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The Association of BMI with Outcomes in Critically Ill Patients with Covid-19

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ABSTRACT

Introduction: The novel systemic acute respiratory syndrome coronavirus (SARSCoV-19) severity has been linked to many risk factors like obesity, advanced age, hypertension (HTN), diabetes mellitus (DM), chronic heart diseases, and lung diseases, with many studies showing their influence and effect on the general population and especially on critically ill patients. We retrospectively studied and correlated BMI with in-hospital mortality, the need for mechanical ventilation, renal replacement therapy (RRT), ICU and hospital length of stay (LOS), and mortality among ICU admitted patients with COVID-19 in King Abdulaziz Medical City (KAMC) in Riyadh, Saudi Arabia.

Methods: A retrospective cohort study was conducted after ethical approval from the institutional review board of King Abdullah International Medical Research Center (KAIMRC). Subjects were identified by the Data management office of KAIMRC. The data was extracted from electronic medical records using a customized data collection sheet. The study included all adult patients (>18 years) who tested positive for COVID-19 by polymerase chain reaction (PCR) and were admitted to the ICU at KAMC from March 2020 until the end of February 2021. Patients where adequate data was not available, and those for whom adequate data on BMI parameters could not be found were excluded. Patient demographics, comorbid conditions, medications, type of ventilation used, and mortality were recorded.

Results: During the study period (2nd of March 2020 until February 28th, 2021) nearly 2000 patients were hospitalized at KAMC with the diagnosis of COVID-19. After excluding the patients who met the exclusion criteria data was collected for 469 critically ill patients, Male (70.9%); female (29.1%). The most common comorbidities in BMI groups were DM (66.5%) and HTN (66%). No significant differences were found regarding the therapies received among these patients. On the Multivariate Cox Model for Determining Predictors of Cumulative Mortality, overweight and obese patient class I had a lower risk of mortality compared to BMI<24.9 (p<0.0087) (0<0.0391, with an overall mortality of (45.6%) in this study.

Conclusion: Obesity increases the risk of ICU admission and one of the major risk factors for severe-critical COVID-19 infection. For ICU patients with COVID-19, We found a lower mortality rate in COVID-19-treated ICU patients who were overweight or obese class I compared to other groups. Further studies should be done to correlate the impact of obesity on critical ill COVID-19 patients.

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Introduction

Since its first appearance in Wuhan, the corona virus disease (COVID19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spread rapidly around the globe at the beginning of 2020. Soon after, the World Health Organization declared the disease as a pandemic, with health authorities throughout the world being challenged due to its emergence. The novel virus's rapid spread and easy method of transmission has made it a top priority to solve. Since then, the virus has infected over 263,000,000 people, resulting in a total of 5,232,562 deaths as of December 2, 2021 [1]. The first confirmed case of COVID-19 in the Kingdom of Saudi Arabia was reported on 02 March 2020. Furthermore, the number of cases has reached 549,877 as of 02 December 2021, with almost 9,000 deaths [2]. COVID-19 severity has been linked to many risk factors like obesity, advanced age, hypertension (HTN), diabetes mellitus (DM), chronic heart diseases, and lung diseases, with many studies showing their influence and effect on the general population and especially on critically ill patients [3-7].

Obesity has always been a concerning worldwide public health burden that has already been shown to be an independent risk factor that strongly affects the prognosis of COVID-19 [3]. According to the World Health Organization, obesity is the excessive or abnormal accumulation of fat or adipose tissue in the body. Defined according to body mass index (BMI). The World Health Organization defines obesity as a BMI (≥30 kg/m2) and overweight as a BMI of (25–29.9 kg/m2) [8]. Even though BMI does not directly measure body fat, it is somehow linked with more direct measures of body fat. Furthermore, BMI appears to be just as strongly linked to a variety of metabolic and disease outcomes as these more direct measures of body fatness. Obesity impairs health via its association with the risk of development of DM, DLP, HTN, and cardiovascular diseases [8]. It has also been shown to increase disease severity, admission rates, and the need for intensive care unit (ICU) and invasive mechanical ventilation (IMV), resulting in a longer hospital stay and higher morbidity and mortality rates [3,9-13]. Obesity is a major health concern, especially in Saudi Arabia, where According to World Atlas data, it is the world's 12th most obese country [14]. Furthermore, previous studies estimated that by 2022, 41% of Saudi men will be classified according to their body mass index as overweight and obese, respectively, compared to 77.7% among women, with an overall rate reaching 59% [15].

