Obesity is a risk factor for COVID-19 infection in Saudi Arabia

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Abstract

Background: Obesity is a global health hazard that has recently been linked to adverse clinical outcomes of COVID-19 infection.

Objective: The aim of this study is to determine the obesity risk factors among hospitalized COVID-19 patients and their influence on the clinical outcomes of the disease

Methods: This is a retrospective observational cohort study of COVID-19 patients admitted to one tertiary hospital in Saudi Arabia from May to July 2020. Patients' demographics, comorbidities and clinical manifestations were collected from the medical records. The clinical outcomes were compared between patients with different categories of body mass index (BMI).

Results: Out of 260 patients who were included in the study, 41.6% were obese. Compared to those patients with normal and overweight BMI, obese patients with COVID-19 were more likely to have hypertension, ischemic heart disease, chronic lung disease and heart failure. Pneumonia (81.1%), ARDS (80.8%), mechanical ventilation (80%), acute kidney injury (74.2%) and heart failure (86.7%) were more prevalent in patients who were either overweight or obese. More than 50% of the patients admitted to the intensive care unit were either overweight or obese, representing nearly 55% of the mortalities. On an average, the BMI of females (32.2 ± 8.3 kg/m²), was significantly higher than males (28.3 ± 5.1 kg/m²), ($P<0.01$) and with higher BMI, the chance of having hypertension increases by threefold ($P<0.01$).

Conclusion: Obesity is very common among hospitalized patients with COVID-19, particularly females. Obese patients were more likely to have cardiovascular risk factors and adverse clinical outcomes.

Keywords: COVID-19, Obesity, BMI, Risk factors, Outcome

Introduction

After more than two years since Corona Virus Disease 19 (COVID-19) was declared a global pandemic, nearly 450 million people (as of March 9, 2022) have been infected with the disease worldwide, and more than 16 million people have lost their lives. In Saudi Arabia, almost 749,000 were affected with more than 9,000 mortalities (1,2). Multiple risk factors have been linked with high morbidity and mortality of COVID-19 worldwide (3,4,5,6).
Numerous reports have highlighted many adverse clinical outcomes in obese patients who develop COVID-19 (3). This could be in part related to the pro-coagulant and pro-inflammatory state associated with obesity, resulting in the amplification of oxidative stress, and impairment of the innate and adaptive immune response to infections. Likewise, comorbidities associated with obesity including other metabolic, cardiovascular, pulmonary, and renal diseases can further aggravate the clinical outcomes of COVID-19 (7,8).

In Saudi Arabia, the latest World Health Survey conducted in 2019, reported that 20% of Saudis were obese, with a higher prevalence in Saudi females (21%) than Saudi males (19%) (4). Studies published in the Middle East and North African (MENA) region, especially in Saudi Arabia, are still scarce considering the high prevalence of obesity in the region.

Thus, the aim of this study is to describe the clinical characteristics of patients with COVID-19 infection admitted to hospitals in Saudi Arabia and identify the obesity risk factors and their impact on the clinical outcomes of the disease by employing the Body Mass Index (BMI) to classify them. The results of this study may help to prioritize patients infected with COVID-19 according to their medical needs with respect to obesity, within the available resources.

Materials and Methods

This is a retrospective observational case-control study from the medical records of patients infected with COVID-19 who were admitted to a tertiary hospital in Riyadh, Saudi Arabia from May to July 2020. Adult patients with confirmed COVID-19 infection by real-time reverse transcription-polymerase chain reaction (RT-PCR) test using the nasopharyngeal swab and between 18–80 years of age were included in the study, while cancer patients, pregnant or lactating women were excluded.

Demographic profile of the patient in addition to Body Mass Index (BMI), comorbidities and clinical manifestations were collected from patients' electronic medical records. The clinical outcomes recorded were the Hospital Length of Stay (LOS), pneumonia, Acute Respiratory Distress Syndrome (ARDS), mechanical ventilation, shock, Acute Kidney Injury (AKI), Acute heart failure (AHF) and death. AKI is defined as an abrupt reduction in kidney function characterized by an elevation in serum creatinine level within 48 hours, with reduction in urine output thus needing dialysis, or a combination of these factors. Meanwhile, AHF is defined as a rapid onset of new or worsening signs and symptoms of heart failure.

