections. Obesity is usually linked to systemic "resistance of insulin," which is interpreted as decreased insulin signalling peripheral organs along with leading to a number of metabolic issues. Insulin resistance is a complicated phenomena involving many components, but obesity-induced adipose dysfunction is a major contributor to the development of systemic insulin resistance. Obesity increases adipose mass significantly, which has a major influence on adipose function and insulin signalling in peripheral organs, including immune cells. In lymphocytes from people with obesity and Type 2 diabetes, the insulin-stimulated signalling pathway is disrupted. In a recent study, Francis M. Finucane and Colin Davenport studied the probable link between insulin resistance and the severity of COVID-19 illness. According to the authors, insulin resistance indicators should be studied for predictive value. There have been no research that particularly look at the relationship between insulin resistance and the severity of COVID-19 illness because

COVID-19 associated myocardial injury

SARS-CoV-2-induced endotheliitis and microvascular dysfunction also impact the myocardium. The cytokine storm reported in severe COVID-19 is hypothesised to produce vascular inflammation, atherosclerotic plaque instability, and myocardial inflammation. Acute COVID-19 cardiovascular syndrome can emerge, characterised by cardiomyopathy, ventricular arrhythmias, and haemodynamic instability. This injury's aetiology is unknown, however it might be connected to myocarditis, microvascular damage, systemic cytokine-mediated injury, or stress-associated cardiomyopathy. ACE2 is found in considerable levels in arterial and venous endothelial cells, pericytes, and cardiomyocytes. As a result, SARS-CoV-2 causes significant acute cellular damage in cardiomyocytes via ACE2-mediated entrance and subsequent viral multiplication. Acute coronary syndrome, acute myocardial damage without obstructive coronary artery disease, arrhythmias, heart failure with or without cardiogenic shock, pericardial effusion, and thromboembolic consequences can all occur in COVID-19 individuals. It is presently unknown if COVID-19 causes CVD or if cardiovascular problems are mostly caused by severe COVID-19. For COVID-19, both pathogenic courses are likely to be significant.

Treatment :With obesity ,COVID-19:Positive

Individuals with COVID infections are frequently managed with supportive care along with intensive care. Despite the possibility for a reduction in morbidity and death if these medications are given more often, many COVID-19 patients will die, as Clifford Lane and Anthony S. Fauci point out. As a result,

experts are optimistic that novel therapeutic agents, such as monoclonal antibodies, more selective immunosuppressive drugs, and Corona vaccinations, can positively reduce the frequency in complications as well as deaths among COVID-19 patients.

Because obese individuals are at a higher chance for a complicated course, it's important to keep track of COVID's clinical status in its acute stage of infection. To detect disease development early in the illness course, biomarkers of pulmonary, cardiac, hepatic, and renal function, as well as glycemic control, should be used. Wherever feasible, treatment for diabetes mellitus should aim to bring hyperglycemia to 125 below level, with medicines that provide the least risk of hypoglycemia, lactic acidosis, ketoacidosis, and fluid retention.

Treatment:With obesity ,COVID-19:Negative

Because the mechanisms by which obesity and poor metabolic health influence the risk of cardiometabolic illnesses and severe COVID-19 are remarkably similar, efforts taken to minimise the risk of cardiometabolic diseases may also reduce the risk of severe COVID-19. Additionally, obesity and poor metabolic health may reduce the efficiency of SARS-CoV-2 immunizations. Immunological senescence and accelerated immune system ageing are seen in patients with obesity, particularly in the CD4⁺, CD8⁺ T cells. Obese people are also less successful at vaccinating against influenza. Furthermore, a higher HbA1c was linked to a worse immunological reaction to influenza A vaccine in 7 T1DM patients and 41 T2DM patients, regardless of age, gender, or BMI.

Obesity and cardiometabolic illness preventive strategies must be implemented at both the patient and community levels. Most expert guidelines for managing obesity and visceral obesity propose a 5–8% reduction in total body weight to prevent cardiometabolic diseases in persons who are overweight or obese. However, greater weight loss may be required in persons with an increased seriousness of obesity (BMI 36.1–40 kg/m²) and 3 (BMI 42 kg/m²) to reduce this risk. Obese persons can lower fat tissue weight along with risk of cardiometabolic disorders by making lifestyle adjustments such as calorie restriction and increased physical activity. According to the PREDIMED study, a Mediterranean diet that was modified ad libitum decreased the graveness of CVS associated actions by 40% in individuals who are at the brink. In comparison to a diet that served as a control.

