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A NON-SYSTEMATIC LITERATURE REVIEW: IMPACT OF OBESITY PLAYS A MAJOR ROLE IN THE SEVERITY OF COVID-19

Liza Virgianti^{1✉}, Febry Istyanto²

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¹Universitas Jenderal Achmad Yani Cimahi, Indonesia
radenliza90@gmail.com

²Politeknik Kesehatan Kementerian Kesehatan Jayapura, Indonesia

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* Corresponding Author:

¹Liza Virgianti, Faculty of Health Science and Technology, Universitas Jenderal Achmad Yani Cimahi, Jl. Terusan Jenderal Sudirman, Cibeber, Kota Cimahi, Jawa Barat, Indonesia 40531, Indonesia,
E-mail: radenliza90@gmail.com, Phone: +62 812-2450-0832

²Febry Istyanto, Politeknik Kesehatan Kementerian Kesehatan Jayapura, Jl. Padang Bulan, RW.2, Hedam, Kec. Heram, Kota Jayapura, Papua 99351, Indonesia,
E-mail: febryistyanto@gmail.com, Phone: +62 821-3345-2012



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ABSTRACT

Covid-19 disease is a worldwide pandemic outbreak involving severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Obesity is known as one of the risk factors at the severity in Covid-19 patients. This is evidenced in the provision of intensive care (ICU) in hospitals or in health care institutions filled with obese patients with a BMI of $>25 \text{ kg / m}^2$. The impact of obesity often jack up the jeopardy of non-communicable diseases, cardiovascular disorders, cancer, diabetes melitus and non-alcoholic fatty liver disease and this often comes together from each individual. This is a non-systematic literature review article created with the collection of various recent scientific articles related to obesity, hypertension, and Covid-19 disease. A search for this article was obtained from NCBI, Web of Science and Google Scholar with keywords used: "Obesity and Covid-19", "Morbid Obesity", "Hypertension", "Comorbidities" and a combination of these keywords. There were 14 core articles. Obesity has been correlated to adaptive immunity dysregulation and failure in antibody formation after infection or vaccination. Thus, the effect of obesity on a person's immunity is said to be important in the severity of the Covid-19 disease

Keywords: Obesity and Covid-19; Morbidity of Obesity; Hypertension; Covid-19 disease.

INTRODUCTION

Covid-19 is an outbreak caused by a corona virus which has another name as a severe acute respiratory event due to coronavirus 2 (SARS-CoV-2). In China, this RNA virus was identified for the first time in Wuhan City, Hubei Province, (Center for Disease Control, 2019). In this case, the development of this outbreak through the main transmission mechanism from one individual to another. Epidemiological investigations have been carried out on animal markets that sell live animals, then they were closed for disinfection (World Health

Organization, 2020). On December 31, 2019, COVID-19 was first reported to the World Health Organization (WHO). Furthermore, WHO officially declared COVID-19 as a world pandemic disease on January 30, 2020 (Wee SL et al, 2020).

Comorbidities in older people such as chronic heart disease, lung disease, kidney disease, diabetes and hypertension are prone to more terrible disease outbreaks with higher mortality rates. Based on the results of the CDC report, the basic conditions that are very universal among those who are hospitalized with COVID-19 are diabetes, chronic lung disease, and cardiovascular disease (Centers For Disease Control, 2020). Obesity is known as a main factor for cardiovascular disease and diabetes mellitus. Not only that, many respiratory complications are connected with obesity, including increased ventilation requirements, increased work of respiration, respiratory muscle inefficiency, and decreased respiratory compliance (Parameswaran et al., 2006). Obesity in China is more prevalent in Italy if we have compared, which may contribute to the different mortality rates between the two countries (Onder G et al., 2020). Another note is that the United States, which currently has the highest mortality rate from COVID-19, has a large prevalence of obesity compared to China when obesity is defined by BMI (Hu C et al., 2018). In fact, from previous experience the impact of obesity has also cost deaths during the H1N1 influenza epidemic, with some immediate challenges facing obese patients both inside and outside the intensive care unit (ICU). This is a concern about the impact obesity has on Covid-19.

The increasing prevalence of obesity has a consequence, namely the burden of disease and its relation to being overweight. Being overweight is associated with an estimated 7.1% of deaths from any cause and 4.9% of disability worldwide (GBD, 2015). There are various comorbidities that facilitate or contribute to a very high prevalence, namely obesity with hypertension in the obese population (Guh DP et al, 2009; Garrison RJ et al, 1987; Shihab HM et al, 2012). Half of hypertensive patients in the US are obese (Egan BM et al, 2014). This makes 33% of the obese population in the US diagnosed with hypertension, compared to 20% of normal weight individuals (Saydah et al, 2014). The association between hypertension and obesity has a multifaceted nature that is closely related to other comorbid obesity. Monitoring and diagnosis of hypertension in obese patients often causes difficulties in measuring the accuracy of blood pressure (Fonseca-Reyes S et al, 2003).

