

High Body Mass Index and Severity of Coronavirus Disease 2019 (COVID-19): A Cohort Study

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Abstract: Background: SARS-CoV-2 disease (COVID-19) has become pandemic all over world. This study aimed to investigate the clinical characteristics and severe outcomes of COVID-19 patients with high body mass index (BMI). Methods: A cohort study included 114 adult patients confirmed COVID-19 were classified by BMI levels on admission: overweight (25–29.9 kg/m²), and obesity (four categories: 30–34.9 kg/m², 35–39.9 kg/m², 40–44.9 kg/m², and ≥45 kg/m²). The rate of pneumonia, severe pneumonia and ICU admission were our primary outcomes, complications and length of hospital stay were the secondary outcome. Results: In Qena University isolation Hospital, study was conducted in 114 patients confirmed COVID-19. The mean age of patients was 42.1±11.1 years and males were 53.5%. Hypertension and diabetes common comorbidities, 54 patients (47.3%) had pneumonia and 28 patients (24.6%) had progressed to severe pneumonia with significant difference across BMI level ($p < 0.05$). The rates of admission to ICU were 13.1%, acute kidney injury (7.8%), acute liver injury (5.2%) and shock (7%), ICU mortality with BMI 40–44.9 kg/m² and ≥45 kg/m² showed 100% mortality among patients admitted ($p < 0.001$), with median of days of hospitalization (12 days). Multivariable analysis demonstrated that; BMI (increase one kg/m²), Hypertension, Dyslipidemia, Lymphopenia, CRP and IL6 independent risk factors for severe illness. Conclusion: Serious outcomes such as severe pneumonia, acute kidney injury and ICU mortality are associated with obesity and COVID-19. Call for future studies to find out the correlation between obesity and COVID-19.

Keywords: High BMI, COVID-19, Sever Pneumonia, IL6

1. Introduction

Coronavirus disease 2019 (COVID-19) has become a worldwide social and medical crisis [1-5]. Acute respiratory distress syndrome (ARDS), multi-organ dysfunction, and other complications are caused by SARS-CoV-2 [6].

Large numbers of comorbidities were associated with minimal clinical outcomes [7], despite of there are very low delicate data about BMI (body mass index) of COVID-19 patients, the refrain of obesity in COVID-19 outcomes must not be disregard [8].

Obesity, defined as excessive accumulation of body fat, is generally determined by body mass index (BMI), calculated by body weight (kg) divided by height squared (m²) [9].

In general, the obesity takes substantial role in the pathogenesis of many diseases due to stimulation of inflammation in the adipose tissue [10].

Angiotensin-converting enzyme 2 (ACE2) is the cell

receptor that host SARS-CoV-2 [11]. ACE2 is widely distributed in multiple organs and tissues as lungs, heart, kidneys, gut, bladder and brain [12-15], which might explain the multiple organ failure in COVID-19 patients. Expression of ACE2 in fat cells was higher than that in lung tissue [16].

Impact of obesity on infectious diseases has been confirmed [17, 18]. Few studies reported the risk and prognosis of COVID-19 with those patients with high body mass index BMI.

Subsequently, this study aimed to examine the clinical features of patients with COVID-19 and different levels of high body mass index levels, investigate the correlation between high body mass index (BMI) and the severity of COVID-19 and to evaluate the risk factors associated with obesity and severe illness..

2. Patients and Methods

From 1 July 2020 to 30 January 2021 at Qena University isolation Hospital, after approval from faculty of medicine and ethical committee this cohort study was conducted in 114 patients with confirmed COVID-19, aged 18 years and older, and BMI $>25\text{ kg/m}^2$ (BMI was classified into the following categories: underweight ($<18.5\text{ kg/m}^2$), healthy weight ($18.5\text{--}24.9\text{ kg/m}^2$), overweight ($25\text{--}29.9\text{ kg/m}^2$), and obesity (four categories: $30\text{--}34.9\text{ kg/m}^2$, $35\text{--}39.9\text{ kg/m}^2$, $40\text{--}44.9\text{ kg/m}^2$, and $\geq 45\text{ kg/m}^2$) [19]. Consent was not obtained because the data were analyzed anonymously.

Diagnosis of COVID-19 was confirmed by positive SARS-CoV-2 RNA in nasopharyngeal swab specimens by real time RT-PCR amplification of SARS-CoV-2.

