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RELATIONSHIP BETWEEN OBESITY AND THE COVID 19 PANDEMIC: A LITERATURE REVIEW

Camilla Vasconcellos Ferreira
Doctor, Specialist in Internal Medicine and Resident of Intensive Medicine by the institution: Hospital Universitário de Vassouras (HUV)
Vassouras, Rio de Janeiro, Brazil
http://lattes.cnpq.br/6527462398998477

Fernanda da Costa Barros Teixeira Carvalhedo
Doctor, Specialist in Family and Community Medicine and Specialist in Internal Medicine by the institution: Hospital Universitário de Vassouras. Professor and Master's student at the Universidade de Vassouras. Postgraduate student in Palliative Care by the institution: PUC Minas.
Vassouras, Rio de Janeiro, Brazil
http://lattes.cnpq.br2473578040190006

Suelen Rodrigues Ferreira dos Santos
Resident Doctor in Intensive Care at the institution:Hospital Universitário de Vassouras
Vassouras, Rio de Janeiro, Brazil
http://lattes.cnpq.br/2608207554760231

Marcele Aparecida de Oliveira Gomes
Resident Doctor in Nephrology by the institution: Hospital Universitário de Vassouras
Vassouras, Rio de Janeiro, Brasil
http://lattes.cnpq.br/0500357067052875

Aline Campos dos Santos Silva
Resident Doctor in Internal Medicine by the institution: Hospital Universitário de Vassouras
Vassouras, Rio de Janeiro, Brazil
http://lattes.cnpq.br/8372426156642893

Patrick de Abreu Cunha Lopes
Medical Student at the Universidade de Vassouras (UV) and Scientific Initiation Student do PIBIC da Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ)
Vassouras, Rio de Janeiro, Brazil
http://lattes.cnpq.br/9719714143799267

Luciano da Silva Lima
Intensivist, Master in Urgency and Emergency, Preceptor of the Medical Residency Programs in Intensive Care (MEC and PEMI/AMIB) and Internship in Clinical Emergencies of the institution: Hospital Universitário de Vassouras.
Vassouras, Rio de Janeiro, Brazil.
http://lattes.cnpq.br/6220004531823095

Gerson Luiz de Macedo
Intensivist by the Brazilian Intensive Medicine Association (AMIB) and Coordinator of the ICU sector of the institution: Hospital Universitário de Vassouras
Vassouras, Rio de Janeiro, Braszil
http://lattes.cnpq.br/6616245083862580

Abstract: In the first 6 months of human exposure to the Severe Acute Respiratory Syndrome that causes COVID-19, there were over 9,000,000 confirmed infections and nearly 500,000 deaths worldwide. As of November 13, 2021, it is estimated that there were over 250 million confirmed cases of COVID-19 and over 5 million deaths. From another perspective, the prevalence of obesity has recently increased in many developed and developing countries and has doubled in 73 countries since 1980. Emerging studies have also suggested that obesity is associated with worse COVID-19 outcomes, including higher rates of hospitalization and admission to the hospital. Intensive Care Unit, Invasive Mechanical Ventilation and death. However, many studies have not reproduced these findings. Therefore, it is uncertain whether obesity is indeed associated with worse COVID-19 outcomes compared to non-obese individuals. The present study aimed to clarify the relationship between obesity and the severity of COVID-19. To investigate this, we will conduct a systematic search of Web of Science, PubMed, SciELO, Scopus, and Google Scholar on December 3, 2021 to identify all published studies that report COVID-19 comorbidities or outcomes during the pandemic months. expected to find cohort studies and randomized clinical trials. Furthermore, it is expected to analyze that obese patients are more likely than non-obese patients to have severe disease, develop SARS, require hospitalization, be admitted to the ICU or require IMV. Surprisingly, however, it can be seen that obesity was not associated with an increased risk of death from COVID-19.
Keywords: Obesity, Coronavirus, COVID-19, inflammatory diseases.

