



Journal of Population Therapeutics & Clinical Pharmacology

Brief Communication

DOI: 10.15586/jptcp.v27iSP1.708

Obesity and higher risk for severe complications of COVID-19: What to do when the two pandemics meet

Alessandra Valerio^{1,2}, Enzo Nisoli^{3,4}, Andrea P Rossi⁵, Massimo Pellegrini^{6,7}, Tiziana Todesco⁸,
Marwan El Ghoch^{9,10*}

¹Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy

²Associate Editor – Journal of Population Therapeutics and Clinical Pharmacology, Brisbane, QLD, Australia

³Center for Study and Research on Obesity, Department of Medical Biotechnology and Translational Medicine, University of Milan, Milan, Italy

⁴Editorial Board Member – Journal of Population Therapeutics and Clinical Pharmacology, Brisbane, QLD, Australia

⁵Division of Geriatrics, Department of Medicine, Healthy Aging Center, University of Verona, Verona, Italy

⁶Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy

⁷Clinical Nutrition Unit, Azienda Unità Sanitaria Locale – IRCCS di Reggio Emilia, Reggio Emilia, Italy

⁸Center for Eating Disorders, District for Health Services, Autonomous Province of Trento, Italy

⁹Co-Editor-in-Chief – Journal of Population Therapeutics and Clinical Pharmacology, Brisbane, QLD, Australia

¹⁰Department of Nutrition and Dietetics, Faculty of Health Sciences, Beirut Arab University, Beirut, Lebanon

Corresponding author: m.ghoch@bau.edu.lb

Submitted: 2 June 2020. Accepted: 7 June 2020. Published: 29 June 2020.

ABSTRACT

The coronavirus disease 2019 (COVID-19) pandemic has spread around the globe, infecting more than ten million individuals, with more than 500,000 dead; about one half of the infected people have recovered. Despite this fact, a subgroup of individuals affected by COVID-19 is at greater risk of developing worse outcomes and experience a high rate of mortality. Data on the association between obesity and

COVID-19 are growing; the available studies, have reported a high prevalence of overweight and obesity in patients experiencing a severe COVID-19 course, with serious complications requiring hospitalization and admission to intensive care units. This paper attempts to highlight potential mechanisms behind the greater vulnerability to COVID-19 of individuals with obesity. The presence of uncontrolled chronic obesity-related comorbidities, particularly pulmonary diseases, can present a primary fertile soil for respiratory tract infection. Combined with immune system impairments, such as alteration in the T-cell proliferation and macrophage differentiation, and the high pro-inflammatory cytokine production by the adipose organ, this may worsen the general condition toward a systemic diffusion of infection. Prevention remains the first line of intervention in these patients that can be achieved by adhering to social distancing and adopting hygiene precautions, combined with a healthy lifestyle. Patients with obesity require preferential access dedicated to primary care services to ensure they are regularly taking their medications for the treatment of any concurrent chronic diseases. Finally, their physicians must promptly manage any medical signs or symptoms in the case of suspected severe acute respiratory syndrome coronavirus-2 (SARS-CoV2) infection to prevent the risk of severe outcomes.

Keywords: *COVID-19, obesity, pandemic, overweight, severe complications, mortality*

THE ERA OF THE COVID-19 PANDEMIC

In the last few months, more than 213 countries and territories around the world have been dominated by an aggressive pandemic of severe acute respiratory syndrome coronavirus-2 (SARS-CoV2) infection, leading to the coronavirus disease (COVID-19) that to date has affected more than ten million people, out of whom nearly five and a half patients have recovered. A subgroup, however faced a serious risk of critical prognosis, requiring intensive care intervention, and deaths have exceeded 500,000.^{1,2} In Italy, nearly 240,000 people have been affected by COVID-19. Of these, nearly 70% have recovered, but the fatal cases have exceeded 34,000. This has resulted in serious difficulties for the Italian national health service, despite it being considered one of the world's leading health services.³ Advanced age and underlying medical conditions are predictors of a worse outcome in patients with COVID-19.³ The medical community works continuously on different fronts trying to find and adopt effective strategies to 1) prevent virus spread, 2) identify medications for the management of critical care and reduce mortality rates, and 3) discover a highly

anticipated vaccine. Moreover, and in the same direction, they are trying to identify factors that may put individuals at higher risk of developing worse outcomes (i.e., severe complications, hospitalization, and mortality), to improve clinical management and limit mortality rates.²

With this aim, the United States Centers for Disease Control and Prevention (CDC), with much caution and based on information derived from clinical practices and expertise, claims that older people and individuals of any age with underlying medical conditions might be at higher risk for severe illness from COVID-19.⁴ This includes patients with:

1. Uncontrolled (moderate to serious) lung - including moderate to severe asthma - heart, liver, and kidney diseases (especially patients requiring dialysis).⁴
2. Compromised immune systems, including those that are drug induced (i.e., cancer patients) and when undergoing organ transplantation.⁴
3. Diabetes and severe obesity (body mass index: BMI \geq 40 kg/m²).⁴

In this direction, recent studies found that obesity is a condition associated with severe complications and higher mortality in COVID-19 disease.^{5,6} This paper attempts to highlight potential mechanisms behind the greater vulnerability to COVID-19 of individuals with obesity. Moreover, we aim to elucidate if special strategies should be adopted to prevent the infection or to improve the prognosis in this patient population.