Baseline demographic data including underlying diseases, smoking status, underlying medical condition, clinical presentations, laboratory, radiological and outcome data were collected from the medical records of patients. Two independent physicians revised the patient data, if the data was obscure or missing, we confirmed it with direct contact with patients' families.

Laboratory data consisted of a complete blood count, coagulation function, serum creatinine (sr.cr), Alkaline phosphatase, Alanine aminotransferase, Total protein, albumin, interleukin 6 (IL6) and C-reactive protein (CRP).

2.1. Definitions

Pneumonia was defined as clinical symptoms of pulmonary infection with lung image suggestive pneumonia. Severe pneumonia having one of the following criteria: respiratory rate >30 breaths/min, severe respiratory distress, or an oxygen saturation $<93\%$ on room air [20]. Acute kidney injury (AKI) was defined as any of the following: increase in serum creatinine $\geq 0.3\text{ mg/dL}$ within 48 hours, increase in serum creatinine to ≥ 1.5 times from baseline, or urine volume $<0.5\text{ mL/kg/h}$ for 6 hours [21]. Patients having an oxygen saturation $<90\%$ despite the use of an oxygen face mask 10 L/minute and respiratory rate ≥ 25 breaths/minute were admitted or transferred to intensive care unit (ICU). The rate of pneumonia, severe pneumonia and ICU admission were our primary outcomes, complications (AKI, abnormal liver function and shock) and length of hospital stay were the secondary outcome.

2.2. Statistical Analysis

Demographic characteristics, underlying diseases, clinical presentation, radiological findings and laboratory finding of the patients are presented as mean and standard deviation (SD) for continuous variables and as frequency (%) for categorical variables and median (interquartile range, IQR) as appropriate for every variable, stratified by high BMI groups. The ANOVA test used for mean difference of continuous variables across high BMI groups. We used Chi-square test

for categorical variables. The rates of study outcomes (pneumonia, severe pneumonia and ICU admission) are illustrated in bar chart stratified by BMI levels. To determine the correlation between high BMI and the severity of illness with COVID 19 we analyzed risk factors using logistic regression models and presented using the odds ratios (OR) and the associated 95% confidence interval (CI).

Statistical significance was considered as $p < 0.05$. The statistical analysis was conducted using IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp).

3. Results

In Qena University isolation Hospital, 114 patients with confirmed COVID-19 were conducted in this cohort study. The mean age of patients was 42.1 ± 11.1 years and males were 53.5% of the patients. Percentage of patients having a BMI $25\text{--}29.9$, $30\text{--}34.9$, $35\text{--}39.9$, $40\text{--}44.9$ and $\geq 45\text{ kg/m}^2$ were 22.8%, 36.8%, 18.4%, 12.2% and 9.6% respectively. 27.1% of the patients were active smokers.

Hypertension and diabetes were common comorbidities. None of the patients with a BMI $25\text{--}29.9$ or $30\text{--}34.9\text{ kg/m}^2$ had dyslipidemia, whereas most patients with a BMI $\geq 45\text{ kg/m}^2$ had dyslipidemia.

The most common symptoms in those patients were fever ($p = 0.01$) and cough ($p = 0.03$), with no significant differences were found in the percentages of sore throat, nasal obstruction, fatigue and myalgia, headache and gastrointestinal (GI) symptoms.

Hemoglobin, creatinine, C-reactive protein, interleukin 6 and alanine aminotransferase, levels significantly elevated in patients with increased BMI levels.

The most common radiological findings presented with those patients was bilateral pneumonia (34.2%). There was a statistically significant difference ($P = 0.05$) in group BMI $\geq 45\text{ kg/m}^2$ in prevalence of bilateral pneumonia and multiple mottling and ground-glass opacity. Baseline characteristics of high BMI patients with COVID-19 at admission are presented in Table 1.

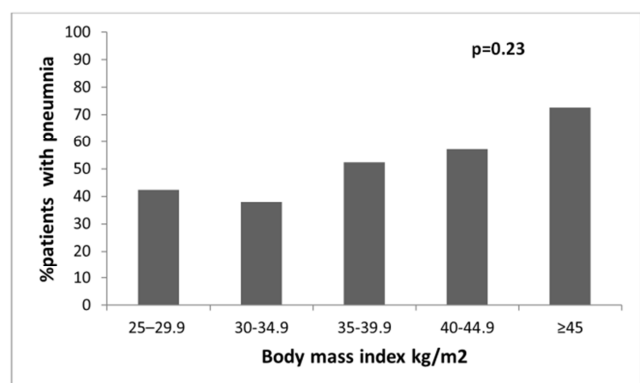


Figure 1. Rate of pneumonia in different high BMI group.