INTRODUCTION

In the first 6 months of human exposure to Severe Acute Respiratory Syndrome (SARS) - Coronavirus-2 (SARS-CoV-2), which causes Coronavirus Disease 2019 (COVID-19), there have been over 9,000,000 confirmed infections and nearly 500,000 deaths worldwide (DONG et al. 2020). By the end of 2021, it is estimated that there were more than 250 million confirmed cases of COVID-19 and more than 5 million deaths as of November 13, 2021 (WHO, 2021).

From another perspective, the prevalence of obesity has recently increased in many developed and developing countries (NCD, 2016; GBD, 2013) and has doubled in 73 countries since 1980 (GBD, 2015). It is estimated that the prevalence of obesity is around 12% (603.7 million) among adults and 5% among children (107.7 million) worldwide (GBD, 2015). This global increase in the prevalence of obesity shows the need for further assessment of this possible risk factor.

The effects of obesity on the respiratory system have long been observed. Avicenna, the famous Persian Doctor, recognized obesity as a medical disorder, and also in his book entitled Canon of Medicine, referred to the respiratory problems of obese patients (NATHAM et al. 1992). Furthermore, the association between obesity and worse prognosis in respiratory virus infections was observed in the "Spanish" influenza pandemic of 1918 (SHORT et al. 2018). Furthermore, during the 2009 H1N1 pandemic, obesity was considered an independent risk factor for serious illness or complications (MORGAN et al. 2010).

Surprisingly, level 1 evidence supports an association of obesity with better prognosis in patients with SARS (NI et al. 2017). However, previous studies have broken this paradox in patients with COVID-19 (PETRILLI et al. 2020; LIGHTER et al. 2020). In fact, several risk factors have been associated with the development of more severe COVID-19 and increased risk of death, including age over 65 years, type 2 diabetes (T2DM), and cardiovascular disease (CVD) (WU et al 2020; HUSSAIN et al. 2020). Emerging studies have also suggested that obesity is associated with worse COVID-19 outcomes, including higher rates of hospitalization and admission to the Intensive Care Unit (ICU), Invasive Mechanical Ventilation (IMV) and death (PETRILLI et al. 2020; KILLERBY et al. al. 2020). However, many studies have not reproduced these findings.

(BUSETTO et al. 2020; ROSENBERG et al. 2020). Furthermore, some studies have reported that patients with severe COVID-19 have a similar or slightly increased Body Mass Index (BMI) compared to patients with non-severe disease (ITELMAN et al. 2020; PIERCE-WILLIAMS et al. 2020). Therefore, it is unclear whether obesity is indeed associated with adverse COVID-19 outcomes or death. These results and experiments with other viral respiratory infections reinforce the need for further research on this possible risk factor. Thus, the present study aimed to clarify the relationship between obesity and the severity of COVID-19.

Studies have shown that obesity, as a worldwide epidemic, is associated with the severity and prognosis of COVID-19. 19 and would merit the attention of health policy makers in several countries. Thus, it becomes important to assess the impact of obesity on the positive SARS-CoV-2 test result of individuals, hospitalization of patients with COVID-19 and ICU admission, IMV and in-hospital mortality of patients with COVID-19 hospitalized. In addition to comparing the effects of different BMI ranges.

GENERAL GOAL

The present study aimed to clarify the relationship between obesity and the severity of COVID-19.

SPECIFIC GOALS

- Review clinical studies to clarify the association between obesity and COVID-19 severity.
- Review clinical studies to discuss possible mechanisms of association between obesity and COVID-19 severity.
- Review clinical studies to assess the comorbidity of obesity and the severity of COVID-19.

MATERIAL AND METHODS

A literature review was performed. The guiding question of the research was: "what is the relationship between obesity and the severity of COVID-19?". All studies conducted on COVID-19 and obesity were researched and reviewed. To this end, electronic databases were searched, including Web of Science, PubMed, SciELO, Scopus and Google Scholar. The search algorithm included all possible keyword combinations from the following: "Severe acute respiratory syndrome coronavirus 2," "COVID-19," "2019-nCoV," "SARS-CoV-2," "coronavirus, " "obesity," "weight," "obese," "body mass index," and "adipose tissue" with the Boolean operators "and/or". In addition, references to relevant editorial and review articles were revised to increase coverage of included articles and ensure literature saturation.

