Review Article

Obesity and Mortality of Hospitalized COVID-19 Patients in Asian and Western Countries: A Systematic Review and Meta-Analysis

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Abstract

Background: The authorities recently emphasized the importance of dietary control for COVID-19 patients in hospitals. However, there is limited detail about the obesity and death of COVID-19 patients who are hospitalized in the Asian and Western countries. The aim of this study was to find the role of obesity and mortality of the hospitalized COVID-19 patients. A systematic review of the studies on obesity and mortality of hospitalized COVID-19 patients in the Asian and western countries. **Methods:** Databases of ProQuest, PubMed, and EBSCO were used to find relevant articles published between January 2020 and March 2021. A total of 3,70,836 patients in 17 studies were included. **Results:** We found significant correlation between obesity and mortality in hospitalized COVID-19 patients (pooled odds ratio [POR] = 1.28, 95% CI: 1.23–1.33). In particular, this study demonstrated that the Asian countries had higher POR (1.44, 95% CI: 1.16–1.79) compared to the western countries (1.28, 95%CI: 1.23-1.33). The heterogeneity calculation showed heterogenous among studies included ($I^2 > 50\%$). **Conclusions:** The mortality of COVID-19-hospitalized patients is related to obesity, which requires a multi-stakeholder mitigation approach to avoid and control obesity and its impacts.

Keywords: *COVID-19, hospitalized, mortality, obesity*

Introduction

The coronavirus disease 2019 (COVID-19) pandemic has been a global challenge, particularly to the low-income and middle-income countries with the double burden of malnutrition. These countries are currently facing health problems due to a high prevalence of both malnutrition and obesity in their population.[1] The previous studies have demonstrated that both malnutrition and obesity are associated with higher hospitalized patients.[2,3]

The double burden is continuing to rise during the COVID-19 pandemic, as the obesity risk increases.[4] Another study suggested that quarantine and isolation measurements had caused changes in the lifestyle and eating habits, which may lead to obesity. A survey study in Italy with large participants had investigated the effect of the pandemic on the eating habits and lifestyle changes, and found that almost 50% of the population had weight gain.[5] Furthermore, another survey study with more than a thousand participants in Jordan, the "Behavior, Knowledge, Stress, and Quality of Life during the COVID-19-induced Confinement (BKSQ-COVID19) project," had analyzed the changes of physical activity and sedentary behavior during the pandemic. This study found that more than 40% of the participants had less sports, walking, and jogging, while about 80% of the participants reported more of all kinds of sedentary behaviors.[6] This leads to serious concerns since it is widely accepted that the obese population is more susceptible to the COVID-19 infection.

This important point is the novelty of this study, particularly in investigating the role of obesity in the mortality of the COVID-19 patients who were treated in both Asian and western countries. This comparison was made as one of the major nutritional problems for decades in the western countries is obesity. However, there has also been an increase in the incidence of obesity in Asian countries, in addition to malnutrition. This phenomenon is a challenge in itself during the COVID-19 pandemic in the

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two regions, and has potentially affected the mortality rate.

Methods

Study design and research sample

To assess the current articles related to obesity with mortality of the hospitalized COVID-19 patients in the Asian and western countries, a systematic review and meta-analysis studies were conducted. The preferred reporting items for systematic reviews and meta-analysis (PRISMA) guidelines was followed in this study.[7]

Eligibility criteria

The included articles limited to the original or research articles with study design of retrospective or prospective study, with English language and with human as study subjects. The study exclusion criteria included full-text version is unavailable, unrelated topics or subjects, and data in publications that could not be extracted or used for further review.

Search approach and study collection

Three databases, that is ProQuest, PubMed, and EBSCO were used to search for relevant articles published between January 2020 and March 2021 with keywords ("obesity" AND "COVID-19" AND "mortality"). In this study, mortality of the hospitalized COVID-19 patients was the dependent variable. The independent variable was obesity (BMI $\geq$ 30 kg/m^2). The literature quest was carried out by two independent investigators. After the initial search, the duplicates were manually deleted, and the title/abstracts were screened for possible relevance. Following that, the full-texts of the possible papers were evaluated using the criterion.

Data extraction

Data were extracted by two separate authors using structured extraction forms that included the author's name and year of publication, region, study design, total sample, characteristics (sex, age, comorbidity), and the effect size. The Newcastle-Ottawa Quality Assessment Scale (NOS) was used to evaluate the articles' quality; 0–3, 4–6, and 7–9 were used to categorize the articles into poor, medium, and high-quality categories.[8] The PRISMA flowcharts were used to illustrate the steps involved in finding the research articles [Fig. 1].

