OBESITY AND COVID-19: THE "MORTAL MARRIAGE" FOR ADULTS?

OBESIDADE E COVID-19: O "CASAMENTO MORTAL" PARA ADULTOS?

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ABSTRACT

Objective: The study aimed to conduct a systematic review to investigate association between obesity and increased COVID-19 mortality. **Methods:** A systematic review was performed using the PubMed, BIREME, and LILACS databases with DeCS/MeSH descriptors, including studies related to obesity and COVID-19 mortality. The search was conducted in English, Portuguese, and Spanish from December 2019 to September 2020. **Results:** Five studies met the inclusion criteria, and two studies showed no significant association ($p > 0.05$) for body mass index (BMI) ≥ 30 and ≥ 40. In adults, the increased mortality rate associated with obesity was significant in two studies with BMI > 30 ($p = 0.0046$) and ≥ 35 ($p = 0.030$). These findings corroborate mortality data for BMI ≥ 40 ($p = 0.02$) and higher intensive care unit admission rates for BMI ≥ 35 ($p < 0.0001$) and between 30 and 34 ($p = 0.006$). **Conclusion:** A correlation between obesity and increased COVID-19 mortality was observed, emphasizing the importance of appropriate treatment of obesity to prevent severe forms of COVID-19.

Keywords: Obesity; COVID-19; Mortality; Hospitalization

RESUMO

Objetivo: Realização de uma revisão sistemática que aborda a associação entre o aumento da mortalidade por COVID-19 relacionada à obesidade. **Métodos:** Foi desenvolvida uma revisão sistemática a partir das bases de dados PubMed, BIREME e LILACS, via descritores DeCS/MeSH, incluindo estudos que abordassem a temática mortalidade por COVID-19 relacionada à obesidade. Os idiomas utilizados foram inglês, português e espanhol. O levantamento bibliográfico foi realizado no período entre dezembro de 2019 e setembro de 2020. **Resultados:** Do total de artigos selecionados, 5 atenderam aos critérios de inclusão, porém, dentre eles, 2 não apresentaram significância ($p > 0,05$), sendo um para IMC ≥ 30 e o outro para IMC ≥ 40. Em populações de adultos, a relação de incremento da mortalidade associado ou não à obesidade teve significância em 2 estudos direto para IMC > 30 ($p = 0,0046$) e IMC ≥ 35 ($p = 0,030$), corroborados por dados de mortalidade para IMC ≥ 40 ($p = 0,02$) e maior admissão na UTI com IMC ≥ 35 ($p < 0,0001$) e IMC 30–34 ($p = 0,006$). **Conclusão:** Definiu-se que há uma correlação entre obesidade e o aumento da mortalidade na infecção por COVID-19, reforçando a relevância do adequado tratamento dessa doença crônica na prevenção de formas graves de COVID-19.

Palavras-chave: Obesidade; COVID-19; Mortalidade; Hospitalização

INTRODUCTION

The first confirmed case of SARS-CoV-2, the virus responsible for COVID-19, was reported to the World Health Organization on December 31, 2019, by Chinese authorities in Wuhan, Hubei, China. Less than four months later, on March 12, 2020, the World Health Organization declared a global pandemic[1].

Experts identified the clinical syndrome, which presented as a respiratory illness with high transmissibility, pathogenicity, morbidity, and mortality[2,3]. COVID-19 leads to respiratory infection characterized by symptoms ranging from mild to severe, such as dry cough, fever, and dyspnea, within 14 days after exposure[1]. Studies identified comorbidities associated with worse outcomes, including diabetes, hypertension, cardiovascular diseases, chronic obstructive pulmonary disease, malignancy, and chronic liver disease[2,3].

Obesity has been identified as a risk factor for increased severity of viral infections. During the 2009 H1N1 outbreak, studies reported that patients with obesity needed more mechanical ventilation and exhibited higher mortality rates. This disproportionate impact of viral illness on patients with obesity suggests a potential risk factor that requires further investigation in the context of the COVID-19 pandemic[4,5].

METHODS

This systematic review was conducted using the databases Latin American and Caribbean Literature in Health Sciences (LILACS), the US National Library of Medicine/National Institutes of Health (PubMed), and the Virtual Health Library (BVS-BIREME) via Health Sciences Descriptors (DeCS) and Medical Subject Headings (MeSH). The search covered publications from December 2019 to September 2020. The descriptors used were obesity, COVID-19, mortality, and hospitalization.

