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REVIEW

The negative impact of obesity on the occurrence and prognosis of the 2019 novel coronavirus (COVID-19) disease: a systematic review and meta-analysis

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Abstract

Purpose The 2019 novel coronavirus (COVID-19) is an emerging pandemic, with a disease course varying from asymptomatic infection to critical disease resulting to death. Recognition of prognostic factors is essential because of its growing prevalence and high clinical costs. This meta-analysis aimed to evaluate the global prevalence of obesity in COVID-19 patients and to investigate whether obesity is a risk factor for the COVID-19, COVID-19 severity, and its poor clinical outcomes including hospitalization, intensive care unit (ICU) admission, need for mechanical ventilation, and mortality.
Methods The study protocol was registered in PROSPERO (CRD42020203386). A systematic search of Scopus, Medline, and Web of Sciences was conducted from 31 December 2019 to 1 June 2020 to find pertinent studies. After selection, 54 studies from 10 different countries were included in the quantitative analyses. Pooled odds ratios (OR) with 95% confidence intervals (CIs) were calculated to assess the associations.
Results The prevalence of obesity was 33% (95% CI 30.0%–35.0%) among patients with COVID-19. Obesity was significantly associated with susceptibility to COVID-19 (OR = 2.42, 95% CI 1.58–3.70; moderate certainty) and COVID-19 severity (OR = 1.62, 95% CI 1.48–1.76; low certainty). Furthermore, obesity was a significant risk factor for hospitalization (OR = 1.75, 95% CI 1.47–2.09; very low certainty), mechanical ventilation (OR = 2.24, 95% CI 1.70–2.94; low certainty), intensive care unit (ICU) admission (OR = 1.75, 95% CI 1.38–2.22; low certainty), and death (OR = 1.23, 95% CI 1.06–1.41; low certainty) in COVID-19 patients. In the subgroup analyses, these associations were supported by the majority of subgroups.
Conclusion Obesity is associated with COVID-19, need for hospitalization, mechanical ventilation, ICU admission, and death due to COVID-19.
Level of evidence Level I, systematic reviews and meta-analyses.

Keywords Obesity · COVID-19 · Hospitalization · Intensive care unit · Mechanical ventilation · Death

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Abbreviations

COVID-19	The 2019 novel coronavirus disease
ICU	Intensive care unit
OR	Odds ratio
CI	Confidence interval
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
BMI	Body mass index
PRISMA	Preferred reporting items for systematic reviews and meta-analyses
RR	Relative risk
GRADE	Grading of Recommendations Assessment, Development and Evaluation
ACE-2	Angiotensin-Converting Enzyme 2

Introduction

The 2019 novel coronavirus (COVID-19), caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), is a viral disease which first diagnosed in late 2019 in Wuhan City of Hubei Province of China, and it is spreading rapidly [1]. Currently, the prevalence of COVID-19 has turned into one of the most critical public health concerns [2]. Recent evidence suggests that the severity of clinical manifestations and mortality rate of the disease varies from person to person and depends on a variety of factors [3]. Given this, the identification of prognostic factors related to COVID-19 and its poor clinical outcomes is urgent to distinguish populations at higher risk for the disease and to better prevention and early treatment of the disease. Since obesity is associated with a mild chronic inflammatory condition [4] and immune dysfunction [5], evidence suggests that obesity may be a risk factor [6], but the findings are still insufficient in this regard. In a single center in France, 75% of individuals with SARS-CoV- 2 infections admitted to the intensive care unit (ICU) had a body mass index (BMI) > 30 kg/m^2. This study showed that with increasing BMI, the severity of the disease and the proportion of patients who need mechanical ventilation increase but no difference in mortality rates was observed between obese and non-obese patients [7]. Findings in Italy revealed that the need for intensive care and the use of a ventilator in overweight and obese patients, despite their younger age, is higher than in normal weight patients [8]. A cross-sectional study in Mexico demonstrated that obesity is one of the most critical risk factors for coronavirus respiratory infection [9]. In contrast, Wu et al. did not considered a statistically significant relationship between obesity and the severity of COVID-19 [10].

Heterogeneous findings may be due to low statistical power, small sample size, unified ethnicity, and differences in age and adjustment level for covariates in individual studies. To date, some meta-analyses [11–14] have attempted to summarize available evidence regarding the relation of obesity to COVID-19 outcomes. Nevertheless, the preliminary meta-analyses included small number of studies, did not comprehensively assess related clinical outcomes, did not assess the influence of potential effect modifiers, such as confounder factors, age, ethnicity and study design, or were conducted on Chinese populations, and thus, were not generalizable to other populations. The current systematic review and meta-analysis study aimed to comprehensively investigate the global prevalence of obesity in patients with COVID-19 and the relation of obesity to COVID-19, COVID-19 severity, and its poor clinical outcomes including hospitalization, ICU admission, need for mechanical ventilation, and mortality.

Methods

This study was performed in a stepwise process in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) [15]. The protocol of this study is registered in PROSPERO (ID: CRD42020203386). This article does not contain any studies with human participants performed by any of the authors.