Data analysis

For further data analysis, the pooled odds ratio (POR) of obesity from the derived data was determined with a 95% confidence interval. The heterogeneity was measured with I^2, and $I^2 > 50\%$ indicated that there was heterogeneity between the studies. If the result was heterogeneous, the random effect model was used, and if the result was homogeneous, the fixed effect model was used. The individual characteristics of the composite poor outcomes were examined in a subgroup analysis. Furthermore, the

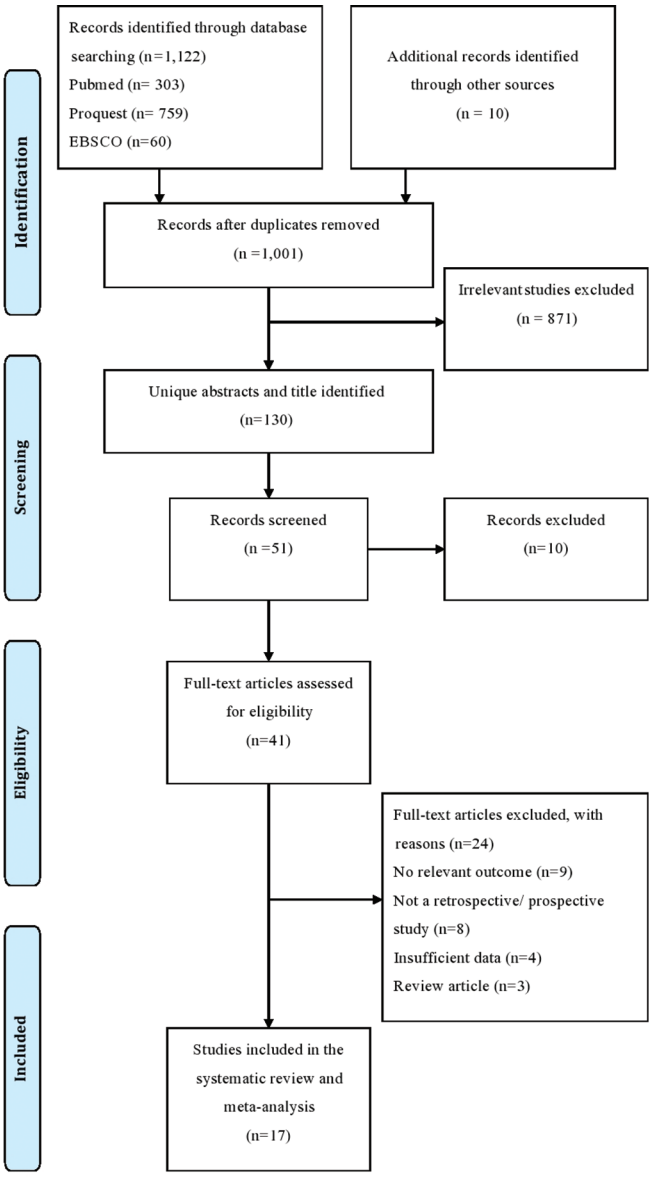

Figure 1: PRISMA flow diagram

findings were viewed as forest plots, and publication bias was assessed using Egger's and Begg's tests. The $P > 0.05$ results from the two tests revealed that there was no publication bias among the studies. STATA 16.0 was used for all data processing and analysis.

Results

Study selection and characteristics

This systematic review study included 17 recent studies conducted to the association of obesity with mortality of the hospitalized COVID-19 patients [Table 1],[4,9-24] The total sample from the included studies was 3,70,836 patients.

Assessment of article quality using NOS

Based on the article quality assessment conducted using NOS, the mean NOS for the 17 reviewed studies was

Table 1: Systematic review of obesity and mortality of hospitalized COVID-19 patients