Studies that examined the association between COVID-19 mortality and obesity were included. The search was conducted in English, Portuguese, and Spanish. The filter "young adult: 19 - 24" was applied, although studies with a higher mean age were not excluded. Studies on COVID-19 mortality with other conditions unrelated to obesity were excluded.

The selection of studies occurred in three stages. First, titles were screened based on the combination of descriptors. Studies that did not meet the eligibility criteria were excluded, along with those with ambiguous or unclear titles. Second, the abstracts were reviewed, and those that not meet the eligibility criteria were excluded. Third, full texts of remaining studies were evaluated, along with additional studies intentionally included for concept definition.

Ten studies were found in the PubMed database. Of these, two were excluded based on their titles, eight abstracts were read, and five were discarded, remaining three studies. In the BVS-BIREME database, five studies were identified that overlapped with the PubMed results. The LILACS database did not show studies using the descriptors. Therefore, no studies from this source were included in the study. After, two additional studies from PubMed were intentionally included and the final sample consisted of five studies.

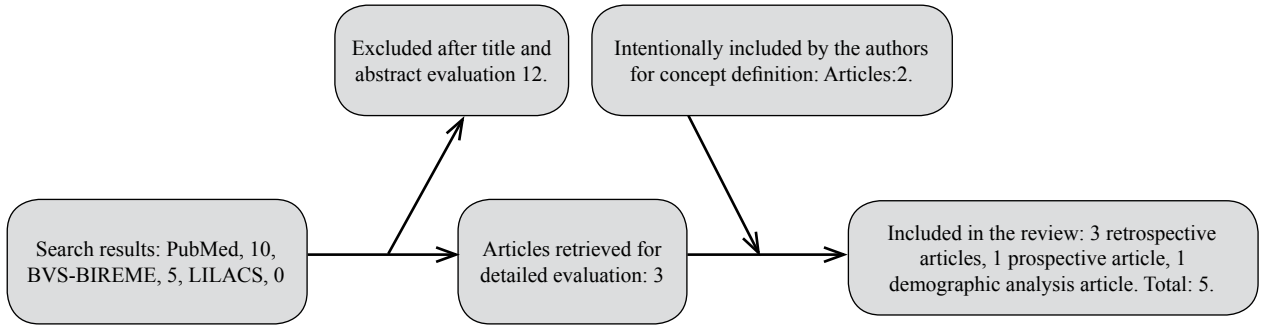

Figure 1. Flowchart of the process of study selections.

RESULTS

The main findings from the five selected studies are presented in Table 1. Steinberg et al. (2020)[4] analyzed mortality in patients aged 18 and 45 years who tested positive for SARS-CoV-2 via real-time reverse transcription polymerase chain reaction (RT -PCR) using nasopharyngeal swab.

This retrospective cohort study was conducted at a high-volume academic medical center in an urban area and an affiliated suburban community hospital. Each results chart was reviewed by at least two investigators and three principal investigators to ensure consensus. Although none of the principal investigators were blinded to the study hypothesis, all variables of interest and goals were clearly defined to minimize interpretive ambiguity. The study included 210 patient charts with demographic data [age, sex, body mass index (BMI)] and three primary outcomes: in-hospital mortality, invasive mechanical ventilation requirement, and hospital admission[4].

Patients who died had a mean BMI of 37.97 (± 7.27) compared with 29.75 (± 6.21) of survivors. In-hospital mortality was significantly associated with a BMI higher than 30 ($p = 0.0046$), suggesting that obesity is an independent risk factor for poor outcomes in young patients with COVID-19[4].

Cummings et al. (2020)6 performed a prospective observational cohort study in two Presbyterian hospitals in New York affiliated with Columbia University Irving Medical Center in northern Manhattan. Patients aged above 18 years, admitted between March 2 and April 1, 2020, with laboratory-confirmed COVID-19 and presenting severe acute hypoxemic respiratory failure were included. RT-PCR confirmed SARS-CoV-2 infection on nasopharyngeal or oropharyngeal swabs tested by the New York State Department of Health between March 2 and March 10, 2020[6].

Among the 1,150 patients who were hospitalized, 257 (22%) were critically ill. The mean period of observation after hospital admission was 19 days. The mean age was 62 years, and 119 (46%) of the critically ill patients had obesity (BMI ≥ 30). The study concluded that severe obesity (BMI ≥ 40) was not a independent risk factor for mortality[6].

