Original Article

Body-mass index COVID-19 severity: A systematic review of systematic reviews

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Abstract

Objectives: Conflicting studies have resulted in several systematic reviews and meta-analyses on the relationship between COVID-19 and body mass index (BMI). **Methods:** This systematic review of systematic reviews followed an umbrella review design, and preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines; Medical literature analysis and retrieval system online (MEDLINE) and SCOPUS databases were searched for systematic reviews on the topic. A predefined screening and selection procedure was done for the retrieved results based on the population, intervention/interest, comparator, outcome, study (PICOS) framework. **Results:** The search strategy yielded 6334 citations. With the predefined selection and screening process, 23 systematic reviews were retrieved for inclusion in the present study. Twenty-three ($n = 23$) systematic reviews met the inclusion criteria. As expected, there was overlap across the reviews in the included primary studies. Available evidence suggests that Class III obesity (morbid obesity) is strongly associated with increased mortality risk in patients with Covid-19. It is difficult to draw a firm conclusion about Class I and Class II obesity due to conflicting outcomes of metanalyses. Increased obesity was consistently associated with increased risk of invasive mechanical ventilation (IMV) in all the reviews with low to moderate heterogeneity. **Conclusions:** Available evidence suggests that Class III obesity (morbid obesity) is strongly associated with increased mortality risk in patients with Covid-19. Increased BMI is positively associated with the risk of IMV and the severity of COVID- care.

Keywords: Body mass index, COVID-19, obesity, SARS-CoV-2, systematic reviews

Introduction

Since the World Health Organization (WHO) declared COVID-19 a pandemic on March 11, 2020,[1,2] several preliminary studies explored the association between increased visceral fat and outcomes in COVID-19 patients.[3,4] In a prospective cohort study of 233 patients of COVID-19 in Italy, Giacomelli reported that patients with obesity had a three-fold higher risk of death as compared to those with a BMI <30 kg/m2.[5] Among 200 patients in New York City with COVID-19, severe obesity (BMI ≥ 35 kg/m2) was associated with higher in-hospital mortality independent of other potentially confounding factors.[6] Simonnet *et al.*[7] demonstrated a higher frequency of obesity among intensive care unit patients

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with SARS-CoV-2-related pneumonia in France. The primary objective of the present systematic review is to identify the relationship between body-mass index and COVID-19 severity and outcomes. The secondary objective of the review is to present a conceptual note on the advantages and limitations of early systematic reviews during the pandemic, which has rapidly evolving epidemiology. To the best of our knowledge, we present the first systematic review of the reviews on the association of BMI and the disease severity in Covid -19 infection.

Methods

We used an umbrella review study design to create an overview of the available evidence on the topic. Umbrella review is a tool in evidence synthesis encompassing a systematic review of systematic reviews where the unit of analysis is a systematic review.[8] The review was undertaken systematically using the method described by Smith *et al*.[9] and preferred reporting items in systematic review and meta-analysis (PRISMA) guidelines.

Eligibility criteria

Population

Adults or children with COVID-19 infection were eligible for inclusion. Studies were included irrespective of the criteria used for confirmation of COVID-19 infection.

Exposure

Obese patients categorized based on BMI or visceral fat quantification on CT scan were eligible for inclusion.

Comparator

Non-obese patients, as evidenced by BMI within normal limits or low visceral adiposity, were included.

Outcomes

All outcomes were eligible (e.g., mortality, ICU admission, invasive mechanical ventilation, increased hospital stay, or severe disease). The primary outcome of interest was mortality and the need for invasive mechanical ventilation.

Study design

A systematic review of systematic reviews.

Inclusion

Systematic reviews were included if they specified a search strategy in at least one literature database and included primary research. No restrictions were placed on the study design of the primary studies.

Exclusion

Literature reviews without a defined research question, search strategy, or the process of selecting articles were excluded.

