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Association of obesity with COVID-19 diseases severity and mortality: A meta-analysis of studies

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**Keywords:** Coronavirus, COVID-19, Obesity, Mortality, Severity

**ABSTRACT**

**Background:** The literature on COVID-19 infection is growing every single day, and evidence of presence or absence of association between obesity and COVID-19 adverse outcomes should be revisited. Therefore, this study summarizes the pooled association of obesity with COVID-19 adverse outcomes and mortality.

**Methods:** We searched PubMed and Science direct databases using specific terms and defined criteria. Data were analyzed using Comprehensive Meta-Analysis V2 (Biostat, Englewood, NJ, USA) random-effect models were used to calculate the odds ratio (OR) with 95% confidence intervals (95% CIs) of infection severity and mortality associated with obesity.

**Results:** Results revealed that obesity is not associated with COVID-19 mortality (OR = 1.1; 95% CI: 0.8 to 1.3) but with other adverse outcomes (OR = 2.4; 95% CI: 1.7 to 3.3).

**Conclusion:** Our findings support previous findings that obesity is associated with COVID-19 severity.

1. Introduction

The 2019 novel coronavirus disease (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which was reported early in December 2019 in Wuhan, China. On March 11, 2020, the World Health Organization announced COVID-19 as a pandemic (Deng et al., 2020). Due to its rapid spread globally, it has resulted in major global public health concerns with an estimated 15–20% of cases requiring hospitalization and 3–5% requiring critical care while the mortality rate of 50–97% in those who need mechanical ventilation. (Argyropoulos et al., 2020; Auld et al., 2020). The main clinical manifestations of the disease were respiratory symptoms including fever, cough, and fatigue and it may progress to pneumonia, acute respiratory distress syndrome (ARDS), shock, and death (Angeli et al., 2020).

Obesity, as defined by a body mass index (BMI) \( \geq 30 \) kg/m\(^2\), is known to be strongly associated with comorbid disorders such as diabetes, cardiovascular disease, and cancer (Pi-sunyer, 2015). It is also linked with respiratory symptoms and diseases, including obstructive sleep apnea syndrome (OSAS), obesity hypoventilation syndrome (OHS), chronic obstructive pulmonary disease (COPD),
asthma, pulmonary embolism, and aspiration pneumonia (Zammit et al., 2010). Furthermore, obesity is a risk factor for bacterial and viral pneumonia, ARDS, and acute respiratory failure after lung transplantation (Fezeu et al., 2011; Gong et al., 2010; Lederer et al., 2011; Mertz et al., 2013).

Regarding obesity and COVID-19, early descriptive studies did not clearly state a direct association between obesity and disease severity, while preliminary data has implicated major risk factors associated with worsening disease severity, including older age and comorbidities such as diabetes and hypertension (Zeng et al., 2020; Zhou et al., 2020).

Many studies have indicated that obesity was more common among cases that required hospitalization or mechanical ventilation (Lighter et al., 2020; Peng et al., 2020). Moreover, subsequent cohort studies from the United States and the United Kingdom indicated that obesity may increase the risk for severe illness and death from COVID-19 (Docherty et al., 2020; Petrilli et al., 2020). There are also emerging data that obesity is an independent predictor of intensive care unit (ICU), as obese patients were more likely to have critical care requirements, ICU admission, or death compared to normal-weight individuals (Hajifathalian et al., 2020).

While other studies did not find any association between obesity and clinical outcomes of COVID-19. For instance, there was no association between overweight and the increase in odds for in-hospital mortality nor between obesity and invasive mechanical ventilatory (IMV) support or supplemental oxygen use/noninvasive ventilatory support in diabetic patients (Longmore et al., 2021).

When comparing hospital admission rates between healthy weight and obese patients with a BMI between 30 and 34.9, results showed no significant difference, and therefore no association between hospital admission and BMI. Moreover, mortality rates were not statistically significant among obese patients with a BMI between 30 and 34.9 in compare with overweight patients with a BMI between 25 and 29.9 (Jiao Yang et al., 2021).