Search strategy

An exhaustive systematic search was conducted by multiple researchers through electronic databases (Scopus, Medline, Web of Sciences) retrieving all potential publications, published from 31 December 2019 to 1 June 2020, investigating the prevalence of obesity among COVID-19 patients or the association of obesity with the risk of COVID-19, COVID-19 severity, death, ICU admission, need for mechanical ventilation, and hospitalization due to COVID-19. The combination of key words was as follows: ("obese" OR "obesity" OR "overweight" OR "body mass index" OR "BMI" OR "adiposity" OR "adipose" OR "body size" OR "weight") AND ("COVID-19" OR "2019 novel Coronavirus" OR "2019-nCoV" OR "SARS-CoV-2" OR "coronavirus 2019"). No restriction filter was applied for primary search and if required, Google translate was used to translate the data into English. Moreover, cross-references within both eligible and review articles were carried out for feasible additional publications.

Inclusion and exclusion criteria

The retrieval publications were screened and abstracted if they met the following inclusion criteria: (a) Observational studies (cohort, case–control, cross-sectional, case series); (b) Studies providing sufficient information for the calculation of relative risk (RR) and/or odds ratio (OR), in cases which critical data were not reported in the eligible articles, we contacted authors; (c) Studies reporting the prevalence of obesity in COVID-19 patients (primary outcome) and/or data on the association between obesity and following secondary outcomes: COVID-19 and COVID-19 severity (severe COVID-19 was defined based on international guidelines or hospitalization, ICU (Intensive Care Unit) admission, need for mechanical ventilator, mortality due to COVID-19 or a combination of these) [16–25]. Duplicates, case reports, reviews, studies with insufficient data after contacting with authors, and abstracts were all excluded, but letters were included. It is worth mentioning that all processes of data extraction were performed by two independent investigators, they verified the validity of extracted data, any potential disagreements were resolved by discussion or, where necessary, by a third investigator.

Data extraction and quality assessment

All required data were extracted conforming to the standardized extraction checklist for the following data: the first author's name, journal and year of publication, variables adjusted for, country of origin, ethnicity, mean, median or range of age, and odds ratio (OR) and corresponding confidence interval (CI) for outcomes. Moreover, Grading of Recommendations Assessment, Development and Evaluation (GRADE) was applied to assess the overall quality of the evidence in each pooled analysis [26].

Statistical analysis

In the current study, odds ratios (ORs) were used to estimate the association of obesity with outcomes. The potential between study heterogeneity was estimated by Cochran's Q-statistic (P value < 0.10 was considered as statistically significant) and I-squared (I^2) tests. Because of a remarkable evidence for heterogeneity, the random-effected model was applied [27, 28]. To assessed the predefined sources of heterogeneity among included studies, subgroup analysis based on obesity severity, study design (cohort vs. non-cohort), ethnicity (Caucasian vs. East-Asian), age category (≥ 50 years vs. ˂ 50 years), and adjustment for covariates (Adjusted vs. Non-adjusted effect size) and univariate random effects meta-regressions based on sex and age of participants were used. Additionally, in sensitivity analysis, we evaluated the conclusiveness and robustness of results by excluding each of the studies from the pooled estimate and analyzing the rest of them. This method enables the assessment of whether the pooled estimates were affected by any individual studies. To discover the risk of publication bias and the small-study effect, Begg's funnel plots and Egger's regression test were estimated (P value < 0.05 was considered as statistically significant) [29, 30]. The funnel plot asymmetry was interpreted as follow: in case of no evidence of publication bias, studies with high precision (large study effects) will be located near the average line, and studies with low precision (small-study effects) will be spread equally on both sides of the average line; any deviation from this shape can indicate publication bias. In the forest plot figures, the areas of the squares for individual studies or diamond-shaped for overall results are inversely proportional to the variances of the log odds ratio estimates, and horizontal lines display CIs. The data analyses were carried out using STATA (version 14.0; Stata Corporation, College Station, TX) and SPSS (version 23.0; SPSS, Inc. Chicago, IL) software.

Results

We identified 956 studies from our preliminary systematic search and four additional records through reference list searching. Of the 960 studies, 54 studies [8, 9, 16–25, 31–72] were eventually eligible to be included in the meta-analysis (Fig. 1); some studies reported data on > 1 pertinent outcome. Of these, there were 52 studies reporting results on obesity prevalence among patients with COVID-19 involving a total of 504,556 cases [8, 9, 16–25, 31–70] and data regarding the secondary outcomes were reported in 43 studies [8, 9, 16–25, 31, 32, 34–38, 42, 43, 45–55, 57–61, 64, 67, 68, 70–72]. A study by Chao et al. [73] was exclusively performed on children and thus was not included in the meta-analysis. Included publications were all observational in nature, published in 2020. The number of COVID-19 participants varied between 16 and 387,109 cases. Participants were from two ethnicities (Caucasian and East-Asian) from 10 different countries, including Mexico, United Kingdom (UK), Italy, United States of America (USA), France, China, Bolivia, Spain, Germany, and Singapore. Further characteristics of included studies are presented in Table 1.

