

## **Relationship between obesity and the occurrence of negative outcome in patients hospitalized with COVID-19: integrative literature review**

**Relação entre obesidade e a ocorrência de desfecho negativo em pacientes hospitalizados com COVID-19: revisão integrativa da literatura**

**Relación entre obesidad y ocurrencia de resultado negativo en pacientes hospitalizados con COVID-19: revisión integradora de la literatura**

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### **Abstract**

**Objective:** To verify the relationship between obesity and the occurrence of negative outcomes in hospitalized patients. **Methodology:** An integrative review was carried out using the National Library of Medicine of the National Institutes of Health (PubMed) and the Virtual Health Library (VLH/BVS) database. **Results:** It was observed that obese patients are 2 to 5 times more likely to need Invasive Mechanical Ventilation (IMV) when admitted to the Intensive Care Unit. Patients with high BMI (obese) and who needed mechanical ventilation had a mortality rate above 60%. The risk increases as the patient has other pathologies, this fact is shown that mortality by COVID-19 has multifactorial causes. **Conclusion:** The study showed that obesity is a risk factor associated with the increased development of the severe form of the disease, usually associated with other pathologies (hypertension, diabetes and cardiovascular diseases). That is, obesity increases the likelihood of unfavorable outcomes.

**Keywords:** Obesity; COVID-19; Risk factors.

### **Resumo**

**Objetivo:** Verificar a relação entre a obesidade e a ocorrência de desfechos negativos em pacientes hospitalizados. **Metodologia:** Foi feita uma revisão integrativa, por meio da base de dados Biblioteca Nacional de Medicina dos Institutos Nacionais de Saúde (PubMed) e Biblioteca Virtual em Saúde (VLH/BVS). **Resultados:** Observou-se que pacientes obesos tem de 2 a 5 vezes mais chances de necessitar de Ventilação Mecânica Invasiva (VMI), quando admitidos em Unidade de Terapia Intensiva. Pacientes que apresentam IMC elevados (obesos) e que precisaram de ventilação mecânica apresentaram mortalidade superior a 60%. O risco aumenta conforme o paciente apresenta outras patologias, tal fato é mostrado que a mortalidade por COVID-19 tem causas multifatoriais. **Conclusão:** O estudo mostrou que a obesidade é um fator de risco associado ao aumento do desenvolvimento da forma grave da doença, geralmente associado a outras patologias (hipertensão, diabetes e doenças cardiovasculares). Ou seja, a obesidade aumenta a probabilidade de desfechos desfavoráveis.

**Palavras-chave:** Obesidade; COVID-19; Fatores de risco.

### **Resumen**

**Objetivo:** Verificar la relación entre obesidad y ocurrencia de desenlaces negativos en pacientes hospitalizados. **Metodología:** Se realizó una revisión integradora utilizando la base de datos de la Biblioteca Nacional de Medicina de los Institutos Nacionales de Salud (PubMed) y la Biblioteca Virtual en Salud (VLH / BVS). **Resultados:** Se observó que los pacientes obesos tienen de 2 a 5 veces más probabilidades de necesitar Ventilación Mecánica Invasiva (VMI)

cuando ingresan en la Unidad de Cuidados Intensivos. Los pacientes con IMC alto (obesos) y que necesitaban ventilación mecánica tenían una tasa de mortalidad superior al 60%. El riesgo aumenta a medida que el paciente resenta otras patologías, este hecho se demuestra que la mortalidad por COVID-19 tiene causas multifactoriales. Conclusión: El estudio mostró que la obesidad es un factor de riesgo asociado al mayor desarrollo de la forma grave de la enfermedad, generalmente asociada a otras patologías (hipertensión, diabetes y enfermedades cardiovasculares). Es decir, la obesidad aumenta la probabilidad de resultados desfavorables.

**Palabras clave:** Obesidad; COVID-19; Factores de riesgo.

## 1. Introduction

In Wuhan, China, at the end of 2019 was observed a series of cases of a new virus that caused respiratory infections. Since then the SARS-CoV-2 (new coronavirus), according to the data released by World Health Organisation, already infected over 215 millions people around the world, what has already resulted in 4,48 millions of deaths. In Brazil, according to the data released by Brazilian government, it's 578.326 deaths already, reaching a 2.8% death rate. (OMS, 2021; BRASIL, 2020) The new coronavirus possess an single-stranded RNA enveloped and the transmission is realized human by human, although in China the bats were established as an important reservoir of the virus. The most common clinic symptoms are: fever and cough; but can include dyspnea, headache, muscle pain and fatigue. Is estimated that 20% of the cases are serious, with a 3% death rate. The COVID-19's complications (respiratory failure, acute respiratory distress syndrome (ARDS), sepsis, septic shock, thromboembolism, and/or multiple organ failure), happens mainly in patients with comorbidities such as hypertension, obesity, diabetes, cardiovascular disease, chronic lung disease, among others. (Hu et al., 2017; Wang, Tang, Wei, 2020; Wang, Horby, Hayden, Gao; 2020)

The (re) emergence of the virus has caused several impacts in many areas of society, such as economy and education, but mostly in the health area. The most critical structural limitation during the pandemic in the country was the low number of ICU beds and mechanical fans needed to deal with the serious cases of the disease, furthermore there were difficulties in the acquisitions of the medicines (sedatives, neuromuscular and cardiotoxic blockers), as well as the rising of the prices, with an increase up to 200% in relation to the usual price. The State University of Campinas estimates that an implantation of an ICU bed is something around R\$ 180.000,00, and the daily cost of it is between R\$ 2.500,00 and R\$ 3.000,00. (UNICAMP, 2020; Paiva, et al., 2020; Holanda & Pinheiro, 2020; Saraiva, et al., 2020)

Given that the damages caused to the patient health and the financial impact related to the treatment of serious cases, it's necessary the identification of the predictive risk factors to the development of the severe stage of the disease. Between the factors we can highlight obesity, given that results between other things in a disregulated immune answer, through the increasing of inflammatory cells, for example, impacting among other things the pulmonary functions. (Kulcsar et al, 2019; Dixon et al, 2018).

