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Obesity and the Risk of Severe COVID-19Illness amongPatients, Depok, Indonesia

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Abstract— **Background**: Corona virus disease (COVID-19) causedby SARS-CoV 2 (SevereAcuteRespiratorySyndrome) has spreadworldwide, infecting morethan 180 millionpeopleand 3.9 milliondeaths. The clinicalmanifestationsof COVID-19 rangefromasymptomaticormildinfectiontosevere illness. This study aimsto examinetheriskofsevere COVID-19 illnessassociatedwithobesity. **Material and Methods**: A cross-sectional study was conducted among COVID-19 patients admittedtotheUniversityHospital in 2020. Patientsages<18yearsandpregnantpeoplewere not includedin theanalysis. Data wereobtainedfrommedicalrecords. Cases wereselected for the analysisonlyif the information wascomplete. There were725 COVID-19 cases included for the analysis. WeusedadjustedPRs (and 95% CI) to estimate the risk of COVID-19severityassociatedwithobesity. **Results**: Of 725 COVID-19 cases, 178 hadseveresymptoms.Patients with hypertension, diabetes, heartdisease and chronickidneydiseasewere more likely to suffersevere COVID-19 symptoms. Aftertakingintoaccountage, gender, diabetes andheartdisease, obesitywasassociatedwithsevere COVID-19 illness(PR 1.78 and 95% CI:1.32-2.38).The risk of COVID-19 severityassociatedwithobesitywereconsistent on levels of age, sex, and comorbidities.
Conclusion : Obesityincreases the riskofseverityin COVID-19. Maintaininghealthy life style, including routine exercise, choice of healthyfood and routine medical checkup mayreduce the risk of COVID-19severity.

Keywords— Obesity, Severity, COVID-19, Indonesia

1. Introduction

At the end of December 2019, the World was shocked with the emergence of several cases of pneumonia of unknown cause which were first reported in Wuhan, China (1). The disease, caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), has spread throughout the World and was named “Coronavirus Disease-19” (COVID-19) in February 2020(2),(3). On March 11, 2020 when the Coronavirus has spread to 114 countries, resulting in more than 118,000 cases and 4,000 deaths, the WHO officially declared COVID-19 a pandemic(4).

The clinical manifestations of COVID-19 range from asymptomatic or mild infection to severe, life-threatening illness(5).Research efforts have been made to identify people who are most at risk of critical conditions and death. Preliminary data refers to individuals who are elderly, and who suffer from diabetes mellitus, cardiovascular disease (including hypertension), respiratory disorders, and kidney disease. With more reports, new evidence has shown a linkin obesity with progression to severe illness in COVID-19 cases that even lead to death(6).Reports from China initially identified hypertension, diabetes, COPD, and cardiovascular disease as the comorbidities most consistently associated with the risk of hospitalization, oxygen therapy requirement, intensive care unit (ICU) admission, and death in patients with COVID-19.

Subsequent reports from the United States and Europe identified another risk factor, namely body mass

index (BMI), in which patients with a higher BMI had a greater risk of hospitalization and severe symptoms requiring respiratory support(7).Although the role of obesity was initially overlooked, recent reports have found that obesity is associated with an increase in the severity of the disease in a person infected with COVID-19(5).

Obesity is one side of the double burden of malnutrition, and today more people are obese than underweight in every region except sub-Saharan Africa and Asia. Previously, obesity was considered a problem that only existed in high-income countries.Overweight and obesity are now increasingly prevalent in low-and-middle-income countries, especially in urban settings. Most children who are overweight or obese live in developing countries, where the rate of increase is moret han 30% higher than in developed countries (8).Meanwhile in Indonesia, RISKESDAS data, The National House hold HealthSurvey, shows a significant increase of obesity, namely 10.5% in 2007, 14.8% in 2013,and 21.8% in 2018(9),(10).