Few studies have measured the association between obesity and COVID-19 in critically ill patients. These studies found a significant damaging association between obesity and increased hospital mortality and morbidity, as well as prolonged length of stay in the ICU [10, 16-20]. Because of the high prevalence of obesity in Saudi Arabia, there is a need to evaluate the association of obesity and outcomes in COVID-19 patients. Therefore, our study aims to evaluate the association of BMI with in-hospital mortality, the need for mechanical ventilation, renal replacement therapy (RRT), ICU and hospital length of stay (LOS) among ICU admitted patients with COVID-19.

Methods

We conducted this retrospective study at King Abdulaziz Medical City (KAMC) in Riyadh, Kingdom of Saudi Arabia. KAMC is a major tertiary care medical center with more than 1600 general inpatient beds and more than 120 critical care beds. The study was approved by the institutional review board of King Abdullah International Medical Research Center, Riyadh, Saudi Arabia. The data management department identified all patients admitted to the KAMC Riyadh with a diagnosis of COVID-19, between the 2nd of March 2020 (when the first case was diagnosed in the Kingdom of Saudi Arabia) and February 28th, 2021. The study included all adult patients (>18 years) who tested positive for COVID-19 by polymerase chain reaction (PCR) and were admitted to the ICU at KAMC from the 2nd of March 2020 until February 28th, 2021. Patients under the age of 18 were excluded, as were those for whom adequate data on BMI parameters could not be found. BMI was classified based on WHO Classification. Those with a BMI<24.9 were used as a reference group. Other classified groups were overweight BMI<29.9, obese class I BMI<35, obesity class II and III with BMI>35. The data was extracted from electronic medical records using a customized data collection sheet. The primary outcome was in-hospital mortality. Secondary outcomes were the need for mechanical ventilation, renal replacement therapy (RRT), ICU and hospital length of stay (LOS) among ICU admitted patients.

The collected variables included the patient's demographics (gender, age, height, weight, and BMI), comorbid conditions such as hypertension (HTN), diabetes mellitus (DM), asthma, coronary artery disease (CAD), heart failure (HF), dyslipidemia (DLP), chronic obstructive pulmonary disease (COPD), and chronic kidney disease (CKD), the use of medications such as tocilizumab, angiotensin-converting enzyme inhibitor (ACEI), insulin, vasopressors, type of ventilation used.

Statistical Analysis

Means and proportions of the study participants were calculated to characterize the study participants, overall and in groups. The primary exposure variable was BMI. To determine the factors associated with BMI, the study participants were divided into four groups based on the patients' BMI. The four groups (BMI <24.9, 25 ≤ BMI<29.9, 30 ≤ BMI<34.9, BMI ≥ 35) were compared using the Chi square or Fisher-exact test for categorical factors and the ANOVA or Kruskal Wallis Test for continuous variables as appropriate. For survival analyses, we generated Kaplan–Meier survival curves, and comparison was done using the log-rank test. Then, a multivariate cox regression model adjusted for covariates (adjusted for age; sex; & comorbidities) were used to estimate the adjusted Hazard ratio (aHR) for death in patients with BMI <24.9 versus other BMI groups (25 ≤ BMI<29.9, 30 ≤ BMI<34.9, BMI ≥ 35). Covariates (age, sex, and comorbidities) were chosen based on univariate testing and clinical relevance. Level of significance was declared at $\alpha = 0.05$. Statistical analysis was conducted using SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

During the study period, nearly 2000 patients were hospitalized at KAMC with the diagnosis of COVID-19. After excluding the patients who met the exclusion criteria, data was collected for 469 critically ill patients of whom 70.9 % were males and 29.1% were females. Patients had a mean age of 62.1 ± 15.18 years, median BMI of 29.1 kg/m2 (IQR, 25.00 – 34.18). BMI > 30 was present in (24.7%) and BMI > 35 was present in (22.6%). The most common co-morbidities among these patients were diabetes (66.5%) and hypertension (66%). Other co-morbidities included dyslipidemia (32.3%), CAD (14.7%), and asthma (12%). The demographics, clinical characteristics and management of the included patients with Covid-19 are summarized in Table 1. There were no significant differences between groups regarding therapies received, including medication, type of ventilation, renal replacement therapy, and vasopressors.