Being the obesity a prevalent disease in the world population, the information about the impact of this risk factor as for the negative outcome of the disease, could be a great value for the directing of the clinic decision, as the rationing of the resources and consequently a reduction of the costs related to this assistance. In this way, the objective of this integrative revision is to verify the relation between obesity and the occurrences of negative outcome in hospitalized patients.

## 2. Methods

This work is an integrative review based on the research question: "What is the relationship between obesity and the occurrence of negative outcomes in patients hospitalized for COVID-19?". This was delimited by the PICO strategy (acronym for Patient, Intervention, Comparison, Results). The steps taken in preparing the study were: elaboration of the research

question, sampling or search in the literature of primary studies, data extraction, evaluation of primary studies, interpretation of results, presentation of the review.

The primary studies were searched from January to 2021, in the following databases: National Library of Medicine of the National Institutes of Health (PubMed) and Virtual Health Library (VLH / BVS).

The controlled descriptors selected in the Health Sciences Descriptors (HSD) of the Virtual Health Library (VLH / BVS) and HSD in PubMed were “Obesity, CoronavirusInfections, Hospitalization, Mortality, Intensive Care Units, Respiration, Artificial” (in English). The descriptors were combined using the Boolean operators, which obtained the following searches: “Obesity AND CoronavirusInfections AND Hospitalization AND Mortality OR Intensive Care Units OR Respiration, Artificial”.

The inclusion criteria were articles whose main and / or secondary objective was to verify and/or establish the correlation between obesity and negative outcomes in patients hospitalized with COVID-19. Regarding the period, foram selecionados artigos publicados no ano de 2020. The search was conducted in Portuguese, Spanish and English. The exclusion criteria were: studies carried out in emergency rooms and outpatient services in hospitals, case reports and studies, pregnant and pediatric patients.

The choice of articles was divided into three stages:

- 1) Search for articles using descriptors in the databases, filtering the period.
- 2) Reading of titles and abstracts by two independent reviewers who decided to include or exclude the article. In case of disagreement, a third reviewer was invited.
- 3) Reading of the articles in full by the reviewers, in order to identify whether the article answered the proposed question.

Articles were identified in the four databases. After applying the criteria, 308 articles were excluded, for the following reasons: Duplicates (136), Secondary Studies and / or Case Report (12), No Answer To The Proposed Questions (83), Studies in Outpatients (16) and studies with pregnant women and pediatric patients (22). Thus, 39 articles were qualified for this review.

### **3. Results**

The information extracted from the primary studies included in the review is shown in Table 1.

**Table 1** - Information extracted from the primary studies.

ID	Title	Author, Year	Language Country	Objective	Methods	n	Sex	Age	Obesity			Statistical Association with Obesity	Conclusion	Limitation
									n	Severe	Death			
01	30-day mortality in patients hospitalized with COVID-19 during the first wave of the Italian epidemic: A prospective cohort study.	Giacomelli et al., 2020	English Italy	Describe the demographic and clinical characteristics of hospitalized patients with COVID-19 and factors associated with the risk of death related to COVID-19.	Prospective cohort study, with data extracted from the clinical records of adult patients.	233	161 (69,1%) Masculine	61	38 (16,3%)	-	25 (65,7%) 25/38	Mortality aHR 3,04 [IC 95% 1,42-6,49]	Obesity is associated with a 3x greater risk of death than patients with a BMI <30 kg/m <sup>2</sup> .	Low number of tests performed at hospital admission; Low number of CT scans performed; Difficulty in determining the effect of medications on the course of the disease;
02	Association of Body Mass Index and Age With Morbidity and Mortality in Patients Hospitalized With COVID-19: Results From the American Heart Association COVID-19 Cardiovascular Disease Registry.	Hendren et al., 2021	English USA	Evaluate the relationship between body mass index and mortality, mechanical ventilation, adverse cardiovascular, renal and venous thromboembolic outcomes in patients admitted with COVID-19	Retrospective study, with data collected from 88 hospitals in the USA.	7606	4207 (55%) Masculine	63	3311 (43,4%) 3311 (43,5%) - Obese Class I: 1623 (21,3%) Class II: 846 (11,1%) Class III: 842 (11%)	VMI Class I: 364 (22,5%); Class II: 214 (25,3%); Class III: 223 (26,6%); (p<0,001)	Class I: 237 (14,6%); Class II: 132 (15,6%); Class III: 223 (26,5%) (p<0,001)	Mortality Class III (HR, 1.30 [95% CI, 1.03-1.63]);  VMI Class I (OR = 1,54 [IC 95%: 1,29-1,84]); Class II (OR = 1,88 [95 % CI: 1,52-2,32]); Class III (OR = 2,08 [95% CI: 1,68-2,58]);	Obesity is associated with increased risk of death, mechanical ventilation, occurrence of thromboembolism and need for dialysis, especially in younger patients.	The non-generalization of data to smaller hospitals. Information may have been underreported. The researchers were unable to assess whether the occurrence of no resuscitation order was a factor that interfered with the established primary outcome.
03	BMI as a Risk Factor for Clinical Outcomes in Patients Hospitalized with COVID-19 in New York.	Kim et al., 2020	English USA	Study the association between BMI and clinical outcomes among patients with coronavirus infection in 2019 (COVID-19)	Retrospective study analyzing electronic medical records of patients diagnosed with Covid-19 admitted to 12 hospitals in the USA.	10.861	6468 (59,6%) Masculine	65	4090 (37,7%) - Obese Class I: 2341 (21,6%) Class II: 990 (9,1%) Class III: 755 (7,0%)	IMV Class I: 517 (22,1%); Class II: 248 (25,1%); Class III: 200 (26,6%); (p<0,001)	Class I: 470 (20,1%); Class II: 207 (20,9%); Class III: 165 (21,9%)	BMI: Class I (OR = 1,48 [IC 95%: 1,27-1,72]); Class II (OR = 1,89 [95 % CI: 1,56-2,28]); Class III (OR = 2,31 [95% CI: 1,88-2,85]);  Mortality Class II: OR = 1,25 [IC 95%: 1,03 -1,52] Class III: OR = 1,61 [IC 95%: 1,30-2,00]	All classes of obesity were associated with increased risk of IMV. In addition, grade II obesity and grade III obesity were associated with greater chances of death. However, among intubated patients, BMI was not statistically associated with the risk of death.	Use of Administrative data that may limit clinical information; Difference between patient populations;
04	Clinical characteristics of coronavirus disease 2019 in a single center of Argentina. Retrospective cohort	Castro et al., 2020	English Argentina	Evaluate the clinical characteristics, evolution and severity of COVID-19 in a third-level hospital in Argentina	Retrospective cohort of 101 patients with COVID-19. Patients were divided according to the presence or absence of	101	54 (53%) Feminine	42	18 (18%)	Pneumonia 8 (31%) (8/26)	-	Severe Pneumonia p (0,061)	There was no significant correlation between obesity and the occurrence of severe pneumonia	Retrospective analysis; Few laboratory and radiological tests; Limited study population;

