

SARS-CoV-2 and Obesity: “CoVesity” - A Pandemic Within A Pandemic

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Abstract

Individuals who are overweight or obese are in a chronic state of low-grade inflammation, making them particularly susceptible to developing severe forms of respiratory failure. Studies conducted in past pandemics link obesity with worse health outcomes. This population is thus of particular concern within the context of the COVID-19 pandemic, considering the cessation of obesity management services. This systematic review highlights (1) the reciprocal link between the obesity and COVID-19 pandemics (2) obesity as a risk factor for more severe disease in past pandemics, (3) potential mechanisms that make obese individuals more susceptible to severe disease and higher viral load, (4) the need to safely resume bariatric services as recommended by expert guidelines, in order to mitigate the health outcomes of an already vulnerable population.

Introduction

On March 11th 2020, Coronavirus Disease–2019 (COVID–19) caused by the novel severe acute respiratory syndrome coronavirus (SARS-CoV–2) was declared a global pandemic by the World Health Organization (WHO)(1). Several conditions have been associated with more severe presentations and hospital admissions, including age, male gender, obesity, hypertension, diabetes, cardiovascular disease, and chronic lung disease (2). Recent studies have reported obesity as an independent predictive factor for worse outcomes, increased complications, and intensive care therapies (3). While these findings enable clinicians to identify at-risk patients more promptly, it also emphasizes the neglected pre-existing obesity pandemic. The WHO estimates that obesity rates have nearly tripled worldwide since 1975 (4). As of 2016, approximately 1.9 billion people are overweight with a body mass index (BMI) of 25–30 and over 650 million are obese with a BMI>30(4). Together, this brings the global obesity rate in adults to about 45%.

Several authors have suggested a link between pandemics and subsequent increases in obesity rates(5–9). The lockdown culture, changes in food-seeking behavior, and more sedentary home-based activities might, in effect, further worsen the obesity pandemic. The cessation of obesity management services including bariatric surgery during the pandemic could further aggravate the situation (10). Given suggestions that the COVID–19 pandemic may never go away(11), it would be particularly useful to know how individuals with obesity are faring during this viral pandemic. If they are experiencing a worse outcome, it might highlight an urgent need to double our efforts aimed at combating obesity.

To our knowledge, there is currently no systematic review in the scientific literature examining the reciprocal relationship of the obesity and COVID–19 pandemics. The purpose of this systematic review was to evaluate the outcomes of COVID–19 patients suffering from obesity and inversely, the effect of the COVID–19 pandemic on the obesity pandemic itself, in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines(12).

Methods

Search strategy and selection of studies:

Scientific publications related to the relationship between obesity and COVID–19 infections were identified using MEDLINE, EMBASE, the Cochrane Review and Scopus databases. Our search terms included coronavirus” OR “COVID 19” OR “COVID 19” OR “COVID–19”, “COVID–19” OR “novel coronavirus” OR “SARS-CoV–2” OR “nCoV19” OR “2019-nCoV”. A separate search using the terms “obes*” OR “overweight*” OR “over-weight*” OR “obesity” OR “BMI” OR “body mass index” OR “adipos*” OR “bariatric surgery” OR “metabolic surgery”. Both strings were combined using the AND modifier. The search included studies published up to May 16, 2020. The reference lists of eligible articles were also hand-searched for additional relevant publications.

Selection of studies: inclusion and exclusion criteria

Inclusion and exclusion criteria were defined *a priori*. Any original study that discussed the impact of obesity on COVID–19 infections and vice versa was included. Given the limited evidence available on this topic, we included articles of all methodologies. Publications in non-English languages and non-clinical studies were excluded. Our search yielded 2,681 studies, as shown in the flow diagram (Figure 1). After removal of duplicates, full-text articles were obtained if their abstracts were considered to be eligible. Each full-text article was assessed independently for final inclusion in this systematic review. The selection was performed by two authors (SC and KZ). In the event of conflicts of opinion, these were planned to be resolved by a third (SM).

Data extraction and quality assessment

The quality of the studies was assessed independently using the Newcastle-Ottawa score (Table 1). Disagreements regarding quality assessment score for each study were resolved by consensus. All but two studies scored highly across all domains and were assessed to be of good quality. SC and KZ independently extracted the following data from each article using a standardized study form: (1) study information, (2) geographic location, (3) research design, (4) study objective, (5) sample size, (6) outcomes, including admission to the intensive care unit, severity of disease, use of mechanical ventilation, and mortality.