Based on this background, there is a double burden of disease that Indonesia is currently facing, namely obesity and COVID-19, where individuals who experience COVID-19 with obesity will develop worsen illness. COVID-19 is a new disease that has emerged since December 2019. COVID-19 has been declared a pandemic because it has spread to more than 200 countries with a large number of cases, including Indonesia.Based on previous studies, it was found that one of the risk factors that worsened COVID-19 patients was obesity. Although currently COVID-19 and obesity are health problems in Indonesia, there are not many studies that examine the relationship between the two. Furthermore, the researchers chose the University of Indonesia Hospital as a place of research because based on the Decree of the Governor of West Java Number 445/Kep.224-Dinkes/2020 regarding the establishment of a referral hospital for handling certain emerging diseases, it is declared as one of the COVID-19 referral hospitals in Depok City, West Java.

This hospital islocated in the city of Depok where cases of COVID-19 continue to increase. In addition, itis a research and training hospital where the available data will be more accurate. To date, there has beenno study regarding the relationship between obesity and the severity of COVID-19 in patients treated at that hospital in 2020. Therefore, researchers are interested in examining how obesity is associated withs everity in COVID-19, and whether ot her factors contribute to the risk of severity of COVID-19 associated with obesity.

2. Material and Methods

Samples

We conducted acrosssectionalstudy among patients who admittedfor Covid-19 infection in The University of Indonesia Hospital, Depok, in March to June 2021. The study protocol was approved by The Research CommitteeUniversity of Indonesia Hospital(Number 0037/SKPE/KKO/2021/00).

We used hospital records to select COVID-19 patients admitted to the hospital between March 2020 and December 2020. We included all adult patients (798 patients) age 18 years old or above during the study period. A total of26 subjects who were pregnant were excluded.

Datafrom medical records were extracted to examine severity of COVID-19 and obesity status.This study defined severity of COVID-19 as havingdifficulty breathing or shortness of breath, chest pain or pressure, loss of speech or movement or had acute respiratory distress syndrome(ARDS).We used body mass index greater than 27 $kg/m^2$to classify obesity. We also obtained other information includingdemographic factors,

hypertension, diabetes mellitus, heart disease, and chronic kidney disease from medical records.We excluded 47 subjects who has missing information, so this has lead 725 subjects eligible for the analysis.

We used descriptive statistics to examine severity of COVID-19 by obesity, age group, sex, hypertension, diabetes mellitus, heart disease and chronic kidney disease. A Prevalence ratio (PR) and 95% confidence interval was derived from modification of Cox proportional hazard by assigning a constant risk periodwas used to estimate the risk of severity of COVID-19 associated with obesity.(11)None of the covariates had changed the estimate for 10% or greater, however, we consideredage and sexbe includedin the final model.Furthermore, stratificationanalyses were performed to evaluate the risks of severity associated with obesity according to levels of age, sex, hypertension, diabetes mellitus, heart disease and kidney disease.

3. Result

Of those who experienced severe COVID-19 32.99% were obese, while 18.99% were not obesed (Table 1). Age group > 50 years experienced more COVID-19 severity (37.20%) than the 18-50 age group (15.97%). More men (29.38%) experienced severe COVID-19 than women (17.82%). This study also showed that the severity of Covid-19 was greater in patients who had comorbidities. Those with hypertension experienced severe COVID-19 by 37.21% than those without hypertension (17.56%). Likewise, the severity of COVID-19 in those with diabetes mellitus, heart disease and chronic kidney disease experienced a greater severity of COVID-19 than those without these diseases (Table I).

Tabel I. FrequencyDistributionofResearchVariablesin Hospitalized COVID-19 Patients Age ≥ 18 yearsatUniversity of Indonesia Hospital in 2020

Variable	COVID-19 Severity				Total	
	Severe		Not Severe			
	n	%	n	%	n	%
Obesity						
Yes	95	32,99	193	67,01	288	39.72
No	83	18,99	354	81,01	437	60.28
Age						
> 50 years	109	37,20	184	62,80	293	
18-50 years	69	15,97	363	84,03	432	100
Sex						
Male	124	29,38	298	70,62	422	100
Female	54	17,82	249	82,18	303	100
Hypertension						
Yes	96	37,21	162	62,79	258	100
No	82	17,56	385	82,44	467	100
Diabetes Melitus						
Yes	82	53,95	70	46,05	152	100
No	96	16,75	477	83,25	573	100
Heart Disease						
Yes	81	53,29	71	46,71	152	100
No	97	16,93	476	83,07	573	100
Chronic Kidney Disease						
Yes	23	56,10	18	43,90	41	100
No	155	22,66	529	77,34	684	100

Multivariable analysis results showsthat obesityincreases the risk of severity of COVID-19 (Table II). After taken into account age and sex,patients with obesity had 1.78 times more likely to experience severity of Covid-19 than than those who did not have obesity (PR1.78; 95% CI1.32-2.38).