Quantitative synthesis of data

Main pooled estimates are summarized in Table 2, and corresponding plots are provided in the Additional file 1. Meta-analysis indicated that the prevalence of obesity was 33% among individuals with COVID-19 (prevalence estimate 33.0%; 95% CI 30.0%–35.0%). Moreover, not only obesity was associated with increased risk of COVID-19 (OR = 2.42, 95% CI 1.58–3.70), but it also was associated with greater risk for disease severity (OR = 1.62, 95% CI 1.48–1.76) and poor clinical outcomes of COVID-19, such as hospitalization (OR = 1.75, 95% CI 1.47–2.09), need for mechanical ventilation (OR = 2.24, 95% CI 1.70–2.94), ICU admission (OR = 1.75, 95% CI 1.38–2.22), and death (OR = 1.23, 95% CI 1.06–1.41) (Table 2). There was significant evidence for

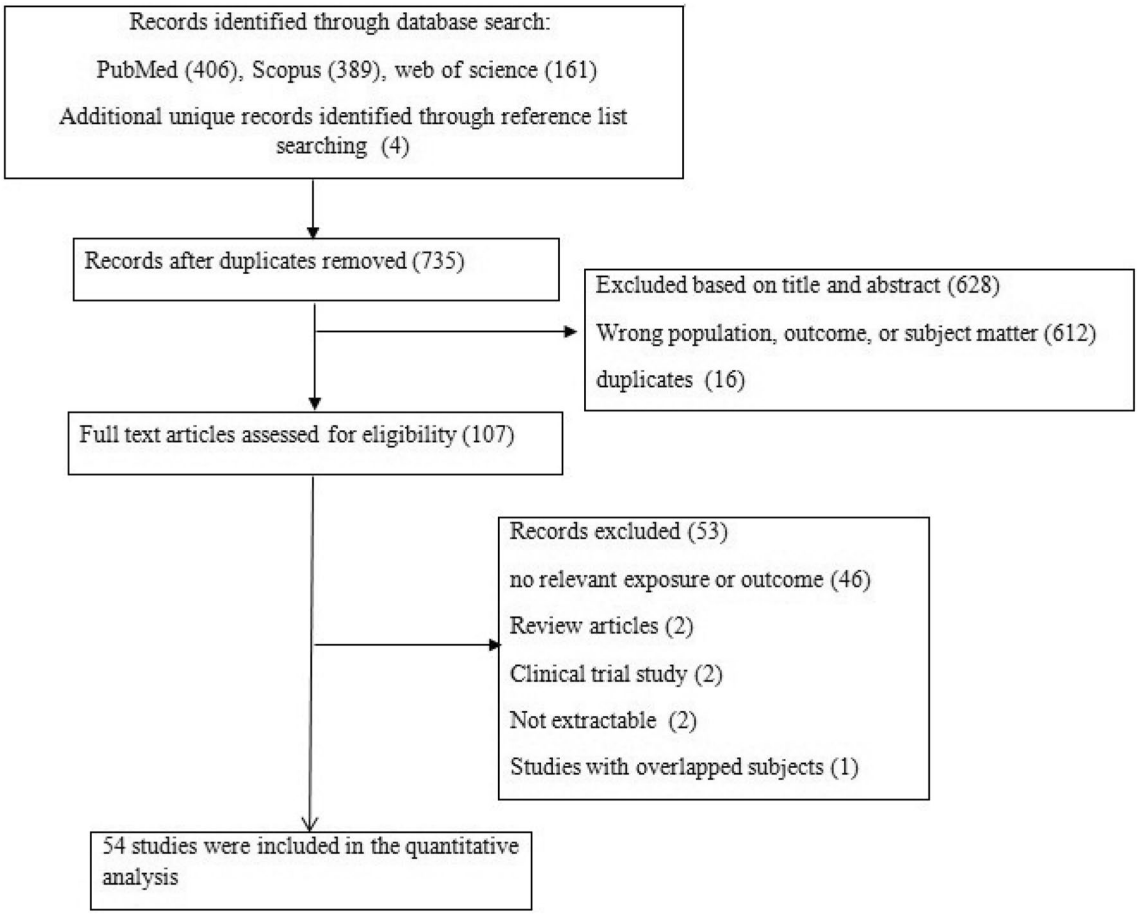

Fig. 1 Flow diagram of the study

heterogeneity across studies in all analyses (Table 2). Meta-regression showed that the relationships between obesity and all outcomes were not affected by sex and age.

Main findings of subgroup analysis

Subgroup analyses have been provided in the Additional file 1. Findings indicate that the relationship between obesity and the occurrence of COVID-19 was independent of study design, the age category of participants, and the level of adjustment for covariates. Nevertheless, this association was not supported in different categories of obesity severity due to the small number of the analyzed studies for each category. Notably, the association of obesity with COVID-19 severity and hospitalization was supported by all subgroups. For mechanical ventilation, the relationship was significant in all subgroups except for patients with Class I/Sever obesity (2 studies), East-Asians (1 study), and patients with age < 50 years (3 studies). For ICU admission, the relationship was significant in all subgroups except for patients with Class I obesity (3 studies) and East-Asians (1 study). Moreover, for death, the findings were supported in cohort studies, patients with Caucasian ethnicity, patients with age < 50 years, and in studies with adjusted effect sizes.

