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AssociationOfObesity With Length Of Stay And Mortality Of SARS COV-2 PatientsIn A National Refferal Hospital Indonesia

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Abstract— **Background**: SARS-CoV-2 patients with obesity have a high risk for severe and critical clinical conditions that require intensive care and have a poor chance of outcome. The aim of this study was to determine association of obesity with length of stay and mortality of SARS-CoV-2 patients in a national referral hospital Indonesia. **Methods:** This study used a retrospective cohort. The research sample was SARS-CoV-2 patients who were treated by pulmonary specialists in the intensive room of Dr. M. Djamil Hospital Padang. The number of samples in this study was 100 subjects. The inclusion criteria in this study were patients aged > 18 years and patients with severe and critical clinical SARS-CoV-2 confirmed who were undergoing treatment in the SARS-CoV-2 isolation intensive room for the period January – December 2021 and there were data on weight and height in the initial assessment on medical record. Data analysis was performed using the Chi-square test. P < 0.05 was significant, and the data were analyzed using the SPSS version 21.0 program. **Results:** SARS-CoV-2 patients with obese who had a length of stay ≥ 14 days (25.0%) more than non-obese (9.6%). This study found that there was an association between obesity and length of stay of SARS-CoV-2 patients (OR = 3.13, 95% CI 1.01-9.70). The majority of obese patients died (81.3%) more than non-obese (57.7%). This study found that there was an association between obesity and mortality of SARS-CoV-2 patients (OR = 3.18, 95% CI 1.28-7.89).**Conclusion:**There was an association between obesity with length of stay and mortality of SARS-CoV-2 patients in a national referral hospital Indonesia. This study can provide input in the therapeutic management of patients with obesity so as to reduce the poor prognosis.

Keywords: Obesity, length of stay, mortality, SARS-CoV-2

Introduction

Obesity is an increasingly important mortality risk factor, partially because it increase the risk of several non-communicable diseases. Pathogenetic mechanisms underlying these diseases appear to be related, at least in part, to a chronic, low-level inflammatory exposure which often accompanies adipose tissue accumulation and promotes the development of metabolic and cardiovascular complications. Furthermore, the thromboembolic risk is known to be higher in patients with obesity than in the general population (such as H1N1 influenza virus), data remain conflicting. Indeed, several reports have suggested that patients with obesity might have a lower mortality rate during severe sepsis than normal-weight patients. Recent studies suggest that obesity might be associated with a higher risk of developing severe COVID-19 respiratory disease. A population-based analysis of a large UK biobank

even suggest a dose-response relationship between the risk of severe COVID-19 disease and increasing BMI, waist circumference, or waist-to-hip ratio. Similar findings were also reported in a meta-analysis involving over 100,000 patients and suggesting an increased risk of critical COVID-19 disease (odds ratio [OR] = 1.09; 95% CI, from 1.04 to 1.14; n = 3825; six studies) and mortality (OR = 1.06; 95% CI, from 1.02 to 1.10; n = 2704; four studies) with each 1 kg/m2 increase in BMI. Other studies also report higher mortality in hospitalized obese COVID-19 patients than in nonobese ones

The prevalence of obesity is increasing both in the general and the critically-ill population, where one out of five hospitalized patients in the intensive care unit (ICU) is obese. While obesity is usually associated with unfavorable clinical outcomes in many clinical settings, observational data suggest that obese patients with acute respiratory distress syndrome (ARDS) may have better outcomes. This phenomenon has been named the "obesity paradox" by some authors. However, the protective effect of obesity in ARDS is not well understood and remains controversial.

This phenomenon seems to be in line with some studies reporting a paradoxical association between overweight and class I obesity and reduced mortality in patients with chronic heart failure. The SARS-COV-2 pandemic has spread across the world and various studies are being conducted to identify groups that are vulnerable to having severe and life-threatening symptoms. Previous studies reported obesity as a risk factor for severe clinical SARS-COV-2, this is because obese and overweight patients tend to have comorbid diseases such as metabolic disease and cardiovascular disease [1]. Another study, in 24 critically ill patients diagnosed with SARS-COV-2, reported that 85% of obese patients require mechanical ventilation, this proportion is higher than non-obese patients [2].