Table II. Risk of severe COVID-19 associated with obesity

	PR	95% CI
Obesity		
Yes	1,78	1.32-2.38
No		

Adjusted for age and sex

Table III shows the association between obesity and severity of Covid-19 according to age, sex, hypertension, diabetes mellitus, heart disease and kidney disease. The risks of severity of Covid-19 associated with obesity were greater than 1.0 for all categories of covariates. The association were stronger among younger age group, women, patients who did not hypertension, diabetes mellitus than among older age group, male, patients with hypertension and diabetes mellitus. Patients who had heart disease or kidney disease have a higher risk of severity of Covid-19 associated with obesity compared compared those who did not have heart disease or kidney disease. However, the PR was not precise amongpatients who had kidney disease due to small number of patients in this category.

Tabel III. Risks of severe COVID-19 associated with obesity based on demographic and other diseases

Variable		COVID-19 Severity		PR
		Severe	Non Severe	
		n (%)	n (%)	
Age				
> 50 years	Obese	51 (47,22)	57 (52,78)	1,51
	Not Obese	58 (31,35)	127 (68,65)	(1,12-2,02)
18-50 years	Obese	44 (24,44)	136 (75,56)	2,46
	NotObese	25 (9,92)	227 (90,08)	(1,57-3,87)
Sex				
Male	Obese	67 (37,64)	111 (62,36)	1,61
	Not Obese	57 (23,36)	187 (76,64)	(1,19-2,17)
Female	Obese	28 (25,45)	82 (74,55)	1,89
	Not Obese	26 (13,47)	167 (86,53)	(1,17-3,05)
Hypertension				
Yes	Obese	51 (42,50)	69 (57,50)	1,30
	Not Obese	45 (32,61)	93 (67,39)	(0,95-1,79)
No	Obese	44 (26,19)	124 (73,81)	2,06
	Not Obese	38 (12,71)	261 (87,29)	(1,39-3,05)
Diabetes Melitus				
Yes	Obese	38 (59,38)	26 (40,63)	1,19

	Not Obese	44 (50,00)	44 (50,00)	(0,89-1,59)
No	Obese	57 (25,45)	167 (74,55)	2,27
	Not Obese	39 (11,17)	310 (88,83)	(1,57-3,30)
Heart Disease				
Yes	Obese	43 (53,09)	28 (39,44)	1,29
	Not Obese	38 (46,91)	43 (60,56)	(0,96-1,74)
No	Obese	52 (23,96)	165 76,04)	1,89
	Not Obese	45 (12,64)	311 87,36)	(1,32-2,72)
Chronic Kidney Disease				
Yes	Obese	14 (93,33)	1 (6,67)	2,69
	Not Obese	9 (34,62)	17 (65,38)	(1,56-4,65)
No	Obese	81 (29,67)	192 70,33)	1,65
	Not Obese	75 (18,00)	337 82,00)	(1,25-2,17)

4. Discussion

The study found that obese COVID-19 patients were 1.68 times more likely to experience severe (severe to critical symptoms) COVID-19 compared to non-obese patients. The increase risk of COVID-19 severity was associated with obesity and were constant through eachstrata of age, sex, and history of comorbidities (hypertension, diabetes mellitus, hearth disease, and kidney disease).