					pneumonia and disease severity.									
05	Characteristics and Risk factors for mortality in patients hospitalized by COVID-19 in a public hospital in Tacna.	Zavaleta et al., 2021	Spanish Peru	Describe the clinical, laboratory and treatment characteristics of patients hospitalized for COVID-19 and determine the risk factors for in-hospital mortality.	Retrospective cohort of adult patients hospitalized by COVID-19. Clinical, laboratory and treatment data were extracted from the medical records of hospitalized patients	351	260 (74,1%) Masculine	61	111 (31,6%)	-	42 (37,8%) (42/111)	-	There was no significant correlation between obesity and the occurrence of pneumonia.	Retrospective analysis; Limited study population;
06	Characteristics, predictors and outcomes among 99 patients hospitalized with COVID-19 in a tertiary care center in Switzerland: an observational analysis	Gregoriano et al., 2020	English Switzerland	Describe the admission characteristics, risk factors and outcomes of patients with 2019 coronavirus disease (COVID-19) hospitalized in a tertiary hospital in Switzerland	Retrospective cohort study included adult patients with (SARS-CoV-2) infection.	99	63 (62,5%) Masculine	67	27 (27%)	Severe 12 (34%) (12/35)	-	Severe OR 1,70 (IC= 0,69-4,22) p = 0,249	There was no significant correlation between obesity and the outcome assessed.	Absence of data in medical records; Patients transferred during hospitalization; retrospective analysis;
07	Clinical characteristics and day-90 outcomes of 4244 critically ill adults with COVID-19: a prospective cohort study	COVID-ICU Group on behalf of the REVA Network and the COVID-ICU Investigators*	English France, Belgium e Switzerland	Describe the severity of acute respiratory distress syndrome (ARDS), the management of ventilation, and the outcomes of ICU patients with laboratory-confirmed COVID-19, and determine risk factors for mortality within 90 days of admission to the ICU.	Multicenter prospective cohort conducted in 138 hospitals in France, Belgium and Switzerland. Demographic, clinical, respiratory support, adjuvant interventions, length of stay in the ICU and survival were collected.	4.244	3159 (74,4%) Masculine	63	1607 (41%)	-	440 (27,3%) 440/1607	-	Mortality was higher in elderly, diabetic, obese and severe ARDS patients.	Absence of data; Lack of standardization in data collection
08	Clinical characteristics and in-hospital mortality of COVID-19 adult patients in Saudi Arabia	Abohmr et al., 2020	English Saudi Arabia	Provide a detailed study of demographic, baseline comorbidities, clinical features, and outcomes for patients with coronavirus disease in 2019 (COVID-19).	Study of case series, of inpatient registration.	768	589 (76,7%) Masculine	≅ 46	143 (18 6%)	ICU 102 (71,3%)	63 (44%) (63/143)	ICU OR = 3,732 [IC = 2.511-5.546]	There was a statistical association between obesity, ICU admission and death.	Limited study population; It was difficult to obtain data on admission;