Sensitivity analysis

In the sensitivity analysis of studies on the relation of obesity to COVID-19 susceptibility and COVID-19 severity, no individual study significantly affected the pooled effect size, showing the reliability of the results. The pooled effect size ranged from 1.83 (95% CI 1.44–2.33) to 2.61 (95% CI 1.64–4.14) for studies on COVID-19 (Additional file 1) and ranged from 1.83 (95% CI 1.44–2.33) to 2.61 (95% CI 1.64–4.14) for COVID-19 severity (Additional file 1).

Publication bias

Egger test revealed no evidence of publication bias for any of the outcomes except COVID-19 severity ($t=2.12$, $P=0.04$), hospitalization ($t=2.48$, $P=0.04$), and need for mechanical ventilation ($t=6.50$, $P=0.001$) (Additional file 1).

Table 1 Characteristics of the included studies

References	Study design	Location	Population				Individuals with obesity	Obesity severity and its definition	Outcome	Adjusted variables in analyses
			No. of participants	% of females	Age (median (IQR), mean ± SD, or range)	Ethnicity				
Hernandez-Garduno [9]	Non-cohort	Mexico	12,304	48.7	48 (38–59)	Caucasian	4717	NR	COVID-19 risk	History of contact with COVID-19, current smoking, cardiovascular, chronic obstructive pulmonary disease, asthma or immunosuppressed conditions
Moriconi [59]	Non-cohort	Italy	100	48	27.02 ± 1.7	Caucasian	29	Obesity BMI ≥ 30 kg/m^2	Death	Crude
Hamer [47]	Cohort	UK	387,109	55.1	56.2 ± 8.0	Caucasian	90,895	Obesity BMI ≥ 30 kg/m^2	Hospitalization	Adjusted for age, sex, education, ethnicity, diabetes, hypertension, cardiovascular disease (heart attack, angina, or stroke)
Zhang [72]	Cohort	China	56	NR	Range 14–45	East-Asian		Obesity BMI ≥ 28 kg/m^2	Death	Crude
Yates [71]	Cohort	UK	882	NR	71 (61–76)	Caucasian		Class I BMI ≥ 30–34.9 kg/m^2 Severe obesity BMI ≥ 35 kg/m^2	COVID-19 risk	Adjusted for potential covariates
Bello-Chavolla [34]	Non-cohort	Mexico	51,633	42.3	46.65 ± 15.83	Caucasian	10,708	NR	Death, hospitalization, ICU admission, mechanical ventilation	Crude
Escalera-Antezana [42]	Non-cohort	Bolivia	107	49	43.9 ± 17.6	Caucasian	6	NR	Death	Crude
Crespo [36]	Non-cohort	Spain	16	25	73.6 ± 4.7	Caucasian	7	NR	Death	Crude

Table 1 (continued)

References	Study design	Location	Population				Individuals with obesity	Obesity severity and its definition	Outcome	Adjusted variables in analyses
			No. of participants	% of females	Age (median (IQR), mean ± SD, or range)	Ethnicity				
Lusignan [38]	Non-cohort	UK	587	47.6	58·0 (34–73)	Caucasian	168	Class I/severe obesity 30–39·9 kg/m^2 Morbid obesity BMI ≥ 40 kg/m^2	COVID-19 risk	Adjusted for hypertension, chronic kidney disease, diabetes, chronic heart disease, chronic respiratory disease, malignancy or immunocompromised, age, sex, ethnicity, socioeconomic deprivation level, household size, settlement or population density, and smoking status
Busetto [8]	Non-cohort	Italy	92	38.1	70.5 ± 13.3	Caucasian	29	Obesity BMI ≥ 25	Death, ICU admission, mechanical ventilation	Age and sex, type 2 diabetes, respiratory chronic diseases and dementia
Fasano [43]	Non-cohort	Italy	105	47.6	70.5 ± 10.1	Caucasian	19	NR	COVID-19 risk	Adjusted for age
Bella [39]	Cohort	Italy	132	31.8	66.0 (55.0–75.8)	Caucasian	18	NR	Obesity prevalence	Crude
Lemyze [54]	Non-cohort	France	44	30	63 ± 10	Caucasian	32	Obesity BMI ≥ 30 kg/m^2 Class I ≥ 30–34.9 kg/m^2 Severe obesity ≥ 35–39.9 kg/m^2 Morbid obesity BMI ≥ 40 kg/m^2	COVID-19 risk	Crude
Dreher [40]	Non-cohort	Germany	50	34	65 (58–76)	Caucasian	17	Obesity BMI ≥ 30 kg/m^2	Obesity prevalence	Crude
Edler [41]	Non-cohort	Germany	80	42	79.2 (52–96)	Caucasian	14	Obesity BMI ≥ 30 kg/m^2	Obesity prevalence	Crude

Table 1 (continued)