Search methods

The search strategy, developed for MEDLINE and SCOPUS (till 01.05.2021) to identify relevant further reviews reference lists of included studies were assessed for eligibility. PubMed search was performed with ("body mass index"[MeSH Terms] OR ("body" [All Fields] AND "mass" [All Fields] AND "index" [All Fields]) OR "body mass index" [All Fields]) AND ("COVID-19" [All Fields] OR "COVID-19" [MeSH Terms] OR "COVID-19 Vaccines" [All Fields] OR "COVID-19 Vaccines" [MeSH Terms] OR "COVID-19 serotherapy" [All Fields] OR "COVID-19 Nucleic Acid Testing" [All Fields] OR "covid-19 nucleic acid testing" [MeSH Terms] OR "COVID-19 Serological Testing" [All Fields] OR "covid-19 serological testing" [MeSH Terms] OR "COVID-19 Testing" [All Fields] OR "covid-19 testing" [MeSH Terms] OR "SARS-CoV-2" [All Fields] OR "sars-cov-2" [MeSH Terms] OR "Severe Acute Respiratory Syndrome Coronavirus 2" [All Fields] OR "NCOV" [All Fields] OR "2019 NCOV" [All Fields] OR (("coronavirus" [MeSH Terms] OR "coronavirus" [All Fields] OR "COV" [All Fields]) AND 2019/11/01[PubDate]: 3000/12/31 [PubDate])) AND severity [All Fields] and SCOPUS database was searched with (TITLE-ABS-KEY (covid 19) AND TITLE-ABS-KEY (body AND mass AND index)) syntax.

Data collection and analysis

Two review authors (AA and NM) independently screened search results.

Selection of reviews

Searches were downloaded into Endnote X7 (Clarivate Analytics, V.7.1 release date April 2, 2014) and de-duplicated. Two researchers (AA and NM) independently screened titles and abstracts. Any paper classified as potentially eligible by either reviewer was ordered as a full text and independently screened by both reviewers. A third researcher reviewed disagreements (MN) where a consensus could not be reached between the researchers.

Data extraction and management

Extracted data included study characteristics, patient characteristics, exposure, comparator, outcome measures, effect estimates, standard error (SE), and confidence interval (CIs) as available. One researcher completed data extraction (MN); a second researcher cross-checked 50% (NM). Both researchers, at a second review, cross-checked discrepancies, and a consensus was reached.

Assessment of methodological quality of included reviews

Quality assessment with the risk of bias in systematic reviews (ROBIS) tool[10] 2) was undertaken by one researcher (NM) and checked by a second (MN). Discrepancies were resolved by discussion.

Data synthesis

A body mass index (BMI) equal to or greater than 25 kg/m^2 is considered overweight, and equal to or greater than 30 kg/m^2 is considered obese.[11] The WHO has different definitions according to the geographical distribution, with overweight in the Asian population as 23 kg/m^2 ≤ BMI <27.5 kg/m^2 and general obesity as a BMI ≥27.5 kg/m^2.[12] The outcomes were

categorized into two groups: mortality and severe disease. The severe disease was further categorized into two groups: use of invasive mechanical ventilation and other outcomes defined as severe disease. This differentiation was done as IMV has been consistently considered a severe disease across all studies. At the same time, the definition of severe disease used in studies has been variable. Each group was further subcategorized according to different obesity classes, and data was extracted separately for each outcome. Each outcome was narratively synthesized, including a number of reviews using the outcome and effect estimates with a 95% confidence interval (CIs) from the source review. Important numerical data was presented in tables for all outcomes measured. All outcomes that were reported in the reviews were included in the report to avoid reporting bias.[13]

Results

Electronic searches identified 6334 records. The full-text screening identified 23 systematic reviews eligible for inclusion. The study screening and selection process for inclusion as per the criteria laid out are as shown in the PRISMA flow diagram [Figure 1].

Study characteristics

Twenty-three ($n = 23$) systematic reviews[14-36] met the inclusion criteria. All the systematic reviews had performed quantitative analysis except one.[31] Reasons for excluding nine studies are as shown in Table 1.[37-45] Twenty ($n = 20$) reviews[14-20,22-24,26,28-34,36,46] reported the association between Obesity and disease severity of covid-19. Out of these, five[14,16,23,26,30] reported severe disease with poor composite outcomes (including mortality). Nineteen ($n = 19$) reviews[14,16,17,19-22,25,33-36,15,18,23,24,26,27,29,30,32] evaluated the effect of obesity on mortality in Covid-19. Out of these, five reviews[14,16,23,26,30] reported mortality along with other poor outcomes. Eight reviews[15,17-19,22,33-35] analysed the association between obesity and the need for invasive mechanical ventilation in Covid-19. Three reviews[16,23,26] analysed the association of obesity with the risk of Covid-19 infection. As expected, there was overlap across the reviews in the included primary studies.

