KJMS / OPEN ACCESS Print ISSN: 2790-0207 Online ISSN: 2790-0215

Original article

Obesity and COVID-19

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DOI: 10.32894/kjms.2021.178314

Abstract:

- ***Background*:** Obesity is a recognized risk factor for severe COVID-19, possibly related to chronic inflammation that disrupts immune and thrombogenic responses to pathogens as well as to impaired lung function from excess weight. Obesity is a common metabolic disease; approximately two in three Iraqi adult participants were overweight/obese. The aim of this study is to investigate the association between COVID-19 disease severity and obesity in a sample of Iraqi patients.
- ***Methods:*** The study included 609 patients with confirmed Covid-19 infection carried out in Azadi and alShifaa14 hospitals and on outpatient cases in Kirkuk city from 1st November 2020 to 30 April 2021 through which BMI was calculated for each patient and correlated with severity.
- ***Result:*** The study showed that majority of patients (77.9%) were overweight or obese., majority of patients (63.5%) were in sever condition, (24.5%) patients were in mild state, and only 2 patients were critical ill. The males gender was associated with more severe cases (p=0.018). Age was associated with more severity (p=0.0001). BMI showed an association with viral disease severity, in which overweight and obese categories were had more severe symptoms (p=0.0001).
- ***Conclusions:*** BMI showed an association with COVID-19 Disease status, in which overweight and obese categories were had more severe symptoms (p=0.0001). The study revealed that males gender were associated with more severe cases of COVID-19 disease status (p=0.018).
- **Keywords:** Obesity, SARS-CoV-2, COVID-19, BMI

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INTRODUCTION

The Coronavirus Disease 2019 (COVID-19), an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has become one of the worst pandemics in this century. The World Health Organization (WHO) announced the confirmation of COVID-19 as a pandemic on March 11th, 2020 (1). As of July 20th, 2021, COVID-19 has affected over 190 million people worldwide, causing more than 4 million of fatalities (2). The clinical outcomes of COVID-19 vary in severity from asymptomatic to lethal (3). In addition to several degrees of pneumonia, COVID-19 may cause injury of many organs including liver, kidneys and heart (4).

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 (m^2) (5). The number of obese people is globally increasing. Adiposity affects adverse health outcomes such as coronary artery disease, cerebrovascular disease, insulin resistance, hypertension and fatty liver disease. Fat accumulation does not only affect mechanical-related health complications, but the abundant adipose tissue also releases many adipokines which play a role in the inflammatory process (6). Nonetheless, the immune system is suppressed in obese people, especially in vulnerable people with multiple comorbidities (7). Obese people may be more susceptible to SARS-CoV-2 infection (8). A pathophysiology of COVID-19 is an immune response dysfunction resulting in damage to multiple organs, particularly the lower airways. Owing to similar pathogenesis, obesity could be correlated to adverse outcomes and severity of COVID-19 (9).

The current coronavirus disease 2019 (COVID-19) outbreak is a worldwide emergency, as its rapid spread and high mortality rate has caused severe disruptions (1). The number of people infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-

2), the causative agent of COVID-19, is rapidly increasing worldwide. Patients with COVID-19 can develop pneumonia (10,11), severe symptoms of acute respiratory distress syndrome (ARDS), and multiple organ failure (12).

SARS-CoV-2 infection can activate innate and adaptive immune responses. However, uncontrolled inflammatory innate responses and impaired adaptive immune responses may lead to harmful tissue damage, both locally and systemically. In patients with severe COVID-19, but not in patients with mild disease, lymphopenia is a common feature, with drastically reduced numbers of CD4+ T cells, CD8+ T cells, B cells and natural killer (NK) cells (13), as well as a reduced percentage of monocytes, eosinophils and basophils (14). An increase in neutrophil count and in the neutrophil-to-lymphocyte ratio usually indicates higher disease severity and poor clinical outcome (5). In addition, exhaustion markers, such as NKG2A, on cytotoxic lymphocytes, including NK cells and CD8+ T cells, are upregulated in patients with COVID-19. In patients who have recovered or are convalescent, the numbers of CD4+ T cells, CD8+ T cells, B cells and NK cells and the markers of exhaustion on cytotoxic lymphocytes normalize. Moreover, SARS-CoV-2-specific antibodies can be detected (15).

