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Original Research Article

Association of obesity with the clinical severity of COVID-19 among hospitalized patients in a tertiary care hospital in Bangladesh

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ABSTRACT

Background: The coronavirus disease 2019 (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is increasingly drawing worldwide attention. Among multiple risk factors, obesity is one of the factors that can influence the disease severity. This study aimed to explore the impact of obesity on the severity of COVID-19 infection.
Methods: This cross-sectional study was conducted in the Department of Respiratory Medicine, Bangabandhu Sheikh Mujib Medical University, Dhaka from September 2020 to February 2021. The Adult (Aged ≥18 years) patients of both genders, who were COVID-19 positive, were included in this study. Ninety-one COVID-19 patients with BMI≥25 kg/m^2 were set as case and another ninety-one patients with BMI<25 kg/m^2 were selected as control. The patient's BMI and waist circumference (WC) were recorded. Disease severity was evaluated by the management of COVID-19 disease guidelines by the World Health Organization (WHO) 2020.
Results: The maximum patients were male (65.38%), in the sixth and seventh decades. The proportion of severe illness was higher in the obese group 69.2% compared to the non-obese 47.3%. Patients with obesity require more ICU support (15.4% versus 5.5%) and invasive mechanical ventilation (9.9% versus 2.2%) compared to non-obese patients. In multivariate logistic regression analysis, after adjusting age, diabetes mellitus, and hypertension, obesity (BMI>25 kg/m^2) was an independent risk factor for severe illness.
Conclusions: Obese patients are associated with severe COVID-19 pneumonia. As BMI increases, disease severity increases, needs more ICU support, and needs more invasive mechanical ventilation.

Keywords: Association, Bangladesh, COVID-19 disease, Obesity, Severity

INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a highly contagious disease and is responsible for pneumonia of unknown origin. At the end of December 2019, a cluster of people in Wuhan, China was affected by the virus. After that, the disease spread rapidly worldwide, affecting millions of people, and was declared a pandemic by the World Health Organization on March 11, 2020. In Bangladesh, the first case was detected on March 8, 2020. Clinical manifestations of COVID-19 range from asymptomatic or mild infection to so severe form that may be life-threatening. The major risk factors for severe disease are extreme age, chronic lung disease, obesity cardiovascular disease, diabetes mellitus, and hypertension. The effect of obesity was initially neglected, but some studies found that obesity is associated with potential severe COVID-19.[1]

Obesity is a non-communicable disease measured by BMI. According to the Asian-Pacific classification, BMI≥25 kg/m^2 is called obese. According to the WHO classification, a BMI≥30 kg/m^2 is called obese. Without any co-morbidity, obesity itself was responsible for a greater risk of severe COVID-19 pneumonia and death. In a French study, in COVID-19 infected patients, the risk of invasive mechanical ventilation admitted to the intensive treatment unit was more than 7-fold higher for those with a body mass index (BMI) >35 compared with a BMI<25 kg/m^2.[2]

The Asia-Pacific classification of BMI has a lower cutoff for overweight and obese categories compared to the World Health Organization (WHO) classification[3]. Waist circumference (WC) is a measure of abdominal obesity. For the Asian population, central or abdominal obesity was defined as a WC≥90 cm for males and ≥80 cm for females.[4] Adipose tissue may be vulnerable to COVID-19-infected patients because angiotensin-converting enzyme 2 receptor expression in adipose tissue is higher than in lung tissue. So, obese patients have worse outcomes, including respiratory failure, the need for mechanical ventilation, and higher mortality.[5] The COVID-19 infection causes an elevated level of angiotensin II. High Ang II levels in the lung can induce pulmonary vasoconstriction leading to ventilation/ perfusion mismatch, inflammation, thrombosis, pulmonary damage, and hypoxemia. Inflammation and oxidative damage promote acute lung injury. Interestingly, Ang II levels decreased in response to dietary weight loss. As such, dietary modification may be beneficial in reducing this potential mechanism of enhanced COVID-19 infection in obesity.[6]

Additionally, obesity is associated with impaired pulmonary function, decreased expiratory reserve volume, functional residual capacity, and respiratory system compliance. Increased abdominal obesity compromises pulmonary function in the supine position by decreasing diaphragmatic function, which impairs the ventilation in the base of the lung, resulting in reduced oxygen levels in the blood.[7] All affect the lung parenchyma and bronchi, responsible for more inflammation and increased morbidity.[6] Obese patients had higher levels of plasma C-reactive protein and lower lymphocyte counts, which are considered two early indicators of severe COVID-19.[8]

A previous study showed that obese patients require more hospital admissions and longer hospital stays. Death is also more common in the obese group.[9] Therefore, the study aimed to assess the effect of obesity on disease severity. It will help with early screening of this high-risk obese group and provide early treatment which may reduce both mortality and morbidity. It will also reduce the cost of unnecessary hospitalization among non-severe cases. This study will add scientific information about obesity and the relationship between obesity and COVID-19 infection.