The Shah et al. (2020)7 study was conducted at Phoebe Putney Health System, the largest community healthcare system in southwest Georgia, which serves over 500,000 people. Patients with COVID-19, confirmed via nasopharyngeal swab and RT-PCR, were hospitalized from May 2 to May 6, 2020. The mean age was 63 years, with 58.2% women and 66.5% had obesity[7].

Morbid obesity (BMI ≥ 40) was present in 25.6% of patients. Of the total 522 patients, 92 (17.6%) died and 430 (82.4%) were discharged. Obesity with a BMI between 30 and 40 was not significant ($p = 0.21$), and morbid obesity was significantly associated with in-hospital mortality ($p = 0.02$), being considered an independent predictor[7].

Lighter et al. (2020)8 retrospectively analyzed BMI by age in symptomatic patients with COVID-19 at a large academic hospital system in New York City, with positive diagnoses confirmed by PCR, between March 3 and April 4, 2020. Critical care was defined based on intensive care admission or documentation of invasive ventilation in electronic medical records8. Among the 3,615 patients who tested positive, 775 (21%) had a BMI between 30 and 34, while 595 (16%) had a BMI of 35 or higher. In total, 1,853 (51%) were discharged from the emergency department, 1,331 (37%) were hospitalized for acute care, and 431 (12%) were directly admitted or transferred to intensive care[8].

Patients aged under 60 years and with a BMI between 30 and 34 had twofold increase in requiring acute care ($p < 0.0001$) and 1.8-fold in needing intensive care ($p = 0.006$) compared with patients with a BMI under 30. Similarly, patients younger than 60 years and with BMI of 35 or higher had 2.2- ($p < 0.0001$) and 3.6- ($p < 0.0001$) fold increased risk of admission to acute and intensive care, respectively. The study suggested that patients with obesity and aged under 60 represent a new epidemiological risk factor contributing to increased morbidity rates in the United States[8].

The retrospective cohort study of Palaiodimos et al. (2020)[9] was conducted at the Montefiore Medical Center, an academic tertiary hospital in the Bronx, New York. The first 200 patients with laboratory-confirmed COVID-19 who were admitted to inpatient medical service or intensive care unit were included and followed for three weeks after admission. Admissions ranged from March 9 to March 22, 2020, with follow-up ending on April 12, 2020[9].

Patients were divided into three groups based on the most recent BMI recorded before or during admission: BMI < 25, 25 ≤ BMI ≤ 34, and BMI ≥ 35.

Severe obesity was defined as a BMI of 35 or higher. A logistic regression model was used to assess baseline variables associated with in-hospital mortality, intubation, and oxygen requirement. The BMI range of 25 to 34 was a reference for dichotomous comparisons with patients who had severe obesity. The mean age was 64 years (IQR: 50 – 73.5)[9].

In-hospital mortality occurred in 24% of patients with higher or severe obesity (BMI < 25: 31.6%; 25 ≤ BMI≤ 34: 17.2%; BMI ≥ 35: 34.8%, p = 0.030). Additionally, patients with severe obesity had a greater need for oxygen (p = 0.004) and were more likely to undergo intubation (BMI < 25: 18.4%; BMI 25 to 34: 16.4%; BMI ≥ 35: 34.8%, p = 0.032)[9].

The study suggested that severe obesity is an independent risk factor for mortality, intubation, and oxygen requirement during COVID-19 hospitalization[9].

Author/year	Sample size	Evaluation of the studied procedure	Individualized p-value /univariate HR* (95% IC)
Cumming M.J. *et al.* (2020)	257	Higher mortality with BMI ≥ 40	HR = 0.76
Steinberg E. *et al.* (2020)	210	Higher mortality with BMI > 30	p = 0.0046
Shah P. *et al*. (2020)	522	Higher mortality with BMI ≥ 30	p = 0.21
Shah P. *et al*. (2020)	522	Higher mortality with BMI ≥ 40	p = 0.02
Lighter J. *et al*. (2020)	3615	Higher ICU admission 30 ≤ BMI ≤ 34	p = 0.006
Lighter J. *et al*. (2020)	3615	Higher ICU admission BMI ≥ 35	p < 0.0001
Palaiodimos L. *et al*. (2020)	200	Higher mortality with BMI ≥ 35	p = 0.030

Table 1. Selected studies, goals, and results.

