Body Mass Index as an independent predictor for Mortality and Severe Disease among Patients with COVID-19

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ABSTRACT

Objective: Worldwide studies reported variable death rates and severe disease among patients with COVID-19. The different rate of obesity across countries is one of the main predictors that may explain the diverse rate of COVID outcomes. This study explored the association between body mass index (BMI) and other predictors of COVID-19 severity and mortality.

Methods: We retrospectively reviewed cases with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections. We used univariate and multivariate logistic regression to understand the relationship between patients' characteristics and severe COVID-19 and mortality.

Results: 297 cases (83%) of 354 COVID-19 cases reviewed were symptomatic. 66 (18.6%) were hospitalized, (5.3%) were admitted to the intensive care unit (ICU), and 2.8% (10/354) died. The risk factors associated with mortality were old age (OR 95% CI 1.08[1.0-1.15]; p<0.03) and high BMI (OR 95% CI 9.29[1.92-44.98]; p<0.006). High BMI was also significantly associated with critical disease (OR 95% CI 5.19[2.18-12.38]; P<0.001)

Conclusion: High BMI was the leading independent risk factor associated with symptomatic COVID-19, severe COVID-19, and COVID-19-related mortality. Medical interventions to prevent and treat obesity are urgently needed to reduce covid-19 related mortality.

Keywords: SARS-CoV-2, COVID-19, Coronavirus Disease, 2019-Novel Coronavirus, BMI, Obesity

INTRODUCTION

The novel coronavirus disease 2019 (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 SARS-CoV-2 emerged in Wuhan in China in December 2019. The World Health Organization (WHO) announced the epidemic of COVID-19 as a pandemic in March 2020 (1). The pandemic has killed millions of humans and disturbed global social and financial activities. By the end of May 2022, there were 525 million reported cases and 6 million deaths globally (2). In Saudi Arabia, during the same period, there were 700,000 COVID-19 cases, and the total number of fatalities reached 9000 (3).

Studies have described diverse rates of covid-19 mortality and disease severity across countries, reflecting the role of viral virulence and host chrachteristics (4, 5). Older age, comorbid conditions, and obesity are the main predictors of covid-19 severity and mortality (6.7.8,9). Previous studies have also found the obesity a predictor of severe influenza infection (10,11,12). Data from Saudi Arabia suggest increasing obesity rates (13,14). However, the association of obesity with SARS-CoV-2 infection in Saudi patients is still unclear. This study described the association between obesity and symptomatic SARS-CoV-2 infection. Specifically, we examined the effect of body mass index (BMI) on the development of COVID-19 symptoms, disease severity, and COVID-19-related mortality. Identifying the high-risk group for the severe disease allows for prompt medical intervention and prioritizes medical resources.

MATERIAL and METHODS

This study was a single-center retrospective observational conducted in National Guard Hospital in Al-Madinah, Saudi Arabia, between April 1 and July 12, 2020. We included Subjects with a positive polymerase chain reaction (PCR) test for SARS-CoV-2Cases and COVID-19 diagnosis, and all data were collected from the hospital's electronic medical records. The institutional review board approved this study on June 1, 2020 (RM20/006/M).

The Abbott Real-time SARS-CoV-2 reverse transcriptase PCR test was used for the qualitative detection of nucleic acid from SARS-CoV-2 from nasopharyngeal (NP) swabs, sputum, or Broncho-alveolar lavage fluid (BAL) nasal swabs. Healthcare workers collected all samples (15).

We defined symptomatic COVID-19 cases as those presented with symptoms of COVID-19 as defined by the Center for Diseases Control (CDC) and WHO and having a positive PCR test for SARS-CoV-2. COVID-19 infection cases were classified as severe if blood oxygen saturation was less than 93% with or without lung infiltrate on chest imaging and critical if one or more of the following were present: acute respiratory distress syndrome (ARDS), sepsis, severe sepsis, septic shock, acute kidney injury (AKI), arrhythmia, myocardial infarction (MI), respiratory failure, disseminated intravascular coagulation and cerebrovascular accident (CVA). We also collected the following variables: gender, sociodemographic, body mass index, smoking, pregnancy (APACHE II), Charlson's comorbidity index, heart failure (HF), Diabetes mellitus (DM), coronary artery disease (CAD), Cerebrovascular accident (CVA), Asthma, Chronic Kidney Disease (CKD), treatment provided during an infection such as antivirals and antimicrobials and home medication were collected the through chart review. Outcomes measured included duration of hospitalization, ICU admission, need for mechanical ventilation, and survival.