Results

Study characteristics (Table 2)

We found twenty-two studies investigating the relationship between obesity and the COVID–19 pandemic (3, 13–32). Of these, sixteen studies evaluated the impact of obesity on COVID–19 infection, including its role as a risk factor. The remaining six studies were on how the pandemic will worsen obesity(3, 29–33). The included studies involved a total sample size of 8,534,930 patients. The Body Mass Index (BMI) was

reported to be above 25kg/m² in all studies. One study used the Edmonton Obesity Staging System (EOSS) to classify its participants, noting that it is a better predictor of all-cause mortality in patients with obesity, as compared to BMI. All patients were reported to have an EOSS of 2–3 (14). Three of the studies were policy statements from national and international organizations for bariatric surgery, and hence deserved mention. The remainder were non-randomized, observational studies.

Discussion

This systematic review of the available evidence highlights the relationship between obesity and the COVID–19 pandemic. Several clinical characterization studies, case series and case reports have shown that obesity is an independent significant predictor of worse outcomes and increased complications from COVID–19 infections. This includes more severe disease, higher rates of hospital admission, intensive care management, and mortality, as compared to lean subjects (summarized in Table 2). Other risk factors include male gender, age, and co-morbidities like hypertension and diabetes.

Our review also suggests that obesity is a significant public health problem that predates the COVID–19 pandemic and will expectedly worsen due to psychological factors, behavioral changes and implemented health policies. The role of obesity in COVID–19 can be contextualized in the wider framework of infectious diseases and needs further attention.

Obesity in pandemics

To date, there is limited evidence elucidating the pathophysiological mechanisms linking obesity and severe COVID–19 disease. SARS-CoV–2 has been shown to gain access to the host via angiotensin-converting enzyme 2 (ACE–2) receptors which are upregulated in adipocyte and adipocyte-like cells such as pulmonary lipofibroblasts. This makes obese and diabetic individuals particularly vulnerable to severe lung infection and may explain the development of associated pulmonary fibrosis (34). Moreover, low-grade systemic inflammation and end-organ damage seen in obese individuals are associated with the development of insulin resistance, type 2 diabetes, hypertension, atherosclerosis, dyslipidemia and asthma—well-known co-morbidities that negatively affect the outcomes of patients with COVID–19(14). Difficult airway management and prone positioning (critical in the treatment of ARDS) which are routinely encountered with elevated BMI, further exacerbate the problem(35, 36).

Additionally, extrapolations can also be made from studies in subjects from past pandemics, given that SARS-CoV–2 has 85% and 50% sequence similarity to known coronaviruses SARS-CoV–1 and MERS-CoV, respectively (37). Increased adiposity has been implicated in higher rates of complications in other pandemics—MERS-CoV, SARS-CoV–1 and H1N1 influenza, including development of acute respiratory distress syndrome (ARDS), acute lung injury (ALI), hospitalization and mortality(38).

During the H1N1 swine flu of 2009, obesity was postulated to be an independent risk factor for increased morbidity and mortality in viral illnesses. In a study that spanned from April to August 2009 in California,

Louie et al. found that over half of 534 adult hospitalized patients with H1N1 were obese, with a BMI >30. Of the 92 cases who died, 61% were obese(5). Fezeu et al. revealed that severely obese H1N1 patients (BMI>40) were twice as likely to be admitted to the intensive care unit, with a higher mortality rate than those with a lower BMI(6).

The outbreaks of MERS and SARS in the early 2000s further established obesity as being positively associated with mortality, along with male gender, older age, hypertension, diabetes, COPD, and chronic heart diseases (9, 39, 40). The clinical features of both of these coronaviruses SARS-CoV-1 and MERS-CoV are similar, and can range from asymptomatic or mild disease, to ARDS and multi-organ failure. However, 75% of MERS cases are associated with underlying comorbidities, with a mortality rate of MERS is 60% in this subgroup, while only 10–30% of SARS patients have underlying health conditions with a mortality rate of 46% within this subgroup(41)