The transmission of infection is mainly person to person through respiratory droplets. Faecal–oral route is possible. The presence of the virus has been confirmed in sputum, pharyngeal swabs and faeces (16). Vertical transmission of SARS-CoV-2 has been reported and confirmed by positive nasopharyngeal swab for COVID-19. The median incubation period of COVID-19 is 5.2 days; most patients will develop symptoms in 11.5 to 15.5 days. Therefore, it has been recommended to quarantine those exposed to infection for 14 days (17).

It has been shown that SARS-CoV-2 disrupts normal immune responses, leading to an impaired immune system and uncontrolled inflammatory responses in severe and critical patients with COVID-19. These patients exhibit lymphopenia, lymphocyte activation

and dysfunction, granulocyte and monocyte abnormalities, high cytokine levels, and an increase in immunoglobulin G (IgG) and total antibodies (18). The immune patterns of COVID-19 include lymphopenia, lymphocyte activation and dysfunction, abnormalities of granulocytes and monocytes, increased production of cytokines, and increased antibodies. Lymphopenia is a key feature of patients with COVID-19, especially in severe cases. CD69, CD38, and CD44 are highly expressed on CD4+ and CD8+ T cells of patients, and virus-specific T cells from severe cases exhibit a central memory phenotype with high levels of IFN-γ, TNF-α, and IL-2. However, lymphocytes show an exhaustion phenotype with programmed cell death protein-1 (PD1), T cell immunoglobulin domain and mucin domain-3 (TIM3), and killer cell lectin-like receptor subfamily C member 1 (NKG2A) upregulation. Neutrophil levels are significantly higher in severe patients, while the percentage of eosinophils, basophils, and monocytes are reduced. Increased cytokine production, especially of IL-1β, IL-6, and IL-10, is another key characteristic of severe COVID-19. IgG levels are also increased and there is a higher titer of total antibodies (19).

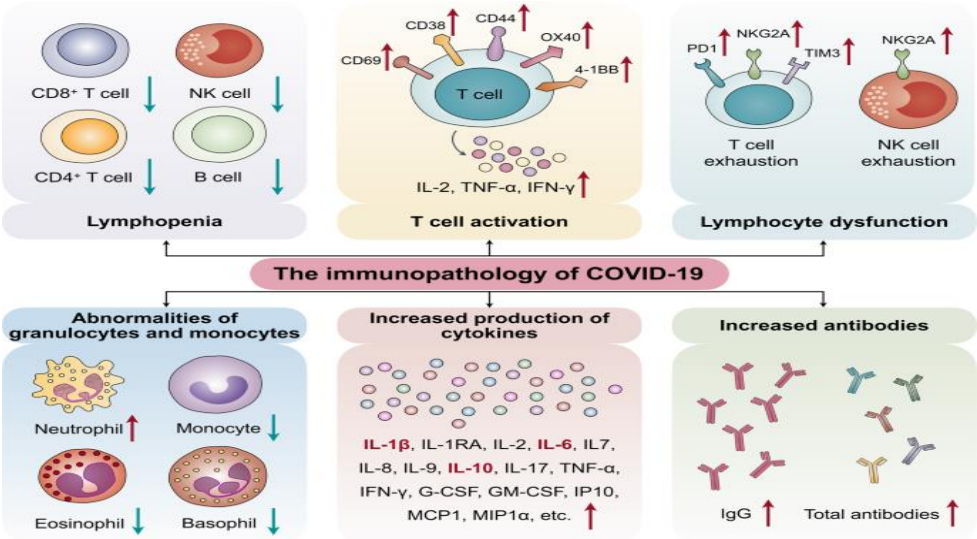

Figure 1. The immunopathology of COVID-19

Increased cytokine production is another key characteristic of severe COVID-19. Most severe COVID-19 cases exhibit an extreme increase in inflammatory cytokines, including IL-1β, IL-2, IL-6, IL-7, IL-8, IL-10, granulocyte-colony stimulating factor (G-CSF), granulocyte macrophage-colony stimulating factor (GM-CSF), interferon-inducible protein-10 (IP10), monocyte chemotactic protein 1 (MCP1), macrophage inflammation protein-1α, IFN-γ, and TNF-α, representing a "cytokine storm" (20).

Age and sex have been shown to affect the severity of complications of COVID-19. The rates of hospitalization and death are less than 0.1% in children but increase to 10% or more in older patients. Men are more likely to develop severe complications compared to women as a consequence of SARS-CoV-2 infection (21). Patients with cancer and solid organ transplant recipients are at increased risk of severe COVID-19 complications because of their immunosuppressed status (31).