Ethical Considerations

The study was approved by the King Saud University (KSU) Institutional Review Board (IRB), (Ref. No. 20/0497/IRB). This study was conducted in accordance with the Declaration of Helsinki. KSU IRB did not require patient consent to review his or her medical record as anonymity in collecting the data was maintained with confidentiality.

Statistical Analyses

All statistical analyses were performed using the Statistical Package for the Social Sciences software, version 22.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were presented as the means ± standard deviations (SDs) and compared using t-test and one-way ANOVA to test the difference between continuous normal variables and three age groups. The categorical data were presented in numbers and percentages (%) and the Chi-square test for dependencies were carried out to determine whether there are significant dependencies between categorical variables and levels of BMI. Multiple regression analysis was used to determine the significant relationships and to arrive at a mathematical model for estimating the BMI based on the independent risk factors. All the statistical tests were considered statistically significant at 5% level of significance.

Results

A total of 304 patients with confirmed COVID-19 were admitted to King Khalid University Hospital in Riyadh, Saudi Arabia between May and July 2020. Forty-four patients were excluded from the study due to incomplete or missing data. The medical records of the remaining 260 patients were retrospectively reviewed. Patients were categorized into three BMI classes; Normal (BMI-19 to 25 kg/m2), Overweight (BMI-25 to 30kg/m2) and Obese (30 to 35 kg/m2 and above). The baseline data is summarized in Table 1. About 20.7% of the patients were in the normal BMI group, 37.7% were overweight and 41.6% were obese. The average mean of the patients' age was 53.9 ±15.2 years, and the majority of the patients were males (68.5%). To test the significant differences in BMI, the ages of subjects were categorized into three different age-groups; <45 years, 45-64 years and ≥65 years. However, there was no significant difference in BMI among the three age groups (p=0.187). For females, the mean of BMI was (32.2 ± 8.3 kg/m²), which was significantly higher than the BMI for males (28.3 ± 5.1 kg/m²), (P<0.01). Obese patients with COVID-19 infection were more likely to have hypertension, ischemic heart disease, chronic lung disease and heart failure compared to those patients within the normal weight or overweight groups. However, this did not reach statistical significance. Meanwhile, the most common initial clinical symptoms on admission of the patients to the hospital were shortness of breath (78.6%, P<0.05), fever (74.2%, P<0.05), and cough (67.2%). The laboratory results showed that prothrombin time (PT) and Activated partial thromboplastin time (APTT) were higher among COVID-19 patients categorized by normal BMI (P<0.001 and P=0.057 respectively).

The baseline data is summarized in Table 1.

Table 1: Baseline characteristics of COVID-19 patients categorized by BMI classes