Table 1. Baseline characteristics of patients with COVID-19 on admission, classified by body mass index levels.

Characteristics	Total N=114	BMI25–29.9 kg/m ² N=26	BMI30–34.9 kg/m ² N=42	BMI35–39.9 kg/m ² N=21	BMI40–44.9 kg/m ² N=14	BMI≥45 kg/m ² N=11	P value
Age (years), mean±SD	42.1±11.1	39.3±12	43.2±12	43.1±15	46.4±11	43.9±12	0.02
Sex, male, number (%)	61 (53.5)	14 (53.8)	14 (33.3)	17 (80.9)	9 (64.2)	7 (63.6)	0.01
Active smoking	31 (27.1)	10 (38.4)	7 (16.6)	7 (33.3)	5 (35.7)	2 (18.1)	0.67
Underlying conditions, number (%)							
Diabetes	17 (14.9)	0 (0)	0 (0)	5 (23.8)	4 (28.5)	8 (72.7)	0.01
hypertension	23 (20.1)	2 (7.6)	1 (2.3)	1 (4.7)	9 (64.2)	10 (90)	0.01
Heart disease	9 (7.8)	1 (3.8)	1 (2.3)	2 (9.5)	3 (21.4)	2 (18.1)	0.23
Chronic liver disease	7 (6.1)	0 (0)	2 (4.7)	2 (9.5)	1 (7.1)	2 (18.1)	0.42
Chronic renal disease	16 (14)	1 (3.8)	1 (2.3)	3 (14.2)	5 (35.7)	6 (54.4)	0.47
COPD	6 (5.2)	2 (7.6)	1 (2.3)	2 (9.5)	1 (7.1)	0 (0)	0.61
Immunosuppression	5 (4.3)	1 (3.8)	1 (2.3)	0 (0)	1 (7.1)	2 (18.1)	0.56
Dyslipidemia	8 (7)	0 (0)	0 (0)	2 (9.5)	3 (21.4)	3 (27.2)	0.03
Signs and symptoms							
Fever >38	89 (78)	23 (88.4)	27 (64.2)	17 (80.9)	13 (92.8)	9 (81.8)	0.01
Sore throat	42 (36.8)	10 (38.4)	10 (23.8)	12 (57.1)	6 (42.8)	4 (36.3)	0.37
Nasal obstruction	37 (32.4)	6 (23)	10 (23.8)	16 (76.1)	3 (21.4)	2 (18.1)	0.41
Cough	63 (55.2)	11 (42.3)	20 (47.6)	13 (61.9)	11 (78.5)	8 (72.7)	0.03
Fatigue and myalgia	54 (47.3)	14 (53.8)	20 (47.6)	10 (47.6)	6 (42.8)	4 (36.3)	0.06
headache	26 (22.8)	9 (34.6)	7 (16.6)	2 (9.5)	5 (35.7)	3 (27.2)	0.73
GI symptoms	42 (36.8)	7 (26.9)	18 (42.8)	7 (33.3)	5 (35.7)	5 (45.4)	0.08
Days of illness at admission (days), mean±SD	6.9±4.1	7±4.0	6.5±4.3	7±3.5	5.6±4.2	4.1±3.2	0.16
Laboratory finding							
Hemoglobin (g/dL), mean±SD	13.5±1.7	12.6±1.4	13.0±1.3	13.6±1.5	13.8±1.5	14.1±1.6	0.02
Absolute lymphocyte count (/mm ³), mean±SD	1954.2±720.7	2094.1±831.2	1953.6±734.0	1870.50±566.3	1865.30±456	1882.63±898	0.09
International normalized ration (IQR)	1.01 (0.97–1.08)	1.02 (0.86–1.06)	1.01 (0.91–1.04)	1.03 (0.90–1.05)	1.01 (0.93–1.05)	1.02 (95–1.08)	0.91
D-Dimer (mg /L)	423 (273–623)	540 (325–945)	624 (321–1243)	1624 (542–2103)	712 (450–847)	1057 (563–1875)	0.31
C-reactive protein (mg/L) (IQR)	9.5 (1.60–14.23)	10.45 (8.45–16.23)	11.45 (8.12–24.87)	13.24 (7.69–20.36)	10.60 (4.01–24.56)	18.36 (7.11–31.25)	0.01
Interleukin 6 (pg/ml)	33.24 (7.8–37.5)	47.23 (19.45–67.45)	45.75 (24.56–68.23)	62.41 (33.10–130.21)	59.12 (31.42–102.45)	55.7 (21.3–124.2)	0.01
Creatinine (mg/dL), mean±SD	0.74±0.25	0.76±0.22	0.72±0.14	0.83±0.16	0.81±0.23	0.90±0.38	0.05
Alkaline phosphatase (U/L), mean±SD	68.3±43.5	67.4±40.6	67.4±14.	73.4±86.8	72.7±39.9	73.7±31.7	0.16
Alanine aminotransferase (U/L), mean±SD	31.45±15.3	26.45±12.3	28.45±12.5	44.45±13.7	66.9±21.2	55.0±32.2	0.01
Total protein (g/dL), mean±SD	78.2±5.8	74.3±5.3	75.1±6.8	78.3±6.1	78.7±4.8	79.1±5.1	0.08
Albumin (g/dL), mean±SD	40.2±3.71	40.7±4.4	41.8±4.9	42.2±4.7	40.5±3.3	41.0±3.0	0.35
Chest x-ray/CT findings							0.05
Normal	14 (12.2)	6 (23)	2 (4.7)	5 (23.8)	1 (7.1)	0 (0)	
Unilateral pneumonia	33 (28.9)	11 (42.3)	13 (30.9)	3 (14.2)	4 (28.5)	2 (18.1)	
bilateral pneumonia	39 (34.2)	9 (34.6)	12 (28.5)	7 (33.3)	7 (50)	4 (36.3)	
Multiple mottling and ground-glass opacity	28 (24.5)	0 (0)	15 (35.7)	6 (28.5)	2 (14.2)	5 (45.4)	