This a non-systematic literature review of articles is very important to review to make it easier for the public to understand the importance of maintaining body weight which affects blood pressure and other congenital diseases. This is very important to stave off the spread and

transmission of COVID-19, especially in the community and it is expected to be understood by all circles of society.

METHOD

This article was created and redeveloped based on a collection of the latest scientific articles related to obesity, hypertension and comorbidities during the COVID-19 period. Search articles based on data from May 2020 to April 2021 with free, full and English text details. The search for this article was obtained from NCBI, Web of science and Google Scholar with the keywords used: "Obesity and Covid-19", "Morbid Obesity", "Hypertension", "Comorbidities" and a combination of these keywords. Obtained 14 core articles which are the type of non-systematic review.

This article is a non-systematic literature review. The assessment of each core article used in this review is based on the guide "*The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to establish certainty in the findings*".

RESULTS

No	Authors	Type of Research	Location	Results
1.	Petrova D et al., 2020	Review Artikel	Spanyol	Obesity has a role in its association with Covid-19 which shows that very obese people have a higher risk of being hospitalized with intensive care also using mechanical ventilation and even death depending on their comorbidities.
2.	Ryan D.H et al., 2020	Review Artikel	Pennington Biomedical Research Center, Baton Rouge Louisiana, USA	Obese communities around the world will be at high risk for severe complications of Covid-19, this increased risk based on chronic disease and driven by obesity. Not only that, even the psychological toll of this pandemic occurred in obese people by isolating themselves and away from the public and experiencing high levels of depression. This needs to be considered by health care providers to combat obesity bias.
3.	Albashir A et al., 2020	Review Artikel	Faculty of Medicine, University of Gezira, Wad	Obesity is a cause of impaired respiratory function which until now is well recognized, even making groups of patients

			Madani City, Sudan	experience a severe clinical course if they are infected by Covid-19, especially for those who are at risk of obesity. Obese patients are potentially more susceptible to COVID-19 transmission and infection when they are exposed to prolonged periods of viral shedding. It has been become a self standing risk factor for obesity for hospitalization for Covid-19, as well as a cause or exacerbation of various comorbidities associated with increased mortality and morbidity among Covid-19 patients.
4.	Fedele D et al., 2021	Review Artikel	Citta della Salute e Della Scienza, Turin, Italy	There are several clinical conditions, which continue to complicate the association with obesity that act as independent risk factors that are useful as the course of severe disease in Covid-19 patients. Even in conjunction obesity can make breathing difficult.
5.	Zhou Y et al., 2020	Review Artikel	Affiliated Hospital of Medical College Qingdao University, Qingdao, China	Previous studies have shown that there are several viruses that play a role in the development of obesity and metabolic disorders that are still associated with obesity. There has been a marked increase in body weight in adenovirus infection. Although still under research the effects of Covid-19 on obesity are still not well explained, but experience with adenovirus and influenza should serve as a warning for obesity treatments.
6.	Finer N et al., 2020	Review Artikel	UCL Institute of Cardiovascular Science, London UK	People who are obese, let alone complications, such as diabetes and hypertension, will be more susceptible to developing serious diseases and requiring hospitalization that allows the use of invasive ventilation.
7.	Huang Y et al., 2020	Review Artikel	Guilin Medical University, China	The increased risk for obesity is more focused on non-communicable diseases, for example, common examples are

				diabetes mellitus, cardiovascular disorders, cancer and non-alcoholic fatty liver disease. In fact, with comorbidities, people with obesity are thought to increase the severity of the disease during Covid-19.
8.	Sanchis-Gomar F et al., 2020	Review Artikel	University of Valencia and INCLIVA Biomedical Research Institute, Valencia, Spain	Obesity accounts for most of the risk factors for cardiovascular disease (CVD), which also include dysglycemia, metabolic syndrome (MetS) and type 2 diabetes mellitus (T2DM), high blood pressure and hypertension (HTN), along with adverse effects on structure and function. cardiovascular. Obesity is also one of the risk factors for the high severity and poor prognosis that occurs in Covid-19 infection. It also occurs in obesity-induced adipose tissue inflammation and has an effect on the immune system that plays a role in the pathogenesis of COVID-19 infection pain.
9.	Yu W et al., 2021	Review Artikel	Sichuan University, Chengdu, China	Obesity is one of the risk factors that can make Covid-19 disease severe through biochemical, immune, physiological, and anatomical mechanisms. There are many countries around the world that are currently closed to curb the dramatic increase in the number of patients in critical condition. Staying at home during the pandemic also changes your lifestyle and sleep patterns which will increase obesity.
10.	Gleeson, L.E et al., 2021	Review Artikel	Trinity College, Dublin, Republic of Ireland	Obesity is associated with adaptive immunity dysregulation and failure of antibody formation after infection or vaccination, severe acute respiratory syndrome coronavirus (SARS-CoV-2) is a virus that does not have an established adaptive immune response on first exposure. This makes the impact of obesity on the immune system play a very important role in the severity of the Covid-19 disease.