METHODS

This cross-sectional study was conducted in the COVID-19 Unit, at Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka from September 2020 to February 2021. A total of 182 patients both male and female were taken as the study population who were RT PCR positive for COVID-19, hospitalized in BSMMU fulfilling the inclusion and exclusion criteria in this study. The severity of COVID-19 was determined by the management of COVID-19 disease guidelines by the World Health Organization (WHO) 2020.[10] Body mass index (BMI) ≥25 kg/m^2 was considered obese.[11] For the Asian population central or abdominal obesity was defined as a WC≥90 cm for males and ≥80 cm for females.[4]

Inclusion criteria

Patients admitted to the COVID-19 ward, at BSMMU with positive RT-PCR reports for COVID-19 disease, age ≥18 years of both sexes, and patients who willing to give informed consent to participate in this study were included.

Exclusion criteria

Patient with bacterial infection evident by procalcitonin >0.5 ng/ml, patient who was on immune-suppressive drugs (e.g. steroid, methotrexate, cyclophosphamide, cyclosporine, azathioprine, mycophenolate mofetil, tofacitinib), pregnancy and recent childbirth, and patient suffering from any malignancy were excluded from this study.

The patients were explained properly about the purpose, procedure, potential physical and psychosocial risks, and right to refuse to participate. They were enrolled upon their voluntary agreement. Adult patients of both genders who were positive RT PCR for COVID-19, aged >18 years, and admitted to BSMMU were evaluated. Information about the demographic variable (age, sex, occupation, education, tobacco intake), and comorbidities (diabetes, hypertension, pre-existing lung disease, chronic kidney disease, cardiovascular disease) was recorded in a data sheet. The symptoms of COVID-19 (fever, cough, shortness of breath, sore throat, malaise, fatigue) were taken. BMI was measured from height and weight. Physical examination (pulse, blood pressure, respiratory rate, oxygen saturation, level of consciousness, flapping tremor) was done. Disease severity was evaluated by the WHO guideline of management of Coronavirus Disease 2019 (COVID-19) on the 12th day of illness. For statistical purposes, COVID-19 patients were categorized into two groups according to their disease severity non-severe (i.e., mild and moderate disease, combined) and severe (severe and critical, combined).

The data was analyzed by using the SPSS program version 23. The categorical variables were described as

frequency and percentages. Continuous variables were described as mean and SD or median as applicable. Means for continuous variables were compared using unpaired t-tests. A comparison of categorical variables was done using the chi-χ^2 test. A multivariate logistic regression analysis was implemented to evaluate the relationship between obesity and COVID-19 infection severity, using odds ratios (ORs) and 95% Confidence interval. A P value of less than 0.05 was considered statistically significant. Informed written consent was taken from every patient before enrollment.

RESULTS

In the severe group mean age was 57.64±10.49 years. Non-severe group mean age was 50.53±9.48 years. The severe group's mean age was more than the non-severe group. There is no association of COVID-19 severity with gender. Smoker was only 13(12.3%) in the severe group and 5 (6.6%) in the non-severe group. Smoking does not affect severity (p value>0.05) (Table 1).

Table 1: Baseline characteristics of the participants (n=182).