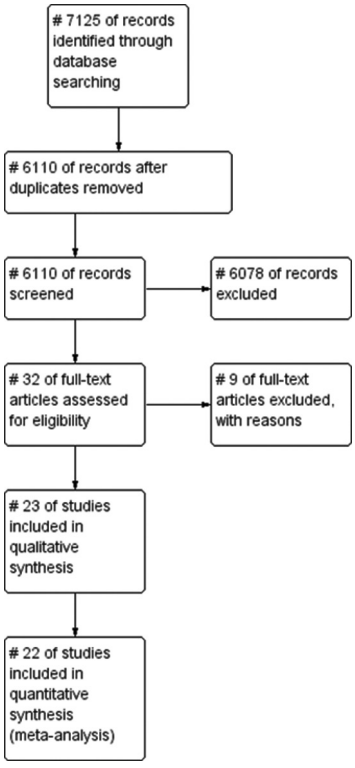

Figure 1: PRISMA flowchart showing process of study selection for the present review

Risk of bias

Fifteen reviews were rated as low-risk bias,[14-19,23-27,29,32,34,36] two as unclear,[28,35] and six as high risk of bias.[20-22,30,31,33] The high risk of bias rating was due to the lack of detail in the search strategy, no attempts to minimize data extraction errors, and no quality assessment of included studies. The risk of bias is shown in Table 2.

Outcome evaluation

Substantial heterogeneity (clinical, methodological, and statistical) was found among the reviews and the primary studies included. Regarding study populations, Asian and non-Asian populations have different cut-offs of anthropometric indices. Physiologically pulmonary reserves are supposed to deplete over time, and age may negatively influence the immunogenic response to infections. Some systematic reviews[26,27,29] attempted to perform a subgroup analysis to deal with age as a confounder variable, but fewer mentioned a priori in the protocol.[26,29] Another approach to address this source of this heterogeneity is to adopt a meta-regression approach used by another set of systematic reviews.[14,17,25,30] However, out of four systematic reviews which conducted meta-regression, only two[14,25] fulfilled the pragmatic criteria of incorporating the ten studies addressing age as a covariate. As a result, there may be more type-II errors in the reviews. The majority of the reviews adopted a combined mix effect approach, which seems sensible as the intuitive probability of covid-19 infection varies chiefly in an unknown manner, and age per se may not influence it directly. Nevertheless, contact network studies have shown that extremes of ages caught infection through the family's middle-aged members (in the age pyramid). Thus, a mixed effect model using age as a random effect and other covariates as fixed effect seem logical and contextual. Although certain expert groups believe that the decision to employ fixed or random effect should be governed by *P* value of I^2 test of heterogeneity, covid-19 being a relatively low and less explored phenomenon, the guidance may be driven more by empirical context.

Disease severity in several systematic reviews was defined on a spectrum from adhering to a guideline,[26,28] disease progression,[17,29] hospital admission requirement,[15,21,30,31,33-35] invasive ventilation[15,17-19,22,33-35] to death,[14,16,17,19-27,29,30,32-36] thus varying widely on clinical plane. These seeming inconsistencies in outcome (from the soft outcome as hospitalisation to the