11.	Michalakakis K et al., 2021	Review Artikel	Division of Obesity	A high BMI in patients will be dangerous and even more contagious in the spread of the virus or infection. This obesity is supported in terms of the mechanisms that apply both to innate immunity and in the development of infection, perhaps partly explaining why obese patients are prone to developing respiratory infections in the context of Covid-19.
12.	Malik P et al., 2021	Review Artikel	Icahn School of Medicine at Mount Sinai, New York, USA	Obesity has added an additional burden to patients as well as health care which results in a poorer overall prognosis. In fact, obesity always has a negative impact on the entire human body such as weakening the immune system to activating excessive pathways and resulting in an increase in overall morbidity.
13.	Yang J et al., 2021	Review Artikel	China Academy of Chinese Medical Sciences, Beijing China	Obesity is able to encourage positive SARS-CoV-2 test results, admission to the ICU, inpatient status of Covid-19 patients in hospitals or health agencies, even to invasive mechanical ventilation therapy, and death of Covid-19 patients who are hospitalized.
14.	Demeulemeester F et al., 2021	Review Artikel	NC Numansdorp, The Netherlands	Being obese increases the risk of infection and complications of SARS-CoV-2. In fact, the immune system is not able to respond to adequate immunity and overcome the disruption to the virus.

DISCUSSION

The discussion should explore the significance of the results of the work, not repeat them. A combined Results and Discussion section is often appropriate. Avoid extensive citations and discussion of published literature. Obesity is one of the factors that influence early morbidity and mortality (Global BMI Mortality Collaboration., 2016) whose consequences are the health and quality life of people who suffer from obesity (Upadhyay J et al., 2018). Obesity has been considered a risk factor for more than 20 chronic conditions such as hypertension, dyslipidemia, type 2 diabetes, stroke, cardiovascular disease, sleep apnea and more than 10 types of cancer

(Upadhyay J et al., 2018; Lauby-Secretan B et al., 2016; Pérez Pérez A et al., 2007). In the first study after publishing that obese subjects were at greater risk of developing serious illness from coronavirus (Stefan N et al., 2020). In detail, this study shows obesity is a risk factor in hospitalization or health care, admission to the ICU and the development of more serious consequences in the cause of death in Covid-19 cases (Simonnet A et al., 2020; Petrilli CM et al., 2020; Lighter J et al., 2020; Caussy C et al., 2020).

There are several biological mechanisms by which the disease Covid-19 may affect more people with obesity. One of them is chronic inflammation that is caused by excess adipose tissue found in obese people. This Covid-19 can exacerbate inflammation further, as well as expose it to higher circulating levels of inflammatory molecules compared to lean subjects (Muscogiuri G et al., 2020). On the other hand, inflammation can produce dysfunction in metabolism such as dyslipidemia, insulin resistance, type 2 diabetes, hypertension, and cardiovascular disease which are considered as risk factors in Covid-19 (Sattar N et al., 2020).

Another common trait found in obesity is vitamin D deficiency, which will increase the risk of systemic infection and can even impair the immune response (Bouillon R et al., 2019). On the other hand, vitamin D supplementation can prevent respiratory infections through several immunoregulatory functions, including reducing the production of pro-inflammatory cytokines by the innate immune system, and reducing the risk of cytokine storms that cause pneumonia (Martineau et al., 2019). That is why several studies have shown that vitamin D deficiency could potentially play a role in the association between obesity and increased susceptibility to complications and death from Covid-19 (Grant W.B et al., 2020).

A research study of French data on people treated with COVID-19 cases showed that obese patients with a BMI of 35 required invasive mechanical ventilation more frequently than lean patients (Simonnet A et al., 2020; Caussy C et al., 2020), without looking at age, gender, diabetes, and high blood pressure (Simonnet A et al., 2020). In the same study, there was a study of 4,103 patients with significant COVID-19 cases in New York that combined obesity with the need for hospitalization and the patient's critical condition (intensive care, mechanical ventilation or death), and regardless of other comorbidities (Petrilli CM et al., 2020). For this study, the prevalence of obesity in hospitalized patients was 40%, while in the non-hospitalized group it was 15%. In fact, a recent study of 16,749 patients in the UK confirmed that obesity was associated with an increased risk of death from Covid-19 (Docherty A.B et al., 2020).