Data are presented as medians (interquartile ranges, IQR), n (%) and mean (SD)

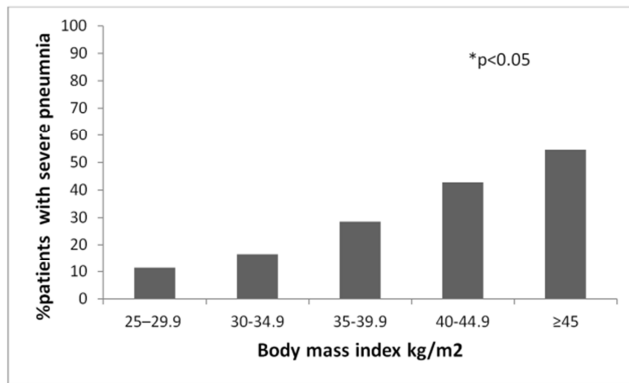
BMI; Body mass index (kg/m²), GI; Gastrointestinal (symptomsa include nausea, vomiting or diarrhea).

*Significant p value <0.05

In our cohort study 54 patients (47.3%) presented with pneumonia and 28 patients (24.6%) had progressed to severe pneumonia. The rates of admission to ICU were 13.1%. The rate of pneumonia tended to increase in patients with higher BMI levels; this rate in patients with BMI ≥45 kg/m² was significantly higher (72.7%) when compared to patients with BMI 25–29.9 kg/m² (42.3%). figures 1, 2, 3.

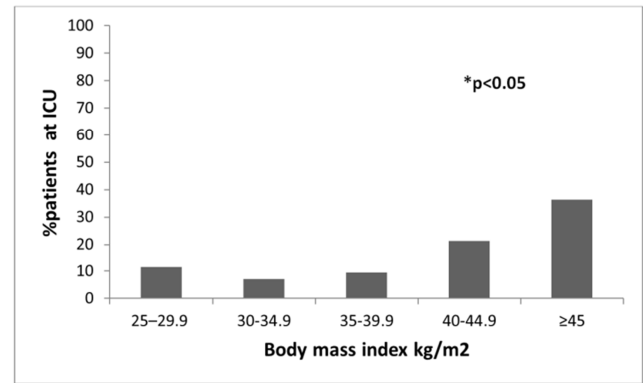
The most common complications in those patients were

acute kidney injury (7.8%) followed by acute liver injury (5.2%) and shock (7%) with no significant difference across BMI level. Regarding the ICU mortality patient with BMI 40–44.9 kg/m² and ≥45 kg/m² showed 100% mortality among patients admitted (3 out of 3 & 4 out of 4) respectively with significant p value <0.001. All patients were discharged from hospital uneventfully with median of days of hospitalization (12 days, P=0.073). Table 2.