Table 1: List of excluded studies with reasons

Study	Journal	Primary objectives	Number of participants	Reason for exclusion
Bhattacharyya, 2021[37]	Research Square	COVID-19's impact is based on symptoms, demographics, comorbidities and demonstrates the association of demographics in cases and mortality in the United States	3745	Included age, sex, race, and comorbidities as risk factors for severity and mortality following COVID-19 but has not included obesity as a risk factor, and BMI was not assessed separately
de Siqueira, 2020[38]	Obesity Research and Clinical Practice			Review articles were also included
Fraser, 2020[39]	Transplantation proceedings	Clinical presentation, treatments and outcomes in liver transplant recipients with COVID-19.	223	Not addressing BMI and COVID-19
Hussain, 2020[40]				Retracted
Maltese, 2020[41]	Journey of clinical medicine	Review on frailty and COVID-19	-	Study design not as per inclusion criteria
Nasiri, 2020[42]	Frontiers in Medicine	Systematic reviews that combine clinical, laboratory, epidemiologic, gender, and mortality findings	5057	Included age, gender, lab parameters, and comorbidities as risk factors for severity and mortality following COVID-19 but has not included obesity as a risk factor, and BMI was not assessed separately
Pal, 2020[43]	Diabetes and Metabolic Syndrome	Review of demographic/biochemical parameters and clinical outcomes of COVID-19 patients with diabetic ketoacidosis (DKA) and combined DKA/HHS (hyperglycaemic hyperosmolar syndrome)	110	BMI was not assessed
Robinson, 2021[44]	Appetite	Weight-related behaviours and weight management barriers among UK adults during the COVID-19 social lockdown	2002	Not as per inclusion criteria
Wang, 2021[45]	Rheumatology International	Risk and clinical outcomes of COVID-19 in patients with rheumatic diseases compared with the general population	2000	Participant information is not as per inclusion criteria.

hard outcome as death) may be a major source of interpretation errors assuming disease severity as a uniform construct for the following reasons. First, hard outcomes such as death always have a lesser probability than soft outcomes such as hospitalisation or non-invasive ventilation. Second, hard outcomes such as death and IMV are more influenced by artefactual causes (described elsewhere in detail). Third, outcomes may not be attributed directly to obesity in the observational world but amalgamate several interactions, terms, and effect modifiers. Fourth, some outcomes like disease progression are an integral part of the natural history of the disease, and they are rather a reflection of the time frame during which patient-reported with disease and may not be attributed to obesity. Fifth, immunological response to the same strain/viral load is reported differentially across the countries and even at the regional and subregional levels. Thus, the outcome of the disease is more ecologically influenced (ecological fallacy) by other macro indicators than micro indicators such as obesity or another clinical parameter.

Discussion

Obesity is frequently associated with high levels of hospitalisation and admissions in intensive care units, with morbidity and mortality rates higher than population averages, indicating that obesity is a significant risk factor.[7] Moreover, obesity is related to the downregulation of the inflammatory pathway, which leads to increased expression of inflammatory molecules, including interleukin-6 (IL-6). Obese patients and a weakened immune system provide the virus with a larger region for replication. Reports indicate that over half of hospitalised patients infected with Hemagglutinin type I and Neuraminidase type I (H1N1) were obese, and most deaths occurred in patients who were morbidly obese.[47] These features suggest that, similar to influenza, obesity may be a significant risk factor in COVID-19.

Fourteen articles presented a meta-analysis of the risk of in-hospital mortality in obese patients with Covid-19. Some reported no association,[17,19,35] or association only in the subgroup of patients, i.e., age ≥60.[29] While others reported some degree of association, those studies analysing association with different obesity classes reported a more significant association and a higher risk of mortality in higher obesity classes.[21,27,33,34,36] A single systematic review found an increased risk of mortality only in patients with fewer comorbidities,[25] suggesting the coexistence of other medical conditions in this subgroup of patients, contributing to poorer outcomes. Across many meta-analyses, there were moderate to high levels of heterogeneity and variation in the effect estimates. Available evidence suggests that Class III obesity (morbid obesity) is strongly associated with increased mortality risk in patients with Covid-19. It is difficult to draw a firm conclusion for Class I and Class II obesity due to conflicting outcomes of metanalyses which is likely due to differences in the methodology (criteria for diagnosis of infection, classification of obesity). Moreover,

Table 2: Risk of Bias Assessment of the included studies (Relevance Assessment)