Table 1: Comparisons of Characteristics of Critically Ill Patients with Covid-19 Based on Their BMI

Variables	All N= 465	BMI <24.9 N=105	BMI = 25-29.9 N=140	BMI = 30-34.9 N=115	BMI > 35 =105	P value
Age, Year- Mean ±Sd	62.1 ± 15.18	62.2 ± 16.42	63.6 ± 16.34	61.8 ± 12.82	60.4 ± 14.83	0.54^
Male Gender-N(%)	330 (71.0)	83 (79.0%)	114 (81.4%)	82 (71.3%)	51 (48.6%)	<0.0001**
Comordities N(%)						
Diabetes Mellitus	310 (66.7)	69 (65.7)	88 (62.9)	77 (67.0)	76 (72.4)	0.47 **
Hypertension	308 (66.2)	63 (60.0)	87 (62.1)	80 (69.6)	78 (74.3)	0.09**
Coronary Artery Disease	69 (14.7)	22 (21.0)	24 (17.1)	9 (7.8)	14 (13.3)	0.04**
Asthma	56 (12.0)	8 (7.6)	11 (7.9)	13 (11.3)	23 (21.9)	0.003**
Chronic Kidney Disease	97 (20.7)	27 (25.7)	27 (19.3)	17 (14.8)	25 (23.8)	0.18**
Chronic Obstructive Pulmonary Disease	19 (4.1)	4 (3.8%)	3 (2.1%)	6 (5.2%)	6 (5.7%)	0.44^^
Dyslipidemia	151 (32.3)	32 (30.5%)	35 (25.0%)	35 (30.4%)	48 (45.7%)	0.006**
Heart Failure	70 (15.0)	20 (19.0%)	19 (13.6%)	13 (11.3%)	18 (17.1%)	0.37**
Icu Management-N(%)						
Invasive Mechanical Ventilation	308 (66.2)	70 (66.7)	88 (62.9)	76 (66.1)	74 (70.5)	0.67**
Continuous Positive Airways Pressure	91 (19.6)	20 (19.0)	33 (23.6)	19 (16.5)	19 (18.1)	0.52**
Helmet	133 (28.6)	29 (27.6)	38 (27.1)	34 (29.6)	32 (30.5)	0.93 **
Bi-Level Positive Airways Pressure	256 (54.7)	48 (45.7)	84 (60.0)	64 (55.7)	59 (56.2)	0.16**
High Flow Nasal Cannula	283 (60.5)	59 (56.2)	87 (62.1)	66 (57.4)	68 (64.8)	0.53**
Prone Positioning	182 (38.9)	25 (23.8)	52 (37.1)	55 (47.8)	49 (46.7)	0.0008 **
Septic Shock	171 (36.6)	42 (40.0)	52 (37.1)	32 (27.8)	44 (41.9)	0.13**
Angiotensin Converting Enzyme Inhibitor Use	82 (17.7)	21 (20.0)	23 (16.5)	18 (15.7)	20 (19.0)	0.81**
Vasopressor Therapy	296 (63.8)	76 (72.4)	79 (56.8)	70 (60.9)	71 (67.6)	0.06**
Insulin Use	383 (82.5)	88 (83.8)	118 (84.9)	92 (80.0)	85 (81.0)	0.72**
Tocilizumab	180 (38.8)	31 (29.5)	51 (36.7)	57 (49.6)	41 (39.0)	0.02**

BMI: Body Mass Index; Sd: Standard Deviation;

The clinical outcomes are presented in Table 2. Overall mortality was (45.7%), of which obese class I (21.4%) and obese class II and III (23.3%). The median ICU length of stay BMI<24.9 was 8.0 (4,16), overweight 11.0 (6,18.5), obese class I 12.0 (5,19), and obese class II and III 11 (5, 22). The number of patients in our cohort study who developed acute kidney injury and required RRT, either continuous renal replacement therapy or hemodialysis, during hospitalization was 144 (31%), with no significant p-value difference between the groups. The mean length of stay in ICU for each group was BMI<24 12.7 ± 14.02, overweight 15.1 ± 14.91, obese class I 14.0 ± 11.09, obese class II 15.0 ± 13.01, with no significant statistical difference between the LOS of the groups.