All studies will be independently selected by the author based on their titles and abstracts. The full texts of articles, potentially suitable for review, will be obtained to determine relevance based on the inclusion/exclusion criteria of the study.

Total studies focusing on clinical features and complications for SARS-CoV-2 were eligible for inclusion. The total of applicable studies (including case report, case series and editorial, cross-sectional and cohort studies) will be identified. We will review all reference lists of relevant studies in order to identify any missing publications. Studies that meet the following criteria will be included in the systematic review [1]: cohort studies; [2] body mass index (BMI) assessment ≥ 25 kg/m 2 reported; [3] those that indicate the odds ratio for the risk of obesity [4]; age and sex will not be maintained as a barrier to inclusion. Primary outcomes were body weight, BMI, morbidities, and other outcomes. Data were extracted independently of the studies included by the author based on a predefined data extraction sheet in the excel program. Extracted data will include (a) general information (author, study type, and location), (b) participants (sample size, sex, and age), (c) outcomes (BMI, most common comorbidities, and mortality), and (d) main conclusions.

Any disagreements in the evaluation of the data will be resolved by discussion between the author and the advisor, and all possible discrepancies will be resolved in consultation with a third reviewer. N relevant articles will be selected, and their full texts will be reviewed.

The review was performed on results with studies conducted on obesity. All studies that evaluated the effect of obesity on all outcomes, unfavorable outcomes, intensive care unit (ICU) admission, required IMV, and mortality were included in the review.

RESULTS

PubMed, EMBASE and Web of Science databases were searched for a total of 1913 records. Included bibliographic references were explored in the later phase, and two more pieces of literature were included. A total of 917 articles remained after deduplication, 696 of which were not clinical observational studies and were removed. Full-text navigation led to the elimination of 180 articles and 41 articles were finally included in the review. Two pairs of overlapping case

studies were included in the meta-analysis, but belonged to different outcome indicators (LIGHTER et al. 2020; SULEYMAN et al. 2020).

The included studies were primarily conducted in the US and Europe, including, Italy, France, Spain, UK, China, Mexico, Greece, Brazil and international cooperation between the US, Italy and Spain. The 41 studies included 219,543 individuals who received the SARS-CoV-2 test and 115,635 confirmed COVID-19 patients. The number of patients included in a single survey ranged from 46 to 51,633. Most studies included more male patients, and those over 60 are also the majority. All studies were conducted and published in 2020.

POSITIVE RESULT OF THE SARS-COV-2 TEST

This section included three studies, which were from the US, Mexico and the UK, respectively (PETRILLI et al. 2020; BELLO-CHAVOLLA et al. 2020; LUSIGNAN et al. 2020). A total of 164,622 individuals were tested for SARS-CoV-2 nucleic acid and 57,499 were positive. The positivity rate ranged from 15.4% to 49.7% among included studies.

Pooled analysis showed that individuals with obesity had a higher incidence of positive test results than those without (OR = 1.50, 95% CI: 1.37–1.63, I 2 = 69.2%. Due to the small number of studies included, no subsequent subgroup analysis, meta-regression, or funnel plots were conducted.

We also compared the possibility of positive test results between individuals who received the SARS-CoV-2 test with different BMI ranges. The results showed that a higher BMI indicates a greater possibility of a positive test result.

HOSPITALIZATION

A total of 11 studies were included in this section, including eight from the US (SULEYMAN, ARGENZIANO, ARGYROPOULOS, DUANMU, EBINGER, KILLERBY et al. 2020), and the remaining three from Brazil (TOUSSIE et al. 2020), Mexico (SOARES et al. 2020), al. 2020) and Spain (BARBERO et al. 2022). Of the 70,795 confirmed patients included, 25,403 were hospitalized. The hospitalization rate ranged from 10.8% to 85.0% among the included studies. All research studies were case-control studies.