Authors	Category: Patients with covid 19 infection (diagnosed by positive RT PCR or chest CT)	Patient (s): Obese/ BMI 30 or more (28 or more in Asians)	Exposure (s): Non obese/BMI less than 30 (or less than 28 in Asians)	Comparator:	Outcome: Severe disease (icu admission, invasive/non-invasive ventilation or death)	Relevance assessment	Does the question addressed by the review match the question you are trying to answer (e.g., in your overview or guideline)?
Booth 2021	Target question						Unclear
	Review being assessed	Age more than 16 with laboratory-confirmed SARS-CoV-2	unclear	no information	risk of specific adverse outcomes	Reasoning	The question matches for the population and outcome but the exposure and the comparison group is not explicitly defined.
Choudhary 2021	Target question						Unclear
	Review being assessed	Age 15 or more with RTPCR proven covid 19 cases	overweight and obesity with standard definition were included.	Healthy patients with optimum BMI	Severe disease (fatality, utilization of health care resources such as increase of hospital stay, ventilation, other services, and comorbidities	Reasoning	The question matches the population and outcome, but the exposure and the comparison group are not explicitly defined.
Chu 2020	Target question						Yes
	Review being assessed	RTPCR or CT proven covid 19 cases	overweight and obesity with standard definition were included.	no information	mortality, severe COVID-19, ICU care, the usage of invasive mechanical ventilation, and disease progression of COVID-19	Reasoning	even if the populaion is not mentioned, it can be assumed. Other PICO are were aligned with our target question
Foldi 2020	Target question						Unclear
	Review being assessed	Patients with obesity			intensive care unit (ICU) admission or invasive mechanical ventilation (IMV)	Reasoning	The question matches the population and outcome, but the exposure and the comparison group are not explicitly defined.
Helvaci 2021	Target question						Unclear
	Review being assessed	patients with COVID-19 RT-PCR)-confirmed	obesity	not mentioned	illness severity	Reasoning	The question matches the population and outcome, but the exposure and the comparison group is not explicitly defined.
Huang 2020	Target question						Unclear
	Review being assessed	Adults with COVID	obesity	Nil	hospitalization, ICU admission, need for IMV, and death	Reasoning	The question matches the population and outcome, but the exposure and the comparison group are not explicitly defined.
Huang 2021	Target question						Unclear
	Review being assessed	Obese and underweight patients with COVID-19		Nil	BMI and mortality	Reasoning	The question matches the population and outcome, but the exposure and the comparison group are not explicitly defined.
Mesas 2020	Target question						Partial
	Review being assessed	confirmed COVID-19 patients	age, sex, and health conditions		in-hospital mortality	Reasoning	Target question demands BMI, reveiw question does not have BMI as main. It is only one of the characteristics
Pranata 2021	Target question						Unclear
	Review being assessed		obesity and increase in		mortality and severity of patient	Reasoning	The question matches the population and

Contd...

Table 2: Contd...

Authors	Category: Patients with covid 19 infection (diagnosed by positive RT PCR or chest CT)	Patient (s): Obese/ BMI 30 or more (28 or more in Asians)	Exposure (s): Non obese/BMI less than 30 (or less than 28 in Asians)	Comparator:	Outcome: Severe disease (icu admission, invasive/non-invasive ventilation or death)	Relevance assessment	Does the question addressed by the review match the question you are trying to answer (e.g., in your overview or guideline)?
			BMI				outcome, but the exposure and the comparison group are not explicitly defined.
Zhang 2021	Target question						Unclear
	Review being assessed				ARDS, hospitalization, ICU admission, need for IMV, and death	Reasoning	PICO not mentioned
Zhao 2020	Target question						Unclear
	Review being assessed		effect of obesity		influenza and COVID-19	Reasoning	research question not specified
Chang 2020	Target question						Unclear
	Review being assessed		patients with obesity		risk of severe COVID-19		The question matches the population and outcome, but the exposure and the comparison group are not explicitly defined.
Ho 2020	Target question						Unclear
	Review being assessed	COVID-19 patients	prevalence of obesity		adverse outcomes such as ICU admission, critical illness, severe disease and mortality.		The question matches the population and outcome, but the exposure and the comparison group are not explicitly defined.
Malik 2020	Target question						Unclear
	Review being assessed	not mentioned	not mentioned		not mentioned		The question matches the population and outcome, but the exposure and the comparison group are not explicitly defined.
Malik 2021	Target question						Low
	Review being assessed		obesity		outcomes in the COVID-19 hospitalizations.		well described and defined terms
Peres 2020	Target question						Yes
	Review being assessed	individuals with COVID-19	overweight or obesity	normal body weight;	clinical, laboratory and image outcomes on COVID-19.		Well described PECO
Poly 2021	Target question						Unclear
	Review being assessed	COVID-19 patients	obesity		an increased rate of mortality		The question matches the population and outcome, but the exposure and the comparison group are not explicitly defined.
Seidu 2020	Target question						Yes
	Review being assessed	SARS-CoV-2	overweight or obesity	normal weight thresholds	have different outcomes		terms described
Soeroto 2020	Target question						Unclear
	Review being assessed		patients with obesity		risk of severe COVID-19		The question matches the population and outcome, but the exposure and the comparison group are not explicitly defined.
Tamara 2020	Target question						Unclear

Contd...