This study is in line with previous studies that found correlationbetween obesity and the COVID-19 severity(2),(12),(13). A study conducted by Cai et al (2020) on 383 patients age ≥18 years in a Chinese hospital found that obese patients also tended to experience cough and fever symptoms compared to non-obese patients. Obese COVID-19 patients had a 3.4 times higher risk of developing severe symptoms compared with non-obese patients (OR = 3.40, 95%CI: 1.40-8.60)(12). The cohort study by Fresan et al (2020) conducted on 433,995 patients age 25-79 years found that the population with class 3 obesity had a 2.3 times the risk of experiencing COVID-19 severity compared to other populations (RR = 2.3; 95% CI: 1.20-4.40) (2). Nakeshbandi et al's (2020) study conducted on 684 patients using a retrospective cohort study design found that the obese population was 2.4 times more likely to experience COVID-19 severity and required intubation compared to other populations (RR = 2.4; 95% CI: 1.5- 4.0)(13).

The risk of developing severe COVID-19 (severe and critical symptoms) associated with obesity may be due to excess adipose tissue in the upper respiratory tract resulting in airway obstruction and a more rapid progression to hypoxia(13).Obese patients also experience an increase in intra-abdominal and restrictive chest wall pressure, which results in decreased forced expiratory volume and forced vital capacity, in addition to decreased diaphragmatic contractility. This contributes to pulmonary dysfunction and subsequent desaturation leading to intubation(6).Obesity is associated with several respiratory disorders, such as obstructive sleep apnea syndrome, asthma, restrictive respiratory syndrome, and obesity hypoventilation syndrome. People with obesity are at particular risk for developing acute respiratory distress syndrome (ARDS), regardless of the etiology of the syndrome(14).

There were 47 subjects not included in the analysis because of missing information. However, selection bias is an unlikely explanation of our finding as the results of sensitivity analyzes by including 47 subjects found the risk of severity of Covid-19 associated with obesity shows a direction of a positive association, namely the PR between 1.22 (95% CI 0.93-1.61) and 2.23 (95% 1.69 – 2.96). Similarly, the risk of severity of COVID-19 according to levels of age, sex, and having comorbidities were consistently greater than 1.

Previous reports found that severity COVID-19 occurred in elderly patients with comorbidities(15). Age 50 years and above is the age where there is a decline in body organ function and if a person is exposed to COVID-19, it is likely to be at risk for severe COVID-19. This study did not find an association between obesity and COVID-19 by increasing age as the risk was lower among the older age group than younger aged group.

This study found that the risk of COVID-19 severity associated obesity was not modified by sex. This contrasts with new research linking a stronger association of COVID-19 severity in men. Research by Sha et al showed that men had a higher risk of COVID-19 severity than women (HR 2,033, 95% CI 1,007–2,098) (16). The main cause of COVID-19 severity is an exaggerated inflammatory response to SARS COV-2 which is associated with high levels of circulating cytokines, such as IL-6(17). foundhigher in men than in women (18).

Individuals infected with COVID-19 with underlying comorbidities can develop severe COVID-19(19). One of the most common comorbidities in COVID-19 patients is hypertension, with a prevalence ranging from 16.9 to 31.2% in hospitalized patients in China (20). A study by Mubarik et al. found that the proportion that experienced severe COVID-19 in patients with hypertension was greater (57.68%) than the group without hypertension (41.88%)(21). In this study while there was an increased risk of COVID-19 severity with obesity among those who had or did not have hypertension, the risk was higher among patients who did not have hypertension than those who had hypertension. The same was also found when the risk was evaluated with diabetes mellitus and heart disease, that the risk of severity of COVID-19 associated with obesity is higher among patients without diabetes mellitus or heart disease compared to those who have this comorbidities(22). However, this study is consistent with the result of previous studies that kidney disease contributes to the risk of severity of COVID-19. Study by Pakhchanian et al observed a higher proportion of patients with kidney disease had severity of COVID-19 compared to those who did not have kidney disease (17.2% vs 3.5%)(23).

The major concern related to the results of this study is the use of hospital medical records as a source of information where information about risk factors for the severity of COVID-19 is limited. The presence of risk factors for severity that are not recorded in medical records, such as smoking, can cause a biased effect estimate caused by residual confounding.

5. Conclusion

In summary, this study suggests that obesity increases the risk of COVID-19 severity. We recommend that further research is carried out that includes other factors associated with the risk of COVID-19 severity.

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