Nevertheless, obesity can contribute to the adverse outcomes of COVID-19 through increased reninangiotensin and aldosterone system (RAAS) activity and insulin resistance. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) penetrates human cells through direct binding with angiotensin converting enzyme 2 (ACE2) receptors on the cell surface, and since obesity is associated with insulin resistance and overactivity of the reninangiotensin-aldosterone system (RAAS), it is implicated with worse COVID-19 outcomes (Bornstein et al., 2020; Lakkis and Weir, 2018). Moreover, the ACE2 expression in adipose tissue is higher than that in the lung, a major target organ affected by COVID-19, and thus, allows entry of SARS-CoV-2 into adipocytes, making adipose tissue an important viral reservoir that allows the spread of infection to other organs (Kruglikov and Scherer, 2020) and thereby explaining how higher levels of adipose tissue as well as ACE2 levels among the obese population exacerbate infection outcomes.

The literature on COVID-19 disease is growing every single day and evidence of presence or absence of association between obesity and COVID-19 adverse outcomes should be revisited. Therefore, this study aims to summarize the pooled association of obesity with COVID-19 adverse outcomes and mortality.

2. Methods

This study is part of a larger protocol that is registered as is registered at PROSPERO CRD42020191768.

2.1. Search strategy

We searched PubMed and Science direct databases until the 9th of August 2020. The following terms were used: (obesity) OR (body mass index) OR (underweight) OR (overweight) OR (weight) OR (body mass) OR (anthropometric) OR (adiposity) OR (anthropometry) AND (covid-19), (Obesity OR Weight OR Overweight OR Anthropometric OR Adiposity OR Body mass index OR BMI) AND (COVID-19).

2.2. Study selection and data extraction

Retrospective and prospective observational studies were retrieved if they met the following criteria: 1) the study provided event rate data on obesity and any adverse outcome such as mortality, severity as defined in the study: Fever, shortness of breath, according to a respiratory rate (RR) ≥ 30 times/min, and oxygen saturation ≤93% in the resting state and arterial blood oxygen partial pressure (PaO2)/oxygen concentration (FiO2) ≤ 300 mm Hg; 2) presented data by obesity status or by body mass index (BMI) categories; 3) patients were adults from the general population diagnosed with COVID-19; and 4) written in English. To minimize selection bias, studies were excluded if they specifically sampled patients with certain illnesses such as organ transplant patients, cancer, or HIV. Moreover, we excluded articles stated as clinical trials, case reports, reviews or systematic reviews, meta-analyses, conference abstracts, animal experiments, international surveys, correspondences, and letters to the editor. Data were extracted by WA and double-checked by FA, and SA. Any discrepancies were resolved by SA. The following pieces of information were extracted using a spreadsheet: authorship, year of publication, country, study type, sample size, study time, age, female percentage, smoker percentage, diagnosis method, exposure and outcomes.

2.3. Study quality

Study quality was assessed using the Joanna Briggs Institute (JBI) critical appraisal checklist for case series to assess the risk of bias (Moola et al., 2017). The JBI assesses the internal validity of studies by considering items related to confounding, selection, and information bias.

2.4. Data analysis

We carried out data analysis using Comprehensive Meta-Analysis V2 (Biostat, Englewood, NJ, USA)) and used random-effects models to estimate the odds ratios (ORs) with 95% confidence intervals (95%CI) of disease adverse outcomes and mortality.
associated with obesity. A p-value of < 0.05 was considered statistically significant. The I^2 statistic (p-value of < 0.1) was used to test for heterogeneity in any analysis. The I^2 statistic estimates the percentage of variation in study results that is explained by between-study heterogeneity rather than sampling error. Usually, an I^2 value > 50% indicates considerable heterogeneity (Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002;). Lastly, Funnel plots and Egger’s test were used to assess the presence of publication bias.

3. Results

Fig. 1 presents the study flowchart. An initial total of 2259 studies were identified using our search terms and a total of 57 studies comprising 272,882 patients were included in the quantitative analysis. Studies were excluded for the following reasons: case reports, clinical trials, reviews or systematic reviews, meta-analyses, correspondence, conference abstracts, animal experiments, international surveys, not enough information on exposure, not relevant content, and no outcome of interest.

