P-ISSN: 2617-9806 E-ISSN: 2617-9814



Impact Factor: RJIF 5.95 www.nursingjournal.net

International Journal of Advance Research in Nursing

Volume 8; Issue 2; July-Dec 2025; Page No. 253-257

Received: 18-06-2025
Accepted: 20-07-2025
Indexed Journal
Peer Reviewed Journal

Case-control study on the influence of obesity on SARS-CoV-2 infection and hospital admission risk in adults

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DOI: https://www.doi.org/10.33545/nursing.2025.v8.i2.D.553

Abstract

Since December 2019, over 7 million deaths have been reported due to the SARS-CoV-2 infection. Recent publications reported risk factors and comorbidities that favor these severe outcomes, being obesity one of them. The aim of this study is to examine the relationship between obesity, infection risk, and disease severity, focusing on hospital admission. The present study consists of an observational, analytical, retrospective case-control study to evaluate whether obesity influences the risk of getting COVID-19 and the likelihood of developing severe disease.

Dependent variables studied were confirmed COVID-19 infection and severe prognosis. The independent variable was obesity, along with sociodemographic variables.

This study did not show an indicate association between obesity and a different risk of contracting SARS-CoV-2. However, the results suggest a possible relationship between obesity and a risk factor for developing severe disease once infected. Due to the low number of hospitalized cases, no statistically significant differences were found.

Keywords: COVID-19, obesity, transmission risk, pandemic

1. Introduction

In December 2019, health authorities in Wuhan reported nearly thirty cases of pneumonia of unknown origin. [1] When the health authorities evaluated the cause behind this disease, they established that the patients were linked epidemiologically. Later, the WHO health department determined that this pneumonia was caused by a novel coronavirus, SARS-CoV-2, which was responsible for COVID-19 [1]. As the virus spread worldwide, it became a pandemic on March 11th, 2020 and from this moment [2], the knowledge about its epidemiology, transmission, symptoms, and treatment started evolving.

To date, 777 million cases have been reported worldwide [3]. While SARS-CoV-2 infection is usually asymptomatic or mild, around 10% of the patients require hospitalization due to complications such as respiratory distress or proinflammatory mediators release [4]. In fact, over 7 million deaths have been reported [5]. There are several risk factors and comorbidities that favor these severe outcomes. To date patients who have cancer, cardiovascular diseases or kidney conditions tend to develop complications due to the SARS-CoV-2 infection, among others [6].

Additionally, it was demonstrated that obesity affects several diseases, such as cardiovascular conditions or cancer. For that, several studies investigated if there is a relationship between obesity and COVID-19, demonstrating

its effect, as it increases susceptibility to infection and complications through several mechanisms like its association with other comorbidities ^[1]. Also, obese patients are prone to develop pulmonary restriction, respiratory muscle weakness, chronic inflammation, or uncontrolled fibrinolysis that raises the risk of thrombosis. ^[7] Furthermore, obesity can affect human immunity, reducing immune defenses against infection ^[8]. Multiple studies state this correlation. For instance, an observational study that was carried out in Italy found that obesity was significantly associated with ICU admission in hospitalized COVID-19 patients ^[9].

These findings must be considered, especially taking into account that the 2023 Spanish National Health Survey reported obesity in 15.2% of men and 15.1% of women aged 18 or older [10]. It is also greater in men between 18-24 and 45-64 years (47.0% men and 32.9% women) and even more above 65 years old (40.1% in women and 32.5% in men) [11], which is considered a risk factor by itself [12].

While it is well known that obesity can lead to a worse COVID-19 outcome, few studies have focused on less populated areas in order to evaluate whether obesity increases the likelihood of infection. The aim of this study was to examine the relationship between obesity, infection risk, and disease severity, focusing on hospital admission due to SARS-CoV-2 infection.

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2. Materials and Methods

We conducted an observational, analytical, retrospective case-control study to evaluate whether obesity influences the risk of getting COVID-19 and the likelihood of developing severe disease. Data were collected from September 1st to September 15th, 2021. The study population consisted of a case group and a control group. Cases were adults (≥18 years) with a positive diagnostic test (PCR or antigen) for SARS-CoV-2 between July 1 and August 31, 2021, in Soria province. Exclusion criteria included being registered outside of the Soria province in the health system. Case group was selected by

simple random sampling, and controls with similar sociodemographic characteristics were randomly selected from the primary care database.