The main complications reported in patients with SARS-CoV-2 may include coagulopathy, mainly disseminated intravascular coagulation, venous thromboembolism, elevated D-dimer and prolonged prothrombin time (31), laryngeal oedema and laryngitis in critically ill patients with COVID-19, necrotizing pneumonia due to superinfection caused by Panton-Valentine leukocidin–secreting Staphylococcus aureus infection which is usually fatal (22), cardiovascular complications including acute pericarditis, left ventricular dysfunction, acute myocardial injury (associated with increased serum troponin), new or worsening arrhythmias and new or worsening heart failure (32), and acute respiratory failure. Approximately 5% of COVID-19 patients require admittance to an intensive care unit because they develop severe disease complicated by acute respiratory distress syndrome (23). Other complications include sepsis, septic shock and multiple organ failure (33), higher risk of death particularly in male patients with severe disease, presence of heart injury and cardiac complications, hyperglycaemia, and patients receiving high doses of corticosteroids (24). Additionally, ventilation-associated pneumonia may occur in up to 30% of patients requiring intensive mechanical ventilation (34), and massive pulmonary embolism complicated by acute right-sided heart failure has also been reported (25).

PATIENT and METHOD

2.1. Study Design

This was a prospective observational cohort study conducted in Kirkuk city over a six-month period, beginning on November 1st, 2020, and ending on April 30th, 2021. The objective of the study was to evaluate the clinical presentation and severity of COVID-19 among patients diagnosed during this period.

2.2. Inclusion Criteria

The study enrolled a total of 609 patients who were confirmed to be infected with the COVID-19 virus. Participants included both outpatient and inpatient cases. Outpatients were those who attended the COVID-19 clinic at Azadi Teaching Hospital, while inpatients were individuals admitted for medical care at either Al-Shifaa Hospital or Azadi Teaching Hospital.

2.3. Clinical Presentation and Severity Classification

The clinical manifestations of COVID-19 among the study participants were categorized based on the World Health Organization (WHO) 2021 classification system, which stratifies disease severity into four levels: mild, moderate, severe, and critical (8). The criteria for each category are as follows:

- **Mild**: Patients presented with symptoms consistent with COVID-19, such as fever, cough, or fatigue, but there was no clinical evidence of pneumonia or hypoxia.
- **Moderate**: Patients exhibited clinical signs of pneumonia (e.g., cough, fever, and fast breathing), but maintained an oxygen saturation (SpO_2) level above 90%.
- **Severe**: Patients showed signs of pneumonia with any of the following:
    1. Respiratory rate greater than 30 breaths per minute,
    2. Severe respiratory distress,
    3. SpO_2 less than 90%.
- **Critical**: Patients developed serious complications such as acute respiratory distress syndrome (ARDS), sepsis, or septic shock.

This classification was used throughout the study to analyze the spectrum and progression of the disease among different patient subgroups.

RESULTS

The results of this prospective observational study include 609 patients diagnosed with COVID-19 in Kirkuk city between November 1, 2020, and April 30, 2021. The mean age of participants was 56.3 ± 17.9 years, ranging from 11 to 91 years. Among them, 59.1% (n = 360) were male, and 40.9% (n = 249) were female.

Regarding comorbidities, diabetes mellitus (DM) was observed in 25.5% of patients (n = 155), hypertension in 35.3% (n = 215), and other comorbidities—such as ischemic heart disease (IHD), chronic kidney disease (CKD), and asthma—in 16.1% (n = 98) (Table 1). Current smokers accounted for 15.1% (n = 92) of the cohort.

Table 1. comorbidities, and smoking status across patients

Variable	Frequency	Percentage
DM		
Diabetic	155	25.5
Not diabetic	454	74.5
Hypertension		
Hypertensive	215	35.3
Not hypertensive	394	64.7
Others(IHD,CKD,Asthma)		
Present	98	16.1
Not present	511	83.9
Smoking		
Current smoker	92	15.1
Non smoker	517	84.9
BMI categories		
Under weight	17	2.8
Normal	118	19.4
Overweight	272	44.7
Obese	202	33.2

In terms of body mass index (BMI), the average BMI was 28.4 ± 5.1 kg/m², ranging from 13 to 46 kg/m². When classified into categories, 2.8% (n = 17) were underweight, 19.4% (n = 118) had normal weight, 44.7% (n = 272) were overweight, and 33.2% (n = 202) were obese (Table 1). In total, 77.9% of patients were either overweight or obese.

Complete blood count (CBC) analysis revealed that lymphopenia was the most prominent abnormality, affecting 89.7% of patients (n = 546). Other hematological findings included leukocytosis (4.1%), increased platelet count (0.8%), and anemia (0.5%). Normal CBC parameters were recorded in only 4.9% (n = 30) of patients (Table 2).