We calculated the mean, median, and standard deviation (SD) for continuous variables and the proportions for categorical variables. We used Fisher exact test to compare categorical variables, The student t-test to compare normal-distributed continuous data, and Wilcoxon Rank-Sum to compare continuous non-normal-distributed variables. We included the variables with a significance level of P-value <0.25 from the unadjusted analysis in the multivariable analysis. We used backward stepwise multivariable logistic regression analysis to identify risk factors for severe diseases and mortality. All p values were two-tailed, and values of less than 0.05 were considered statistically significant. Data analysis was performed using STATA version 13 (STATA cooperation, Texas, USA).

RESULTS

From April 1, 2020, to July 12, 2020, 354 COVID-19 cases had a positive PCR test for SARS-CoV-2; we included these cases in this analysis. Of the total cases, 297 (83%) cases presented with COVID-19 symptoms. The most common initial symptoms were fever (67%), cough (55%), sore throat (43%), and fatigue (28%). Of the symptomatic cases, 66 (18.6%) were hospitalized, and of those (5.3%) were subsequently admitted to the intensive care unit (ICU). The

median length of stay for the hospitalized cases was 11(5-15) days.

Table 1 shows the baseline demographic and clinical characteristics of symptomatic cases. The median age was 42 (31-58) years, and females represented (52%) of the total cases. The most common chronic comorbidities for the patients were DM (24%), asthma (8%), and CAD (7%). Among hospitalized cases, the most frequent complications observed were septic shock 31(13%), AKI 17 (7%), and respiratory failure 13 (4%). While (4%) cases were treated with Hydroxychloroquine, the most common antivirals used were the combination of Ribavirin plus lopinavir-ritonavir plus interferonbeta1b (8%). In addition, 20% of the cases were treated with antimicrobials for concomitant bacterial pneumonia, and 3% received both convalescent plasma and tocilizumab.

Of the total symptomatic cases, 81 (27%) had severe COVID-19 disease. In unadjusted analysis, the risk factors associated with severe disease included older age (p<0.011), high BMI (BMI over 30 kilogram/meter square) (p<0.001), high Charlson's comorbidity score (p<0.01), and heart failure (p<0.002) (Table 1). In the multivariable analysis, the only factor significantly associated with severe disease was older age (OR 95% CI 2.2[1.2-4.1]; p<0.010).

Of the total cases, 19(6.4%) developed critical diseases (**Table 2**). In unadjusted analysis, the risk factors associated with the critical illness were older age (p<0.001), high BMI (p<0.001), high Charlson's comorbidity score (p<0.001), and high APACHE II score (p<0.001). In multivariable logistic regression analysis, the factors significantly associated with the critical disease were older age (OR 95% CI 1.05[1.00-1.10]; p<0.018) and high BMI (OR 95% CI 5.59[2.32-13.46]; p<0.001). In an additional model which included Charlson's comorbidity index to adjust for chronic comorbidity, the only variable which remained significantly with the critical disease was high BMI (OR 95% CI 5.19[2.18-12.38]; p<0.001)

In this cohort of COVID-19 cases, the median BMI was 29(27-30) kg/m2, and 112(46%) of the subjects had a BMI >30 Kg/m2. Compared to cases with a high BMI (< 30 Kg/m2), subjects with a low BMI (>30 Kg/m2) were older (p<0.029); had a higher mean Charlson's comorbidity index (p<0.032); and were more likely to have CAD (p<0.001), CHF (p<0.001), asthma (p<0.001) and COPD (p<0.027) (**Table 3**). In multivariable logistic regression analysis, the high BMI cases were more likely to have symptomatic COVID-19, critical illness, and higher mortality than those with a low BMI. These findings remained the same after we adjusted for the comorbidities in the model (**Table 4**).