Table 2: Comparisons of Outcomes of Critically Ill Patients with Covid-19 Based on Their BMI

Variables	All N= 465	BMI <24.9 N=105	BMI = 25-29.9 N=140	BMI = 30-34.9 N=115	BMI > 35 =105	P value
Icu Mortality-N(%)	212 (45.6)	56 (53.3)	60 (42.9)	46 (40.0)	50 (47.6)	0.21 **
Icu Length of Stay, Days- Mean ±Sd	14.3 ± 13.40	12.7 ± 14.02	15.1 ± 14.91	14.0 ± 11.09	15.0 ± 13.01	0.13 ^
Hospital LOS, Days- Mean ±Sd	24.0 ± 22.68	23.9 ± 23.52	25.2 ± 23.68	23.7 ± 21.60	22.9 ± 21.87	0.76 ^
Mechanical Ventilation Duration, Days- Mean ±Sd	12.1 ± 14.20	11.3 ± 15.30	12.5 ± 15.68	11.1 ± 11.82	13.3 ± 13.61	0.36 ^
Deep Venous Thrombosis-N(%)	61 (13.1)	16 (15.2)	16 (11.4)	15 (13.0)	14 (13.3)	0.86**
Pulmonary Embolism-N(%)	40 (8.6)	9 (8.6)	12 (8.6)	10 (8.7)	9 (8.6)	1.00**
Tracheostomy-N(%)	59 (12.7)	15 (14.3)	15 (10.7)	17 (14.9)	12 (11.5)	0.71**
Renal Replacement Therapy-N(%)	144 (30.8)	35 (33.3)	42 (30.0)	28 (24.3)	39 (37.5)	0.19**

ICU: Intensive Care Unit; LOS: Length of Stay

Multivariate Cox Model was used for determining predictors of mortality, and we found that overweight and obesity class I when compared to normal BMI, both were significantly associated with lower risk of mortality (p<0.01) (p<0.04).(Table 3, Figure 1)

Table 3: Multivariate Cox Model for Determining Predictors of Cumulative Mortality

Variables	Hazard Ratio	95% Confidence interval	P-value
Age Per Each One Year Increase	1.038	1.03-1.05	<.0001
Female vs Male	1.022	0.72-1.46	0.90
BMI = 25-29.9 vs BMI <24.9	0.587	0.39-0.87	0.01
BMI = 30-34.9 vs BMI <24.9	0.628	0.40-0.98	0.03
BMI ≥ 35 vs BMI <24.9	0.752	0.48-1.18	0.22
Hypertension Vs No Hypertension	1.040	0.69-1.56	0.85
Heart Failure Vs No Heart Failure	0.787	0.50-1.23	0.29
Coronary Artery Disease Vs No Coronary Artery Disease	0.870	0.55-1.38	0.55
Tocilizumab Vs No Tocilizumab	0.848	0.61-1.18	0.33
Prone Vs No Prone	1.130	0.81-1.58	0.47