References	Study design	Location	Population				Individuals with obesity	Obesity severity and its definition	Outcome	Adjusted variables in analyses
			No. of participants	% of females	Age (median (IQR), mean ± SD, or range)	Ethnicity				
Cummings [37]	Cohort	USA	257	33	62 (51–72)	Caucasian	119	Morbid obesity BMI ≥ 40 kg/m^2	Death	Interleukin-6 and D-dimer concentrations, age and sex, symptom duration before hospital presentation, hypertension, chronic cardiac and pulmonary disease, and diabetes
Suleyman [68]	Non-cohort	USA	463	55.9	57.5 ± 16.8	Caucasian	262	Morbid obesity BMI ≥ 40 kg/m^2	Hospitalization, ICU admission, mechanical ventilation	Race, age, sex, obstructive sleep apnea, diabetes, hypertension, coronary artery disease, congestive heart failure, chronic kidney disease, end-stage renal disease, cancer
Giacomelli [45]	Cohort	Italy	233	30.9	61 (50–72)	Caucasian	38	Obesity BMI ≥ 30 kg/m^2	Death	Age, being treated with at least one anti-hypertensive agent, disease severity, presence of anemia, lymphocyte count, D-dimer, C-reactive protein, creatine kinase
Hajifathalian [46]	Cohort	USA	770	39.2	64 ± 16.7	Caucasian	277	Obesity BMI ≥ 30 kg/m^2	Death, ICU admission, mechanical ventilation	Adjusted for age, race/ethnicity, and troponin I level

Table 1 (continued)

References	Study design	Location	Population				Individuals with obesity	Obesity severity and its definition	Outcome	Adjusted variables in analyses
			No. of participants	% of females	Age (median (IQR), mean ± SD, or range)	Ethnicity				
Hur [49]	Cohort	USA	486	44.2	59 (range 19–101)	Caucasian	259	Class I/severe obesity 30–39·9 kg/m^2 Morbid obesity BMI ≥ 40 kg/m^2	Mechanical ventilation	Demographics and medical history
Khoury [17]	Cohort	USA	178	100	32 (27–36)	Caucasian	98	Obesity BMI ≥ 30 kg/m^2	Severity (severe COVID-19 was defined as dyspnea (patient reported), respiratory rate 30 breaths per minute or higher, oxygen saturation 93% or less on room air, or findings consistent with pneumonia on chest X-ray, or a combination of these)	Crude
Huang [18]	Cohort	China	202	42.6	44.0 (33.0–54.0)	East-Asian	24	Obesity BMI ≥ 28 kg/m^2	Severity [defined by guidelines for the diagnosis and treatment of novel coronavirus (2019-nCoV) Infection by the National Health Commission (trial version 5)]	Type 2 diabetes, lactate dehydrogenase, albumin; C-reactive protein

Table 1 (continued)

References	Study design	Location	Population				Individuals with obesity	Obesity severity and its definition	Outcome	Adjusted variables in analyses
			No. of participants	% of females	Age (median (IQR), mean ± SD, or range)	Ethnicity				
Gao [19]	Non-cohort	China	150	37.3	48	East-Asian	75	Obesity BMI ≥ 25 kg/m^2	Severity (based on National Health Commission & State Administration of Traditional Chinese Medicine. Diagnosis and treatment protocol for novel coronavirus pneumonia (trial version7)	Age, sex, smoking status, hypertension, diabetes, and dyslipidemia
Chao [73]	Cohort	China	323	48.6	61 (range 23–91)	East-Asian	13	Obesity BMI ≥ 30 kg/m^2	Severity (based on the clinical presentation at the time of admission)	Crude
Ong [60]	Cohort	Singapore	91	44	51 (35–61)	East-Asian	40	Obesity BMI ≥ 25 kg/m^2	Death, ICU admission, mechanical ventilation	Crude
Memtsoudis [58]	Non-cohort	USA	107	NR	61.5 (27–86)	Caucasian	37	Obesity BMI ≥ 30 kg/m^2	ICU admission	Crude
Lokken [56]	Non-cohort	USA	107	100	29 (26–34)	Caucasian	37	Obesity BMI ≥ 30 kg/m^2	Obesity prevalence	Crude
Zheng [20]	Non-cohort	China	66	25.8	47	East-Asian	45	Obesity BMI ≥ 25 kg/m^2	Severity [guidelines for the diagnosis and treatment of novel coronavirus (2019-nCoV) infection by the National Health Commission (trial version 5)]	Adjusted for age, sex, smoking, type 2 diabetes, hypertension, and dyslipidemia
Knight [52]	Cohort	UK	407	100	NR	Caucasian	140	Obesity BMI ≥ 30 kg/m^2	COVID-19 risk	Crude
Kuderer [53]	Cohort	USA	892	50	66 (57–76)	Caucasian	172	NR	Death, obesity prevalence	Adjusted for age, sex, and smoking status

Table 1 (continued)