Clinical Study and Results

Individuals associated to Body Mass Index of 31 to 37 were 1.5 times at an incidence to be accepted to acute care & 1.9 times more at an incidence to be accepted to critical care for ARDS involving in a study including 4,000 COVID-19 affected individuals, including 218 obese individuals under the age of 55. Individuals with a Body Mass Index of 37 and above were 1.3 times more likely than those with Body Mass Index of less than 28 were accepted to immediate care unit and 4.5 times were accepted to ICU[17]. A study of 792,123 young people aged 17 to 35 who were hospitalised with COVID-19 found that a considerable number of them had unfavorable outcomes: 23% required critical care, 13% required artificial breathing, and 2.9 percent died. This in-hospital death rate is decreased in case of older COVID-19 patients, but nearly twice for young Corona virus disease of 2019 patients.. Obesity, HTN and DM are all related with an increased risk in negative outcomes. Younger individuals who had more than one of these disorders had the same risks as middle-aged adults who did not have them [18]. Similar findings were seen in an older cohort, with 46 percent of individuals admitted to the ICU having a Body Mass Index that exceeded 29 and 27 percent having a Body Mass Index that exceeded 34. Patients requiring invasive artificial breathing increased as their Body Mass Index increased, with the largest proportion happening in those with a Body Mass Index with levels higher than 34 [19].

Obese women with polycystic ovarian syndrome have been identified as a medically underserved and likely increased risk category for COVID-19 issues. Researchers detected 23,363 women with PCOS and chose in random 87,675 women of similar age and general practice in a population-based analysis [20]. Women with PCOS exhibited a 54 percent higher incidence of COVID-19 infection after controlling for age, Body Mass Index, and impaired glucose control, which remained at 27 percent higher than controls. The increased cardiac associated risk with Polycystic ovarian syndrome leads to a higher incidence of COVID-19-related illnesses, constituting a separate sub-group of women.

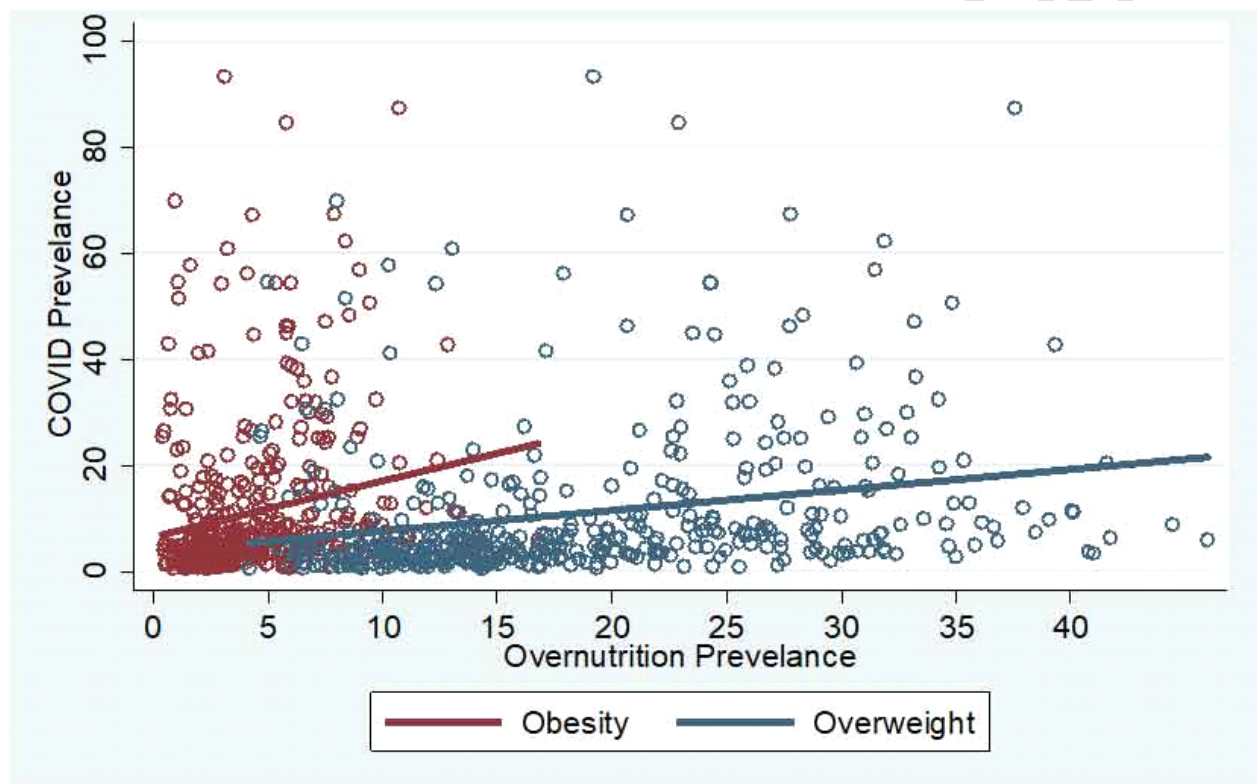


Figure 5 : Prevalence of COVID with obesity

Conclusion

In recent years, India has seen an upsurge in incidences of malnutrition. Lifestyles have grown increasingly sedentary as a result of stay-at-home instructions to combat the development of Covid-19. There is some evidence that greater consumption of processed foods during lockdown has raised the likelihood of being overweight or obese. While the multiple health consequences of being overweight are already widely established, the positive association between morbidity and death from Covid-19 and being overweight has to be communicated to the public in order to provide urgency to individual preventative actions. Evidence also suggests that Covid-19 vaccinations have a decreased effectiveness in overweight or obese people. It is not unlikely that such vaccinations will produce less antibodies,