There is discrepancy among researchers regarding the correlation between obesity and a higher transmission risk. For that reason, this study has calculated sample size taking into account the percentage of SARS-CoV-2 prevalence among Spanish population in 2021 being 18.6% [13] a 95% confidence interval, and a 5% maximum error, requiring 227 participants per group. Ultimately, 300 individuals were included in each group. Figure 1 demonstrates the case-selection flow diagram.

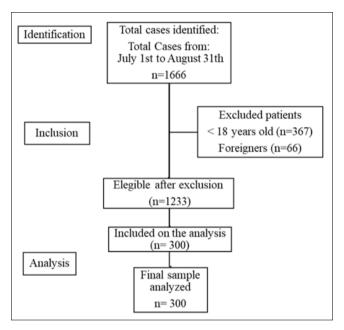


Fig 1: Flowchart for case selection

From the 1233 eligible cases, a random sample of 300 was selected for inclusion in the analysis.

Dependent variables studied in this project were: confirmed COVID-19 infection (positive PCR or antigen test) [14] and severe prognosis requiring hospitalization. The independent variable was obesity, defined as BMI higher than 30 kg/m², [15] along with sociodemographic variables (age, sex and Primary Care Area. Data was extracted from electronic patients records (Medora and Jimena systems), which include weight, height, and automated BMI calculation. Records were accepted as valid if updated within the past year. Hospitalization was considered if it occurred in July or August 2021.

Qualitative variables were described using frequencies and percentages, and the quantitative variables were described with mean, standard deviation, and range. Chi-square tests assessed associations between obesity and infection risk first

and later hospitalization risk among infected patients. Odds ratios (ORs) were calculated with 95% confidence intervals. Statistical analyses were performed using SPSS v25.

The study was approved by the Burgos and Soria Research Ethics Committee for Medical Products. The study followed the principles of the Declaration of Helsinki ^[16]. All data was anonymized with coded identifiers, stored in an encrypted database, and handled in accordance with EU GDPR (Regulation 2016/679) and Spanish data protection law (LOPD-GDD 3/2018).

3. Results: After conforming the group's case group by simple random sampling, control group was selected matching in age and sex distribution. Table 1 summarizes sociodemographic data used in this study.

Table 1: Soc	ciodemographic characteristics of pati	ients
	Case group (n=300)	

Variable	Case group (n=300)	Control group (n=300)		
Women n (%)	134 (44.6)	134 (44.6)		
Men n (%)	166 (55.3)	166 (55.3)		
Average age (range)	32.92 (18-90)	33.62 (18-90)		
Standard Deviation	17.89	17.35		
Primary Care Area				
Ágreda n (%)	8 (2.67)	9 (3)		
Almazán n (%)	26 (8.67)	24 (8)		
Arcos de Jalón n (%)	10 (3.33)	6 (2)		

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Berlanga de Duero n (%)	7 (2.33)	5 (1.67)
Burgo de Osma n (%)	13 (4.33)	17 (5.67)
San Esteban de Gormaz n (%)	1 (0.33)	18 (6)
Gómara n (%)	1 (0.33)	7 (2.33)
Ólvega n (%)	17 (5.67)	15 (5)
Pinares n (%)	8 (2.67)	14 (4.67)
San Leonardo de Yagüe n (%)	25 (8.33)	10 (3.33)
Soria Rural n (%)	29 (9.67)	21 (7)
San Pedro Manrique n (%)	8 (2.67)	2 (0.67)
Soria Norte n (%)	68 (22.67)	70 (23.33)
Soria Sur n (%)	79 (26.33)	82 (27.33)

The prevalence of obesity was also calculated in both the case and control groups relative to the exposure factor under investigation (obesity). The findings are summarized in Table 2.

Table 2: Results of the analysis of case and control groups with respect to the exposure factor.

	Case group (COVID-19 positive)	Control group (COVID-19 negative)	Total
Obese, n(%)	19 (6.33)	18 (6)	37
Not obese, n(%)	281 (93.66)	282 (94)	563
Total, n(%)	300 (100)	300 (100)	

OR (95% CI): 1.06 (0.54-2.06) Chi-square: 0.029, p=0.865.