09	Clinical characteristics and outcomes in women and men hospitalized for coronavirus disease 2019 in New Orleans.	Yoshida et al., 2021	English USA	Determine if sex differences exist in clinical characteristics and outcomes of adults hospitalized for coronavirus disease 2019 (COVID-19) in a US healthcare system.	Demographic data, comorbidities, presenting symptoms and laboratory results. Outcomes included admission to the intensive care unit (ICU), invasive mechanical ventilation (IMV), and hospital death.	776	476 (61,4%) Women	≅ 60	411 (53%)	-	-	ICU Obesity: OR 1.55 [IC 1.10-2.17] BMI >40: OR 2.48 [IC 1.43-4.29]  VMI Obesity: OR 2.41 [IC:1.63-3.56] BMI 35-39.9: OR 2.68 [IC 1.42-5.06]; BMI >40: OR 3.85 [IC:2.07-7.17]	Obesity was associated with Mechanical Ventilation at a lower BMI (> 35) in women, but the effect of morbid obesity (BMI ≥ 40) was similar in both sexes. When multivariate analyzes were performed by race, obesity was associated with greater odds of ICU, IMV and death in black patients in general. However, obesity was not associated with death in non-black women and men.	Limited population; Limited number of patients from some ethnic groups, such as Asians and Native Americans, preventing more accurate racial/ethnic stratification in the analysis.
10	Clinical characteristics and outcomes of critically ill patients with COVID-19 admitted to an intensive care unit in London: A prospective observational cohort study	Thomson et al., 2020	English United Kingdom	Understand the clinical characteristics and outcomes of patients admitted to a United Kingdom ICU with severe COVID-19.	Prospective observational cohort of all patients with COVID-19 admitted to a large United Kingdom ICU.	156	112 (72%) Masculine	62	31 (20,1%)	-	-	Death OR 3,06 [IC 95% 1,16-8,74];	Obese patients in the ICU were 3 (three) times more likely to evolve to death.	The screening and criteria used to identify patients who require (and are suitable for) admission to the ICU may have affected our cohort composition and, potentially, relationships between exposures and outcomes.
11	Clinical Characteristics and Outcomes of Patients Hospitalized for COVID-19 in Africa: Early Insights from the Democratic Republic of the Congo	Nachega et al., 2020	English Congo Republic	Describe the clinical, laboratory and outcome characteristics of patients hospitalized with COVID-19 in the DRC and differentiate them from other non-African populations.	Cohort using data routinely collected from the DRC Ministry of Health Multisectoral Response Committee database COVID-19	766	500 (65,3%) Masculine	46	39 (5,1%)	Serious 22 (56,4%) (22/39)	17 (43%) (17/39)	Death aHR 2,30 [ IC 95% 1,24-4,27]	Obesity increases the risk of death by 2 (two) times.	It was not possible to compare clinical characteristics between hospitalized patients with COVID-19 and outpatients.
12	Clinical Characteristics and Prognosis of 244 Cardiovascular Patients Suffering From Coronavirus Disease in Wuhan, China.	Peng, et al., 2020	English China	Summarize the clinical characteristics and laboratory indicators of patients with COVID - 19 with CVD, especially critically ill patients.	Clinical, laboratory and outcome data were collected from the patients' medical records and compared between the 2	244	131 (53,69%) Feminine	61	80 (32,7%) BMI ≥24	-	34 (42,5%) (34/80)	Death Obesity: OR 8,43 [IC 95% 3,81-18,64]	Overweight/obesity combined with coronary heart disease, severe hypoxia and lactic acid accumulation resulting from respiratory failure	Descriptive study; Limited number of cases;

					groups								are related to unfavorable outcomes.	
13	Clinical characteristics and risk factors associated with severe COVID-19: prospective analysis of 1,045 hospitalized cases in North-Eastern France, March 2020.	Kaeuffer et al., 2020	English France	Identify predictive risk factors for serious illness and death in France	Prospective non-interventional study of hospitalized COVID-19 adult patients. Severe illness was defined by composite criteria, including death or admission to the ICU within 7 days of hospitalization	1045	612 (58,6%) Masculine	66	351 (39,1%) (351/897)	Serious 164 (46,7%) (164/351)	-	Serious illness Obesity: OR 2,2 [IC 95% 1,5–3,3];  Death Obesity: OR 1,4 [IC 95% 0,7 - 2,5]	Obesity is a risk factor for severe COVID-19, but it is not related to the death of hospitalized patients.	Possible lack of data; self-report of comorbidities; There were no d-dimer tests and/or other inflammatory markers.
14	Clinical outcomes and inflammatory marker levels in patients with Covid-19 and obesity at an inner-city safety net hospital.	Mostaghimi, et al., 2020	English USA	Characterize the association between clinical outcomes in patients with obesity and inflammatory markers	Retrospective cohort where there was a comparison between outcomes and inflammatory markers in patients with Covid-19 stratified by BMI and T2D.	791	460 (58,2%) Masculine	65	363 (45,9%)	ICU 98 (52,4%)	-	Death BMI $\geq$ 35: aOR = 4,27 [IC 95% 1,69–10,82]	Obese patients had a higher transfer rate to the ICU (27.1% vs 20.7%, p = 0.04). BMI $\geq$ 35 was associated with a two-fold greater risk of transfer to the ICU and a four-fold greater risk of all-cause mortality;	Limited data, observational study
15	Comorbidities and Mortality in Patients With COVID-19 Aged 60 Years and Older in a University Hospital in Spain.	Posso et al., 2020	English Spanish	To analyze whether the type of comorbidities increases the risk of in-hospital mortality in patients with COVID-19 aged 60 years or more treated at the university hospital	Retrospective evaluation of prospectively collected data from clinical records	834	446 (53,5%) Feminine	$\cong$ 72	55 (6,6%)	-	12 (21,8%) (12/55)	Death aOR 1,21 [CI95% 0,60-2,45] p > 0,05	There was a higher risk of obese patients evolving to death, but the correlation was not significant.	Limited number of cases; Absence of information in medical records; It was not possible to establish the effect of treatment on the outcome;
16	Comorbidity and clinical factors associated with COVID-19 critical illness and mortality at a large public hospital in New York City in the early phase of the pandemic (March-April	Filardo et al., 2020	English USA	Evaluate demographic data, comorbid conditions and clinical factors associated with critical illness and mortality among patients diagnosed with COVID-19	Retrospective study of patients diagnosed with COVID-19	337	182 (67,4%) Masculine	58	109 (41,8%) (109/261)	ICU 59 (54,1%) (59/109)	35 (32,1%) (35/109)	Mortality (aRR 1,37, 95% CI 1,07-1,74)	There was a statistical association between obesity and increased mortality.	Retrospective analysis (no data)