Variable	Total (n = 260)	Normal (n =54)	Overweight (n = 98)	Obese (n = 108)	*P* value
Age (year)	53.9± 15.2	51.2 ± 17.7	54.8 ± 14.1	54.5 ± 14.8	0.187
<45 yrs		20(37.0)	28(28.6)	30(27.8)	
45 – 64 yrs		22(40.7)	44(44.9)	52(48.1)	0.761
65 or more yrs		12(22.3)	26(26.5)	26(24.1)	
Sex (%)					
Male	178 (68.5)	40 (74.1)	79 (80.6)	59 (54.6)	0.000*
Female	82(31.5)	14(25.9)	19(19.4)	49(45.4)	
Nationality (%)					
Saudi	114 (43.8)	20 (37.0)	34 (34.7)	60 (55.6)	0.006*
Non-Saudi	146 (56.2)	34 (63)	64 (65.3)	40 (44.4)	
Civil Status, Married (%)	152 (58.5)	29 (53.7)	63 (64.3)	60 (55.6)	0.326
Blood Pressure					
SBP (mmHg)	125.5 ± 20.7	126.2 ± 22.7	126.1 ± 20.3	124.6 ± 20.1	0.872
DBP (mmHg)	71.3 ± 12.5	69.2 ± 12.3	72.8 ± 11.3	70.9 ± 13.5	0.984
Smoking History (%)					
Smoker	20 (7.7)	4 (7.4)	10 (10.2)	6 (5.6)	0.415
Non-smoker	240 (92.3)	50 (92.6)	88 (89.8)	102 (94.4)	
Comorbidities ((%)					
HTN	119 (45.8)	20 (37.0)	41 (41.8)	58 (53.7)	0.082
DM	116 (44.6)	27 (50.0)	41 (41.8)	48 (44.4)	0.625
IHD	29 (11.2)	6 (11.1)	9 (9.2)	14 (13.0)	0.691
CKD	25 (9.6)	8 (14.8)	9 (9.2)	8 (7.4)	0.316
CLD	20 (7.7)	5 (9.3)	4 (4.1)	11 (10.2)	0.231
HF	23 (8.8)	4 (7.4)	8 (8.2)	11 (10.2)	0.804
CVA	18 (6.9)	6 (11.1)	5 (5.1)	7 (6.5)	0.367
Clinical Symptoms (%)					
Cough	174 (67.2)	34 (63.0)	68 (70.1)	72 (66.7)	0.662
Fever	192 (74.4)	33 (62.3)	79 (81.4)	80 (74.1)	0.036*
SOB	202 (78.6)	36 (67.9)	85 (86.7)	81 (76.4)	0.021*
Sputum	39 (15.0)	6 (11.1)	16 (16.3)	17 (15.7)	0.663
Hemoptysis	3 (1.2)	0 (0)	3 (3.1)	0 (0)	0.081
Sore Throat	25 (9.6)	4 (7.4)	11 (11.2)	10 (9.3)	0.737
Neurological symptoms	25 (9.6)	7 (13.0)	9 (9.2)	9 (8.3)	0.631
Diarrhea	51 (19.7)	9 (16.7)	18 (18.4)	24 (22.4)	0.629
Nausea and vomiting	53 (20.4)	10 (18.5)	18 (18.4)	25 (23.1)	0.647
Abdominal Pain	20 (7.7)	5 (9.3)	5 (5.1)	10 (9.3)	0.476
Laboratory results					
HbA1c (mmol/L)	8.2 ± 8.3	7.7 ± 2.2	7.4± 2.0	8.8 ± 10.9	0.625
D-dimer (mcg/L)	2.1 ± 3.6	3.6 ± 5.3	2.6± 4.9	1.5 ± 1.8	0.426
HDL(mmol/L)	0.98 ± 0.48	0.9 ± 0.4	1.0± 0.5	1.0 ± 0.5	0.141
LDL(mmol/L)	1.94 ± 0.99	1.9 ± 1.1	2.2± 0.9	1.8 ± 1.0	0.872
PT (seconds)	15.3 ± 4.3	17.5 ± 6.9	14.7± 2.1	15.1 ± 4.4	0.001*
A PTT (seconds)	40.6 ± 8.3	44.1 ± 10.2	39.6± 6.0	40.3 ± 8.9	0.057
Ferritin (mcg/L)	1110.3±1567.6	1275.7±1849.9	1113.4±1033.1	1068.1±1747.5	0.059
LDH (U/L)	434.1 ± 177.7	418.3 ± 147.2	492 ± 166	407.3 ± 186.1	0.579

Data are presented as mean ± standard deviation or number (%);* Statistically significant; SBP- systolic blood pressure; DBP- diastolic blood pressure; HTN- hypertension; DM, diabetes mellitus; IHD-ischemic heart disease; CKD-chronic kidney disease; CLD-chronic lung disease; HF-heart failure, CVA-cerebrovascular accident; SOB-shortness of breath; HbA1c-glycated haemoglobin ; HDL-high density lipoprotein; LDL-low density lipoprotein; PT-prothrombin time; aPTT- activated partial thromboplastin time ; LDH-lactate dehydrogenase