Table 1 summarizes the characteristics of the included studies. Studies were conducted in different parts of the world including China, the USA, Italy, Germany, Spain, France, Mexico, Taiwan, Brazil, Switzerland, and Rhode Island. All studies were published in 2020. Most studies were cohort studies, prospective cohort and retrospective cohort, and case series. Some studies did not provide a specific definition of obesity. Other studies defined obesity as a BMI ≥ 30 while Studies from Asia defined obesity as BMI ≥ 28. COVID-19 was diagnosed using tests including reverse-transcription polymerase chain reaction (RT-PCR) and real-time RT-PCR (rRT-PCR). For the majority of the studies included in this analysis, the diagnosis of COVID-19 complied with the World Health Organization interim guidance 2020 (World Health Organization, 2020). Studies reported outcome data on adverse clinical outcomes including: mortality (n = 20), ICU admission (n = 12), invasive mechanical ventilation (IMV) or intubation (n = 14.), acute respiratory distress, ARDS, (n = 4) and pneumonia (n = 2).

Data analyses revealed that obesity is not associated with COVID-19 mortality (OR = 1.1; 95%CI: 0.8 to 1.3) (Fig. 2), but was associated with other adverse outcomes (OR = 2.4; 95%CI: 1.7 to 3.3) (Fig. 3). Heterogeneity measured by I^2 was 79% for mortality and 97% for severity. Usually, an I^2 value > 50% indicates considerable heterogeneity. Studies defined severity using various terms such as hospital admission, severe symptoms, ICU admission, mechanical ventilation, and mortality (Argenziano et al., 2020; Argyropoulos et al., 2020; Claudia et al., 2020; Gavin et al., 2020; Giacomelli et al., 2020). COVID-19 severity refers to oxygen saturation < 90% on room air, respiratory rate > 30 breaths/min in adults or signs of severe respiratory distress (accessory muscle use,
inability to complete full sentences) as defined according to the interim guidelines from the World Health Organization (World Health Organization, 2020). Some studies measured outcomes that can be considered as a measure of COVID-19 severity. Thus, these studies were considered to measure the severity of COVID-19 disease and analyzed. A few studies did not clearly define severity. For example, Zhang et al. Gao et al., Wang et al., Deng et al. (Deng et al., 2020; Gao et al., 2020; Wang et al., 2020; Zhang et al., 2020) defined severity as severe illness while Cai et al. defined severity as exacerbation of the disease (Cai et al., 2020b).

As shown in Fig. 4 that evaluates publication bias using a funnel plot based on mortality. A visual symmetry indicates the absence of publication bias. Also, Egger’s test revealed no significant publication bias (Egger’s test: \( p = 0.99369 \)). However, Fig. 5 shows a funnel plot based on severity that indicates publication bias (Egger’s test: \( p = 0.01937 \)).

### 4. Discussion

This analysis pooled the results from recent publications on the association of obesity with COVID-19 adverse outcomes and mortality. Evidence accumulated to date shows that obesity is associated with COVID-19 adverse outcomes but not mortality.

Several potential mechanisms could explain how obesity may lead to adverse COVID-19 outcomes. The first possible mechanism is that adipose tissue produces and secretes several pro-and anti-inflammatory cytokines that have been engaged as active players in the development of metabolic diseases such as type 2 diabetes mellitus and cardiovascular disease (Lee et al., 2013). In particular, the increased level of cytokines like interleukin 6 in obese people, stimulates the liver to produce and secrete C-reactive protein (Ellulu et al., 2017). C-reactive protein is associated with adverse outcomes in patients suffering from COVID-19 (Alzoughool et al., 2020).

Numerous studies in humans described the relation between excess adiposity and impaired immune function, they revealed that the incidence and severity of infectious diseases are higher in obese individuals as compared to healthy individuals (Martí et al., 2001; Torres et al., 2018). On the other hand, ACE2, the receptor used by coronaviruses to enter the affected cells, was found to be highly expressed in adipocytes of obese patients (Frel et al., 2020). This could also add another good possible explanation and support our results as it was previously discussed in more depth that the adipose tissue of obese patients could play a role in the progression of severe COVID-19 through secreting pro-inflammatory cytokines, mitochondrial dysfunction, and impaired immune response to viral infection all of which boost the formation of cytokines that lead to poor progression of even mild COVID-19 cases (Yu et al., 2022).