First author, year	Year of study	Region	Study design	Total samples	Characteristics	Obesity with mortality of hospitalized COVID-19 patients (OR, 95% CI)	NOS
Rapp *et al*.[4]	2021	New York	Retrospective	4,062	Sex (M, 2,333; F, 1,769); age of M vs F (<40 years, 7.1% vs 5.8% ; 40-69 years, 53.0% vs 41.1%; ≥70 years, 39,9% vs 53.1%); comorbidity M vs F (hypertension, 32.4% vs 39.0%; asthma, 2.9% vs 7.4%; diabetes, 22.5% vs 25.4%)	1.53, 1.21-1.94	7
Olivas Martínez *et al*.[9]	2021	Mexico	Prospective	800	Sex (61% were male); age (the average age was 51.9 years); comorbidity (hypertension, 30.0%; diabetes, 26%)	1.62, 1.14-2.32	7
Carrillo Vega *et al*.[10]	2020	Mexico	Retrospective	10,544	Sex (64.99% were men); age (the average age was 54.24 years); comorbidity (diabetes, 29.97%; CVD, 5.14%; CKD, 4.24%; COPD, 5.09%, asthma, 3.98%)	1.74, 1.35-2.26	8
Czernichow *et al*.[11]	2020	France	Prospective	5,795	Sex (M, 3,791; F, 2,004); age (the average of M vs F, 60.3 years vs 58.9 years); comorbidity (hypertension, 52%; sleep apnea, 5%; dyslipidemia, 7%; diabetes, 39%; heart failure, 4%; CKD, 8%; cancer, 12%)	1.89, 1.45-2.47	8
Filardo *et al*.[12]	2020	New York	Retrospective	337	Sex (67.4% were male); age (the median age was 58 years); comorbidity (CVD, 51.5%; pulmonary, 13.3%; CKD, 7.0%; diabetes, 33.0%; HIV, 1.9%; cancer, 2.6%)	1.37, 1.07-1.74	7
Giacomelli *et al*.[13]	2020	Italia	Prospective	233	Sex (69.1% were male); age (the median age was 61 years)	2.01, 1.07-3.81	7
Halvatsiotis *et al*.[14]	2020	Greece	Retrospective	90	Sex (80% were male); age (the median age was 66.5 years); comorbidty (CVD, 21.1%; diabetes, 18.9)	2.35, 0.90-6.15	6
Kim *et al*.[15]	2020	Korea	Prospective	5,628	Sex (M, 1,723; F, 2,334); age of obese vs malnutrition (50-59 years, 21.4% vs 8.1%; 20-29 years, 19.0% vs 25.1%); comorbidity of obese vs malnutrition (diabetes, 15.9% vs 7.3%; hypertension, 29.0% vs 11.3%)	2.28, 1.23-4.25	7
Klang *et al*.[16]	2020	New York	Retrospective	3,406	Sex (M, 1,723; F, 2,334); age (<50 years, 17.0%); comorbidity (hypertension, 40%; diabetes, 40%; CKD, 28.3%; hyperlipidemia, 18.3%; heart failure, 16.7%; cancer, 15.0%; CAD, 10.0%)	5.1, 2.3-11.1	7
Nakeshbandi *et al*.[17]	2020	New York	Retrospective cohort	504	Sex (52.0% were male); age (the average age was 68.0 years); comorbidity (hypertension, 83%; diabetes, 53%; hyperlipidemia, 35%; CAD, 19%; CKD, 16%; COPD, 8%; asthma, 8%)	1.3, 1.0-1.7	8

Contd...

Table 1: Contd...

First author, year	Year of study	Region	Study design	Total samples	Characteristics	Obesity with mortality of hospitalized COVID-19 patients (OR, 95% CI)	NOS
Palaiodimos *et al*.[18]	2020	New York	Cohort	200	Sex (51.0% were female); age (the median age was 64 years); comorbidity (hypertension, 76%; hyperlipidemia, 46.2%; diabetes, 39.5%)	3.78, 1.45-9.83	7
Parra-Bracamonte *et al*.[19]	2020	Mexico	Retrospective	331,298	Sex (53.8% were male); age (the median age was 44 years); comorbidity (hypertension, 20.0%; diabetes, 16.2%)	1.22, 1.17-1.27	8
Pettit *et al*.[20]	2020	Chicago, U.S	Retrospective cohort	238	Sex (47.5% were male); age (the average age was 58.5 years); comorbidity (hypertension, 52.9%; diabetes, 28.6%; pulmonary disease, 26.5%; CVD, 21.4%)	1.7, 1.1-2.8	7
Shah *et al*.[21]	2020	Southwest Georgia	Retrospective	522	Sex (58% were male); age (the median age was 63 years); comorbidity (hypertension, 79.7%; diabetes, 42.3%)	2.29, 1.11-4.69	7
Steinberg *et al*.[22]	2020	New Jersey, U.S	Retrospective cohort	210	The ages of 18-45 years	6.29, 1.76-22.46	6
Tartof *et al*.[23]	2020	Southern California, U.S	Retrospective cohort	6,916	Sex (M, 3,111; F, 3,805); age (the median age was 49 years)	2.68, 1.43-5.04	7
Zhang *et al*.[24]	2020	China	Retrospective	53	The ages of 14-45 years	1.35, 1.07-1.70	5
Total samples				370,836			
The mean score NOS							7.00±0.79

CAD, coronary artery disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; M, male; F, female; CI, confidence interval; NOS, Newcastle-Ottawa Quality Assessment Scale; OR, odds ratio

7.00 ± 0.79, which means that the articles reviewed had high quality and low-risk of bias.