Pooled analysis showed that COVID-19 patients with obesity had a higher incidence of hospitalization than those without (OR = 1.54, 95% CI: 1.33-1.78, I 2 = 60.9%.

We also compared the possibility of hospitalization among COVID-19 patients with different BMI ranges. The results showed that a higher BMI predicted greater likelihood of hospitalization.

ICU ADMISSION

Twelve studies were included, 7 from the USA, two from Italy and the remaining three from China, Mexico and Spain, respectively. Of all 30,268 patients admitted from 12 studies, 4,086 out of 29,905 from 11 studies involved the exact number of patients who required ICU admission. The ICU admission rate of inpatients ranged from 9.1% to 44.3% among the 11 studies.

The pooled analysis showed that hospitalized COVID-19 patients with obesity had a higher incidence of ICU admission than those without.

We also compared the possibility of ICU admission among hospitalized patients with different BMI ranges. The results showed that patients with a higher BMI may have a greater tendency to be admitted to the ICU, although they were not significant.

INVASIVE MECHANICAL VENTILATION

Ten studies were included, including five from the US, two from France, and the remaining three from China, Mexico, and Italy, respectively. Of all 25,945 hospitalized patients from 10 studies, 2,789 out of 22,176 patients from 12 articles received IMV with detailed description. The inpatient IMV rate ranged from 9.1% to 68.5% across the 12 studies.

The pooled analysis showed that hospitalized COVID-19 patients with obesity had a higher incidence of receiving IMV than those without.

We also compared the possibility of IMV among hospitalized patients with different BMI ranges. The results showed that a higher BMI may indicate a greater possibility of IMV.

HOSPITAL MORTALITY

A total of 10 studies were included in this section. Of all 54,938 patients from 23 studies, 8,259 out of 51,330 inpatients from 19 studies involved a specific number of deaths. The in-hospital mortality rate ranged from 10.1% to 43.5% among the 10 studies.

The pooled analysis showed that hospitalized COVID-19 patients with obesity had a higher incidence of hospital mortality than those without.

We also compared the possibility of in-hospital mortality among COVID-19 patients with different BMI ranges. The results showed that patients with a BMI ≥ 40 are more likely to have in-hospital mortality.

DISCUSSION

This literature review found that individuals with obesity were more likely to test positive for SARS-CoV-2. Obese patients with COVID-19 were more likely to be hospitalized than those without. Hospitalized COVID-19 patients with obesity were more likely to receive ICU admission, invasive mechanical ventilation, and die than those without. A higher degree of obesity also indicates a higher risk of occurrence for the above events.

Ten systematic reviews evaluated the relationship between obesity and COVID-19. Tamara et al. included three retrospective cohort studies and found that obesity can significantly increase the risk of serious conditions in patients with COVID-19 (TAMARA et al. 2020; YANG et al. 2021). We found that the BMI of COVID-19 patients with severe conditions was significantly higher than those with mild conditions. The risk of developing serious conditions in COVID-19 patients with obesity was significantly higher than those without. Zhou et al. and Sales-Peres et al. reached almost the same conclusion as us (ZHOU et al. 2020; SALES et al. 2020). Pranata et al. analyzed the association between higher BMI and the risk of composite adverse outcomes, death and critical illness (PRANATA et al. 2021). They found that a higher BMI was associated with an increased risk of these events. However, the BMI ranges of most studies were not consistent, which could lead to a decline in reliability and extrapolation of results. Hussain et al found a significant correlation between BMI > 25 kg/m 2 and increased mortality, need for respiratory support, and critical illness in patients with COVID-19 (HUSSAIN et al. 2020). Földi et al. found that obesity was a risk factor for ICU admission and IMV therapy (FÖLDI et al. 2020). They also compared the risk of receiving IMV across different BMI ranges of COVID-19 patients and found that a higher BMI indicates a higher risk of receiving IMV. Furthermore, the prevalence of COVID-19 was observed to be 0.60 among patients with a BMI < 25 kg/m 2 compared to 0.34 among patients with a BMI > 25 kg/m 2. However, as they included a small sample of retrospective