References	Study design	Location	Population				Individuals with obesity	Obesity severity and its definition	Outcome	Adjusted variables in analyses
			No. of participants	% of females	Age (median (IQR), mean ± SD, or range)	Ethnicity				
Cai [21]	Non-cohort	China	383	53	48 (39–54)	East-Asian	41	Obesity BMI ≥ 28 kg/m^2	Severity (defined by the presence of any of the following conditions: (1) significantly increased respiration rate of ≥ 30 times/minute; (2) hypoxia, i.e., oxygen saturation (resting state) ≤ 93%; (3) blood gas analysis, i.e., partial pressure of oxygen/fraction of inspired oxygen ≤ 300 mmHg; or (4) the occurrence of respiratory or other organ failure that required intensive care unit monitoring and treatment, or shock)	Adjusted for age, sex, epidemiological characteristics, days from disease onset to hospitalization, presence of hypertension, diabetes, cardiovascular disease, chronic obstructive pulmonary disease, liver disease, and cancer, and drug used for treatment

Table 1 (continued)

References	Study design	Location	Population				Individuals with obesity	Obesity severity and its definition	Outcome	Adjusted variables in analyses
			No. of participants	% of females	Age (median (IQR), mean ± SD, or range)	Ethnicity				
Kalligeros [50]	Cohort	USA	103	38.8	60 (50–72)	Caucasian	49	Class I $\geq$ 30–34.9 kg/m^2 Severe obesity BMI $\geq$ 35 kg/m^2	ICU admission, mechanical ventilation	Adjusted for age, race, and gender, Heart disease: heart failure, coronary artery disease and cardiomyopathy; lung disease: chronic obstructive pulmonary disease, asthma, interstitial lung disease, and pulmonary hypertension
Klang [51]	Cohort	USA	3406	31	40.68	Caucasian	1231	Class I/severe obesity 30–39·9 kg/m^2 Morbid obesity BMI $\geq$ 40 kg/m^2	Death	Age, male, sex, coronary artery disease, heart failure, hypertension, diabetes, hyperlipidemia, chronic kidney disease, history of cancer, smoking and race
Petrilli [22]	Cohort	USA	5279	50.5	54 (38–66)	Caucasian	2162	Class I/severe obesity 30–39·9 kg/m^2 Morbid obesity BMI $\geq$ 40 kg/m^2	Hospitalization, severity (defined as requiring intensive care, mechanical ventilation, discharge to hospice care, or death)	Adjusting for personal characteristics and comorbidities
Palmieri [62]	Cohort	Italy	3032	NR	range: 5–105	Caucasian	335	NR	Obesity prevalence	Crude
Richardson [65]	Non-cohort	USA	4170	39.7	63 (52–75)	Caucasian	1733	Obesity BMI $\geq$ 30 kg/m^2 Severe obesity BMI $\geq$ 35 kg/m^2	Obesity prevalence	Crude

Table 1 (continued)

References	Study design	Location	Population: No. of participants	% of females	Age (median (IQR), mean ± SD, or range)	Ethnicity	Individuals with obesity	Obesity severity and its definition	Outcome	Adjusted variables in analyses
Auld	Cohort	USA	217	55.2	64 (54–73)	Caucasian	21	Morbid obesity BMI ≥ 40 kg/m^2	Death	Crude
Sabatino [66]	Non-cohort	Italy	76	47	34.7	Caucasian	7	NR	Obesity prevalence	Crude
Barrasa [33]	Non-cohort	spain	48	44	63 ± 12	Caucasian	23	BMI ≥ 30 kg/m^2	Obesity prevalence	Crude
Kayem [23]	Non-cohort	France	617	100	NR	Caucasian	139	Obesity BMI ≥ 30 kg/m^2	Severity (defined as requiring any respiratory support)	Crude
Lighter [55]	Cohort	USA	3615	NR	Age ≥ 60 Age < 60	Caucasian	1370	Class I ≥ 30–34.9 kg/m^2 Severe obesity BMI ≥ 35 kg/m^2	ICU admission	Crude
Tatum [69]	Cohort	USA	125	54.8	58.7 ± 14.8	Caucasian	83	NR	Obesity prevalence	Crude
Price-Haywood [64]	Cohort	USA	2798	60	54.16	Caucasian	1727	Obesity BMI ≥ 30 kg/m^2	Death, Hospitalization	Race with the additional covariates of age, sex, Charlson Comorbidity Index score, residence in a low-income area, insurance plan
Mani [57]	Cohort	USA	184	39.67	64.72 ± 14.87	Caucasian	66	Obesity BMI ≥ 30 kg/m^2 Class I ≥ 30–34.9 kg/m^2 Severe obesity ≥ 35–39.9 kg/m^2 Morbid obesity BMI ≥ 40 kg/m^2	Death, mechanical ventilation	Crude
Argenziano [31]	Non-cohort	USA	841	40.4	63.0 (50.0–75.0)	Caucasian	352	Obesity BMI ≥ 30 kg/m^2	ICU admission	Crude
Simonnet [7, 67]	Cohort	France	124	27	60 (51–70)	Caucasian	59	Class I ≥ 30–34.9 kg/m^2 Severe obesity BMI ≥ 35 kg/m^2	Mechanical ventilation	Age, sex, diabetes, hypertension, dyslipidemia
Garg [44]	Non-cohort	USA	151	NR	≥ 18	Caucasian	73	Obesity BMI ≥ 30 kg/m^2	Obesity prevalence	Crude