Characteristics age (years)	Obese (n=91)	Non obese (n=91)	P-value
Mean±SD	55.23±11.77	54.12±9.73	0.489
Sex			
Male	54 (59.3)	65 (71.4)	0.087
Female	37 (40.7)	26 (28.6)	
Smoking status			
Smoker	11 (12.1)	7 (7.7)	0.321
Non-smoker	80 (87.9)	84 (92.3)	
Symptoms			
Fever	90 (98.9)	87 (95.6)	0.368
Cough	68 (74.7)	66 (72.5)	0.737
SOB	58 (63.7)	44 (48.4)	0.037*
Headache	10 (11.0)	11 (12.1)	0.817
Fatigue	43 (47.3)	48 (52.7)	0.553
Sore throat	16 (17.6)	8 (8.8)	0.080
Diarrhea	9 (9.9)	8 (8.8)	0.799
Nasal congestion	1 (1.1)	6 (6.6)	0.118
Loss of smell	34 (37.4)	28 (30.8)	0.348
Loss of taste	36 (39.6)	37 (40.7)	0.880
Co-morbidity			
Hypertension	58 (63.7)	39 (42.9)	0.005*
Diabetes mellitus	48 (52.7)	46 (50.5)	0.767
Cardiovascular disease	4 (4.4)	8 (8.8)	0.232
CKD	5 (5.5)	2 (2.2)	0.444
Pre-existing lung disease	0 (0.0)	7 (7.7)	0.014
Severity of the disease			
Severe	63 (69.2)	43 (47.3)	0.003*
Non-severe	28 (30.8)	48 (52.7)	
Severity of the disease			
Mild	4 (4.4)	7 (7.7)	0.022*
Moderate	24 (26.4)	41 (45.1)	
Severe	49 (53.8)	36 (39.6)	
Critical	14 (15.4)	7 (7.7)	
ICU and mech. ventilation status			
ICU	14 (15.4)	5 (5.5)	0.029*
Invasive mechanical ventilation	9 (9.9)	2 (2.2)	0.029*

*= significant.

Among hypertensive patients, severe was 64 (60.4%), non-severe was 33 (43.4%). Among diabetes mellitus patients, severe was 66 (62.3%), and non-severe was 28 (36.8%). So hypertension and diabetes, both affected COVID-19 severity (Table 2).

The highest number of severe patients was in the obese group (BMI: 25-29.9 kg/m^2) and it was 45 (42.5%). The highest number of non-severe patients was in the non-obese group (23.0-24.9 kg/m^2) and it was 31 (40.8%). BMI: 25.0-29.9 range, severe versus non-severe was 45

(42.5%) versus 18 (23.7%), and BMI≥30 severe versus non-severe was 18 (17.0%) versus 10 (13.2%); respectively (p value <0.05) (Table 1). Female with waist circumference (cm) ≥80 cm was associated with more severe 34 (97.1%) COVID-19 infection (p value <0.05).

In univariate logistic regression age>60 years, diabetes mellitus, hypertension, and BMI>25 kg/m^2 all have a role in severe COVID-19 infection. Multivariate logistic regression shows age >60 years, diabetes mellitus, and BMI>25 kg/m^2 were independent risk factors for severe COVID-19 pneumonia. After adjustment of age, diabetes mellitus, and hypertension, obese patients with BMI>25 kg/m^2, were at 2.412-fold odds of developing severe disease (OR: 2.412; 95% CI: 1.252-4.646: p=0.008) (Table 3).

Table 2: Characteristics of the participants according to obesity (n=182).

Characteristics Age (years)	Severe (n=106)	Non-severe (n=76)	P value
Mean±SD	57.64±10.49	50.53±9.48	<0.001*
Sex distribution			
Male	71 (67.0)	48 (63.2)	0.593
Female	35 (33.0)	28 (36.8)	
Smoking status			
Smoker	13 (12.3)	5 (6.6)	0.205
Non-smoker	93 (87.7)	71 (93.4)	
Co-morbidities			
HTN	64 (60.4)	33 (43.4)	0.024*
DM	66 (62.3)	28 (36.8)	0.001*
CKD	5 (4.7)	2 (2.6)	0.471
Cardiovascular disease	5 (4.7)	7 (9.2)	0.228
Pre-existing lung disease	4 (3.8)	3 (3.9)	0.952
BMI			
Non-obese			
<18.5	2 (1.9)	2 (2.6)	0.047*
18.5 - 22.9	15 (14.2)	15 (19.7)	
23.0 - 24.9	26 (24.5)	31 (40.8)	
Obese			
25.0 - 30.0	45 (42.5)	18 (23.7)	
>30	18 (17.0)	10 (13.2)	
Waist circumference (cm)			
Male			
<90	25 (35.2)	20 (41.7)	0.476
≥90	46 (64.8)	28 (58.3)	
Female			
<80	1 (2.9)	6 (21.4)	0.020*
≥80	34 (97.1)	22 (78.6)	

*= significant.

Table 3: Logistic regression of severity of COVID-19 (n=182).