Prevalence of obesity in the whole study was 6.16%, while in the case group was 6.33% and 6.0% in the control group. We did not demonstrate evidence of an association between obesity and COVID-19 infection risk (p=0.865, OR=1.06, 95% CI: 0.54-2.06).

To evaluate the risk of developing a severe form of the disease, Table 3 examines the association of the factor of obesity, comparing this information with the group of cases that required hospitalization with those that did not.

Table 3: Results of the analysis of case and control groups with respect to the exposure factor.

	Hospitalizated	Not hospitalizated	Total
Obese, n(%)	2 (18.18)	17 (5.89)	19
No obese, n(%)	9 (81.81)	272 (94.11)	281
Total, n(%)	11 (100)	289 (100)	

OR (95% CI): 3,55 (0.712-17.763) Chi-square: 2.70, p=0.100

When analyzing hospitalization among infected patients (Table 3), obesity prevalence was 18.18% in hospitalized vs. 5.88% in non-hospitalized cases. The Chi-square test (90% CI) didn't show statistical significance (p=0.100). The OR of this analysis is 3.55 (95% CI: 0.712-17.763). Although a higher proportion of obesity is observed among hospitalized patients, the association does not demonstrate reach statistical significance.

4. Discussion

This study did not show an association between obesity and a different risk of contracting SARS-CoV-2. However, the results suggest a possible relationship between obesity and a risk factor for developing severe disease once infected, but due to the low number of hospitalized cases, no statistically significant association differences are found.

Previously, several researchers stated that obesity was correlated with worse prognosis of the disease ^[1]. Recent studies investigate this relationship, which can be explained through several mechanisms. On one hand, SARS-CoV-2 spike protein binds to the angiotensin-converting enzyme 2 (ACE2) receptor that is express throughout the body, but especially on adipocytes ^[8].

On the other hand, obesity may cause a chronic

proinflammatory state, reducing immune response.^[7] These factors, combined with comorbidities associated with obesity, such as diabetes, hypertension or cardiovascular diseases, could explain why obesity is a risk factor for developing a severe form of the COVID-19.

A project that studied Italian population, with a sample of 482 patients reported a significant increase in respiratory failure [OR: 2.32, 95% CI (1.31-4.09)] and ICU admission [OR: 4.96, 95% CI (2.53-9.74)] in patients with a BMI higher than 30 ^[9]. Another cohort study conducted in France with 128 patients admitted to the ICU showed that obesity was more frequent in patients admitted due to SARS-CoV-2 infection compared to the control group ^[17]. A meta-analysis including a total of 4,444 patients showed that obese individuals have a higher risk [OR: 2.31, 95% CI (1.3-4.12)] of having a worse prognosis compared to non-obese individuals ^[18].

These results are consistent with our study, in which an OR of 3.55, 95% CI (0.712-17.763) and an obesity prevalence of 18.18% among hospitalized patients were observed, compared to a prevalence of 5.88% (similar to the prevalence in the random control sample) in positive patients who did not require hospitalization. The differences observed between the obesity prevalences in SARS-CoV-2infected patients across the studies mentioned may be due to variations in population obesity prevalence in different countries. In 2016, the World Health Organization estimated the obesity rates on Italy, France, the United States, and Spain were 23.7%, 25.7%, 26.5%, and 35%, respectively [1]. In the present study, the obesity prevalence was 6.16% in the overall study population, 6.33% in cases and 6% in control, which is much lower than the prevalence estimated by the WHO. This may be due to the average age of the sample (32.92 for cases and 33.62 for the control group), since visits to health centers are less frequent among young people, possibly leading to underdiagnosis.