*significant p value <0.05

Figure 2. Rate of severe pneumonia in different high BMI group.



*significant p value <0.05

Figure 3. Rate of intensive care unit (ICU) admission in different high BMI group.

Table 2. Outcomes of COVID-19 patients with high BMI.

Characteristics	Total N=114	BMI25–29.9 kg/m ² N=26	BMI30–34.9kg/m ² N=42	BMI35–39.9 kg/m ² N=21	BMI40–44.9 kg/m ² N=14	BMI≥45 kg/m ² N=11	P value
Complications							
Acute kidney injury	9 (7.8)	2 (7.6)	2 (4.7)	2 (9.5)	1 (7.1)	2 (18.1)	0.130
Abnormal Liverfunction	6 (5.2)	1 (3.8)	0 (0)	2 (9.5)	1 (7.1)	2 (18.1)	0.181
Shock	8 (7)	0 (0)	1 (2.3)	1 (4.7)	3 (21.4)	3 (27.2)	0.311
ICU mortality	10 (66.6)	0 (0)	1 (2.3)	2 (9.5)	3 (21.4)	4 (36.3)	*0.001
Length of hospital stay (days)	12 (7–22)	9 (11–19)	11 (7–17)	9 (6–15)	11 (8–18)	11 (9–24)	0.073

Data are presented as medians (interquartile ranges, IQR), n (%)

^a(total number of patients admission to intensive care unit=15 (10 death)).

*significant p value <0.001.

Table 3. Multivariable Analysis of Risk Factors associated with high BMI and COVID 19 patients.

Risk Factors	Odds Ratio (95% CI)	P value
Age	1.06 (1.13-1.84)	0.041
sex	1.89 (1.06-2.64)	0.052
BMI (per 1kg/m ² increase)	1.21 (1.12-1.91)	*0.001
Hypertension	4.56 (2.36-7.37)	*0.001
diabetes	1.866 (1.023-3.405)	0.120
Dyslipidemia	3.367 (1.750-6.479)	*0.001
Fever >38	2.27 (1.41-3.32)	0.012
Cough	3.17 (1.19-10.31)	0.014
Gastrointestinal symptoms (diarrhea, vomiting)	3.77 (1.28-4.34)	0.024
Lymphopenia	3.53 (1.89-7.11)	*0.001
Albumin	0.97 (0.75-0.99)	0.004
Serum creatinine	1.08 (1.01-1.81)	0.031
C reactive protein	1.04 (1.02-1.06)	*0.001
Interleukin 6	4.71 (3.04-11.72)	*0.001

*Significant p value<0.001

The cohort of this study comprised of 114 COVID 19 patients with high BMI >25kg/m². Multivariable analysis found that; BMI (per 1kg/m² increase) (OR1.21 95% CI (1.12-1.91) P<0.001), Hypertension (OR 4.56 95% CI (2.36-7.37) P<0.001), Dyslipidemia (OR 3.367 95% CI (1.750-6.479) P<0.001), Lymphocytes (decrease) (OR3.53 95% CI (1.89-7.11) P<0.001), C reactive protein (OR1.04 95% CI (1.02-1.06) P<0.001) and Interleukin 6 (OR4.71 95% CI (3.04-11.72) P<0.001) were independent risk factors and related to pneumonia, severe pneumonia, AKI, and ICU

stay. Table 3.

4. Discussion

114 patients with confirmed COVID-19 BMI >25 kg/m² in Qena isolation university hospital were allocated in this study. The mean age of the most of the patients were 42.1±11.1 years. Approximately 77% of the patients were obese over 30kg/m². 47% of the patients were diagnosed with pneumonia and a 15.7% of the patients with pneumonia had

progressed to severe pneumonia (8.7% presented with severe pneumonia). The high BMI ($40\text{--}44.9\text{kg/m}^2$ & $\geq 45\text{kg/m}^2$) were significantly associated with severe pneumonia, ICU admission and mortality.

Similar to a previous study [22], in this study the rate of pneumonia and severe pneumonia were high among patients with high BMI levels. obese patients ($\text{BMI} \geq 45\text{kg/m}^2$) with COVID-19 were at higher risk of severe pneumonia, comparing to COVID-19 patients with over weight ($\text{BMI} 25\text{--}29.9\text{kg/m}^2$).

Fever and cough as a presented symptoms were common in obese patients ($\text{BMI} \geq 45\text{kg/m}^2$) which reflect the pulmonary inflammation. The laboratory investigations and radiological findings (14 patients 12.2% normal findings) demonstrated the severity of illness in obese patients.