Another possible mechanism that supports our finding is the association between obesity and thrombosis, whereas obesity induces thrombosis via two suggested mechanisms; proinflammatory and hypofibrinolytic (Blokhin and Lentz, 2013). The activation of prothrombotic signaling pathways in vascular cells is considered one of the primary outcomes of the chronic inflammatory state of obesity (Levi et al., 2012).

### Meta Analysis

Fig. 2. Forest plot of the odds ratios of obesity in non-survivor compared to survivor COVID-19 patients.
Meta Analysis

Fig. 3. Forest plot of the odds ratios of obesity in severe compared to non-severe COVID-19 cases.

Fig. 4. Funnel plot for publication bias based on mortality.
Table 1
Design and characteristics of the included studies on obesity and COVID-19.

| Study                        | Country          | Study Design                  | Age years | Female % | Current smoker % | Diagnosis method | Sample size | Exposure | Exposure definition | Exposure (n) | Nonexposure (n) | Outcome                  | Outcome definition          |
|------------------------------|------------------|-------------------------------|-----------|----------|------------------|------------------|-------------|----------|---------------------|--------------|------------------|---------------------------|-------------------------------|
| Giacomelli et al. (2020)     | Italy            | A prospective cohort study    | 61.0      | 30.90%   | History of smoking = 30% | RT-PCR           | 233         | Obesity  | BMI ≥30              | 38           | 195              | mortality                 | died during hospitalization |
| Nguyen et al. (2020)         | Paris            | Retrospective cohort study    | 64.8      | 34.40%   | 4.70%            | RT-PCR           | 279         | BMI      | BMI >25              | 122          | 71               | Unfavourable outcome     | artificial ventilation or death |
| Xie et al. (2020)            | China            | Retrospective cohort study    | 55        | 39.40%   | 13.50%           | RT-PCR           | 104         | Obese    | BMI ≥28              | 12           | 92               | without outcome improvement | ICU pts |
| Argyropoulos et al. (2020)   | USA              | Retrospective observational   | 52.5      | 44.50%   | Not measured     | RT-PCR           | 205         | Obesity  | BMI ≥30              | 48           | 157              | Severity                  | hospitalized/not hospitalized |
| Kalligeros et al. (2020)     | Rhode Island     | Retrospective cohort study    | 60        | 38.80%   | 11.70%           | RT-PCR           | 103         | BMI      | BMI >25              | 49           | 54               | Severity                  | ICU-admitted/Non-ICU intubated/non intubated |
| Mani et al. (2020)           | USA              | Retrospective cohort study    | 64.72     | 39.67%   | Not measured     | PCR              | 184         | Obesity  | BMI ≥30              | 66           | 118              | Severity                  | Death or Intubation         |
| Anderson et al. (2020)       | USA              | Retrospective cohort study    | 67        | 42%      | 13.60%           | RT-PCR           | 2466        | Obesity  | BMI >25              | 259          | 1853             | Severity                  | Pts with need for ventilation death |
| Karagiannidis et al. (2020)  | Germany          | Observational cohort study    | 68.3      | 48.10%   | Not measured     | RT-PCR           | 10,021      | Obesity  | BMI ≥30              | 513          | 9508             | Severity                  | mortality                        |