Obese individuals may be more infectious

Several human and animal studies have demonstrated a positive correlation between infectivity and increased weight. Maier et al. demonstrated that symptomatic obese individuals shed influenza A particles up to 104% longer than their lean counterparts(42). Similarly, in a study of 178 young adults, Yan et al. concluded that the concentration of viral RNA found in aerosols from collected breath correlated positively with BMI(43). The obesity microenvironment may also be conducive to the development of more virulent viral strains. For example, obese mice models infected with influenza were observed to have a decreased type I interferon response, and had increased viral replication as compared to non-obese mice(44). There is a paucity of evidence on the infectivity of obese individuals in the COVID-19 pandemic, but extrapolations can be made from investigations on other viruses. While the pathophysiology of SARS-CoV2 infection has not been completely elucidated, it has been proposed that the virus gains entry into cells through ACE2-dependent mechanisms, much like SARS-CoV and human respiratory coronavirus NL63(45). It is spread by human-to-human transmission via droplets, aerosolized particles, and direct contact(46). Infection has been estimated to have an incubation time varying from 2 to 14 days, with a mean of 6.4 days(46, 47). Taking into considering prolonged viral shedding and increased viral load in expired air in obese persons, longer quarantine periods should be considered in individuals with increased adiposity as compared to their lean counterparts(48).

Viral infections may induce obesity

The association between obesity and viral infection is not unidirectional. Certain infections by pathogens like adenovirus 36 (Ad36) have been demonstrated to induce obesity. In a systematic review published in 2020, Kim et al. conclude that Ad36 infection increases adipogenesis (through hypertrophy and hyperplasia) in animals and is associated with human obesity. Moreover, Ad36 infection was shown to induce acute and chronic inflammation leading to angiogenesis in fatty tissues(49). Another systematic

review by Xu et al. concludes that *Helicobacter pylori* infection may be a risk factor for the development of obesity(50). However, a causal relationship cannot be established due to the nature of the study design of the included studies.

Indirect impact of COVID19 on the obese population and obesity services

We have recognized that obesity is a risk factor for poor outcomes in COVID–19 infection(28, 51). However, it is inevitable that the pandemic will only exacerbate the existing levels of obesity for several reasons. Firstly, the lifestyle of the average individual during a state of social isolation and global unrest will drastically change. Specifically, in the early phases of the pandemic and during lockdown measures, there will likely be a tendency towards an unhealthy diet coupled with a sedentary lifestyle (52). Over a longer time, this may lead to considerable weight gain for most people. Secondly, the reallocation of hospital resources from elective surgeries to managing COVID–19 patients has led to the nationwide pause of most bariatric surgery as well as most other multidisciplinary services that comprise of the tier 3 weight management programs (31). This is not only to free up inpatient capacity and redirect healthcare workers towards managing COVID–19 patients, but also to avoid intraoperative risks of viral contagion among patients and staff(29). Hence, there is a pre-existing level of obesity that we have not managed yet. In combination, we predict a rise in obesity and its complications in the post-COVID era (53).

Globally, the majority of governments have instituted a “lockdown” approach in an effort to limit the transmission of COVID–19 cases. While this has been proven to be effective as containment measures, there are multiple negative effects of this approach. From an obesity perspective, it is highly likely that the cessation of active lifestyles will lead to an increase in weight gain amongst a significant proportion of the population(33). This can be attributed to a reduction in physical exercise as well as poorer dietary lifestyle. In the early phases of the outbreak, panic-buying and stockpiling depleted most stores of perishable healthy food items, including meat, fruits and vegetables(54). These reactions had severe repercussions on both food access and utilization(55). Consequently, most people had to rely on unhealthy food items as sustenance. Previously, Scully et al had shown that both lockdown and confinement would also lead to erratic dietary patterns and frequent snacking, both of which are associated with higher caloric intake and increased risk of obesity(56). Furthermore, studies from China showed a negative impact on psychological health, which has previously been linked to unhealthy dietary patterns and poor quality of the diet (30, 57, 58). Hence, the current lockdown is likely to increase the prevalence of obesity, and we should actively seek measures to overcome them.

The COVID–19 crisis has led to the cessation of most elective surgical procedures globally at different times. In the UK, NHS England has asked for elective procedures to be halted for three months starting from April 15, 2020 (59, 60). Accordingly, early guidelines from the International Federation for the Surgery of Obesity and metabolic disorders (IFSO) recommended postponing any bariatric procedure(31). But, delaying bariatric surgery extends the progression of metabolic complications of obesity, including

type 2 diabetes, obesity hypoventilation syndrome, obesity-associated heart failure and cancers(61–66). This directly increases the disease burden amongst patients. For example, previous modelling work and the multi-cantered Swedish Obesity Study have consistently showed longstanding disease as a strong predictor of disease remission(67–69). The impact of cancelling elective bariatric surgery will be expensive. Previous economic analyses have shown that diseases that can be corrected with surgery is more cost-effective than medical management. For example, the management of type 2 diabetes with several medications is far more costly than bariatric surgery. Hence, delaying surgery for these patients will make it less cost-saving over time.