Overweight and obese SARS-COV-2 patients are associated with poor outcomes. Previous research on the effect of obesity and poor outcomes in a cross-sectional study of 8,261 SARS-COV-2 patients showed that obese patients (Body Mass Index (BMI) > 30 kg/m2)) had a higher mortality rate of 13.6% than patients with BMI < 30 kg/m2 by 7.1% [3,4]. SARS-COV-2 patients with a BMI >25 kg/m2 can increase the risk of death in SARS-COV-2 patients by 18.92% [4]. Other studies have reported that SARS-COV-2 patients with a BMI > 30 kg/m2 have a longer duration of hospital stay (21±8 days) compared to patients with BMI <30 kg/m2 (13±7) days [4,5].

In the subset of patients with the most severe forms of COVID-19 (critical COVID-19 disease, as defined by the World Health Organization [19]), limited data are available. Few studies measured the association between obesity and hospital mortality in this patient population, and among those who did, most included both critically ill and hospitalized patients with a less severe form of the disease. Among studies that focused on critically-ill patients, a significant harmful association between obesity and hospital mortality has not been observed consistently. A recent systematic review of predictors of in-hospital mortality in COVID-19 concluded that obesity was only associated with mortality in studies that included fewer critically-ill patients. However, these studies used ill-specified multivariable models that did not focus on the association between obesity and hospital mortality and used heterogeneous obesity categorizations. Thus, the association between obesity, defined as a high body mass index (BMI), and hospital mortality specifically in critical COVID-19 patients is not yet well-defined.

Compared to China, in these westernized societies the population is older, and there is a much higher prevalence of obesity. These features might aggravate the severity of the disease, given the greater frailty of the population and the well-established mechanical restrictive pattern imposed by high body weight to the respiratory system dynamic. Furthermore, in obese patients there is an increased prevalence of respiratory diseases, including chronic obstructive pulmonary disease (COPD) and sleep apnea. These factors might explain the greater severity, hospitalization and mortality from H1N1 virus infection observed in obese compared to non-obese patients. Recent studies have suggested that BMI represents a risk factor for severe complications in patients with COVID-19. Epidemiological data of the Italian Health Institute (Epicentro) have shown that in people died with positive SARS-COV-2 swab the prevalence of obesity was 11%.

SARS-CoV-2 patients with obesity have a high risk for severe and critical clinical conditions that require intensive care and have a poor chance of outcome [7]. The aim of this study was to determine association of obesity with length of stay and mortality of SARS-CoV-2 patients in a national referral hospital Indonesia [8].

Materialsand Methods

1.1 Studydesign andresearchsample

This study used a retrospective cohort analysis among SARS-COV-2 patients who are treated by pulmonary specialists in the intensive room of Dr. M. Djamil Hospital Padang. From January – December 2021, data was collected from medical records [9]. The number of samples in this study was 100 subjects. The sampling technique used is convenience sampling [10]. The inclusion criteria in this study were patients aged >18 years and patients with confirmed clinical severe and critical SARS-COV-2 undergoing treatment in the SARS-COV-2 isolation intensive room at Dr.M. Djamil Hospital Padang for the period January – December 2021 and there were weight and height data in the initial assessment of the medical record. The exclusion criteria in this study were pregnant women, SARS-COV-2 patients with ascites and/or anasarca edema at the time of initial admission [11]. The patient went home at his own request while being treated in the SARS-COV-2 isolation intensive room at Dr. M. Djamil Hospital Padang.

1.2 Statistical analysis

Quantitative data were expressed as mean ± SD or median [interquartile range], for variables with normal or skewed distribution, respectively. Continuous variables with a normal distribution were compared by the Student t test, while the variables with a skewed distribution by the Mann Whitney U test. Categorical data, expressed as percentage, were analysed with X2 test. In order to identify the variables, at admission, maximally contributing to the duration for obtaining a negative oropharyngeal or nasal swab, and the length of hospital stay, respectively, two partial least square (PLS) regressions [were generated. Variables with Variable Importance in Projection (VIP, expressing a measure of a variable's relevance in the model) greater than 1,50 were considered significant for association with the

dependent variable (duration for a negative swab, or length of hospital stay). The same method has been used in order to identify the variables maximally contributing to group separation of subjects between survisors and dead.

1.3 Data collection and operational definition

This research has passed the ethical review by the research ethics commission at RSUP Dr. M Djamil Hospital Padang. The independent variable in this study was obesity (obese, 25 kg/ m2; non-obese, < 25 kg/m2) [6]. The dependent variable was length of stay (≥ 14 days; <14 days) [7], and mortality of SARS-COV-2 patients (death; survive) [7].