| Berenguer et al. (2020)      | Spain            | Retrospective cohort study    | 70        | 39%      | 6.70%            | RT-PCR           | 4035        | Obesity  | BMI ≥30              | 497          | 3109             | Severity                  | mortality                        |
| Claudia et al. (2020)        | Switzerland      | Retrospective cohort study    | 67        | 37%      | 8%               | PCR              | 99          | obesity | BMI ≥30              | 27           | 72               | Severity                  | severe COVID-19 progression/ICU transfer |
| Argenziano et al. (2020)     | USA              | Retrospective cohort study    | 63        | 40.40%   | 4.90%            | RT-PCR           | 1000        | obesity  | BMI ≥30              | 352          | 489              | Severity                  | Admitted to ICU               |
| Tousie et al. (2020)         | USA              | Retrospective cohort study    | 39        | 38%      | 15%              | RT-PCR           | 338         | obesity  | BMI ≥30              | 133          | 205              | Severity                  | hospital admission and intubation, Mechanical Ventilation ICU admission or Mortality |
| Gavin et al. (2020)          | USA              | Retrospective cohort study    | 60        | 48.60%   | 7.10%            | PCR              | 140         | obesity  | BMI ≥30              | 75           | 65               | severity                  |                                         |
| Buckner et al. (2020)        | USA              | Retrospective cohort study    | 69        | 50%      | 26%              | RT-PCR           | 105         | obesity  | BMI ≥30              | 44           | 49               | severity                  |                                         |
| Huang et al. (2020)          | China            | Retrospective cohort study    | 44.0      | 42.60%   | Smoking history:7.9% | RT-PCR           | 202         | obesity | BMI ≥28              | 24           | 178              | severity                  |                                         |
| Giacomelli et al. (2020)     | Italy            | Retrospective cohort study    | 61.0      | 30.90%   | History of smoking = 30% | RT-PCR           | 233         | obesity  | BMI ≥30              | 38           | 195              | mortality                 | died during hospitalization |
| Shah et al. (2020)           | USA              | Cohort study                  | 63.0      | 58.20%   | 17%              | PCR              | 522         | obesity  | BMI ≥30              | 347          | 175              | mortality                 | died during hospitalization |
| Sinha et al. (2020)          | USA              | Cohort study                  | 59.0      | 36.90%   | Not measured     | PCR              | 255         | obesity  | BMI ≥30              | 135          | 120              | Severity                  | died during hospitalization |
| Langer-gould et al. (2020)   | USA              | Retrospective cohort study    | 59.3      | 31.70%   | Ever smoker = 31.75% | RT-PCR           | 93          | obesity | BMI ≥30              | 55           | 38               | mortality                 | died during hospitalization |
| Mccullough et al. (2020)     | USA              | Retrospective cohort study    | 63.3      | 36.80%   | Ever smoker = 3.80% | RT-PCR           | 756         | obesity  | BMI ≥30              | 267          | 449              | mortality                 | died during hospitalization |