	2020).													
17	COVID-19 Experience in a Wisconsin Academic Medical Center.	Kolinski et al., 2020	English USA	Describe the demographic characteristics and outcomes of patients admitted with COVID-19.	We performed a retrospective analysis of data obtained for patients with COVID-19 admitted from March 14, 2020 to April 19, 2020.	178	93 (55%) Masculine	65	80 (48%) (80/168)	ICU 50 (62,5%) (50/80)	-	ICU p= 0,021	There was a statistical association between obesity and admission to the ICU.	
18	COVID-19 hospitalizations in Brazil's Unified Health System (SUS).	De Andrade et al., 2020	English Brazil	Understand the profile of hospital admissions of COVID-19 in the Unified Health System (SUS) and identify the factors associated with the occurrence of hospital deaths related to the disease, considering the characteristics of the patient and the care provided. focusing on regional variations.	Analysis of medical records of hospitalized patients over 18 years of age in the SUS	89.450	50539 (56,5%) Masculine	60	665 (0,7%)	-	224 (33%) 224/665	Mortality OR: 1,8 [IC 95% 1.5-2,25] p<0.0001	Obesity was statistically associated with a greater chance of hospital death (56.3% higher among obese people compared to non-obese people).	High underreporting; Data from the public network only;
19	Demographic and clinical features of critically ill patients with COVID-19 in Greece: The burden of diabetes and obesity.	Halvatsiotis, et al., 2020	English Greece	To investigate the association between type 2 diabetes mellitus, other underlying diseases and obesity with the outcomes of critically ill patients with Covid-19 in Greece.	Retrospective multicenter study, data and outcomes of 90 critically ill patients confirmed by RNA 2109-nCoV from 8 hospitals across Greece were analyzed.	90	72 (80%) Masculine	65	31 (34,4%)	-	12 (38,7%) 12/31	Obesity was more frequent (46.2%) among the deceased than among the survivors (26.7%) (p = 0.077)	The p value suggests that there may be a relationship between obesity and mortality	Retrospective data; Absence of test results;
20	Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterization Protocol: prospective observational cohort study.	Docherty, et al., 2020	English United Kingdom	Describe the clinical characteristics of inpatients with 2019 coronavirus disease (covid-19) in the UK	Prospective observational cohort study with rapid data collection and near real-time analysis.	20.133	12068 (59,9%) Masculine	73	2.215 (11%)	-	-	Mortality HR 1.33 [IC 95% 1.19-1.49] p<0,001	Obesity was associated with higher hospital mortality.	Absence of records in medical records;



21	Features of patients that died for COVID-19 in a hospital in the south of Mexico: A observational cohort study.	Ruíz-Quiñonez et al., 2021	English Mexico	Evaluate demographic characteristics, clinical characteristics and pharmacological treatment of individuals who died from COVID-19 in southern Mexico.	Observational study including information from 185 deceased people with a confirmed diagnosis of COVID-19. Data were retrieved from medical records.	185	95 (60,1%) Masculine	≈ 59	41 (25,9%)	-	-	Mortality HR 1.92	Epidemiological data from COVID-19 in Mexico indicate that obesity is a risk factor for death and a partial mediator of the effects of diabetes on reduced survival	Absence of records in medical records;
22	ICU outcomes in Covid-19 patients with obesity.	Parikh et al., 2020	English USA	A study explores the clinical relationship between obesity and Covid-19 in patients admitted to an intensive care unit (ICU) in a tertiary hospital.	We conducted a retrospective cohort study of adult patients with laboratory-confirmed severe acute respiratory syndrome coronavirus 2	160	46 (55,4%) Masculine	≈ 56	83 (52%)	IMV 52 (62,6%) (52/83)	26 (31,3%) (26/83)	IMV OR: 2.0 [IC 95% 1.1-3.8]	Obese patients were twice as likely to need mechanical ventilation. However, there was no significant relationship between obesity and death.	Small sample size; Absence of records in medical records;
23	Obesity and the Risk of Intubation or Death in Patients With Coronavirus Disease 2019.	Frank, et al., 2020	English USA	To characterize the impact of obesity on disease severity in patients with coronavirus disease.	Retrospective cohort study.	305	128 (42%) Feminine	60	127 (42%)	-	-	IMV ≥ 30 kg/m2 to < 35 kg/m2 HR: 2.1 [IC 95% 1.2-3.9]  Mortality BMI ≥ 35 kg/m2 HR: 2.0 [IC 95% 1.1-3.6] p = 0.02	Obesity was an independent risk factor for IMV and death.	Small sample size; Absence of BMI registration;
24	Obesity is Associated with Increased Risk for Mortality Among Hospitalized Patients with COVID-19.	Petti, et al., 2020	English USA	Determining whether obesity is a risk factor for mortality among patients with COVID - 19.	Study was a retrospective cohort.	238	113 (47,5%) Masculine	≈ 58,5	146 (61,3%)	ICU 38 (26%) 38/146  IMV 23/146 (15,7%)	14 (9%) (14/146)	Mortality OR: 1.7 [IC 95% 1,1-2,8] p = 0,016	Obesity was considered a significant predictor of mortality among hospitalized patients with COVID - 19 after adjusting for age, sex and other comorbidities.	Small sample size and the fact that it is a retrospective analysis.
25	Obesity predisposes to the risk of higher mortality in young COVID-19 patients.	Zhang, et al., 2020	English China	Check whether obesity is a risk factor associated with death in young patients	Study was a retrospective cohort.	53	-	-	-	-	12 (27,9%) 12/43	Mortality OR: 1,3 [IC 95% = 1,075-1,70] p = 0,010	Obesity was a risk factor associated with the occurrence of mortality	Limited number of sample size
26	Obesity prolongs the hospital stay in patients affected by COVID-19, and may impact on SARS-COV-2 shedding.	Moriconi, et al., 2020	English Italy	Investigate whether obesity is a predictor of worse outcome in patients with COVID.	This retrospective observational study was based on medical records of hospitalized patients.	100	57 (57%) Masculine	69	29 (29%)	-	5 (17,2%) 5/29	-	In partial least squares regression, there was no statistical association between obesity and mortality.	Sample size;