Obesity and mortality of the hospitalized COVID-19

Forest plots of the association of obesity and mortality of the hospitalized COVID-19 patients in Figure 2 showed obesity with mortality of the hospitalized COVID-19 patients (POR = 1.28, 95% CI: 1.23–1.33). Heterogeneity in the studies test was conducted to assess the association of obesity and mortality of the hospitalized COVID-19 patients (I^2 = 74.2%, I^2 > 50%), showing a variation in the heterogenous studies on the mortality of the hospitalized COVID-19 patients.

The results of the Egger's and Begg's test to assess publication bias among the studies included on obesity with mortality of the hospitalized COVID-19 patients [Figure 3]. Figure 3 found that there was not any significant publication bias for the studies included on obesity with mortality of the hospitalized COVID-19 patients (Egger's and Begg's test result, P > 0.05).

Table 2: Obesity and mortality of hospitalized COVID-19 patients in Asian and Western Countries

Countries	Number of Studies	Pooled odd ratio (95% CI)	I^2 (%)	Begg's test	Egger's test
Asian	2	1.44 (1.16-1.79)	58.5	0.510	0.100
Western	15	1.28 (1.23-1.33)	76.1	0.083	0.108

Obesity and mortality of the hospitalized COVID-19 patients in Asian and western countries

Table 2 described that the Asian countries had the highest POR of obesity (1.44, 95% CI: 1.16–1.79) compared to the western countries (1.28, 95% CI 1.23–1.33) with mortality of the hospitalized COVID-19 patients. The heterogeneity in the studies was conducted to assess the association of obesity and mortality of the hospitalized COVID-19 patients in the Asian and western countries (I^2 > 50%), showing a variation in the heterogenous studies on the occurrence of mortality of the hospitalized COVID-19 patients in the Asian and western countries. There was not any significant publication bias for the studies included on obesity with mortality of the hospitalized COVID-19 patients in the western and Asian countries.

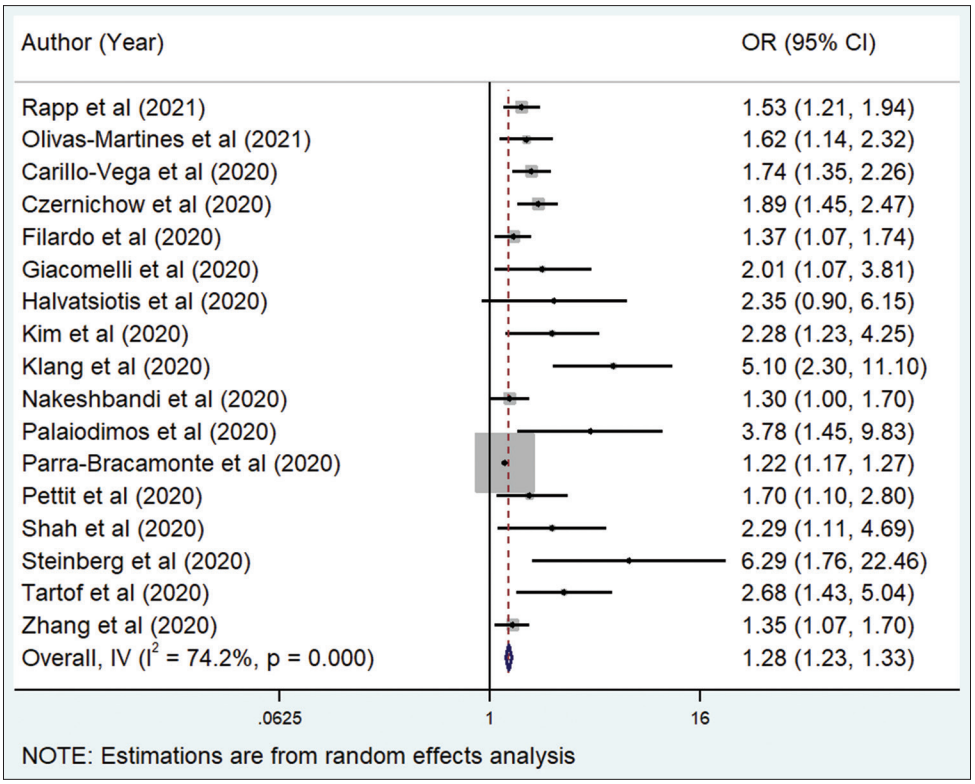

Figure 2: Forest plots the association of obesity and mortality of hospitalized COVID-19 patients