(continued on next page)
| Study                  | Country | Study Design          | Age (years) | Female % | Current smoker % | Diagnosis method | Sample size | Exposure | Exposure definition | Exposure (n) | Nonexposure (n) | Outcome | Outcome definition                              |
|-----------------------|---------|-----------------------|-------------|----------|------------------|------------------|-------------|----------|---------------------|--------------|-----------------|---------|------------------------------------------------|
| Ciceri et al. (2020)  | Italy   | Cohort study          | 65.0        | 27.10%   | Not measured     | RT-PCR           | 410         | BMI ≥ 30 | 78                  | 332          | mortality        | outcome: died during hospitalization/no outcome: discharged pts critical illness (intensive care, mechanical ventilation, discharge to hospice care, or death) intubated pts (require invasive mechanical ventilation) Died in the ICU |
| Petrelli et al. (2020)| USA     | Prospective cohort study. | 54.0        | 50.50%   | 5.50%            | RT-PCR           | 5279        | BMI ≥ 30 | 1865                | 3414         | Severity         | Severity |
| Hur et al. (2020)     | USA     | Retrospective observational study | 59.0        | 44.20%   | 33.50%           | RT-PCR           | 486         | BMI ≥ 30 | 259                 | 227          | Severity         | Severity |
| Auld et al. (2020)    | USA     | Observational cohort study | 64.0        | 45.20%   | Not measured     | PCR              | 217         | Obesity ≥ 40 | 21                  | 196          | Mortality        | severity: (1) shortness of breath, according to a respiratory rate (RR) ≥ 30 times/min; (2) an oxygen saturation ≤ 93% in the resting state; and (3) arterial blood oxygen partial pressure (PaO2)/oxygen concentration (FiO2) ≤ 300 mm Hg. |
| Deng et al. (2020)    | China   | Retrospective cohort study | 33.75       | 44.60%   | Not measured     | RT-PCR           | 65          | BMI ≥ 28 | 10                  | 55           | Severity         | Severity |
| Halasz et al. (2020)  | Italy   | Retrospective cohort study | 64          | 18.20%   | Not measured     | RT-PCR           | 242         | Obesity ≥ 30 | 48                  | 143          | Mortality        | non survivors |
| Wang et al. (2020)    | China   | Retrospective cohort study | 44.3        | 44.80%   | Not measured     | RT-PCR           | 297         | BMI ≥ 28 | 40                  | 257          | Severity         | Severity |
| Hu et al. (2020)      | China   | Retrospective cohort study | 61          | 48.60%   | Not measured     | RT-PCR           | 323         | Obesity ≥ 30 | 13                  | 310          | severity         | not defined |
| Urra et al. (2020)    | Spain   | Retrospective cohort study | 61.8        | 39.50%   | Not measured     | RT-PCR           | 172         | Obesity ≥ 30 | 17                  | 155          | severity         | ICU admission |
| Klang et al. (2020)   | USA     | Retrospective cohort study | less than 50 (43.25) and more than 50 (72) | 42.43%   | 23.30%           | PCR              | 3406        | BMI ≥ 30 | 1231                | 2175         | mortality        | non survivors |