The overall mortality rate was 2.82% (10/354). Most deaths occurred among patients aged 60 years or older, and no death occurred in patients younger than 45 years. All deaths occurred within 60 days of hospitalization; of those (80%) occurred within 30 days of admission. In multivariable logistic regression analysis, risk factors associated with mortality included older age (OR 95% CI 1.08[1.0-1.15]; p<0.03) and high BMI (OR 95% CI 9.29[1.92-44.98]; (p<0.006). Again, when we included Charlson's comorbidity index in the model, the only variable significantly associated with mortality was high BMI (OR 95% CI (8.12[1.6-2 40.54]; p<0.011) (**Table 4**).

Table 1. Baseline Clinical Characteristics of Severe and Non-Severe COVID-19 Cases from April 1 to July 30, 2020

Characteristics	Total N: 297	Non-severe COVID-19 n / (N %) 216(72.73)	Severe COVID-19 n/ (N %) 81(27.27)	P-value
Age (years)				
Mean	45(16.83)	43(16)	49(17)	0.0111
Median	42(31-58)	41(31-56)	51(33-64)	
Age groups (years)				
> 20	8(3)	3(4)	0	
20-39	122(41)	92(43)	30(37)	0.029
40-59	95(32)	72(33)	23(28)	
>60	71(24)	43(20)	28(35)	
Male	124(48)	98(46)	44(54)	
Female	152(52)	115(54)	37(56)	0.240
Body mass index (kg/m^2)				
Mean	29(3)	27(2)	32(3)	
Median	29(27-30)	28(27-29)	32(31-32)	0.0001
Body mass index <30	161(54)	161(84)	0(0)	0.0001
Body mass index >30	112(46)	31(16)	81(100)	
Smoking	14(5)	10(5)	4(5)	0.999
Pregnancy	6(2)	6(3)	0(0)	0.194
APACHE II score				
Mean	13.7(13)	6.9(5.2)	15.4(14)	0.1193
Median	9.5(5-20)	6.5(2-12)	10(5-23)	
Charlson's comorbidity index				
Mean	1.5(2.4)	1.3(2.1)	2.1(2.8)	0.01
Median	0(0-2)	0(0-2)	1(0-3)	
Heart failure	18(6)	7(3)	11(13)	0.002
Diabetes mellitus	72(24)	56(26)	16(20)	0.290
Coronary artery disease	23(7)	17(8)	6(7)	0.999
Cerebrovascular accident	7(2)	5(2)	2(2)	0.999
Asthma	22(8)	16(8)	6(7)	0.999
Chronic obstructive pulmonary disease	4(1)	2(1)	2(2)	0.303
Chronic Kidney Disease	9(3)	4(2)	5(6)	0.068
Home medication				
Aspirin	47(16)	34(16)	13(16)	0.859
NSAID	7(2)	7(3)	0(0)	0.195
ACEI/ARBs	37(13)	28(13)	9(12)	0.843

Data are presented as mean (SD) or median (IQR), as appropriate, unless otherwise indicated. Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blockers; ARDS, NSAID, nonsteroidal anti-inflammatory drug; BMI, body mass index; Kg/m2, kilogram/meter square; COVID-19, coronavirus disease 2019; P-value significant if <0.05

Table 2. Baseline Clinical Characteristics of Critical and Non-Critical COVID-19 Cases from April 1 to July 30, 2020

Characteristics	All 296	Non-critical n / (N %) 277(93.58)	Critical n / (N %) 19(6.42)	P-value
Age (years)				
Mean	45(16.8)	44(16)	63(13)	0.0000
Median	42(31-58)	41(31-57)	65(56-74)	
Age groups (years)				
< 20	8(3)	8(3)	0	
20-39	122(41)	121(44)	1(5)	0.000
40-59	95(32)	91(33)	4(21)	
>60	71(24)	57(20)	14(74)	
Male	124(42)	145(53)	12(63)	
Female	152(52)	130(47)	7(37	0.236
Body mass index (kg/m^2)				
Mean	29(3)	29(3)	34(6)	
Median	29(27-30)	29(27-30)	32(32-33)	0.0000
Body mass index <30	160(59)	160(63)	0(0)	0.0000
Body mass index >30	112 (41)	93(37)	19(100)	
Smoking	14(5)	13(5)	1(5)	0.609
Charlson's comorbidity index				
Mean	1.5(2.4)	1.3(2.1)	4(3.3)	0.000
Median	0(0-2)	0(0-2)	4(2-8)	
SOFA score (mean)	4.6(5)	2.2(3.1)	9.6(4.3)	0.000
SOFA score (median)	3(0-8)	1(0-4)	9(7.5-12.5)	
APACHE II score				
Mean	13.8(13))	6(4.1)	28.3(212)	0.000
Median	9.5(5-20)	6(2-9)	27(19-33)	
Heart failure	19(6)	0(0)	19(100)	0.000
Diabetes mellitus	72(24)	67(24)	5(26)	0.788
Coronary artery disease	26(8)	7(3)	19(100)	0.000
Cerebrovascular accident	7(2)	5(2)	2(10)	0.068
Asthma	26(9)	7(3)	19(100)	0.000
Chronic Kidney Disease	9(3)	4(2)	5(56)	0.000
Home medication				
Aspirin	47(16)	40(15)	7(37)	0.859
NSAID	7(2)	7(3)	0(0)	0.999
ACEI/ARBs	37(13)	32(11)	5(26)	0.052