27	Obesity and smoking as risk factors for invasive mechanical ventilation in COVID-19: A retrospective, observational cohort study.	Monteiro et al., 2020	English USA	Describe the trajectory of respiratory failure in COVID-19 and explore factors associated with the risk of invasive mechanical ventilation (IMV).	Retrospective and observational cohort study with electronic medical records of hospitalized adult patients.	112	74 (66%) Masculine	61	40 (36%)	IMV 17/40 (42,5%)	-	IMV OR 5.82 [IC 1,74-19,48] p=0,004	Obesity was associated with a greater need for IMV among hospitalized patients.	-
28	Outcomes for patients with COVID-19 admitted to Australian intensive care units during the first four months of the pandemic.	Burell et al., 2020	English Australia	To describe the characteristics and outcomes of patients with COVID-19 admitted to intensive care units (ICUs) during the first months of the pandemic in Australia.	Prospective observational cohort study in 77 ICUs across Australia.	204	140 (69%) Masculine	63	81 (40%)	IMV 52/81 (64,1%)	8 (9,8%) 8/29	Death OR 0,32 [IC 0,13-0,79]	There was no statistical correlation between death and mortality.	Non-exploitation of decision-making regarding admission to the ICU. And the observational nature of the study.
29	Relationship between obesity and severe COVID-19 outcomes in patients with type 2 diabetes: Results from the CORONADO study.	Smati et al., 2021	English France	To assess the relationship between body mass index (BMI) classes and COVID-19 early prognosis in hospitalized patients with type 2 diabetes (DM2).	From the CORONAVIRUS-SARS-CoV-2 and Diabetes Outcomes (CORONADO) study, an analysis was performed in patients with DM2.	1965	1267 (64%) Masculine	71	805 (41%)	IMV 195 (24%) 195/805	78 (9,6%) 78/805	IMV Class II: 1,94 [IC 1,36-2,76], p = 0,0003 Class III: 2,63 [IC,81-3,83], p <0,0001	There was an association between obesity and intubation, but there was no statistical association with mortality.	The specificity of patients: hospitalized with DM2; Short follow-up period;
30	Risk factors for mortality in hospitalized patients with COVID-19 at the start of the pandemic in Belgium: a retrospective cohort study.	Van Halem et al., 2020	English Belgium	Identify the main risk factors for hospital mortality of patients with COVID.	Retrospective cohort study, with data collection through electronic medical records.	319	191 (60%) Masculine	74	54 (23%) 54/230	-	19 (35,1%) 19/54	-	In the univariate analysis, patients with obesity had an overall increased risk of death, while overweight, on the other hand, showed a trend toward lower mortality.	The retrospective cohort was carried out in a single center; There was no correction for multiple comparisons, making predictors with p values close to 0.05 less likely to be true associations.
31	Selective CD8 cell reduction by SARS-CoV-2 is associated with a worse prognosis and systemic inflammation in COVID-19 patients.	Urta et al., 2020	English Spain	To analyze comorbidities, inflammation indicators such as CRP and the neutrophil/lymphocyte ratio, as well as the count of blood cells with T lymphocyte subtypes in patients hospitalized with Pneumonia COVID-19.	A retrospective case-control study was carried out in patients with COVID-19 pneumonia admitted to the University Hospital of Ciudad Real (Spain)	172	104 (60%) Masculine	-	17 (9%)	ICU 7/17 (25%)	-	ICU OR = 4,72 [IC 95% 1,614-13,830, p=0,005]	There was a statistical association between obesity and admission to the ICU	-