Regarding the relationship between obesity and the risk of infection, several studies evaluated this relationship; however, results differ depending on the population studied. Regarding disease severity, numerous studies report a significantly worse prognosis. Obesity has commonly been associated with greater susceptibility to infections. Petrakis

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[19] conducted a study focused on the relationship between obesity and COVID-19, observing more severe symptoms and a worse prognosis for individuals with this condition, with differences of up to 5 points on the BMI index between patient groups who developed worse symptoms versus those who did not. According to the study, obesity may negatively influence the outcome of the disease, mainly due to the proinflammatory state and decreased immunity in these subjects. These findings are also shown in the meta-analysis published by Yang [18], where after analyzing six studies, it was determined that individuals with severe COVID-19 generally have a higher BMI, while obese patients were more likely to develop severe disease once infected with COVID-19, with a OR of 2.31. In this study, a causal relationship between obesity and the risk of infection could not be established, obtaining an OR of 1.06. However, increasing the confidence interval did reveal significance regarding the risk of hospital admission.

Study limitations include the fact that some cases are asymptomatic. This percentage is difficult to calculate, and previous studies indicate rates ranging from 1.2% in a study conducted in China to 33% in the seroprevalence study conducted in Spain [20, 21]. The control group was not diagnosed with coronavirus disease, but this does not demonstrate guarantee that they did not undergo an asymptomatic infection.

A strength of this study is that data were collected via simple randomization, reducing selection bias with a control group similar in age and sex. Additionally, this study reports that while SARS-CoV-2 affects obese patients in terms of their prognosis, with higher risk of hospitalization, it does not correlate with a higher chance of getting infected.

A further limitation of this study is that only bivariate analyses were performed. Although a multivariable logistic regression could have provided adjusted estimates, particularly for age and sex, the limited number of hospitalized cases made such an approach statistically unreliable. As a result, the study should be interpreted as an exploratory analysis.

The limitations that this study may have include possible undiagnosed asymptomatic cases among controls. On the other hand, some strengths include random sampling and reliable BMI data from primary care measurements, minimizing self-report bias.

This study is reproducible and clinically relevant, with a population attributable fraction of 13% for hospitalization risk in obese patients. These findings suggest that obese patients with COVID-19 may benefit from protocols that consider obesity as a risk factor for viral infections, in order to minimize complications of these types of diseases.

This research highlights the need to continue investigating viral entry mechanisms and the relationship between obesity and the risk of infection, aiming for the implementation of preventive measurements for patients with obesity to avoid virus infection, and in case the patient is infected, obesity should be considered a risk factor for worse prognosis, focusing more on patient monitoring and early detection of potential complications.

Future research should clarify the biological mechanisms correlating obesity to severe disease and investigate whether it independently increases susceptibility to infection.

5. Conclusions

The findings suggest a possible association of obesity and risk of getting hospitalized but due to the low number of hospitalized cases, no statistically significant association differences was found. This study may help raise awareness among the population and healthcare professionals, promoting active patient monitoring, appropriate treatment, and encouraging policymakers to allocate resources to increase resources for health education.

International studies support our results. An Italian cohort (n=482) reported increased risk of respiratory failure (OR: 2.32) and ICU admission (OR: 4.96) with a BMI index higher than 30. A French ICU cohort (n=128) showed higher obesity rates among COVID-19 patients versus non-infected persons. A meta-analysis (n=4,444) found obesity associated with worse outcomes (OR: 2.31).

In our sample, obesity prevalence was lower than WHO national estimates, between 6% and 23-35%, possibly due to the younger average age (32-33 years) and underdiagnosis in primary care.

While evidence on obesity increasing infection risk is inconsistent, its link to severe disease is consistently strong. The proinflammatory state and affected immunity system likely explain a worse outcome, as reported by Petrakis and Yang. Our OR of 1.06 suggests no infection risk increase, but the OR of 3.55 supports higher hospitalization risk.

Obese patients are at higher risk of severe COVID-19 requiring hospitalization, though obesity does not demonstrate appear to increase infection risk itself. This evidence underscores the need for active case detection, appropriate clinical management, and enhanced public health education and resources.

6. Acknowledgments

We thank the urban COVID Unit of Soria province for their support in conducting this study.

7. Funding

This study received no financial support from public, private, or non-profit entities.

8. Conflict of Interest

The authors declare no economic or personal conflicts of interest.

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How to Cite This Article

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Álvarez-Ruiz M, Pérez-Rivas FJ. Case-control study on the influence of obesity on SARS-CoV-2 infection and hospital admission risk in adults. International Journal of Advance Research in Nursing. 2025;8(2):253-257

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