An increasing number of research studies are trying to link obesity to the severity or mortality of COVID-19 (Copin et al., 2020; Sanschis-Gomar et al., 2020). For example,

preliminary epidemiological data from the Centers for Disease Control and Prevention in the US, showed that among Covid-19 patients with obesity, 69% had a body mass index (BMI) between 30 and 40 kg/m², and 30.1 % were severely obese with a BMI of 40 kg/m² (Garg S et al., 2020). Not only that, the level of obesity that has been standardized against gender and age has a severity of Covid-19 cases with a total of 340 patients in France, which is significantly higher than the French adult population in general (Caussy C et al., 2020). However, on the other hand, there is still no comprehensive review of this association and it deserves to be studied systematically. In this systematic review we summarize the epidemiological characteristics (hospitalized or diagnosed) of obese Covid-19 patients, in which obesity is determined by local BMI classification criteria.

Obesity can also increase the risk of common non-communicable diseases such as cardiovascular disorders, diabetes mellitus, cancer, and non-alcoholic fatty liver disease, and often coexist in one individual. The comorbidities that are thought to increase the likelihood of severe illness from Covid-19 are for people with obesity (Muscogiuri G et al., 2020; Zhou Y et al., 2020; Hussain A et al., 2020).

The previous experience regarding the discussion of the impact of obesity on deaths from H1N1 influenza showed that obese patients would become sick and require intensive care which poses many challenges in handling. They will be more challenging to intubate and image. This is because the challenge of getting access from a vein, even obesity has been shown to increase the risk of catheter infection and blood flow that needs to be obtained in the ICU (Dosset LA et al., 2009). Obese people will be more difficult to position and transport by nursing staff and at higher BMI levels may require special beds and positioning or transport facilities are not often available outside specialized bariatric surgery units (Jackson Leach R et al., 2020).

Studies have shown that obese patients are potentially more infectious than lean people in the setting of viral infection. First, in that the viral shedding in obesity increases the duration, obese patients have 42% longer viral shedding symptoms when compared to non-obese people (Maier H et al., 2018). Second, obesity will be characterized by a delayed state and capacity to produce interferon in both human and animal studies (Klinkhammer J et al., 2018; Honce R et al., 2020). Third, a positive relationship was found in BMI with the level of infectious virus in the exhaled air (Yan J et al., 2018).

In most patients admitted to the ICU will experience or recover from a life-threatening situation. The BMI of Covid-19 patients will correlate significantly with ICU care (Ortiz-Brizuela E et al., 2020; Hajifathalian K et al., 2020). In a research study in Hubei Province, China, patients with a BMI > 25 kg/m² were 22.1% of the 172 severe to critically ill Covid-19

patients (Hu L et al., 2020). Some experts argue that the high obesity rate among intensive care patients who will become infected with SARS-CoV-2 may depend on local obesity rates (Caussy C et al., 2020). However, on the other hand there was a series of 3,615 patients with Covid-19 cases from New York, USA, those under 60 years old with a BMI of 30 to 34 kg/m² had a 1.8-fold increase in the likelihood of admission to the ICU when compared with patients BMI <30 kg/m². Not only that, in the case of Covid-19 patients in the ICU already had a higher BMI when compared to non-ICU patients (BMI, median 30.5 kg/m² vs 28.77 kg/m²). Interestingly, in USA there are 39.8% of patients transferred to the ICU in countries with high obesity rates (Kalligeros M et al., 2020) and in Italy (19%) (Lagi F et al., 2020), which is significantly higher than in China (5.4% non-Hubei region) (Huang R et al., 2020) and Korea South (13.3%) (Hong KS et al., 2020), which have low obesity rates. In consideration of this likely to be due to differences in health technology as well as varying degrees of aging, we only need to emphasize the importance of obesity's role in the severe form of Covid-19 cases. In fact, it is very possible also to those caused by chronic diseases associated with obesity. Among the 1,591 patients admitted to the ICU for Covid-19 patients in Lombardy, Italy, 68% (95% CI, 65%-71%) patients had at least one comorbidity, including hypertension (49%), cardiovascular disease by (21%), hypercholesterolemia by (18%), and diabetes by (17%) (Graselli G et al., 2020), and have all been associated with obesity in previous studies (Khan SS et al., 2018; Mohan V et al., 2020; Aune D et al., 2018).

CONCLUSION

Obesity greatly affects the severity of the Covid-19 disease. Especially in patients who have comorbidities. This allows treatment for a longer period of time or to avoid something bad.

COMPETING INTEREST

Authors declare that we have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

AUTHORS' CONTRIBUTION

Corresponding author and the second author conceptualized, designed, prepared the initial draft and framework also interpreted the data.

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