Data are presented as mean (SD) or median (IQR), as appropriate, unless otherwise indicated. Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blockers; ARDS, NSAID, nonsteroidal anti-inflammatory drug; BMI, body mass index; COVID-19, coronavirus disease 2019; Kg/m2, kilogram/meter square; Sofa, Sequential Organ Failure Assessment; APACHE II score, acute Physiologic Assessment and Chronic Health Evaluation score; P-value significant if <0.05

Table 3. Baseline Clinical Characteristics of Obese and non-Obese COVID-19 Cases from April 1 to July 30, 2020

Characteristics	ALL 272	Non-Obese n/ (N %) 160(59)	Obese n/ (N %) 112(41)	P-value
Age (years)				
Mean	29(3)	44(16)	49(18)	
Median	29(27-31)	41(31-55)	50(33-63)	0.029
Age groups				
< 20	6(2)	5(3)	1(1)	0.076
20-39	108(40)	67(42)	41(37)	
40-59	89(33)	56(35)	33(29)	
>60	69(25)	32(20)	37(33)	
Male	130(48)	74(47)	56(50)	0.623
Female	140(52)	84(53)	56(50)	
Smoking	12(4.5)	7(4.43)	5(4.63)	0.581
Comorbidity				
Heart failure	19(7)	0	19(16)	0.001
Coronary Artery Disease	26(10)	0	26(23)	0.001
Chronic Kidney Disease	9(3)	4(3)	5(4)	0.495
Asthma	26(10)	0	26(23)	0.000
COPD	4(1)	0	4(4)	0.027
Diabetes mellitus	68(25)	42(26)	26(23)	0.572
Cerebrovascular accident	7(3)	5(3)	2(2)	0.703
Charlson's comorbidity index				
Mean (DS)	1.5(2.4)	1.43(2.3)	1.9(2.6)	0.032
Median (IQR)	0(0-2)	0(0-2)	1(0-3)	
APACHE II score (Median, IQR)	9.5(5-20)	7(3-12)	10(5-23)	0.235
Outcomes				
Mortality	10(3.6)	0	10(9)	0.001
Critical COVID-19	19(7)	0	19(17)	
Severe COVID-19	81(30)	0	81(72)	0.001
Home medication				
Aspirin	45(17)	29(18)	16(15)	0.617
ACEI/ARBs	36(13)	21(13)	15(14)	0.855

Data are presented as mean (SD) or median (IQR), as appropriate unless otherwise indicated; n of all patients (%) or a proportion of subset, n/N (%); ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blockers; BMI, body mass index; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019.Obese BMI >30 Kg/m2, kilogram/meter square; Non-Obese BMI <30 Kg/m2; P-value significant if <0.05

Table 4. Multivariable Analysis of the Risk Factors for Mortality, Critical Illness, and Symptomatic COVID-19, with and without Adjustment for Charlson's Comorbidity Score

Outcomes	Risk factors	AOR	95% CI	P-value	AOR	95% CI	P-value
COVID-19 symptoms	BMI	1.23	1.10-1.37	0.001	1.23	1.10-1.37	0.001
	Age	0.02	1.00-1.05	0.012	1.02	0.99-1.05	0.115
	Charlson's comorbidity	-	-	-	1.02	0.99-1.05	0.522
COVID-19 critical illness	BMI	5.59	2.32-13.46	0.001	5.19	2.18-12.38	0.001
	Age	1.05	1.00-1.101	0.018	1.01	0.96-1.08	0.583
	Charlson's comorbidity	-	-	-	1.31	0.92- 1.86	0.129
COVID-19 mortality	BMI	9.29	1.92-44.98	0.006	8.12	1.62-40.54	0.011
	Age	1.08	1.00-1.15	0.03	1.05	0.96-1.15	0.251
	Charlson's comorbidity	-	-	-	1.18	0.96-1.16	0.439