There are several solutions for the afore-mentioned issues. Firstly, there should be a coordinated effort from governments and food and beverage industry to ensure an adequate supply chain to prevent food insecurity. There needs to be increased public awareness about the “lockdown lifestyle” can make them obese and provide strategies to avoid it. Already, WHO has provided a list of exercises that can be performed at home to stay physically active(70). Secondly, in the context of a long backlog of operations and patients with higher likelihood of complications, it is possible that there will be a shortage of staff and hospital beds to accommodate this surge. Traditionally, patients have been listed for surgery on a first-come-first-serve basis, prioritized on clinical need. Now, we must generate guidelines for prioritizing patients based on disease severity, taking into account any co-existing microvascular and macrovascular complications of obesity (indicators of organ dysfunction)(71). For example, the Diabetes Surgery Summit (DSS) recommends that patients using insulin and patients with disease duration longer than 5 years be prioritized(32). In the meanwhile, patients should be optimized for surgery and ensure that their weight and metabolism is controlled through lifestyle and pharmacological measures. Surgery should be expedited for patients not responding to such conservative measures. Obesity management / bariatric surgical teams must be advocates for their patients during these difficult times, otherwise there is a significant risk of the patients’ needs being ignored due to continued public perception, that obesity is still a choice and not a disease(72). Through these measures, we may be able to mitigate the afterburn of COVID–19 on the bariatric population.

Conclusion

COVID–19 is an unprecedented viral pandemic which is highly infectious and carries a mortality rate of nearly 7%. Obesity, a pandemic in itself, is an independent factor for having a worse outcome among COVID–19 patients. The dual pandemic—CoVesity, will have a detrimental outcome in the short, medium and long term. We should aim at a phased and safe return of obesity/bariatric services based on expert consensus, guidelines and recommendations from the relevant national and international bodies. There are already safe and reproducible proven interventions for the obesity pandemic that existed prior to COVID–19 and that will continue long after the virus is no longer an issue.

Declarations

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There are no funding sources to disclose.

Conflict of interest:

The authors declare that they have no conflict of interest.

Ethical approval

For this type of study, formal consent is not required.

Informed consent

This research was done without patient involvement. Patients were not invited to comment on the study design and were not consulted to develop patient relevant outcomes or interpret the results. Patients were not invited to contribute to the writing or editing of this document for readability or accuracy. There are no plans to disseminate the study results to patients or the public.

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Tables

Table 1: Quality assessment of studies using the Newcastle-Ottawa scale

Study	Authors	Study design	Selection	Comparability	Exposure	Quality
Obesity and COVID-19 Severity in a Designated Hospital in Shenzhen, China.	Cai et al	Retrospective study	***	*	**	Good
COVID-19 and the role of chronic inflammation in patients with obesity.	Chiappetta et al	Retrospective study	**	*	*	Poor
Characteristics of Emergency Department Patients With COVID-19 at a Single Site in Northern California: Clinical Observations and Public Health Implications.	Duanmu et al	Cross-sectional study	**	*	**	Good
Obesity Is a Risk Factor for Greater COVID-19 Severity.	Gao et al	Case control study	**	*	**	Good
Association of Obesity with Disease Severity among Patients with COVID-19.	Kalligeros et al	Retrospective cohort	**	*	***	Good
Obesity could shift severe COVID-19 disease to younger ages.	Kass et al	Observational	***	*	**	Good
Obesity in patients younger than 60 years is a risk factor for Covid-19 hospital admission.	Lighter et al	Retrospective study	***	*	***	Good
Association of higher body mass index	Ong et al	Retrospective study	***	*	***	Good

(BMI) with severe coronavirus disease 2019 (COVID-19) in younger patients.							
Effects of COVID-19 Lockdown on Lifestyle Behaviors in Children with Obesity Living in Verona, Italy: A Longitudinal Study	Pietrobelli et al	Longitudinal cohort study	**	*		**	Good
High prevalence of obesity in severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) requiring invasive mechanical ventilation.	Simonnet et al	Retrospective cohort study	**	*		***	Good
Clinical and Chest Radiography Features Determine Patient Outcomes In Young and Middle Age Adults with COVID-19.	Toussie et al	Retrospective study	**	**		**	Good
Bariatric Surgical Practice During the Initial Phase of COVID-19 Outbreak.	Aminian et al	Retrospective cohort study	**	*		***	Good
COVID-19 and the role of chronic inflammation in patients with obesity.	Chiappetta et al	Retrospective study	**	*		*	Poor
Obesity as a Risk Factor for Greater Severity	Zheng et al	Retrospective study	**	**		**	Good

Due to technical limitations, Table 2 is provided in the Supplementary Files section.