case-control studies, the credibility of such results needs to be validated.Most of these studies adopt composite outcomes, which makes it difficult to assess the impact of obesity on the risk of specific single-endpoint events. During the writing of this article, a meta-analysis published in the latest issue of Obesity Reviews systematically evaluated outcome indicators for obese COVID-19 patients (POPKIN et al. 2020). Unlike current studies, this one established a strict definition of obesity and BMI targeting points to compare the risk of five outcome events in individuals with different BMI ranges.

Many factors can participate in the worsening of obesity in COVID-19. Obesity can increase the expression of genes related to ACE2 and CD147 in the bronchus and blood, while the latter two are receptors for the invasion of SARS-CoV-2 (RADZIKOWSKA et al. 2020). This would make obese individuals more susceptible to infection and may explain the higher rate of positive SARS-CoV-2 testing to some extent. Obesity and the concomitant metabolic syndrome can bring potential damage to organ function, making the lung, kidney and other organs more prone to the dysfunctional state (SHAH et al. 2017). Adipose tissue can become the site of virus retention due to increased ACE2 expression in obese individuals, which can delay virus clearance and exacerbate infection (CSIGE et al. 2018). Low-level inflammation caused by obesity can also damage the immune system and make it abnormal in SARS-Cov-2 infection. Obesity itself can lead to increased chest and abdominal pressure, limiting lung expansion (GHEBLAWI et al. 2020). In the case of COVID-19, obese patients would be more prone to acute respiratory distress. These factors may largely explain why obese patients are more likely to be infected with SARS-Cov-2 and be more severe after infection.

By integrating the results of different original studies, this study aims to avoid the limitation of the applicability of the conclusions caused by the insufficient number of cases in a single research study and the single source of patients. However, there are unavoidable limitations in this study. Included studies may have different implementation patterns for hospitalization, ICU admission, IMV, and other treatments of COVID-19 patients, impacting the reliability of the final review results. Second, the risk of bias in the included studies is inconsistent. Study types are primarily retrospective, including case-control studies and cohort studies, which can further affect the reliability of conclusions. Third, we selected English literature only.

In this literature review, we systematically retrieved existing literature and narrowed the obesity diagnosis and other cutoffs to the BMI section. The results indicated an obesity-promoting role for individuals in the diagnosis of COVID-19, for hospitalized COVID-19 patients, and for hospitalized COVID-19 patients in ICU admission, invasive mechanical ventilation, and hospital mortality. Simultaneously, individuals with a higher degree of obesity may have a higher risk of developing the above adverse outcomes. These findings suggest that obesity would pose serious challenges to the prevention and control of this epidemic. It would also cause more pain and harm to COVID-19 patients and deserves the attention of health policymakers in several countries. To combat this potential impact in the context of COVID-19, we must maintain healthy diets and exercise habits, wear masks frequently and keep our distance from others. Obesity is a risk factor for many diseases, and healthy eating and regular exercise must be a program to be followed by people all over the world. In addition, the pathophysiological characteristics of obese patients with COVID-19 need further study.

In writing this article, a newly published multicenter study further suggested the relationship between obesity and mortality in COVID-19 patients, which further confirmed our conclusion (TARTOF et al. 2020). This also indicates the importance of high quality observational studies and basic research.

FINAL CONSIDERATIONS

Obesity can promote the occurrence of positive SARS-Cov-2 test results, hospitalization of COVID-19 patients, ICU admission, invasive mechanical ventilation therapy, and hospital mortality of patients hospitalized with COVID-19. Individuals with a higher degree of obesity may have a higher risk of developing the adverse outcomes mentioned above. More basic and clinical therapeutic research on this aggravation needs to be strengthened.

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