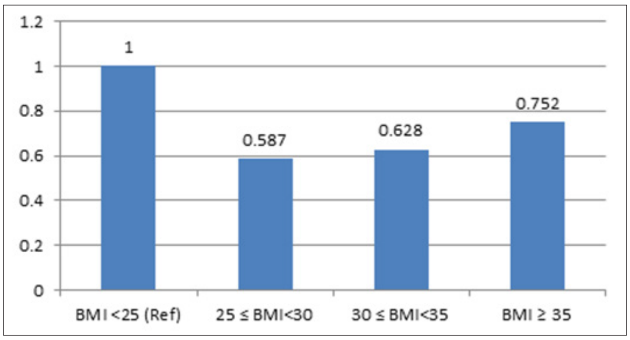

Figure 1: Adjusted hazard ratio of mortality for BMI groups

Discussion

According to initial findings from Wuhan, BMI is linked to severe COVID-19 and an increase in mortality and morbidity [21]. During the COVID-19 pandemic, obesity was associated with a worse clinical outcome of SARS-CoV-2 infection. This may be because of the chronic low-grade inflammation, impaired immune response, and metabolic disorders in obese patients [22]. Clinical features and pathophysiology of how obesity can affect or worsen the infection COVID-19 have been studied and reported [23]. Furthermore, obesity increases the risk of multiple comorbidities considered to be risk factors for severe complications of COVID-19, specifically, diabetes mellitus, hypertension, cardiovascular disease, non-alcoholic fatty liver disease, and obstructive sleep apnea [24, 25]. Moreover, obesity may impact COVID-19 severity according to several different mechanisms, including abnormal ventilation, impaired immune response to viral infection, endothelial dysfunction, and extensive coagulopathy [23, 25-29].

Based on our knowledge, this study is the first study that investigates the association between BMI and the outcome of COVID-19 patients in ICU setting at a Tertiary Care Medical Center in Middle East. In this cohort study, the associations of BMI with multiple severe outcomes in ICU patients with COVID-19 pneumonia were investigated, including invasive mechanical ventilation therapy, type of required ventilation, ICU length of stay, severity of ARDS, and death. Patients were categorized into 4 groups based on their BMI, BMI <24.9 (22.6%), overweight (30.1%) obesity class I (24.7%) and obesity class II and III (22.6%). We found that patients with obesity had no significantly increased risk of invasive mechanical ventilation therapy, ICU admission, or developing ARDS.

Over 75% of our patients had either moderate or severe acute hypoxemic respiratory failure. The percentage of patients who required invasive mechanical ventilation during hospitalization in our study was 308 (66.2%) for median durations of 9 days [1,17]. No statistical difference was found between the groups. Some studies reported that obese patients required more IMV than the other groups, with a significant P value. For example, one study reported that obese patients have twice the odds of receiving mechanical ventilation than non-obese [17]. While we reported 66.2% of patients who required invasive mechanical ventilation, other studies reported (82.4%, 68.6%, and 79%), respectively [30-32]. Furthermore, many patients also required non-invasive ventilation during the admission, like BIPAP and CPAP 346 (74.4%) using face mask as helmet interface, 133 (28.6%), and high-flow nasal cannula 280 (60.2%), and some of the patients received the non-invasive ventilation either before or after the initiation of invasive mechanical ventilation. The higher proportion of patients requiring IMV in our cohort study could be explained by the severity of PaO2/FiO2, as many of the patients (44.5%) had a ratio of less than <100.

The overall mortality among our patients was (45.6%). We tested BMI groups <24.9 vs overweight and obese class I and we found that to be statistically significant (p<0.0087) (0<0.0391), which means that overweight and obese patient class I had a lower risk of mortality compared to BMI<24.9. In comparison to other studies, they found that obesity almost doubles mortality in patients hospitalized with COVID-19 [33]. whereas some studies discovered that lower BMI>24.9 was associated with increased mortality in COVID patients [34,35]. Moreover, a study from Wuhan, found a U-shaped relationship, that is consistent with our study, between BMI and in-hospital mortality (underweight and obese class III) but more significant for underweight [36]. One hypothesis behind that is the obesity paradox, which is an inverse correlation between body mass index (BMI) and mortality. The underlying mechanism responsible for the Obesity Paradox is still unknown. Preconditioning, which is a chronic proinflammatory state in obesity that creates a protective environment, limiting the detrimental effects of a more aggressive second hit, such as ventilator-induced lung injury or sepsis, is one proposed pathophysiological mechanism to explain the decreased mortality in critically ill patients with obesity [37].

In conclusion, the association between BMI and the severity of COVID-19 is an important finding and should be explored more. In this cohort study, contrary to our hypothesis, overweight and obese I patient were found to have a lower mortality risk compared to the normal weight group. Further studies are needed to explore the obesity paradox theory.

Declarations

Ethical Approval

The study protocol has been approved by the National Guard Health Affairs Institutional Review Board (NRC21R/162/04), Riyadh, Kingdom of Saudi Arabia.

Competing Interests

The authors declare that they have no competing interests.

Funding

Not Applicable

Applicable of Data and Materials

The data that will support the findings of this study are available from the corresponding author upon reasonable request as per the regulations of King Abdullah International Medical Research Center (KAIMRC).

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