Initial treatment given upon admission in the hospital were cephalosporin antibiotics (89.2%), azithromycin (62.3%), and steroids (61.8%). Regarding the outcome of the patients with COVID-19 infection, pneumonia (81.1%), ARDS (80.8%), mechanical ventilation (80%), shock (57.9%), acute kidney injury (74.2%) and heart failure (86.7%) were more prevailing in patients who were either overweight or obese. Furthermore, more than 50% of the patients admitted to ICU were either overweight or obese and their mean LOS of 22.9 ± 18.1days and 16.1 ± 13.6 days respectively, and nearly 30% of obese patients in the study have died (Table 2).

A multiple linear regression model was used to evaluate the association between risk factors of COVID-19 patients and BMI. Several demographic and comorbidities were identified. Moreover, a stepwise logistic regression model was used to reduce them to 3 so that only the significant predictor variables are entered into the regression equation one at a time. Thus, it can be observed that the BMI of females was significantly higher than males (P<0.01), and the higher the BMI of a person, the greater the chance to have hypertension (P<0.01). However, in the outcome, it was observed that with higher BMI, the likelihood of developing shock was reduced (P<0.01). Table 3 presents the univariate and multivariate linear regression analyses of risk factors associated with high BMI for COVID-19 patients.

Table 2. Treatment and Outcome of COVID-19 patients classified by BMI Classes

Variable	Total (n = 260)	Normal (n =54)	Overweight (n = 98)	Obese (n =108)	*P* value
Treatment (%)					
Steroids	160 (61.8)	31 (57.4)	65 (67.0)	64 (59.3)	0.396
Antibiotics	232 (89.2)	44 (81.5)	91 (92.9)	97 (89.8)	0.093
Hydroxychloroquine	40 (15.4)	12 (22.1)	21 (21.4)	7 (6.5)	0.004*
Azithromycin	162 (62.3)	31 (57.4)	69 (70.4)	62 (57.4)	0.111
Anti-viral	14 (5.4)	3 (5.6)	5 (5.1)	6 (5.6)	0.988
Outcome (%)					
Pneumonia	222 (85.4)	42 (77.8)	84 (85.7)	96 (88.9)	0.167
ARDS	26 (10.0)	5 (9.3)	10 (10.2)	11 (10.2)	0.979
Mechanical Ventilation	60 (23.2)	12 (22.2)	20 (20.4)	28 (26.2)	0.610
Shock	19 (7.3)	8 (14.8)	7 (7.1)	4 (3.7)	0.037*
AKI	62 (23.8)	16 (29.6)	16 (16.3)	30 (27.8)	0.084
HF	15 (5.8)	2 (3.7)	4 (4.1)	9 (8.3)	0.326
ICU admission	136 (52.3)	21 (38.9)	54 (55.1)	61 (56.5)	0.084
LOS (day)	17.9 ± 14.6	14.3 ± 5.3	22.9 ± 18.1	16.1 ± 13.6	0.222
Death	71 (27.3)	14 (25.9)	25 (25.5)	32 (29.6)	0.777

Data are presented as mean ± standard deviation or number (%); * Statistically significant; ARDS- Acute Respiratory Distress Syndrome; AKI- acute kidney injury; HF- heart failure; ICU-Intensive Care Units; LOS-Length of Stay

Table 3. Univariate and multivariate linear regression analyses of risk factors associated with BMI for COVID-19 patients

Table 3. Univariate and multivariate linear regression analyses of risk factors associated with BMI for COVID-19 patients