Figures

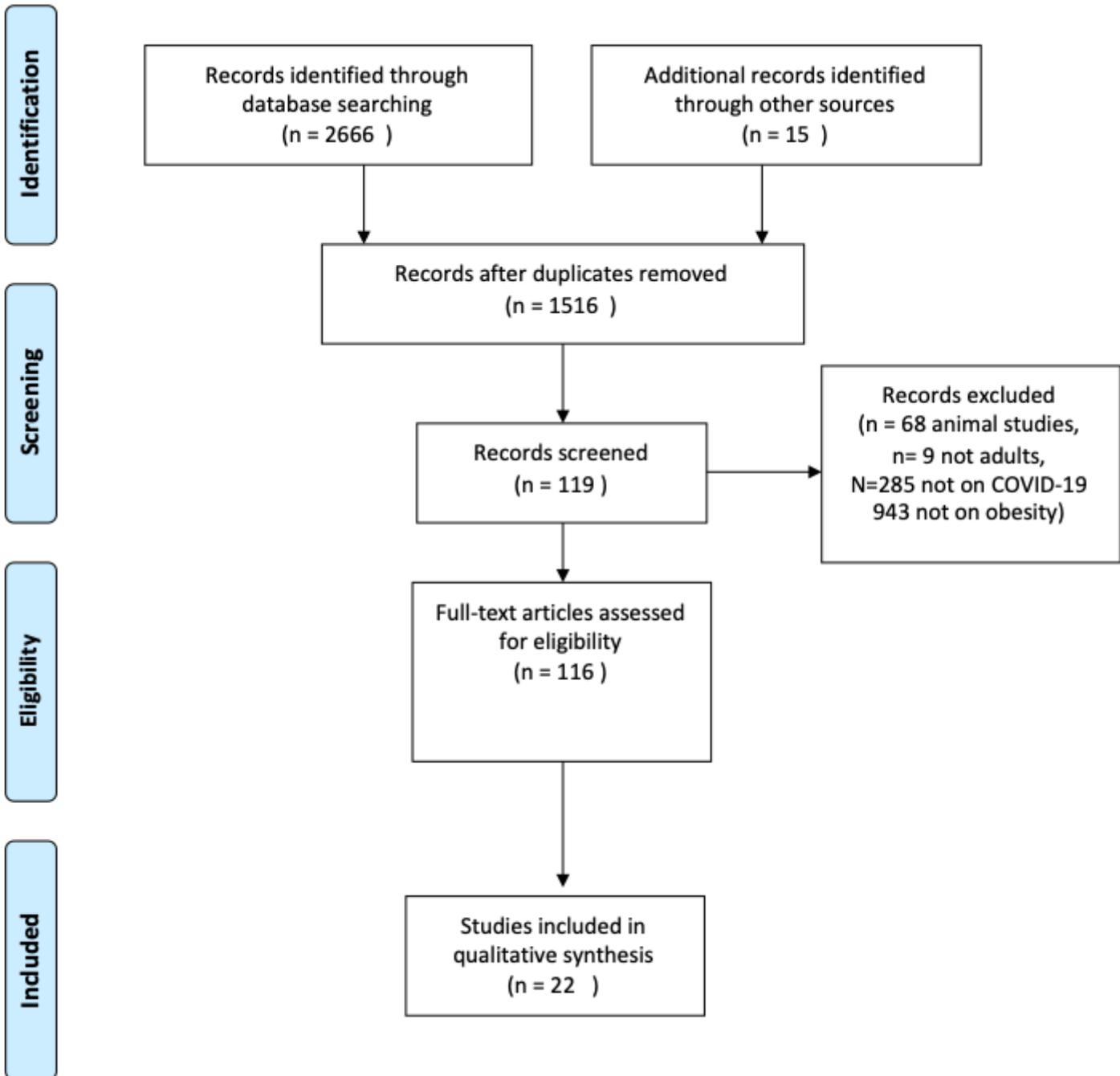


Figure 1

PRISMA diagram for study selection

Supplementary Files

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- [Table2.docx](#)