Table 3: Subgroup analysis based on age, sex, severity of COVID-19, comorbidity, and hospitalization in ICU with mortality of hospitalized obese COVID-19 patients

Subgroup	Weight (%)	Pooled odd ratio (95% CI)	I^2 (%)
Age (≥50 years)	16.28	3.12 (2.01-4.23)	93.76
Sex (male)	22.15	1.45 (1.40-1.50)	0
Severity of COVID-19 (severe)	2.07	1.35 (1.04-1.66)	0
Severity of COVID-19 (critical)	1.95	1.73 (1.34-2.13)	0
Diabetes mellitus	18.56	1.25 (1.12-1.39)	53.98
Hypertension	19.51	1.10 (0.95-1.25)	66.28
Chronic kidney disease	12.71	1.63 (1.45-1.82)	35.98
Cancer	3.37	1.26 (0.46-2.05)	9.11
Hospitalization in ICU	3.41	6.19 (4.09-8.30)	89.62

Subgroup analysis

Subgroup analyzes were presented based on age, sex, severity of COVID-19, comorbidity, ICU admission, and mortality of the hospitalized obese COVID-19 patients [Table 3]. Table 3 presented the results of the subgroup analysis, showing that obese COVID-19 patients admitted to the ICU have a high risk of dying during hospitalization (POR = 6.19, 95% CI: 4.09–8.30), followed by age ≥50 (POR = 3.12, 95% CI: 2.01–4.23), critical severity (POR = 1.73, 95% CI: 1.34–2.13), chronic kidney disease (POR = 1.63, 95% CI: 1.45–1.82), male (POR = 1.45, 95% CI: 1.40–1.50), severe severity (POR = 1.35, 95% CI: 1.04–1.66), cancer (POR = 1.26, 95% CI: 0.46–2.05), diabetes mellitus (POR = 1.25, 95% CI: 1.12–1.39), and hypertension (POR = 1.10, 95% CI: 0.95–1.25).

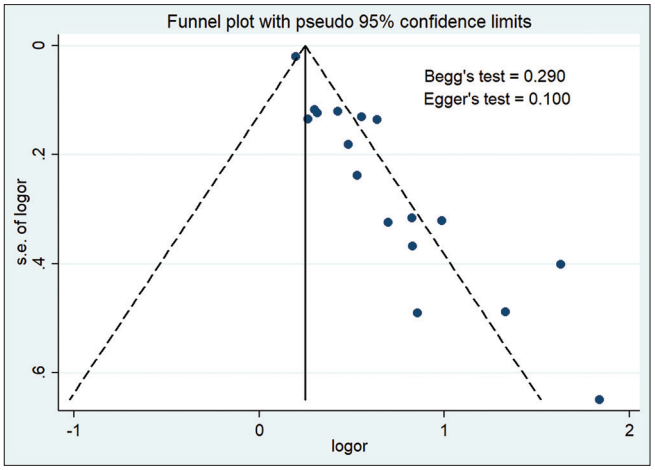

Figure 3: The results of Egger's and Begg's test to assess publication bias among studies included on obesity with mortality of hospitalized COVID-19 patients

The subgroup heterogeneity test on the mortality of the hospitalized obese COVID-19 patients found that there was heterogeneous variation (I^2 > 50%) in the combined studies based on subgroup variables (age ≥ 50 years, diabetes mellitus, hypertension, chronic kidney disease, and hospitalization in the ICU). However, male, severe and critical severity, and cancer were found to be homogeneous the variations (I^2 < 50%) in the combined studies.