Table 2: Contd...

Authors	Category: Patients with covid 19 infection (diagnosed by positive RT PCR or chest CT)	Patient (s): Obese/ BMI 30 or more (28 or more in Asians)	Exposure (s): Non obese/BMI less than 30 (or less than 28 in Asians)	Comparator:	Outcome: Severe disease (icu admission, invasive/non-invasive ventilation or death)	Relevance assessment	Does the question addressed by the review match the question you are trying to answer (e.g., in your overview or guideline)?
	Review being assessed	COVID-19 patients	impact of obesity		Requirement of advanced medical treatment		The question matches the population and outcome, but the exposure and the comparison group are not explicitly defined.
Yang 2020	Target question						Unclear
	Review being assessed	not mentioned	not mentioned		Not mentioned		The question matches the population and outcome, but the exposure and the comparison group are not explicitly defined.
Yang 2021 Jun	Target question						Unclear
	Review being assessed	COVID-19 patients	obesity		An increased rate of mortality		The question matches the population and outcome, but the exposure and the comparison group are not explicitly defined.
Yang 2021 Nov	Target question						Unclear
	Review being assessed	positive SARS-CoV-2 test result	obesity		Hospitalization of COVID-19 patients, intensive care unit (ICU) admission, invasive mechanical ventilation (IMV), and in-hospital mortality		The question matches the population and outcome, but the exposure and the comparison group are not explicitly defined.

synthesising multiple meta-analyses data that include overlapping primary studies has the potential to overestimate the strength of the findings; therefore, it is essential to be mindful of the limited evidence on which our conclusions are based.

All reviews analysing the association between BMI and the use of IMV consistently reported the increased risk of IMV in obese patients with Covid-19. Overall heterogenicity among the primary studies included was low to moderate. In the subgroup analysis of BMI classes,[18,33,34] a linear relation was found with higher BMIs associated with a greater risk of the need for IMV. The outcome of the disease is influenced to a greater extent by cointerventions (clinical care, family support, timely intervention, compliance), and covid-19 seems to be no exception. Most of these variables are difficult to measure directly and demand the incorporation of other techniques like psychometrics. The quantitative analysis in included reviews uniformly suggests an association between higher BMI and severe covid-19 disease. At the same time, some reviews used predefined criteria to classify a severe disease; the definition of severe disease is not uniform across the reviews.[15,26,28] Some of the reviews also included hospital admission or duration of stay as criteria for severe disease.[15,16,26,30,33,36] The criteria for admission vary across the hospitals depending upon the local policy, which may have changed as the pandemic progressed depending on the patient load and the available resources. However, as the criteria of severe disease were predefined in the reviews, despite the variability in the criteria used across reviews, it may be concluded that obese patients with covid 19 infection are more likely to need intensive care.

Heterogeneity and meta-analysis errors

Only 11 of these have had their protocol registered (Ten on international prospective register of systematic reviews (PROSPERO) and one on international platform of registered systematic reviews and meta-analysis protocols (INPLASY)). It is possible that the authors were unaware of each other's research. Registering reviews allows transparency of methods and avoids unnecessary duplication. All except one[30] systematic review formally appraised the quality of the included studies. The I^2 value describes the percentage of total variation across studies due to heterogeneity rather than chance.[48] Examining the meta-analyses highlights low to high levels of statistical heterogeneity. Differences in criteria for diagnosis of Covid-19 and classification of obesity and how outcomes were measured may also have contributed to between-study heterogeneity. For example, some reviews also included radiologically suspected cases of Covid 19 without reverse transcription-polymerase chain reaction (RTPCR) confirmation,[20,23,24,26,28,36] whereas it was unclear in some.[19,29-31] Similarly, some reviews used different criteria to define obesity in Asian and western populations,[19,23,26,31,33,35] others used common criteria that too different (either ≥30[15,30,33,34,36] or ≥25.[18,24,29]

Strengths

How all systematic reviews tackled the artefactual elements in a single study is also another point of concern. It is a well-known

fact that there is no uniformity in the treatment algorithm across the countries, and the decision for step-up or step-down care varies widely from centre to centre. A systematic review, while combining the studies, might address this issue only when treatment protocols are explicitly presented in the studies. Multiple databases were searched for studies, and study selection was undertaken by two researchers, reducing the risk of error and bias. A mapping of the studies included in the reviews was undertaken to consider individual studies being included in multiple reviews and hence double-counting studies.