Variables	Univariate OR (95% CI)	P value	Multivariate OR (95%CI)	p-value
Age (>60 years)	3.395 (1.693-6.807)	<0.001	2.926 (1.414-6.055)	0.004
Hypertension	1.986 (1.092-3.610)	0.025	1.219 (0.623-2.383)	0.564
Diabetes mellitus	2.829 (1.538-5.203)	0.001	2.555 (1.313-4.972)	0.006
BMI (>25 kg/m^2)	2.431 (1.329-4.445)	0.004	2.412 (1.252-4.645)	0.008

DISCUSSION

The COVID-19 disease is a highly contagious infection that affects people of all ages and can be fatal in the elderly. Among other risk factors, diabetes mellitus, hypertension, cardiovascular disease, obesity, and chronic lung disease seem to increase the risk of adverse COVID-19 outcomes. Obesity is now a serious global health problem. The global prevalence of obesity is increasing day by day.

The mean age of the obese group was 55.23±11.77 years, and the non-obese group was 54.12±9.73 years. Among the study population, the maximum number of patients was male (65.38%). Gao et al conducted a cohort study of laboratory-confirmed COVID-19 patients, our demographic findings, almost matched with this study.[8]

In this study, we found that age >60 years was a strong risk factor for severe COVID-19 pneumonia. This might be due to older age being associated with many comorbidities, poor immune response, and old patients being more prone to infection. These findings were similar to the observation done by Liu et al.[12] We also found no association between smoking and severity, probably due to the lower proportion of smokers. It was consistent with Farsalinos et al study.[13]

In our study, the most common symptoms were fever, cough, and shortness of breath, which is similar to the Aggarwal et al study.[14] During infection, shortness of breath (63.7%) was a more prevalent symptom in the obese group than the non-obese group. This might be due to obesity's reduced expiratory reserve volume and functional residual capacity, so the ventilation in the base of the lung is impaired. Wang et al found no significant differences in clinical symptoms among patients with different BMI.[15] In our study, co-morbidities, like diabetes and hypertension were more frequent in severe COVID-19 patients in comparison to non-severe COVID-19 patients, p value <0.05. Honardoost et al also describe in their study that co-morbidity like diabetes, and hypertension are associated with worse COVID-19 outcomes.[16]

In our study, out of 182 patients, 106 (58.24%) progressed to severe COVID-19. Among them, in the obese group, severe patients were 63 (69.2%), and in non-obese severe patients 43 (47.3%), a p-value of 0.003. These results were consistent with the findings of Goa et al and Cai et al.[8,9] Our study revealed that among obese patients, critical case 14 (15.4%), which was more than non-obese patients 7 (7.7%). Goossens et al explain in their study that obesity is associated with impaired lung function, systemic low-grade inflammation, higher susceptibility to infections, impaired immune response to infectious agents, and increased activity of the RAAS; all are responsible for severe COVID-19 infection.[17]

Our study reveals, in normal weight (18.5-22.9) severe patients were 15 (14.2%), in over-weight (23.0-24.9) severe patients were 26 (24.5%), in obese I (25.0-29.9) severe patients were 45 (42.5%). This result was consistent with Simonnet et al, Kalligeros et al, and Sahin et al study.[1,18,19]

Abdominal obesity or central obesity is assessed by waist circumference. COVID-19 severity is also associated with abdominal adipose tissue distribution.[20] In South Asian females had higher central obesity in comparison to men.[21] Our study result also reveals central obesity was more in females than males. Petersen et al found in their study, that higher upper abdominal circumference was associated with ICU treatment and/or mechanical ventilation.[22] In our study, a female waist circumference ≥80 cm was associated with severe COVID-19 pneumonia. In the supine position, the patient's ventilation may be more difficult with the decreased diaphragmatic movement, so in the base of the lung, ventilation is also impaired, resulting in reduced oxygen-saturated blood levels.[23]

In multivariate logistic regression analysis, it was revealed that the severity of COVID-19 infection was independently associated with age >60 years, diabetes mellitus, and obesity. After adjustment of age, diabetes mellitus, and hypertension, obese patients with BMI>25 kg/m^2, were at 2.412-fold odds of developing the severe disease (OR: 2.412; 95% CI: 1.252-4.646: P=0.008). Gao et al, Wang et al, and Cai et al results were also similar to our study.[8,9,15]

This study has some limitations. The study had a limited sample size, which could impact the generalizability of the findings to other populations. The study also did not account for all potential confounding variables that could impact the association between obesity and COVID-19 severity, which could impact COVID-19 severity. There might be a slender chance of selection bias.

CONCLUSION

Obese patients are associated with severe COVID-19 pneumonia. As BMI increases, disease severity increases, needs more ICU support, and needs more invasive mechanical ventilation. Additional research is needed to better understand the relationship between obesity and COVID-19 severity, including the mechanisms by which obesity impacts COVID-19 outcomes and the potential impact of weight loss interventions on COVID-19 severity.

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