1.4 Dataprocessing and analysis

Frequency and percentage were utilized for categorical data, whereas the mean was used for numerical variables. Data analysis was performed using the Chi-square test. $P < 0.05$ was significant, and the data were analyzed using the SPSS version 21.0 program [7,8].

2. Results

Characteristics of obese and non-obese SARS-COV-2 patients in intensive care.

Table1. Characteristics of obese and non-obese SARS-COV-2 patients in intensive care

Characteristics	Obese (n=48)	Non-obese (n=52)	p-value
Demographics, f(%)			
Age (years)			0.503[a]
<50	11 (57.9)	8 (42.1)	
50-59	13 (52.0)	12 (48.0)	
60-69	15 (48.4)	16 (51.6)	
≥ 70	9 (36.0)	16 (64.0)	
Sex			0.030[a*]
Male	22 (37.9)	36 (62.1)	
Female	26 (61.9)	16 (38.1)	
Clinical severity, f(%)			1.000[a]
Severe	40 (47.6)	44 (52.4)	
Critical	8 (50.0)	8 (50.0)	
Inflammation marker, median (min-max)			
Procalcitonin	0.75 (0.05-171.00)	0.27 (0.05-171.42)	0.375[b]
IL-6	73.70 (1.70-1,482.00)	42.10 (1.50-902.80)	0.570[b]
Ferritin	1,107.58 (11.30-12,001.00)	1,201.00 (11.30-12,001.00)	0.083[b]

D-Dimer	3,494.50 (587.00-7,1901)	3,231.50 (216.00-1,0001.00)	0.221[b]
Comorbid, f(%)			
Hypertension	16 (48.5)	17 (51.5)	1.000[a]
Diabetes mellitus	22 (71.0)	9 (29.0)	0.004[a*]
Liver disease	1 (100.0)	0	n/a[a]
Cancer	1 (50.0)	1 (50.0)	1.000[a]
Pulmonary disease	1 (33.3)	2 (66.7)	1.000[a]
Kidney disease	8 (57.1)	6 (42.9)	0.653[a]
Immunodeficiency	0	1 (100.0)	n/a[a]
Number of comorbid, f(%)			0.118[a]
None	14 (36.8)	24 (63.2)	
1	21 (50.0)	21 (50.0)	
> 1	13 (65.0)	7 (35.0)	

a, Chi-square test; b, Mann-whitney test; *, $p<0.05$ considered significant

Table 1 found that there were no differences in age, clinical severity, inflammation markers, comorbid hypertension, liver disease, cancer, pulmonary disease, kidney disease,immunodeficiency and number of comorbids for obese and non-obese SARS-COV-2 patients ($p>0.05$) [14]. However, there were differences in gender and diabetes mellitus in obese and non-obese SARS-COV-2 patients ($p<0.05$).

Association of obesity with length of stay of SARS-CoV-2 patients in a National Referral Hospital Indonesia (Table 2).

Table 2. Association of obesity with length of stay of SARS-CoV-2 patients in a National Referral Hospital Indonesia

Obese	Length of stay (f/%)		Total (f/%)	p-value	OR (95% CI
	≥ 14 days	< 14 days			
Obese	12 (25.0)	36 (75.0)	48 (100.0)	0.041	3.13 (1.01-9.70)
Non obese	5 (9.6)	47 (90.4)	52 (100.0)		
Total	17 (17.0)	83 (83.0)	100 (100.0)		

Table 2 showed SARS-CoV-2 patients with obese who had a length of stay ≥ 14 days (25.0%) more than non-obese (9.6%). This study found that there was an association between obesity and length of stay of SARS-CoV-2 patients (OR = 3.13, 95% CI 1.01-9.70). Association of obesity with mortality of SARS-CoV-2 patients in a National Referral Hospital Indonesia (Table 3).

Table 3. Association of obesity with mortality of SARS-CoV-2 patients in a National

Referral Hospital Indonesia

Obese	Mortality (f/%)		Total (f/%)	p-value	OR (95% CI
	Death	Survive			
Obese	39 (81.3)	9 (18.8)	48 (100.0)	0.020	3.18 (1.28-7.89)
Non obese	30 (57.7)	22 (42.3)	52 (100.0)		
Total	69 (69.0)	31 (31.0)	100 (100.0)		

Table 3 showed the majority of obese patients died (81.3%) more than non-obese (57.7%). This study found that there was an association between obesity and mortality of SARS-CoV-2 patients (OR = 3.18, 95% CI 1.28-7.89).