32	Severe Obesity as an Independent Risk Factor for COVID-19 Mortality in Hospitalized Patients Younger than 50.	Klang et al., 2020	English USA	To analyze obesity as an independent risk factor for mortality in hospitalized patients under 50 years of age.	We retrospectively analyzed data from patients with COVID-19 hospitalized in a large academic hospital system in New York City.	3406	1961 (57,5%) Masculine	-	1231 (36%)	-	-	≤50 anos: BMI >40 (OR = 5,1); > 50 anos: BMI >40 (OR = 1,6);	Hospitalized patients under 50 years of age with severe obesity are more likely to die from COVID-19.	Retrospective study; small number of patients under 50 years old
33	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.	Palaiodimos et al., 2020	English USA	Evaluate the characteristics and baseline outcomes of patients hospitalized with COVID-19 in the Bronx and investigate whether obesity is associated with worse outcomes regardless of age, sex, and other comorbidities.	Retrospective study with review of electronic medical records,	200	102 (51%) Feminine	64	162 (81%)	IMV 35 (21,6%) 35/162 ICU 29 (17,9%) 29/162	36 (22%) 36/162	Mortality BMI ≥ 35kg/m <sup>2</sup> : OR 3,78 [IC 95%: 1,45–9,83] p= 0,006	Severe obesity was associated with higher hospital mortality, even after adjusting for other potentially confounding factors.	Retrospective study and reduced sample size
34	The impact of obesity on COVID-19 complications: a retrospective cohort study.	Nakeshbandi et al., 2020	English USA	To elucidate the association between obesity and COVID-19 outcomes.	Retrospective cohort study of patients hospitalized with COVID-19.	504	263 (52%) Masculine	68	215 (43%)	IMV 60 (28%) 60/215	87 (42,4%) 87/215	Mortality RR 1,3 [IC 95% 1,0–1,7] p=0,04 IMV RR 2,4 [IC 95% 1,5–4,0] p = 0,001	Overweight and obese patients who have COVID-19 are at increased risk of mortality and intubation compared to those with normal BMI.	Retrospective observational study, and presence of confounding bias for some outcomes.
35	The importance of overweight in COVID-19: A retrospective analysis in a single center of Wuhan, China.	Rao et al., 2020	English China	Evaluate the association between overweight and severity, drug response and clinical outcomes of the new coronavirus 2019 disease (COVID-19).	Retrospective cohort study, with review of medical records.	240	129 (53,8%) Feminine	48	114 (47,5%)	Severe Pneumonia 73 (64%) 73/114	-	Severe Pneumonia OR 3,075 [IC 95% 1,18 -7,96], p= 0,021	Overweight is associated with a severe form of pneumonia, but it is not associated with death.	Descriptive study with reduced sample size.
36	The obesity paradox: Analysis from the SMAteo COvid-19 REgistry (SMACORE) cohort.	Biscarini et al., 2020	English Italy	To examine the correlation between obesity, 30-day mortality and admission to the Intensive Care Unit (ICU) in patients with Covid-19.	Retrospective cohort study with revised medical records and analysis of demographic, clinical, and outcome data.	427	291 (68,1%) Masculine	67	74/331 (22,3%)	ICU 21 (28,4%) 21/74	25 (33,8%) 25/74	ICU OR 1,96 [IC 95% 1,03-3,75] p= 0,001	Obesity was associated with ICU admission, but it was not associated with death.	Descriptive study, with reduced sample size, and non-differentiation of BMI calculation between adipose and muscle tissue.

37	The relationship between obesity, hemoglobin A1c and the severity of COVID-19 at an urban tertiary care center in New York City: a retrospective cohort study.	Randhawa et al., 2021	English USA	Determine whether obesity and diabetes are risk factors for serious outcomes in COVID-19 and compare patient outcomes in these two conditions.	Retrospective cohort study.	302	195 (64,5%) Masculine	-	152 (50,3%)	IMV 71(46,7%) 71/152	-	Patients with obesity and/or diabetes were more likely to develop ARDS (79 patients x 57 patients, p < 0.0001) and to be IMV (71 patients x 45 patients, p = 0.0031)	Patients with obesity and/or diabetes were more likely to experience serious complications but had insignificant differences in mortality	Absence of blood gas data; Distribution of body fat in the elderly.
38	The role of obesity in inflammatory markers in COVID-19 patients.	McNeill et al., 2021	English USA	Evaluate inflammatory markers in obese and non-obese individuals hospitalized for COVID-19.	Retrospective cohort study.	781	453 (58%) Masculine	61	349 (45%)	ICU 129 (37%) 129/349  IMV 109 (31%) 109/349	49 (14%) 49/349	Mortality OR 2,20 [IC 95% 1,31-3,70] p= 0,003)	Obesity was associated with mortality	There may have been an investigation bias, as inflammatory markers were not measured at defined intervals. In addition, the fact that it is a single-center research.
39	The swedish covid-19 intensive care cohort: Risk factors of ICU admission and ICU mortality.	Ahlström et al., 2021	English Sweden	To assess the impact of pre-COVID-19 medications, the comorbidity-related risk for ICU admission as an indicator of severe disease in COVID-19, and the effect of these factors on the risk of mortality in the ICU.	Retrospective study of data analysis of patients admitted to the ICU	1981	1465 (74%) Masculine	61	123 (6,2%)	-	19 (15,4%) 19/123	ICU OR 2,37 [IC 95% 1,81-3,11] p= 0,001	Obesity was related to admission to the ICU, but it was not related to death from COVID-19.	Patients who were referred to the ICU, but who were not admitted due to wear and tear on the healthcare system.

Source: Research Protocol (2020).

Among the observed data shown in the table above, there is a prevalence of males (77%) with an average age of 61 years, demonstrating that this is an elderly population. When evaluating the incidence of obese patients hospitalized by Covid-19, the mean was 33%, compared to obese patients who required Invasive Mechanical Ventilation (IMV) it was approximately 37%.

#### 4. Discussion

The surveys carried out in the USA corresponded to 37.5% (15) of the studies included in this review, while 35.89% (14) studies were carried out in European countries. Although Vasconcelos et al., (2020) demonstrate that China stood out in scientific production related to COVID-19, presenting the largest number of publications related to the topic in 2019 and 2020, the leading role of obesity-related research in the US may be a reflection of the high incidence of this comorbidity, being present in 35% of the North American population, as described by De Sousa et al., (2008). Thus, there was greater concern about the implications of the correlation between obesity and the occurrence of COVID-19 in the context of the pandemic.

Regarding the adopted methodology, 89.7% (35) of the studies were carried out through retrospective data review. According to Fernandes et al, (2005), among the weaknesses/limitations of this type of study there is the information bias and the inability to control confounding variables (lack of information), this fact corroborates the data collected from the studies in this review where the potential or the real lack of information was one of the points most evident as limitations in the studies, along with the sample size and the difficulty of measuring outcomes in a pandemic scenario.

There was great variation in the number of patients in the populations studied, with samples ranging from 53 to 89,450 participants, with an average of 3864 participants per survey. Regarding the characteristics of the population, the average age was 61 years among the studies, this information was not found in 04 studies. The prevalence of older adults in the samples is evident, which according to the authors may also have corroborated for the outcomes. Matsudo et al, 2000 says that there is evidence in the literature that aging brings neuromotor, metabolic and anthropometric variations to the population.