THE HEAVY BURDEN OF OBESITY

Obesity is best described as an increase in fat deposition in the adipose tissue.⁷ The World Health Organization (WHO), however, uses BMI to define obesity in adults⁷; individuals with a BMI ≥ 30 kg/m² are classified as affected by obesity.⁸ The prevalence of obesity has dramatically increased in the last three decades: it has become one of the most serious health conditions worldwide, to the extent that it is now considered a pandemic.⁸ Moreover, it is widely known that obesity is associated with several medical complications (i.e., high blood pressure, dyslipidemia, insulin resistance, type 2 diabetes mellitus, coronary artery disease, pulmonary diseases, and several cancer types) and psychosocial comorbidities (i.e., depression, eating disorders, impairment of health-related quality of life: HRQoL), and an increased rate of mortality worldwide.⁸

THE BI-DIRECTIONAL INTERACTION BETWEEN OBESITY AND COVID-19 DISEASES

Even though the underlying mechanisms are still unclear, increasing evidence suggests an association between obesity and infectious diseases.⁹ Several factors have been identified that appear to increase the risk of acquiring infection with worse outcomes, especially pulmonary infections, in people with obesity.¹⁰ Growing data are now available in the COVID-19 scenario, where obesity seems to increase the risk of hospitalization⁶ and admission to intensive care units (ICU)

for COVID-19¹¹, and has been considered as a risk factor for greater severity of the disease and higher mortality.^{5,11} Notably, obesity appears to be the main predictor of severe COVID-19 symptoms in younger people.¹² In patients under the age of 60, those with obesity had almost double the risk of being admitted to critical care compared to normal-weight patients.¹² Similarly, data from the H1N1 pandemic, which occurred a decade ago, also offer useful lessons, due the considerable similarity with COVID-19.¹³ In fact, in 2009, more than 50% of H1N1 cases in adults in California were affected by obesity.¹⁴ Moreover, obesity was associated with a higher admission rate and a longer stay in ICU¹⁵, and eventually with a higher rate of mortality due to the H1N1 infection.¹⁶ All of these are strong indications of the close association between obesity and poorer outcomes in H1N1.¹⁷ At that time, several hypotheses were formulated regarding the association between H1N1 and obesity which in our opinion can be extendible to the COVID-19 disease. We briefly mention here the most plausible explanation.

Firstly, the presence of uncontrolled chronic obesity-related comorbidities (e.g., type 2 diabetes, cardiovascular and renal diseases, among others)¹⁸ makes this population more vulnerable. Especially comorbidities with pulmonary complications may present a primary fertile soil for respiratory tract infection¹⁰, such as 1) restrictive lung diseases, 2) lower operating lung volumes, 3) obstructive sleep apnea, 4) increased risk of pulmonary embolism, and 5) dysregulated pulmonary immune response.

Secondly, immune system impairments due to the increased and abnormal fat deposition in individuals with obesity may add insult to injury, facilitating a systemic diffusion of infection^{19, 20}, and make the condition difficult to tame or/and treat. These include: 1) impaired cross-communication between adipocytes and the immune system, due to dysregulated secretion of adipokines (leptin and adiponectin) affecting the

functionality of several immune cells 2) altered T-cell proliferation and macrophage differentiation (i.e., decreased CD8+ T cells, reduced natural killer [NK] cell activity and antigen presentation of dendritic cells), 3) increased cytokine production (i.e., Interleukin 6; Interferon gamma; Tumor Necrosis Factor alpha). Interestingly, disturbed NK cell function has been proposed as a determinant of the high incidence of H1N1 infections in individuals with obesity.²¹ Recently, in the same direction, Diao and colleagues from Wuhan reported similar findings in patients with COVID-19; T-cell counts were found to be dramatically reduced, and the surviving T cells appeared to be functionally exhausted.²²

Finally, the increased incidence of nosocomial infections in patients with obesity when compared with their normal weight counterparts²³, the lack of full knowledge about optimum antimicrobial doses suitable for patients with obesity that fit their body mass²⁴, the poor wound recovery with impaired repair of damaged epithelial surface²⁵, the elevated levels of oxidative stress as well as inflammation²⁶, and the logistic barriers in the management of individuals with obesity during hospitalization, may also lead to difficulties in treating these patients in time, with possible life-threatening consequences.²⁷

CONCLUSION

Individuals with obesity, especially those in the severe obesity classes or those with related comorbidities, are at a higher risk of developing more serious symptoms and complications due to COVID-19. The two conditions may reciprocally and negatively influence each other. Effective strategies that prevent this group of individuals from being infected (i.e., adhering to social distancing and adopting the recommended hand washing and hygiene precautions) undoubtedly form the first line of defense.²⁸ These precautions should be combined with a

healthy lifestyle based on healthy eating and appropriate hydration, regular and moderate physical activity, and adequate rest and sleep.²⁸ Weight-management programs (i.e., internet-based self-administered intervention) are of utmost importance.²⁹ They provide an indispensable opportunity to avoid any additional weight gain that may lead to clinical deterioration of obesity and its correlated comorbidities.³⁰ Last but not least, patients with obesity need a preferential access dedicated to primary care services. Polypharmacy is usually an issue for these patients,³¹ which by itself increases the risk of adverse drug events, drug–drug interactions, and non-adherence to medication.^{32–34} To keep these comorbidities under control, general practitioners must ensure that these patients are regularly and correctly taking medications for the treatment of chronic conditions such as diabetes, high blood pressure, and dyslipidemia. Careful management of any medical signs or symptoms and prompt intervention in cases of suspected SARS-CoV2 infection is necessary for early diagnosis of COVID-19 to prevent the progression of the disease towards severe outcomes. Such precautions are needed both at home and during hospital care.

CONFLICTS OF INTEREST

None.

FUNDING

None.

DATA AVAILABILITY STATEMENT

Not applicable.

COMPLIANCE WITH ETHICAL STANDARDS

Not applicable.

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