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| Study                  | Country     | Study Design                           | Age years | Female % | Current smoker % | Diagnosis method | Sample size | Exposure | Exposure definition | Exposure (n) | Nonexposure (n) | Outcome           | Outcome definition             |
|-----------------------|-------------|----------------------------------------|-----------|----------|------------------|------------------|-------------|----------|---------------------|---------------|-----------------|------------------|----------------------------------|
| Dreher et al. (2020)  | Germany     | case series observational study         | 65        | 34%      | 6%               | RT-PCR           | 50          | obesity | BMI ≥30              | 17            | 33              | severity          | ARDS requiring ventilatory support |
| Price et al. (2020)   | USA         | observational study                     | 64        | 47.48%   | Not measured     | PCR              | 239         | obesity | BMI ≥30              | 112           | 119             | severity          | ICU admission                    |
| Lodigiani et al. (2020)| Italy      | retrospective cohort study             | 66        | 32%      | 11.60%           | PCR              | 388         | obesity | BMI ≥30              | 87            | 274             | severity          | ICU admission                    |
| Goyal et al. (2020)   | USA         | Retrospective Cohort Study              | 66.5      | 40%      | 5%               | RT-PCR           | 1687        | obesity | BMI ≥30              | 525           | 1162            | mortality          | death                           |
| Cai et al. (2020)     | China       | case series                            | 34.63     | 52.20%   | Not measured     | RT-PCR           | 383         | obesity | BMI ≥28              | 41            | 342             | mortality          | death                           |
| Palaiodimos et al. (2020)| USA       | retrospective cohort study             | 64        | 51%      | 32.50%           | PCR              | 200         | obesity | BMI ≥35              | 46            | 154             | mortality          | death                           |
| Pettit et al. (2020)  | USA         | retrospective cohort study             | 58.5      | 52.50%   | Not measured     | RT-PCR           | 238         | obesity | BMI ≥30              | 146           | 92              | mortality          | death                           |
| Hajifathalian et al. (2020)| USA      | retrospective cohort study             | 64        | 39.20%   | Not measured     | RT-PCR           | 770         | obesity | BMI ≥30              | 277           | 493             | Severity           | ICU admission                    |
| Moriconi et al. (2020)| Italy      | retrospective cohort study             | 69.5      | 48%      | 17%              | RT-PCR           | 100         | obesity | BMI ≥30              | 29            | 71              | Severity           | chronic obstructive pulmonary disease (COPD) death |
| Nakeshbandi et al. (2020)| USA       | retrospective cohort study             | 68        | 48%      | 14%              | RT-PCR           | 504         | Obesity | BMI ≥30              | 215           | 289             | Mortality          | death                           |
| Petersen et al. (2020)| Germany     | cross-sectional                        | 65.6      | 40%      | 13.33%           | PCR              | 30          | obesity | BMI ≥25              | 19            | 11              | severity           | ICU with mechanical ventilation mechanical ventilation |
| Steinberg et al. (2020)| USA       | retrospective cohort study             | no median age | not measured | not measured     | RT-PCR           | 210         | obesity | BMI ≥30              | 100           | 110             | severity           | ARDS not survived                  |
| Tsai et al. (2020)    | Taiwan      | retrospective cohort study             | 41        | 50%      | Not measured     | RT-PCR           | 28          | obesity | BMI ≥25              | 7             | 21              | severity           | pneumonia                       |
| Zhang et al. (2020)   | China       | retrospective cohort study             | 62        | 51.40%   | Not measured     | RT-PCR           | 74          | overweight | BMI ≥23              | 58            | 16              | Severity           | Disease severity                   |
| Gao et al. (2020)     | China       | cohort study                           | 48        | 37.30%   | Not measured     | RT-PCR           | 150         | obesity | BMI ≥25              | 50 *75        | 100 *75         | Severity           | severity of illness               |
| Ferrando et al. (2020)| Spain       | prospective cohort study CoHORT study | 64        | 31.90%   | Not measured     | PCR              | 742         | obesity | not defined            | 262           | 419             | severity           | Mild and severe ARDS               |
| Russo et al. (2020)   | Italy       | prospective cohort study CoHORT study | 67.7      | 40.10%   | 8.30%            | RT-PCR           | 192         | obesity | not defined            | 26            | 166             | mortality          | not survived                   |
| Antinori et al. (2020)| Italy       | prospective cohort study single center | 63        | 25.75%   | Not measured     | RT-PCR           | 35          | Obesity | not defined            | 3             | 32              | Severity           | ICU admission                    |
| Guillo et al. (2020)  | France      | retrospective cohort study single center| 62        | 44%      | Not measured     | RT-PCR           | 129         | obesity | not defined            | 25            | 104             | Severity           | death or intubation at 3 weeks follow-up. |
| Bartoletti et al. (2020)| Italy      | retrospective cohort study single center | 65.7      | 36.70%   | Not measured     | RT-PCR           | 1113        | obesity | not defined            | 196           | 917             | Severity           | Severe respiratory failure       |
| (Hernandez-Galdamez et al., 2020) | Mexico    | retrospective cohort study cross-sectional study | 45.7    | 45.29%   | 7.79%            | RT-PCR           | 110,987    | Obesity | not defined            | 41,344         | 69643           | severity           | Hospitalized pts                  |
| Harmouch et al. (2020)| USA         | retrospective cohort study             | 63        | 42.90%   | 34.10%           | RT-PCR           | 563         | obesity | (stated as morbid obesity) | 120          | 443             | mortality          | died during hospitalization       |