Obese people also have change in the respiratory system (restrictive pulmonary pattern). Altered respiratory mechanics, increased pulmonary resistance, and decreased respiratory muscle length and lung volume can impair respiratory system compliance [23].

The results in our study similar to those that found an increased risk for hospitalization, ICU admission, invasive mechanical ventilation, and death within increasing the BMI also the risk for severe COVID-19-associated illness [24, 25].

As obesity closely related to increased morbidity and mortality to infectious diseases, [26–28] in this retrospective cohort study, 114 COVID-19 patients were overweight/obese. Commonly overweight (26 patients)/obesity (88 patients), the worst outcomes regarding complications and ICU mortality were in BMI $40\text{--}44.9\text{kg/m}^2$ and $\geq 45\text{kg/m}^2$.

The current study also proved that high BMI (severe obesity) patients were at higher risk and unwell. We also observed that patients had several underlying diseases, such as hypertension and chronic kidney disease.

Mostly of our study patients have underlying medical conditions, so bacterial and viral infection could infect efficiently. The greater number of comorbidities (serious heart conditions, diabetes, chronic kidney disease) in obese patients increases the severity of COVID-19 [29, 30].

Immune dysregulation, comorbidities, and an impaired respiratory system could be a pathogenic link with the obesity and severity of illness with COVID-19 [31]. The main mechanism of lung injury and multiorgan failure in COVID-19 is proinflammatory cytokines (cytokine storm). Interleukin (IL)-1, IL-6, IL-8, IL-10, tumor necrosis factor- α , c-reactive protein, and resistin are proinflammatory mediators that overproduce from dysfunctional adipocytes in obesity which aggravate the COVID-19 severity [32, 33].

We found some biochemical indicators, including CRP ($p=0.01$), IL6 ($p=0.01$), serum creatinine ($p<0.05$) and ALT ($p=0.01$) significantly increased with increasing BMI (severe obesity), indicating the more active inflammation, injury of kidney and liver were significantly elevated in the blood of those patients.

We detected AKI, acute liver injury and shock as complications in those patients and main causes of death in ICU mortality, various mechanisms induce AKI in COVID-

19 including thrombotic events, cytokines storm and obesity inflammatory mediators, and direct viral injury [31, 34]. severe pneumonia and respiratory failure requiring invasive mechanical ventilation all are risk factors of AKI [35].

This study included six patients had HBV and 18 patients had HCV infection all of them previously received treatments and medical consultation. There is multiples factors for liver injury in patients with COVID-19 such as inflammatory response, direct viral invasion, anoxia, and pre-existing chronic liver disease [36]. Abnormal liver function test as alanine aminotransferase has been found in obese patients with COVID-19.

Several studies investigated that obese had delayed responses to influenza virus and poorly recovered [37–39]. The same clinical response were noticed in COVID-19 patients with obesity. In this study we compared different high BMI level regarding the length of hospital stay, we found no significant different across high BMI level.

The risk factors for severe outcomes illness in COVID-19 patients were calculated by multivariable analysis, high BMI (per 1kg/m^2 increase), hypertension, Dyslipidemia, Lymphopenia, CRP and increased IL6 were independent risk factors for severe Outcomes COVID-19 patients.

Another theory supported our study results is the widely distributed of ACE2 in the fat cells as it assist the viral entrance [40].

In this study, a prospective cohort we allocated all confirmed COVID-19 cases overweight or obese, it represent all of different high BMI COVID-19 patients. All the patients have been observed clinically until improved or died, all the data were completed and analyzed so the final clinical outcomes were accurate. However this study has limitations.

First, we estimated risk for severe COVID-19 across high BMI only in hospitalized patients.

Second, we didn't evaluated the treatment regimens in the analysis, but all patients received our hospital protocol for COVID-19 cases as appropriate.

Third, the BMI of some older adults might have been misclassified.

Finally, small sample size.

5. Conclusions

Our cohort study demonstrated that, the rate of severe pneumonia, adverse outcomes, ICU admission and mortality increase with increasing BMI in obese patients with COVID-19. In our study the higher the BMI, dyslipidaemia, elevated CRP and IL6, were independent risk factors for severe illness and adverse outcomes in obesity with COVID-19 infection. Preventing COVID-19 in adults with higher BMIs remains important issue to be concern.

Conflict of Interest

The author does not have any possible conflicts of interest.

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