BMI, body mass index; Kg/m^2, kilogram/meter square AOR, adjusted odds ratio; CI, confidence interval; COVID-19, coronavirus disease 2019; P value significant if <0.05, Age in Years

DISCUSSION

Here we described the clinical characteristics and risk factors associated with COVID-19 severity and mortality, and we examined the effect of obesity on COVID-19 outcomes. Of all cases reviewed (83%) were symptomatic, (18%) were hospitalized, (14%) had severe diseases, and (5%) were admitted to the ICU. The above rates are comparable to the rates of symptomatic and severe COVID-19 reported from China during the early periods of this pandemic.4 The reported rates of COVID-19 severity and mortality were variable between countries. These differences have been attributed to the demographic characteristics and prevalence of chronic comorbidities in these countries (16).

In this study, about one-third of the symptomatic cases developed severe COVID-19. Older age and obesity were the main predictors for severe and critical COVID-19 disease. Besides, our data suggest a trend toward an association between severe COVID-19 and pre-existing heart failure and CKD. Many studies demonstrated a similar association between age and obesity with COVID-19 severity (17,18,19,20). Older age and obesity have also been shown to be associated with severe influenza infection (21).

This study's mortality rate was 2.8%, comparable to the mortality rates reported in most other countries. Here, we found the main risk factors associated with mortality were older age and high BMI. Several studies also found an association between mortality and these risk factors (18). Many mechanisms may explain the differential risk of old age in COVID-19 mortality, including age-dependent defects in the immune response to viral infections and the presence of comorbidities. We found no association between age and mortality after adjusting for comorbidities. This suggests that the effect of age on mortality could be due to comorbidities. Many studies that have found an association between older age and mortality also reported higher rates of comorbidities among elderly patients (22).

Our data suggest that obesity is a significant risk for symptomatic COVID-19, severe COVID-19 disease, and mortality. Many recent studies reported similar findings (23,24). Alarmingly, 46% of the COVID-19 cases in our cohort cases were obese. Our high rate of obesity in our institution aligns with the prevalence of Obesity in the country (25) In this study, high BMI cases were older and had more comorbidities than cases with low BMI. However, our data suggest that high BMI was an independent predictor of COVID-19 severity and mortality. The association between high BMI and poor clinical outcomes in the H1N1 influenza infection supports our findings (26). A few mechanisms may explain the association between obesity and COVID-19 severity. Obesity causes a state of chronic inflammation and produces cytokines that increase cytokine storm risk in severe COVID-19 cases (27,28). Nonetheless, the exact mechanism of this association remains unclear as many studies showed that obesity increases the risk of death from any critical illness (29,30).

Our study findings have many implications. We described the number of COVID-19 cases that required hospital and ICU admissions, which projects hospital resources needed in this pandemic. Risk stratification of severe COVID-19 patients using age and BMI may facilitate early medical intervention to improve outcomes, prioritizing the use of the medical resource and early decisions for care goals. High BMI is a modifiable risk, and weight reduction should be encouraged to improve baseline population health.

Our study has several limitations. Due to the relatively small sample size and low rate of deaths in our cohort cases, we could not identify cardiovascular diseases, DM, and CKD as risk factors for COVID-19 mortality, which other studies have shown. However, we found a trend toward this association in the univariate analysis. Since this is a retrospective study, we could not obtain all baseline clinical characteristics and complete follow-up outcomes. Nevertheless, most of our patients seek medical care in the same healthcare system linked to electronic medical records.

CONCLUSION

This is the first study to describe the clinical characteristics, severity, and mortality of COVID-19 cases in Medina in Saudi Arabia. High BMI was an independent risk factor associated with symptomatic COVID-19, severe COVID-19, and death. Therefore, interventions to prevent and treat Obesity may reduce COVID-19 severity and related mortality.

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