necessitating further booster doses in this population (Pellini et al. 2021). With few vaccinations available, obese and overweight people may be a target category that should be prioritised in the country's immunisation policy. Due to a convoluted framework and other obesity-related clinical features, obese COVID-19 patients may have grave respiratory failure in need of mechanical ventilation. The cytokine storm in COVID-19 affected individuals are triggered by a second rate chronic inflammatory state in obese patients and it can reveal a variety of hidden pathological diseases and associated complications. Infectious pathogens sensitize a variety of receptors in adipocytes, leading in the activation of cytokine-mediated signaling pathways and the generation of pro-inflammatory cytokines and acute phase reactants. Distribution of body fat appears play a vital role in the relation b/w Body Mass index associated obesity along with a drastic COVID infection, with visceral fat cells rapidly pushing the likelihood of a serious COVID infection. Risk assessment instruments such as Body Mass Index, height weight ratio, circumference of the waist are important[21]. : The measurement of visceral fat and abdominal circumference might be utilized to profile younger obese individuals who in the front line of Corona virus disease of 2019 infection associated death, making it a COVID-19 risk assessment approachment.

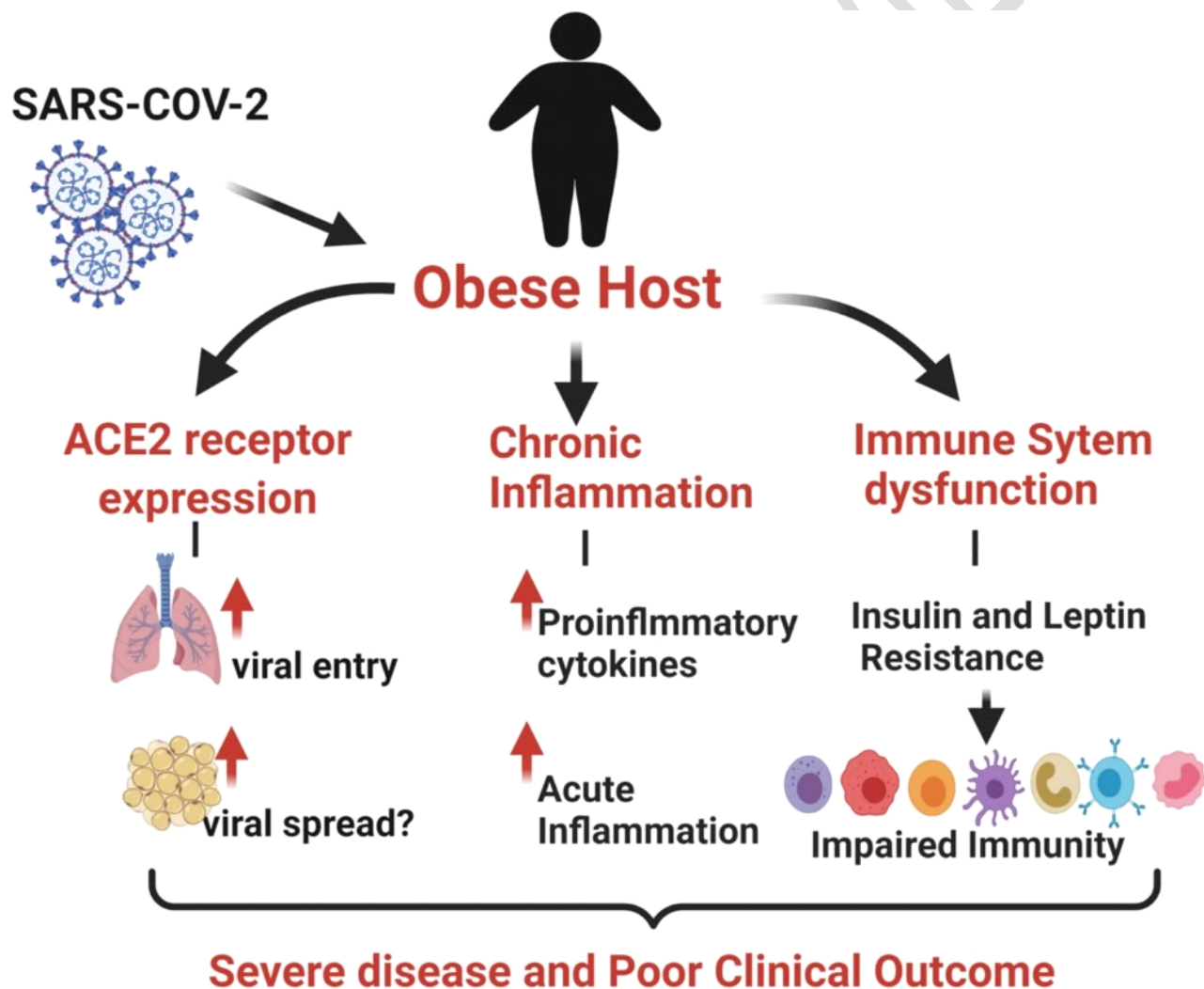


Figure 6 : severe disease and poor clinical outcome

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