Risk Factor Variables	Univariate analysis Unstandardized coefficients				Multivariate analysis Unstandardized coefficients			
	B	SE	95% CI	P value	B	SE	95% CI	P value
Age (yr)	0.03	0.03	-0.02, -0.08	0.275	0.01	0.03	-0.05, 0.07	0.750
Male sex (vs female)	3.83	0.84	2.18, 5.49	0.000*	3.59	0.86	1.89, 5.30	0.000*
Smoker (vs non-smoker)	-0.16	1.52	-3.16, 2.83	0.915	1.39	1.49	-1.53, 4.32	0.350
Comorbidity present (vs not present)								
Hypertension	2.95	0.79	1.39, 4.51	0.000*	3.49	0.94	1.65, 5.34	0.000*
Diabetes mellitus	-0.16	0.81	-1.77, 1.44	0.841	-1.45	0.88	-3.18, 0.28	0.099
Ischemic Heart Disease	0.15	1.29	-2.38, 2.69	0.905	-0.78	1.38	-3.51, 1.94	0.571
Chronic Kidney Disease	-0.99	1.37	-3.69, 1.71	0.472	-0.71	1.48	-3.63, 2.21	0.632
Chronic lung Disease	2.50	1.51	-0.48, 5.48	0.100	2.10	1.50	-0.85, 5.06	0.163
Heart Failure	3.44	1.72	0.04, 6.83	0.047*	0.98	1.54	-2.06, 4.01	0.527
Cerebrovascular accident	-2.19	1.59	-5.32, 0.94	0.170	-3.13	1.75	-6.59, 0.39	0.076
Outcome								
Pneumonia	1.61	1.14	-0.64, 3.86	0.160	1.41	1.17	-0.90, 3.73	0.230
ARDS	0.56	1.35	-2.10, 3.22	0.676	1.15	1.49	-1.79, 4.09	0.440
Mechanical Ventilation	0.42	0.96	-1.47, 2.32	0.659	1.78	1.38	-0.94, 4.50	0.199
Shock	-3.64	1.54	-6.67, -0.60	0.019*	-4.70	1.77	-8.19, -1.21	0.009*
Acute Kidney Injury	1.14	0.95	-0.73, 3.01	0.231	0.78	1.03	-1.26, 2.81	0.453
Heart Failure	3.44	1.72	0.04, 6.83	0.047*	2.06	1.92	-1.73, 5.85	0.285
ICU patients	1.22	0.81	-0.37, 2.81	0.131	1.11	0.95	-0.76, 2.99	0.243
LOS (day)	-0.03	0.03	-0.08, 0.02	0.222	-0.04	0.03	-0.09, 0.01	0.144
Death	-0.10	0.91	-1.89, 1.69	0.910	-0.89	1.29	-3.43, 1.64	0.488

Legend: ARDS, Acute Respiratory Distress Syndrome; ICU, Intensive Care Unit; LOS, length of stay; * Statistically significant

Discussion

The findings of the present study showed a high prevalence of obesity among hospitalized patients with COVID-19 in Saudi Arabia particularly among females. In the same line, obese patients with COVID-19 had high probability of hypertension as compared to the non-obese. There was a trend toward adverse outcome among obese patients, however the difference was not statistically significant.

Our findings were in agreement with a previous study from Saudi Arabia which reported that 45.8% of COVID-19 patients were obese (9). Lower prevalence of obesity was reported from China (10) probably reflecting the local prevalence of obesity in different countries. Nevertheless, obese patients in general seem to be more vulnerable to infections. A study conducted in Sweden has reported that there were increased incidence of varying infections in obese men and women as well as subjects with a low level of physical activity compared with more physically active subjects for both genders (11).

In the present study, hypertension was more common among obese patients with COVID-19. A population based cross-sectional study in Al Kharj, Saudi Arabia reported that being overweight was associated with the highest risk of hypertension (OR = 4.98 [95% C.I. = 1.98–12.52], P = 0.001). Those who were classified as class I obese had 3.5 times the risk of hypertension compared with the non-obese group (OR = 3.49 [95% C.I. = 1.42– 8.63], P = 0.007) (12). Another study which was conducted in Saudi Arabia between 1995 to 2005 reported that the prevalence of hypertension was around 26% among the 15–70 years' age group, and by 2010, hypertension was classified as the leading risk factor for death in Saudi Arabia (13,14,15,16). In the present study obese patients were more likely to have hypertension, which can partly contribute to a worse outcome of COVID-19 infection.