*HR: Relative Risk; BMI: body mass index; ICU: intensive care unit

DISCUSSION

Considering the results obtained, a few studies have directly examined obesity as an independent risk factor for COVID-19 mortality. The selected studies were methodologically heterogeneous, which limited comparisons due to diverse variables and associations. However, Palaiodimos et al. (2020)4, Steinberg et al. (2020)7, and Shah et al. (2020)9 reported direct associations between increased COVID-19 mortality and populations with BMI ≥ 35, > 30, and ≥ 40, respectively.

The study by Lighter et al. (2020)8, involving 3,615 patients, demonstrated an increased rate of intensive care unit admissions in patients aged under 60 years with a of 35 or higher, or between 30 and 34. Moreover, Palaiodimos et al. (2020)9 observed an increased need for intubation and supplemental oxygen during hospitalization in patients with a BMI of 35 or higher, which corroborates the findings of Lighter et al. (2020), suggesting a link between higher BMI and disease severity. These results are significant in COVID-19 mortality8,9.

Cumming et al. (2020)6 identified several comorbidities, such as hypertension, chronic heart disease, pulmonary disease, and diabetes, associated with mortality from COVID-19, with were assessed as relative risk, with a hazard ratio of 0.76. Although a hazard ratio below one does not indicate an independent risk factor, this does not imply irrelevance, as it contributes to the observed mortality outcomes4-6.

The limitation of this systematic review was the scarcity of studies on increased COVID-19 mortality associated exclusively with obesity. Most studies assess a set of comorbidities that include obesity due to its cause-and-effect relationship. Therefore, further studies are needed to evaluate the impact of obesity on mortality in patients with COVID-19.

CONCLUSION

A correlation between obesity and increased mortality in SARS-CoV-2 infection was identified, which reinforces the importance of proper management of obesity to prevent severe forms of COVID-19.

REFERENCES

1. Muscogiuri G, Pugliese G, Barrea L, Savastano S, Colao A. Commentary: Obesity: The "Achilles heel" for COVID-19? Metabolism. 2020; 108:1 54251. doi:10.1016/j.metabol.2020.154251.
2. Zhu N, Zhang D, Wang W, et al. A new coronavirus from pneumonia patients in China, 2019. N Engl J Med. 2020; 382 (8): 727-33.2.
3. Huang C, Wang Y, Li X, et al. Clinical characteristics of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet.2020; 395 (10223): 497-506.
4. Steinberg E, Wright E, Kushner B. In Young Adults with COVID-19, Obesity Is Associated with Adverse Outcomes. West J Emerg Med. 2020; 21(4): 752-5. Published. 2020 Jun 15. doi:10.5811/westjem.2020.5.47972
5. Dietz W, Santos-Burgoa C. Obesity and its implications for COVID-19 mortality. Obesity (Silver Spring). 2020;28(6):1005.
6. Cummings MJ, Baldwin MR, Abrams D, Jacobson SD, Meyer BJ, Balough EM, et al. Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. Lancet. 2020 Jun 6; 395(10239): 1763-70. doi: 10.1016/S0140-6736(20)31189-2. Epub 2020 May 19. PMID:32442528; PMCID: PMC7237188.
7. Shah P, Owens J, Franklin J, Mehta A, Heymann W, Sewell W, et al. Demographics, comorbidities and outcomes in hospitalized Covid-19 patients in rural southwest Georgia. Ann Med. 2020 Nov; 52(7): 354-60. doi: 10.1080/07853890.2020.1791356. Epub 2020 Jul 13. PMID: 32620056.
8. Lighter J, Phillips M, Hochman S, Sterling S, Johnson D, Francois F, et al. Obesity in Patients Younger Than 60 Years Is a Risk Factor for COVID-19 Hospital Admission. Clin Infect Dis. 2020 Jul 28; 71(15): 896-7. doi: 10.1093/cid/ciaa415. PMID: 32271368; PMCID: PMC7184372.
9. Palaiodimos L, Kokkinidis DG, Li W, Karamanis D, Ognibene J, Arora S, et al. Severe obesity, increasing age and male sex are independently associated with worse in-hospital outcomes, and higher in-hospital mortality, in a cohort of patients with COVID-19 in the Bronx, New York. Metabolism. 2020 Jul; 108: 154262. doi: 10.1016/j.metabol.2020.154262. Epub 2020 May 16. PMID: 32422233; PMCID: PMC7228874.