Table 2. CBC manifestation

		Frequency	Percent
Valid	anemia	3	.5
	Increase PLT	5	.8
	leukocytosis	25	4.1
	lymphopenia	546	89.7
	Normal	30	4.9
	Total	609	100.0

Chest CT scans were evaluated for lung involvement. The results showed that 20% of patients had 10–30% lung involvement, 36.1% had 31–60% involvement, and 20% had more than 60% involvement. Meanwhile, 23.8% of patients had no abnormal findings on CT (Table 3). Analysis of CT involvement by BMI (Table 4) showed that among patients with ≥30% lung involvement, the majority were overweight (45%) or obese (41.7%). Those with <30% lung involvement were also predominantly overweight or obese (58.8% and 25.5%, respectively). Notably, patients with normal CT findings were more likely to have a normal BMI (40.7%) or be overweight (33.8%).

Table 3. percentage of lung involvement by CT scan

CT %		Frequency	Percentage from total
Valid	10 - 30	122	20.03
	31- 60	220	36.1
	> 60	122	20.03
	normal	145	23.8
	Total	**609**	**100.0**

Table 4. Association between CT involvement and BMI

			BMI				Total
			Under weight	Normal	Over weight	Obese	
CT Involvement	<30 %	Count	0	16	60	26	102
		% within CT	0.0%	15.7%	58.8%	25.5%	100.0%
	≥30%	Count	5	43	163	151	362
		% within CT	1.4%	11.9%	45.0%	41.7%	100.0%
	Normal	Count	12	59	49	25	145
		% within CT	8.3%	40.7%	33.8%	17.2%	100.0%
Total		Count	17	118	272	202	609
		% within CT c	2.8%	19.4%	44.7%	33.2%	100.0%

In terms of disease severity, most patients had severe COVID-19 (63.5%), followed by mild (24.5%), moderate (11.7%), and critical illness (0.3%) (Table 5). A gender-based comparison (Table 6) revealed that severe disease was more common in males (61.5%) than females (38.5%). All patients who developed critical illness were male.

Table 5. Severity of COVID-19 infection

		Frequency	Percent
COVID-19	Mild	149	24.5
	Moderate	71	11.7
	Severe	387	63.5
	Critical	2	.3
	Total	609	100.0

Table 6. Association between severity and gender

		Mild N. (%)	Moderate N. (%)	Severe N. (%)	Critical N. (%)	Total N. (%)
Gender	Female	76 (51)	24 (33.8)	149 (38.5)	0 (0)	249 (40.8)
	Male	73 (49)	47 (66.2)	238 (61.5)	2 (100)	360 (59.1)
Total		149 (100)	71 (100)	387 (100)	2 (100)	609 (100)

Associations between comorbidities and disease severity (Table 7) showed that patients with diabetes, hypertension, or other chronic conditions were significantly more likely to develop severe disease ($p < 0.0001$). For instance, 37.2% of diabetic patients had severe illness, compared to only 15.5% who were moderate, and none with mild or critical disease. Similarly, hypertension was present in 49.6% of those with severe illness.

Table 7. Association between severity and Comorbidities

		Mild N. (%)	Moderate N. (%)	Severe N. (%)	Critical N. (%)	P value
DM	Yes	0	11 (15.5)	144 (37.2)	0	**0.0001**
	No	149 (100)	60 (84.5)	243 (62.8)	2 (100)	
HTN	Yes	4 (2.7)	19 (26.8)	192 (49.6)	0	**0.0001**
	No	145 (97.3)	52 (73.2)	195 (50.4)	2 (100)	
Other	Yes	6 (4.0)	12 (16.9)	78 (20.2)	2	**0.0001**
	No	143 (96.0)	59 (83.1)	309 (79.8)	0 (100)	

Smoking status was also analyzed in relation to severity (Table 8). Among current smokers, 17.1% had severe disease, while none developed critical illness. However, the majority of severe cases occurred among non-smokers (82.9%).

Table 8. Association between severity and Smoking

		Mild N. (%)	Moderate N. (%)	Severe N. (%)	Critical N. (%)	Total N. (%)
Smoking	No	128 (85.9)	66 (93.0)	321 (82.9)	2 (100)	517 (84.9)
	Yes	21 (14.1)	5 (7.0)	66 (17.1)	0	92 (15.1)
Total		149(100)	71(100)	387(100)	2(100)	609(100)

When severity was analyzed in relation to BMI (Table 9), obesity and overweight were significantly associated with severe disease. Of those with severe COVID-19, 45.7% were overweight and 40.3% were obese. Meanwhile, underweight and normal BMI were more frequently observed in milder cases.