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Table 1 (continued)

| Study                  | Country   | Study Design          | Age years | Female % | Current smoker % | Diagnosis method | Sample size | Exposure definition | Exposure (n) | Nonexposure (n) | Outcome       | Outcome definition                        |
|------------------------|-----------|-----------------------|-----------|-----------|------------------|------------------|-------------|---------------------|--------------|----------------|--------------|---------------------------------------------|
| Soares et al. (2020)   | Brazil    | cohort study          | less than and more than 60 | 55.16%    | 2% *50%          | RT-PCR           | 10,713      | obesity             | not defined  | 597            | 10116         | mortality non survivors                  |
| Leonardi et al. (2020) | Italy     | retrospective study   | 61        | 36%       | Not measured     | RT-PCR           | 189         | obesity             | not defined  | 14             | 175           | severity critical illness                |
| Goshua et al. (2020)   | USA       | cross-sectional study | 62        | 40%       | Not measured     | PCR              | 68          | obesity             | not defined  | 25             | 43            | severity ICU admission                   |
| Baqui et al. (2020)    | Brazil    | cross-sectional study | 56.1      | 42%       | Not measured     | RT-PCR           | 7371        | obesity             | not defined  | 324            | 7047          | mortality died during hospitalization ICU and non ICU admission |
| Hirsch et al. (2020)   | USA       | Cohort study          | 64        | 39.10%    | Not measured     | BMI >30 obese, morbid obesity not specified | 5449        | obesity             | obese + morbid obese − total = 3518 | Acute Kidney Injury (AKI) |                        | Acute Kidney Injury developed during hospitalization. |
In addition to the above possible mechanisms, we should mention that obesity causes mechanical compression of the diaphragm muscle, chest cavity, and lungs, leading to restrictive pulmonary damage (Mafort et al., 2016). Besides, obese persons are normally with a reduced lung volume and capacity as compared to healthy persons (Melo et al., 2014), leading to adding more stress on COVID-19 patients. Also, complications of obesity such as hypertension (Naeini et al., 2021), diabetes (Shrestha et al., 2021), and sleep apnea (Abdelmassih et al., 2021) may contribute to the disease severity and mortality. Hypertension increases the OR of severe COVID-19 outcomes by 2.5 times through dysregulation of the immune system including CD8\(^+\) T cell dysfunction and possible overproduction of proinflammatory cytokines (Naeini et al., 2021). COVID-19 patients with diabetes have higher ICU admission and intubation rates as it is suggested that the production of cytokines involved in inflammation and oxidative stress are enhanced by high blood glucose levels (Shrestha et al., 2021). Sleep apnea that is prevalent among obese patients causes systemic intermittent hypoxia leading to reduced levels oxyhemoglobin saturation (Abdelmassih et al., 2021) and thus the need for ventilation.

Our results are in line with several previous meta-analyses. For instance, Yang and his colleagues found that positive COVID-19 detection was more obvious among obese cases and hospitalization rates were higher for obese compared with normal BMI patients (Jun Yang et al., 2021). Moreover, of a total of 124 patients, 47.6% of cases were obese (BMI >30) and 28.2% were severely obese (BMI >35), in addition to 85.7% of total hospitalized patients cases who required mechanical ventilation their BMI was relatively higher, therefore there is a significant association between IMV introduction and BMI (Simonnet et al., 2020a). Similarly, obesity is highly associated with positive COVID-19 test, higher risk of ICU admission, critical illness, and mortality, furthermore, higher BMI was linked with higher rates of ICU admissions and critical illness (Ho et al., 2020). Another meta-analysis found that overweight individuals were at a higher risk of 1.31 times to develop severe COVID-19 symptoms while the risk among obese individuals was 2.41 times higher compared to healthy individuals (Islam et al., 2021). Obesity is associated with the risk of many diseases including acute respiratory distress syndrome, chronic inflammation, decreased immune system and increased susceptibility of individuals to infections (Hegde et al., 2013; Heredia et al., 2012). Thus, obesity may act as an independent risk factor for poor progression of COVID-19 (Tamara and Tahapary, 2020).

Our work as well as previous meta-analyses are not without limitations that consequent to limitations in the literature. First, studies have different definitions of severity. Second, studies define obesity using different BMI cut-off points. Nevertheless, evidence to date from multiple meta-analyses indicates obesity may exacerbate COVID-19 symptoms and higher BMI is significantly associated with IMV introduction for patients, consequently, obesity may be a marker of poor prognosis and patients with high BMI should be monitored closely and managed carefully in order to clinically manage the disease (Ho et al., 2020; Simonnet et al., 2020b; Jun Yang et al., 2021).

In conclusion, our findings support previous findings in the other meta-analysis, hence, COVID-19 obese patients should be monitored for likely progression to severe outcomes.

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**CRediT authorship contribution statement**

**Suhad Abumweis**: Conceptualization, Formal analysis, Methodology, Visualization, Project administration, Resources, Supervision, Interpretation: all authors, Writing – review & editing, all authors. **Waed Alrefai**: Conceptualization, Data curation, Methodology, Visualization, Writing – review & editing, Interpretation: all authors; . **Foad Alzoughool**: Conceptualization, Data curation, Methodology, Writing – review & editing, Interpretation: all authors.

**Declaration of competing interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.
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