Table 1 (continued)

References	Study design	Location	Population				Individuals with obesity	Obesity severity and its definition	Outcome	Adjusted variables in analyses
			No. of participants	% of females	Age (median (IQR), mean ± SD, or range)	Ethnicity				
Palaiodimos [61]	Cohort	USA	200	51	64 (50–73.5)	Caucasian	46	Severe obesity BMI ≥ 35 kg/m^2	Death, mechanical ventilation	Smoking and diabetes, age, sex, race, heart failure, coronary artery disease, chronic kidney disease or end-stage renal disease, chronic obstructive pulmonary disease
Cariou [35]	Cohort	France	1127	35.1	69.8 ± 13.0	Caucasian	428	Class I/severe obesity 30–39·9 kg/m^2 Morbid obesity: BMI ≥ 40 kg/m^2	Death	Age and sex
Buckner [24]	Cohort	USA	93	50	69 (range 23–97)	Caucasian	44	Obesity: BMI ≥ 30 kg/m^2	Severity (defied as a composite endpoint of admission to an intensive care unit (ICU) or death)	Crude
Piva [63]	Cohort	Italy	33	9.1	64 (59–72)	Caucasian	6	NR	Obesity prevalence	Crude
Toussie [70]	Cohort	USA	313	38	39 (31–45)	Caucasian	133	Class I/severe obesity 30–39·9 kg/m^2 Morbid obesity BMI ≥ 40 kg/m^2	Hospitalization, mechanical ventilation	Adjusted for chest X-ray Severity Score
Caussy [16]	Non-cohort	France	340	42	≥ 18	Caucasian	85	Obesity BMI ≥ 30 kg/m^2	ICU admission, severity (defined as ICU admission) COVID-19 risk	Age and sex

Table 1 (continued)

References	Study design	Location	Population: No. of participants	% of females	Age (median (IQR), mean ± SD, or range)	Ethnicity	Individuals with obesity	Obesity severity and its definition	Outcome	Adjusted variables in analyses
Docherty [25]	Cohort	UK	16,081	40.1	72.9 (58.0–82.0)	Caucasian	1685	Clinician defined	Death	Age, sex, chronic cardiac disease, chronic pulmonary disease, chronic kidney disease, chronic neurological disorder (such as stroke), dementia, and liver disease

BMI body mass index, *NR* not reported, *IQR* interquartile range, *ICU* intensive care unit

Evaluation of quality of evidence according to the GRADE

The quality of evidence for each of the outcomes is as follows: very low (COVID-19 hospitalization), low (COVID-19 severity, death, ICU admission, and need for mechanical ventilation), moderate (the risk of susceptibility to COVID-19) (Additional file 1).

Discussion

The current meta-analysis showed that the prevalence of obesity was 33% among individuals with COVID-19. Not only was obesity associated with increased occurrence of COVID-19, but it was also associated with greater odds of developing critical conditions (e.g. hospitalization, mechanical ventilation, ICU admission), and mortality. Notably, these associations were consistently observed among Caucasians. To the best of our knowledge, this is the first study that has provided a comprehensive evaluation of both occurrence and prognosis of COVID-19 in relation to obesity.

The 33% prevalence of obesity among patients with COVID-19 corroborates a recent review that has shown obesity is the most prevalent comorbidity among patients with severe or fatal COVID-19 (42%) [12]. Similar observations have been reported in other respiratory-related outbreaks including MERS-CoV [74], influenza [75], and SARS-CoV [76]. Moreover, the positive association of obesity with the occurrence and severity of COVID-19 is in line with similar reviews that only included initial studies from China [14].

In the current study, obesity was associated with poor prognosis of COVID-19 by increasing the need for hospitalization, mechanical ventilation, ICU admission, and even mortality. This finding was in the line with a current systematic review that included mostly case report, case series, letter to editor, and comments [77]. That review found that obesity was associated with the increasing prevalence of hospitalization (average of 20.4%) and greater lethality (average of 20.4%) in the patient with COVID-19 [77]. The contribution of obesity to diseases severity and the requirement of advanced medical care in COVID-19 has been also stated in another initial review that only included three studies [78]. Our study also further added to a meta-analysis by Földi et al. that showed obesity is a risk factor for both ICU admission and mechanical ventilation requirement in COVID-19 patients [11]. Nevertheless, the study by Földi et al. did not investigate the relation of obesity to the risk of mortality, and hospitalization due to COVID-19. This is of particular importance since restricted IUC capacity has created great concern across the world. As such, knowledge of relevant risk factors can help clinicians better identify and guide the high-risk populations for making the most

Table 2 Overall pooled odds ratio for the association between obesity and risk of susceptibility to COVID-19 and its poor clinical outcomes