More than two thirds of the study patients were males. Numerous reports have been published on gender differences in COVID-19 outcomes (11) and although, varying evidence did not show a strong difference between genders regarding infection with COVID-19, male patients tend to have both higher severity and fatality rates. These variances may be due to higher levels of angiotensin-converting enzyme 2 (ACE2) and transmembrane protease serine 2 (TMPRSS2) in males. Hormonal influences on the immune response as well as differences in behavior can also contribute to the greater severity and fatality in COVID-19 observed among more men than women (17). This study can be compared to previously published studies which observed that the majority of the COVID-19 patients were males (9).

Shock is a clinical state of circulatory failure; it is an indicative of diminished oxygen delivery at the cellular level. It has been reported that patients infected with COVID-19 who required intensive care unit (ICU) admission, had up to 67% probability of developing shock (3,18). A retrospective cohort study of 1,019 COVID-19 patients conducted in New York City at the height of the pandemic, reported that obesity is independently associated with an increased risk for septic shock (19). In the present study, only 7% of the total patients developed shock during the course of their hospital admission, moreover, obesity was inversely related to developing shock as an outcome (p .009).

The potential impact of obesity on the outcome of septic patients is quite controversial. In most animal studies, obesity resulted in altered inflammatory response, higher number of complications, and escalated mortality among obese animals (20,21). On the contrary, some human studies showed that obesity has a beneficial effect wherein, an observational cohort study with 1,400 adult patients analyzed with severe sepsis, found that obesity shielded against death (22). Another study, reported an improved short-term survival in overweight and obese patients with septic shock despite equal severity of illness upon presentation and co-morbidities (20). In addition, overweight and obese patients had lower degree of inflammatory response as shown by lower IL-6 levels, and less coagulation derangement than normal weight patients (20). In the present study we observed that obese patients had a lower level of D-Dimer, PT, APTT and ferritin than patients with normal BMI. This might in part indicate a lower inflammatory response and explain the lower number of obese patients who developed shock, however this needs to be confirmed in larger studies.

Pneumonia, ICU admission, mechanical ventilation and death were higher among obese patients, although the difference did not reach statistical significance. This is probably due to the small number of patients and the high prevalence of DM (50%) in patients with normal BMI, who's average HbA1c was 7.7 mg/dL. DM on its own merit is associated with higher in-hospital complications among COVID-19 patients (7).

An earlier record-based case-series study conducted in Saudi Arabia, reported that ICU admission was significantly higher in obese patients (p=0.001) (23). Similarly, another study reported higher mortality and worse clinical outcome in obese patients (24). A study conducted in France with over 130,000 patients admitted to hospital with COVID-19 validated that obesity, diabetes and arterial hypertension are related to the severity and mortality among patients with existing comorbidities and requiring more invasive mechanical ventilation (18).

Limitations of this study include the small number of patients and the retrospective nature of the study which did not allow measuring adipose tissue-related cytokine concentrations (e. g. interleukin [IL-6], monocyte chemotactic protein [MCP]-1, tumor necrosis factor [TNF]-α, as well as other serum adipokines such as leptin and adiponectin. Other measures of obesity that could be relevant are the visceral fat area (VFA), upper abdominal perimeter, subscapular and triceps fat thickness.

Conclusion

Based on the findings of this study it can be safely contended that obesity is highly prevalent among patients infected with COVID-19 in Saudi Arabia. Given their increased risk toward an adverse outcome when infected with COVID-19, it is vital to recognize the distinctive hazards that obese patients face. This can help to establish a strategy with efficient and effective triaging and clinical evaluation for patients with obesity. This study also highlights the importance of controlling obesity and hypertension at the community level.

Declaration of Competing Interest

The authors of this study has no known competing financial interests or personal relationship that could appeared to influence the work reported in this paper

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