Discussion

Our study shows that obesity is associated with a more severe respiratory presentation of COVID-19 and a more severe increase in inflammatory markers, possibly leading to higher oxygen requirements on admission, prolonged oxygen requirements during hospitalization, delayed viral clearance and extended hospital stay. hospital. This characteristic, however, does not translate into a higher risk of death in subjects with obesity compared with patients without obesity.

SARS-CoV-2 patients with obese who had a length of stay ≥ 14 days (25.0%) more than non-obese (9.6%). This study found that there was an association between obesity and length of stay of SARS-CoV-2 patients (OR = 3.13, 95% CI 1.01-9.70). The majority of obese patients died (81.3%) more than non-obese (57.7%). This study found that there was an association between obesity and mortality of SARS-CoV-2 patients (OR = 3.18, 95% CI 1.28-7.89).

Central and general obesity have been shown to be risk factors for hospitalization for COVID-19 infection [15]. The known increased risk is evident even with modest weight gain [16]. Previous studies reported that obese COVID-19 patients had a higher ARDS incidence (46%) than non-obese patients (23%) [8]. Another study in COVID-19 patients with a BMI >40 kg/m2 was 1.5 times more often require intensive care compared to patients with BMI <25 kg/m2 [17].

In another recent paper [24] it has also been described that of 124 patients admitted to ICU for COVID-19, almost half of them were affected by obesity, and a higher BMI was associated with an increased risk of mechanical ventilation. Nearly 90% subjects requiring invasive mechanical ventilation had class II or III obesity. Previous reports on hospitalized patients also observed that patients with higher BMI were associated with increased morbidity and longer duration of stay, so that high BMI was also considered a major risk factor for cost and length of hospital stay [18]. Obese patients were observed to be hospitalized longer in the intensive care unit (ICU) than those with normal weight [19]. In our cohort of patients, the prevalence of obesity (28%) in COVID-19 patients is higher compared to that (11%) reported by Italian Health Institute (Epicentro). This difference could have

multiple explanations; first of all, our cohort is relatively small; moreover, out patients were older and represented a selected population, with greater clinical impairment and need for hospitalization compared to the total SARS-COV-2 confirmed cases in Italy.

Obese patients have an increased risk of exacerbations when they have a viral respiratory infection [20]. A study in Sweden of 1,649 COVID-19 patients undergoing intensive care, reported that a high BMI was associated with an increased risk of death during intensive care as well as an increased duration of stay in the ICU [14,15]. The results of this study concluded that obesity can be an independent risk factor for severe outcome in COVID-19 patients undergoing intensive care, so that BMI measurements are recommended to be included in the severity assessment for COVID-19 patients admitted to the ICU [16,17]. There is growing evidence that obesity increases the risk of hospitalization, severity, and in some cases death from COVID-19 infection, this raises the possibility that obesity independently increases the risk of severity of COVID-19 and other respiratory viral illnesses [12,13,14].

It should be highlighted, however, that the estimated duration of the viral shedding calculated in our report might be inaccurate. Indeed, the days of viral shedding were counted starting from the date of the first positive swab performed upon admission to the Emergency Department. Information regarding the exact onset of the clinical symptoms was not systematically recorded. Another limitation of the present study is represented by the small number of patients included in our cohort, associated with a lack of a better characterization of adiposity. While in a routine clinical setting the most commonly used definition of obesity is based on the presence of a BMI >30 kg/m2, it is well established that other measures such as waist-to-hip ratio might provide better information on the amount of visceral vs. subcutaneous adipose tissue; thus they might better reflect the presence of a pro-inflammatory environment related to fat accumulation. However, in the setting of an acute medical ward, with the huge burden of patients faced during phase 1 of the pandemic, collection of these measures was practically impossible. Finally, we did not have information on the severity of insulin resistance associated with obesity, which is known to have an impact on the risk of cardiac dysfunction and CVD-related mortality [30]. Phase 2 of the pandemic might represent an excellent opportunity for deepening our knowledge and acquiring further information regarding the potential influence of waist-to-hip ratio and the levels of insulin resistance on the association between obesity and severity of the SARS-CoV-2 infection.

In a national referral hospital in Indonesia, there was an association between obesity and the length of stay and mortality of SARS-CoV-2 patients [19,20]. This research can help with the therapeutic care of obese people to improve their prognosis [30].

Conclusion

There was an association between obesity with length of stay and mortality of SARS-CoV-2 patients in a national referral hospital Indonesia. This study can provide input in the therapeutic management of patients with obesity so as to reduce the poor prognosis.

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Conflict of interest statement

There are no competing interest declared by the authors.

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