
Obesity as a risk factor for Covid- 19 mortality: an overview of published meta-analyses

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Abstract: Obesity and Covid-19 affected the world in the form of pandemics. With this brief review was investigated whether obesity is a risk factor for Covid-19 mortality. The search procedure was performed in the PubMed database with restrictions on meta-analysis (MAs), systematic reviews (SRs), and papers published in the English language. A total of 326 papers were obtained, 11 of which were eligible for analysis according to the aim of this study. The reported odds ratio (OR) range was 1.05-3.76, and the reported hazard ratio (HR) was 2.1, but significant heterogeneity was evidenced by I² values up to 89.1%. Eight MAs and SRs reported an association between obesity and an increased risk of Covid-19 mortality or severe disease, while two studies found no association. One study reported that the risk of Covid-19 mortality is related to morbid obesity with body mass index (BMI)≥40 kg/m². Good quality MAs and SRs requires good quality of the included studies, which was a great challenge during the Covid-19 pandemic.

Keywords: Obesity, Covid-19, Mortality

1. Introduction

Obesity is a major health problem worldwide and is associated with epidemic proportions [1]. According to a report published by the World Health Organization (WHO), almost one-third of the world's population is obese or overweight, with approximately 2.8 million people deaths per year [2]. Various chronic diseases are associated with obesity or being overweight [3]. Moreover, obesity is a predisposing factor for poor prognosis in viral diseases [4]. WHO classifies obesity according to body mass index (BMI). Obese individuals are classified according to BMI into class I (30-35 kg/m²), class II (35-40 kg/m²), and class III (≥40 kg/m²) [2]. WHO announced the global pandemic of COVID-19 on February 11, 2020 [5]. Even nowadays, a quick Pub Med search ending with July 14, 2023, revealed 373,914 papers published on the "Covid 19" term. This study aimed to descriptively summarize the main findings from available

systematic reviews (SRs) and meta-analyses (MAs) referring to obesity (overweight) as a risk factor for Covid-19 mortality.

2. Search procedure and discussion

The search procedure was performed on June 21, 2023, in the PubMed database using the following search query: (((obesity) AND (Covid 19)) AND (mortality)) AND (prognosis) with activated filters restricted to MAs, SRs, and papers published in English. A total of 326 papers were obtained, 21 of which were SRs and MAs. Ten studies were excluded because they did not address the aim of this study and 11 studies were analyzed [6-16]. The reasons for exclusion were gravidity, kidney injury, thyroid disorders, no reported mortality, *Candida auris* infections, and age below 18 years etc. Odds ratios (OR) or hazard ratios (HR) were used as measures of the associations [18]. The reported OR range was 1.05-3.76, and the reported HR was 2.1 [6-16]. Heterogeneity, which might introduce a certain bias, was measured using Cochran's Q and I² statistics. Levels that correspond to low, medium, and high heterogeneity follow I² values of 25%, 50%, and 75% [17]. Reported I² values varied from 7.49%-89.1% [6-16]. Due to the constraints of this paper format, this brief review omitted formal statistical measurements, and the main findings are explained descriptively. In addition to this short form of review, we acknowledge certain limitations.

The emergence of SARS-CoV-2 has changed people's lives in many ways. During the COVID-19 pandemic, in addition to sedentary behavior, changes in diet, poor nutrition, and increased BMI were observed during the pandemic compared to the period before the pandemic [19]. Of the 11 studies reviewed, eight reported that obesity is a risk factor for Covid-19 mortality [6-13], seven studies for severe disease [6-8, 10-12, 16], and two reported no association [15, 16]. One study reported that the risk of Covid-19 mortality was related to morbid obesity (BMI≥40 kg/m²) (three studies included in MA; OR 3.76, 95% CI 2.67-5.28, I²=0%, p=0.665) [14].

It was assumed here potential sources of the heterogeneity and proposed recommendations for further MAs and SRs. At the beginning of the pandemic, it was difficult to draw precise conclusions because there were many uncertainties about the virus; however, they were urgently needed for patient care. MAs or SRs published close to the beginning of the pandemic had small (two or more) numbers of studies included in MA and SR [6, 14, 15]. Even though two studies are required to perform MA, more quality papers included in MA produce more certainty about the summary results [18]. Even larger numbers of the studies were included in the MA, the smaller number of studies were included in the formal MA, where mortality was the endpoint (i.e., 88/3 and 40/10) [9, 13]. The majority of studies confirmed the association between Covid-19 mortality and obesity, but the presence of medium or high levels of heterogeneity according to the I² values ≥50% and ≥75%, and p values ≤0.05, were observed [6-16]. This should be considered when accepting or rejecting the main findings of particular MAs or SRs. Heterogeneity is always present, according to the Cochrane Handbook for Systematic Reviews of Interventions [18]. A rapid pace in publications during the Covid-

19 pandemic, prevented constant updating during work on the particular MA. Procedures in MA require a statement about their limitations. All of the studies investigated here [6-16] had statements about their limitations, which we extracted and summarized [Table 1]. However, papers in non-English languages are usually rejected. Most studies reported hospital mortality. Mortality out of the hospital was hard to identify and report. Obesity is associated with other comorbidities; thus, it is difficult to interpret obesity as an independent risk factor for Covid-19 mortality. Although, morbid obesity is a risk factor for mortality with or without Covid-19 [2].

Table 1. Reported main limitations from the studies.

<i>Finding</i>	<i>Author, year</i>
<i>Limited number of studies included in the MA</i>	Deng 2014
<i>Lack of definition for obesity and the severity of the disease in COVID-19</i>	Deng 2014
<i>Not uniform definition of the obesity:</i>	Raiesi,2022;
<i>national cut-points (BMI>25 kg/m²), or WHO definition (BMI>30 kg/m²)</i>	Zhao,2020
<i>Recall bias; reporting bias</i>	Hoong, 2021
<i>Hospitalisation may differ between hospitals-not uniform population of included studies</i>	Hoong 2021;
<i>Overlap of some participants included in the MA</i>	Huang 2020;
<i>Differences between self-reported and measured BMI</i>	Najafabady,2023
<i>Independent risk for mortality of comorbidities, other than Covid-19</i>	Ng, 2021;
<i>The confounders other than pooled adjusted OR/HR might be accounted for.</i>	Pranata, 2021;
<i>Majority retrospective studies which is less reliable compared to prospective studies</i>	Pranata, 2021
<i>Omitted comorbidities of the obese patients. The included studies varied in their differentiation of patients' disease severity according to the clinical definition.</i>	Raiesi, 2022;
<i>Alpha and Beta variants were considered, without the risk factors within the post-Omicron strain (B.1.1.529) context</i>	Vardavas, 2022
<i>Cross sectional, and retrospective studies. Some studies had small sample sizes.</i>	Aghilli,2021;
	Zhao, 2020

Our findings are consistent with those of previous reports [20]. The authors pointed to caution in interpretation of the results since the evidenced and proven low quality of MAs and SRs [20]. True significance in the relationship between obesity and Covid-19 mortality is a challenge for future MA with good quality of included studies, following strict rules and procedures.

3. Conclusions

The majority of MAs and SRs investigated here have reported an association between obesity and an increased risk of severe disease and Covid-19 mortality. Some studies found no relationship between obesity patients with Covid-19 mortality. Others found that during the pandemic, persons with BMI> 40 kg/m² were more vulnerable to mortality than other obesity classes. According to WHO recommendations, obesity is preventable. Even evidence of considerable heterogeneity in the MAs and SRs, Covid-19 mortality and obesity should be investigated in future MAs and SRs by following strict methodological procedures with included high-quality papers.

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