Together, these results underline the significant associations between COVID-19 severity and comorbidities, smoking, BMI, and gender, with obesity and chronic diseases notably contributing to worse clinical outcomes.

Table 9. Association between severity and BMI

		Mild N. (%)	Moderate N. (%)	Severe N. (%)	Critical N. (%)	Total N. (%)
BMI	Under	12 (8.1)	0	5 (1.3)	0	17 (2.8)
	Normal	59 (36.6)	8 (11.2)	49 (12.7)	2 (100)	118 (19.4)
	Over	51 (34.2)	44 (62.0)	177 (45.7)	0	272 (44.7)
	Obese	27 (18.1)	19 (26.8)	156 (40.3)	0	202 (33.2)
Total		149(100)	71(100)	387(100)	2(100)	609(100)

DISCUSSION

Obesity has long been identified as a significant risk factor for developing severe forms of COVID-19, a relationship that is likely rooted in chronic inflammation which impairs both immune responses and thrombogenic regulation in affected individuals (9). In the current study, we included 609 patients diagnosed with COVID-19 to investigate the impact of obesity on disease severity, reaffirming this established correlation (9).

Our findings revealed that approximately two-thirds of the studied patients were either overweight or obese, which closely aligns with the national prevalence of obesity reported in Iraq (10). Furthermore, our results are comparable to those of a large meta-analysis which indicated that the prevalence of obesity among COVID-19 patients is around 34% (11).

In terms of gender distribution, our study observed a slightly higher number of male patients, a trend that is consistent with findings from a study conducted in China, which demonstrated an approximately equal distribution of COVID-19 cases among males and females (12). However, when it comes to disease severity, male patients in our study were more likely to develop severe illness. This pattern is consistent with other studies which have reported that men are more susceptible to severe COVID-19 compared to women (13,14,15). This discrepancy may be partly explained by hormonal differences that modulate immune responses, rendering men more vulnerable to the inflammatory and thrombotic complications of the disease.

Laboratory parameters such as D-dimer and C-reactive protein (CRP) were also found to be elevated in patients with more severe disease in our cohort. These biomarkers were significantly associated with severe COVID-19, consistent with other research findings suggesting that elevated D-dimer and CRP levels at the time of hospital admission could serve as simple yet valuable predictors for the development of critical illness and the need for intensive care unit (ICU) admission (16,17).

When examining the relationship between obesity and COVID-19 severity, our data showed a clear association, where patients in the overweight and obese BMI categories were more likely to exhibit severe symptoms. This observation is corroborated by several reports and meta-analyses that have examined the clinical impact of obesity on COVID-19 outcomes. While the association between obesity and increased mortality

remains inconclusive, pooled analyses have consistently demonstrated that obese COVID-19 patients face a significantly higher risk of hospitalization and ICU admission (18,19).

Obesity, as a growing global health issue, also contributes to the presence of multiple comorbidities known to exacerbate the severity of COVID-19. This may be due in part to its effect on immune system dysfunction and its mechanical impact on respiratory function. Specifically, obesity impairs the immune response and reduces lung capacity and reserve, which in turn complicates ventilation efforts in severely ill patients (20,21).

Overall, our findings contribute to the growing body of evidence that underscores the importance of managing obesity not only as a chronic condition but also as a modifiable risk factor in the context of the COVID-19 pandemic.

CONCLUSION

BMI showed an association with COVID-19 status, in which overweight and obese categories were had more severe symptoms (p=0.0001). The study revealed that males gender were associated with more severe cases of COVID-19 status (p=0.018).

RECOMMENDATION

It is recommended that special attention be directed toward individuals with obesity who contract COVID-19, given their increased vulnerability to severe disease outcomes. Early identification, prompt medical intervention, and targeted management strategies should be prioritized for this high-risk group in order to mitigate the progression and complications of the infection. By adopting proactive measures, healthcare providers can play a vital role in reducing the burden of severe illness among obese patients affected by COVID-19.

Ethical Clearance:

Ethical approval was obtained from the scientific and ethical committee of the Iraqi Board for Medical Specialization, and verbal informed consent was secured from all participants after explaining the study's aims and ensuring data confidentiality.

Financial support and sponsorship:

Nil.

Conflicts of interest:

There are no conflicts of interest.

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