Outcome	Combined sample size (*n*)	Articles (*n*)	Effect sizes (*n*)	I^2 (%)	$P_{\text{for heterogeneity}}$	OR (95% CI)	References
COVID-19 risk	14,669	7	12	93.0	≤0.001	2.42 (1.58–3.70)	[9, 16, 38, 43, 52, 54, 71]
COVID-19 severity	479,052	37	76	66.8	0.05	1.62 (1.48–1.76)	[8, 16–25, 31, 32, 34–37, 42, 45–53, 55, 57–61, 64, 67, 68, 70, 72]
Hospitalization	447,595	6	8	73.3	≤0.001	1.75 (1.47–2.09)	[22, 34, 47, 64, 68, 70]
Mechanical ventilation	54,459	11	18	48.5	0.01	2.24 (1.70–2.94)	[8, 34, 46, 49, 50, 57, 60, 61, 67, 68, 70]
ICU admission	58,055	10	14	74.0	≤0.001	1.75 (1.38–2.22)	[8, 16, 31, 34, 46, 50, 55, 58, 60, 68]
Death	78,260	18	24	60.6	≤0.001	1.23 (1.06–1.41)	[8, 25, 32, 34–37, 42, 45, 46, 51, 53, 57, 59–61, 64, 72]

use of available facilities to reduce morbidity and mortality outcomes of COVID-19 infection.

Although the underlying mechanism linking obesity to COVID-19 has remained to be elucidated, several potential pathways may justify this association through chronic inflammation, higher Angiotensin-Converting Enzyme 2 (ACE-2) concentration, and functional restrictive capacity of the lung. Chronic inflammation is accompanied by the increased level of *C-reactive protein*, interleukin 6, and adipokines, all of which can suppress the immune system and put the body at greater risk for the COVID-19 infection [67, 79]. Moreover, ACE-2 receptors—responsible for facilitating COVD-19 entry into cells—can be expressed in different parts of the body including adipose tissue [80]. That is, greater adiposity is equal to having more ACE-2 receptors and subsequently be more susceptible to catch COVID-19. Finally, individuals with obesity have physiological respiratory dysfunction which can increase the risk for hypoventilation [81], and thus may contribute to a worse prognosis of COVID-19.

Strengths and limits

The limitations of this study should be reported. Studies used different criteria to define obesity such that some studies define obesity based on national cut-points (BMI > 25 kg/m^2), while others used the WHO definition of obesity (BMI > 30 kg/m^2). Also, the included studies did not mention the detailed comorbidities of obese patients, such as diabetes and hypertension. Additionally, although we divided disease severity based on clinical symptoms, ICU care and death, the included studies still varied in their differentiation of patients' disease severity in clinical definition, with classifications of "mild, moderate, severe, and critical", "ordinary and severe/critical", "common and severe", and "non-severe and severe" disease. A high heterogeneity existed between studies; however, subgroup analyses were conducted to trace potential sources. As another limitation, because of the unavailability of data for Africa, data obtained from the studies included in the present meta-analysis were categorized into just two ethnicities (Caucasian and East-Asian), limiting the expandability of our findings to African descent populations. Nonetheless, this is the first study that provided an extensive evaluation of health literature to assess the association of obesity with odds of occurrence and prognosis of COVID-19. This study brings attention to obesity as an important risk factor for COVID-19, which has dire consequences in relation to morbidity, mortality and the financial burden generated by the current pandemic. We followed a rigorous methodology as all stages were conducted by two reviewers independently including study selection, data extraction, and quality appraisal. The large sample size and extensive coverage of different regions around the world will increase the power and representativeness of the results to the whole patient population worldwide.

Conclusion

In conclusion, obesity was associated with the occurrence and poor prognosis of COVID-19. As the main concern is that vaccines might be less effective for obese people [82], more attention should be paid to prevent and treat COVID-19 in obese patients.

What is already known on this subject?

Previous studies have reported that obesity might be related to poor prognosis of COVID-19; however, due to low statistical power, small sample size, heterogeneity of ethnicity, and differences in age and adjustment level for covariate, the results of studies were inconclusive.

What does this study add?

This meta-analysis confirmed that obesity is associated with COVID-19 and its poor clinical outcomes. Thus, it is highly recommended to consider obesity status in prognostic scores and improvement of guidelines for the clinical care of patients with COVID-19 and even for vaccination.

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Authors' contributions SA and NG designed the study. MA, HM and TR searched, screened and selected the articles. NS, MD, BR and SH extracted the data from the articles. SA and HM performed data analysis and interpretation. TR drafted the manuscript. All authors contributed in writing and editing of the manuscript. SA supervised the study.

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Declarations

Conflict of interest All authors declared that they have no competing interests.

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Consent for publication This is formally to submit the article entitled "The negative impact of obesity on the occurrence and prognosis of the 2019 novel coronavirus (COVID-19) disease: a systematic review and meta-analysis" prepared by the Tehran University of Medical Sciences for review and, hopefully, publication in your prestigious journal. The authors would like to advise that all authors listed have contributed to the work. All authors have agreed to submit the manuscript Eating and Weight Disorders—Studies on Anorexia, Bulimia and Obesity. No part of the work has been published before. There is no conflict of interest in this paper.

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