Limitations

With the present review, we also present a concept that umbrella reviews are a valuable tool to summarise the evidence of the highest standard in a broad topic and rapidly changing evidence landscape.[8] Twenty-three reviews included in this review were published within 11 months (between May 2020 to April 2021). As similar search strategies and search dates were used in a majority of the systematic reviews, inevitably, many of the included studies were the same across reviews. We observed that 23 reported systematic reviews were based on 302 and had heterogeneous criteria of selections. Additionally, these studies were based on heterogeneous inclusion and exclusion criteria. It can be inferred that with this amount of heterogeneity, it is difficult to draw concrete conclusions. This gives us a message that there is a need for more homogenous data collection in primary studies; otherwise, the systematic reviews based on these studies will further enhance the heterogeneity. All systematic reviews were included irrespective of their risk of bias scoring. It could be argued that several reviews were stretching the traditional definition of a systematic review; however, they did hold to the protocol definition with an electronic database search strategy and included primary evidence.

Systematic reviews and meta-analyses: Future and challenges

Systematic reviews and meta-analyses are considered the most potent tools for evidence synthesis and are crucial for evidence generation. Multiple systematic reviews have been published concisely, leaving the readers unsure of the varied conclusions. We have witnessed a couple of Cochrane systematic reviews and several non-Cochrane systematic reviews on different questions related to COVID-19. However, the significant challenges are the rapidly evolving disease landscape, epidemiology, treatment options, and emerging risk factors and outcomes. One of the critical limitations of systematic review during the recent pandemic is ever-changing evidence. Living systematic reviews are apt for such situations, which necessitate a change in the methodology of the systematic reviews.[49,50] Cochrane published guidelines on conducting a systematic living review in 2019; still, there is no well-established guideline as to when such a pandemic is rapidly evolving disease should be updated and when not.[50] Rapid dissemination of evidence base for body-mass-index and severity of COVID-19 and outcomes were essential for policymaking, identifying vulnerable population, and appropriate allocation of resources at the peaks of the pandemic. However, most of the case series on the matter were prone to biases. In addition, obesity is a proinflammatory state, and COVID-19 also has inappropriate inflammation responses. Therefore, there are biases even in the systematic reviews conducted early, which cannot be removed entirely.

Conclusion

Available evidence suggests that Class III obesity (morbid obesity) is strongly associated with increased mortality risk in patients with Covid-19. It is difficult to draw a firm conclusion about Class I and Class II obesity due to conflicting outcomes of metanalyses. Most of the reviews suggested evidence of moderate strength for the relation with increased BMI and increased risk for IMV. Despite the variability in the criteria used across reviews, it may be concluded that obese patients with covid 19 infection are more likely to need intensive care. We further found that umbrella reviews provide a better evidence synthesis in rapidly changing disease epidemiology where early and quick systematic reviews are published.

Key messages

- As we have identified in our study, though most of the systematic reviews on body-mass-index and COVID-19 implicate a positive association between obesity and severe COVID-19, the accuracy of data analysis is still questionable.
- There are methodological changes advised for early systematic reviews and guidelines for conducting systematic living reviews that must be updated.
- With the present study, we attempted to find the current evidence on the relationship between BMI and severity and outcomes of COVID-19, and the study suggests that a systematic review of early systematic reviews in a rapidly changing disease epidemiology yields a more accurate evidence base and helps in understanding inherent biases which can be avoided in the future studies.
- Living systematic review is a recent concept to address the challenges of traditional systematic review during a pandemic. However, updating a systematic review is a major challenge, as we found in our study that none of the systematic reviews were further updated.

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Conflicts of interest

There are no conflicts of interest.

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