Discussion

Our finding demonstrated that mortality of the COVID-19 hospitalized patients is related to obesity (POR = 1.28, 95% CI: 1.23–1.33). Obesity is associated with inflammation and may worsen the COVID-19 condition.[25] In particular, obesity causes systemic chronic low-grade inflammation, and increases the inflammatory biomarkers, including macrophages, increases leptin, and neutrophil chemotaxis. Obesity enables amplified inflammatory response, cytokine storm, IL-6 overproduction, and lung injury, and reduced natural killer cell cytotoxicity.[26]

Moreover, our study had confirmed the association between obesity and COVID-19 mortality with a heterogeneous result of heterogeneity association. A significant correlation between obesity and COVID-19-related death had been confirmed by several large studies. Another study had analyzed COVID-19 death rates from 30 industrialized countries, and found that the obesity rate is the strongest associated with COVID-19 death rate.[27] A study with almost 7,000 patients using multivariable Poisson regression method had showed that even after adjustment for obesity-related comorbidities, there was a J-shaped association between the BMI and COVID-19 mortality. However, this study showed that only BMI of ≥40 kg/m^2 that increase the risk of death significantly.[23] Several previous studies also demonstrated that only the BMI ≥ 35 kg/m^2 significantly increasing the risk of mortality in COVID-19 patients.[28,29] The different cut-offs on obesity on the previous original studies are potentially affected the result of our study.

The results of the subgroup analysis in this study found an increased risk of death in the obese COVID-19 patients, namely those having an age of ≥50 years, males and severe and critical severity. This finding shows in detail which groups need more attention and prioritized intensive care and protection to reduce the risk of death. In addition, obese people are a high-risk and difficult group of patients to treat for COVID-19, needing longer time in the hospital and complete care of comorbidities and complications.[30] Obese people must also be quarantined for longer than those with a normal BMI because of the prolonged virus shedding.[31] Although it was not an objective measurement, the impression of weight increase during the lockdown was noted in half of the respondents in an Italian poll,[32] which might imply a possible rise in obesity. This may increase the number of people who are at risk of acquiring serious illnesses COVID-19.

Furthermore, this study found that obesity had a higher Pooled Odds Ratio in the Asian countries than in western countries in terms of the mortality of the hospitalized COVID-19 patients. The heterogeneity estimates indicated that the included studies were heterogeneous. The cause of the high risk of death from COVID-19 in obese patients in the Asian countries compared to western countries in the results of this study can be caused by several factors. First, this situation can occur because in the Asian countries, there are still disparities in health facilities and the availability of various health workers in several countries in the Asian region which of course are still not as good as in the western countries.[33,34] For example, Germany has more time to prepare laboratory and intensive care capacities for the COVID-19 patients.[35,36] This is different in the Asian countries, where during the pandemic, it was unavoidable that the health workers were overwhelmed and patients who showed severe symptoms had the opportunity to miss the hospital for treatment.[37] The reason is simple. The health facilities are already overcapacity.[38,39]

Second, the number of hospital beds can also play a role, especially for countries with low capacity who are forced to make decisions about which COVID-19 cases are prioritized for treatment.[34] Third, previous studies found obesity rates in COVID-19 patients were found to be high in Bangladeshi/Pakistani and also identified a high chance of COVID-19 death which was three times higher for Bangladeshi/Pakistani compared to white people.[40] However, given the heterogeneity between these studies, it is necessary to have further research to validate the role of obesity and other risk factors that contribute to mortality outcomes of the inpatients.

Finally, there are several limitations to this study. First, the comorbidity and seriousness of the studied population were different. Second, COVID-19 mortality in obese children was not included in the study, so it is not explained. Third, compared to prospective studies, most of the studies included were retrospective, which are less reliable. Fourth, we didn't include articles written in non-English, which could limit epidemiological data from non-English papers.

The findings of this study highlight the serious clinical health implications of increasing body mass index in the community. In the health care sector, it is recommended that there is an intensive management of COVID-19 disease, especially among obese patients. However, in addition to taking curative actions in the health care sector, it is necessary to pay attention to preventive and promotive measures to reduce the increase in obese patients being hospitalized due to COVID-19. Therefore, people need to regularly control their weight to avoid obesity and other health problems. Apart from that also to always apply a healthier lifestyle. Try to eat balanced nutritious foods. Exercise is also needed even though during the pandemic people are doing more activities at home. After that, the government through relevant stakeholders needs to campaign and enforce discipline in carrying out health protocols (wearing masks, washing hands with soap and running water, maintaining distance, staying away from crowds and limiting mobilization and interaction) to the public so that they cannot be ignored.

Suggestions for further research, it is necessary to conduct research with a prospective design in the areas identified in this study which have not been investigated much, namely Africa, Asia and South America to strengthen the results of studies that have been carried out previously.

Conclusions

Our study confirmed that mortality of COVID-19 hospitalized patients is related to obesity, which requires a multi-stakeholder mitigation approach to avoid and control obesity, and its impacts.

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Conflicts of interest

There are no conflicts of interest

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