In the studies analyzed, there was a prevalence of males in 77% (30) of the researches, only 01 article did not take gender into account. This is consistent with some studies that confirmed that men have characteristics that enhance the disease, due to greater disregard for health and low use of primary and secondary care, being at greater risk of clinical decompensation (Camarano, 2002; Almeida et al., 2015).

For the definition of obesity, the classification proposed by the WHO was used, in which the BMI that determines obesity is above 30kg/m<sup>3</sup>. It was possible to identify the information on the prevalence of obesity in 37 studies, 01 there was no information on the number of obese patients in relation to the population studied, and in another study, the BMI value >24kg/m<sup>2</sup> was considered for statistical analysis purposes. That would fit the overweight classification, according to the WHO. The percentage incidence of obese patients hospitalized by Covid in the extracted data ranged from 0.7% to 81%, with a mean of 33%. Even before the new coronavirus pandemic, obesity was already considered a global challenge, however, with the restrictions established by governments and health promotion/protection entities that aimed to reduce the circulation of the virus, there was na increase in the sedentary and weight gain (Posso et al., 2020).

Insulin resistance, changes in metabolism, hyperglycemia, and increased inflammatory markers are just some of the changes Obesity itself is a metabolic entity characterized by changes related to its occurrence. This, combined with vascular and pulmonary alterations, as well as the increased expression of the angiotensin 2 converting enzyme, and the adipose tissue itself, which can behave as a means for intense viral replication, thus creating na exacerbated immune response, make this comorbidity na important predictive and prognostic factor for understanding the course of the disease and its severity (Saryer et al., 2020; Guzik et al., 2020; Shah et al., 2021).

Of the evaluated articles, 23 brought data from obese patients who had severe complications, some of them evaluating more than one outcome: invasive mechanical ventilation (IMV) (n 9) and/or admission to the intensive care unit (n 9) and/or occurrence of severe pneumonia (n 2), or only outcomes defined as severe (n 3). The percentage of obese hospitalized patients who required IMV ranged from 15.7 to 64.1%, with an average of approximately 37%, while the percentage of obese patients with COVID who were admitted to the ICU ranged from 17.9% to 62.5% with an average of 41%. And the relationship between obesity and mortality was assessed in 24 articles, with a death rate ranging from 9% to 65.7%, with a mean death rate of 29.7%. It is worth noting that among the articles mentioned, there were 02 (two) studies that showed the relationship between obesity and the IMV and mortality outcomes, stratifying by degree of obesity according to the WHO classification, in these it was shown that the greater the degree of obesity, the higher the percentage of patients who evolve with IMV and death.

Regarding statistical associations (odds ratio, relative risk and hazard ratio), 06 (six) studies evaluated the correlation between obesity and IMV in 100% of them there was a statistical correlation, which showed that obese patients are 2 to 5 times more likely to need VMI. When the outcome evaluated was admission to the ICU, in all 06 (six) articles that evaluated this outcome, there was a positive correlation, as the occurrence of obesity makes the patient with COVID 1.5 to 4.7 times more likely to be admitted to the intensive care unit. In one of the studies where there was stratification by race, only obese blacks were associated with intensive care. The occurrence of death in obese patients was evaluated in 29 articles, of which 17 (58.6%) showed a significant correlation between obesity and increased mortality, one of the studies showed an 8-fold increase in the chances of death in obese patients.

Some studies report that when considering a scenario of mechanical ventilation, obese patients would be subject to longer periods of intubation, greater difficulty in weaning from mechanical ventilation and handling by professionals in non-specialized health centers, factors that could contribute for unfavorable outcomes (Severin et al., 2020; Stefan et al., 2020). Muscogiuri et al., (2020), points out that patients with COVID with a BMI value above 30 kg / m<sup>2</sup> and who were referred for mechanical ventilation had a mortality rate of 60.9%. Furthermore, it was also observed that the recommendation and need for mechanical ventilation increased with the degree of obesity, which may explain the variability between studies. In addition, it is difficult to obtain the patients' BMI data, since most of the time this value is obtained in an estimated way during hospitalization.

In the study by Thomsom et al. (2020), the absence and unclear criteria for admission to the intensive care units (ICU) would be a confounding factor in the analysis of admitted patients. In this regard, some scores created to assess hospitalized patients with COVID are already available, which aim to identify those who need intensive support in less time, helping clinical decision-making in a stressful and low-resource context (Zhao et al., 2020; Kumar et al., 2020)

Louie et al. (2011) and Dawood et al. (2009) reported during the H1N1 influenza epidemic a large proportion of hospital admissions and mortality were associated with obesity, and now a growing number of studies suggest that the outcomes of obese patients are worse compared to non-obese patients. Obese individuals who became infected with the coronavirus. It is a fact that mortality from COVID has multifactorial causes, among which we can highlight: diabetes, cardiovascular, cerebrovascular, pulmonary diseases and advanced age are some of the predictors already identified (Muscogiuri et al., 2020; Li et al., 2020; Du et al., 2020; Kang et al., 2020; Ruan et al., 2020; Grasselli et al., 2020).

## 5. Conclusion

According to the studies analyzed, they showed that obesity increases the incidence of unfavorable outcomes, such as increased ICU admission, increased intubation and invasive mechanical ventilation, that is, obesity is a risk factor for the development of the severe form of the disease. The findings of this study also concluded that mortality was associated in 50%



of the studies. It is important to mention that obesity is usually associated with several other pathologies, such as: hypertension, diabetes and cardiovascular diseases, which are also a risk factor for the development of the severe form of COVID -19. Therefore, there is a need for studies that seek to correlate to which dangers obese individuals and those with comorbidities are exposed.

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