Combination of obesity and co-morbidities leads to unfavorable outcomes in COVID-19 patients

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A B S T R A C T
Objective: Obesity has been described as a significant independent risk factors of COVID-19. We aimed to study the association between obesity, co-morbidities and clinical outcomes of COVID-19.
Methods: Clinical data from 417 patients were collected retrospectively from the Al Kuwait Hospital, Ministry of Health and Prevention (MOHAP), Dubai, United Arab Emirates, who were admitted between March and June 2020. Patients were divided according to their body mass index (BMI). Various clinical outcomes were examined: presenting symptoms, severity, major co-morbidities, ICU admission, death, ventilation, ARDS, septic shock and laboratory parameters.
Results: The average BMI was 29 ± 6.2 kg/m². BMI alone was not associated with the outcomes examined. However, class II obese patients had more co-morbidities compared to other groups. Hypertension was the most significant co-morbidity associated with obesity. Patients with BMI above the average BMI (29 kg/m²) and presence of underlying co-morbidities showed significant increase in admission to ICU compared to patients below 29 kg/m² and underlying co-morbidities (21.7% Vs. 10.53%), ARDS development (21.7% Vs. 10.53%), need for ventilation (8.3% Vs. 1.3%), and mortality (10% Vs. 1.3%).
Conclusions: Our data suggests that presence of underlying co-morbidities and high BMI work synergistically to affect the clinical outcomes of COVID-19.

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1. Introduction
The coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has swept through the globe since the first reports in Wuhan, China in January 2020. As of August 31, 2020, the number of confirmed COVID-19 cases is 25,100,000 and the death toll has reached 844,000. Researchers are racing to understand the virus and the risk factors that lead to a more severe outcome of COVID-19. Notably, the presence of the following risk factors have been described as important predictors of severity of COVID-19; diabetes, hypertension, age, cardiovascular disease and obesity (Grasselli et al., 2020; Hernández-Garduño, 2020; Zhou et al., 2020). Although most individuals who are infected by SARS-CoV-2 show mild to moderate symptoms such as cough, fever and sore throat, a significant minority, and especially individuals with the risk factors described above, show much more severe symptoms which can lead to critical illness and even death.

Obesity, as defined by a body mass index (BMI) of ≥30 kg/m², has gained attention as one of the most important risk factors associated with severe outcome of COVID-19 (Hernández-Garduño, 2020; Tamara and Tahapary, 2020). In fact, studies in the United Kingdom have shown that areas with higher rates of overweight/obese individuals are associated with higher rates of mortality (Hamer et al., 2020). This association has been linked to the “cytokine storm” where SARS-CoV-2 infection leads to the release of...
pro-inflammatory cytokines with detrimental effects on various organs (Kim and Nam, 2020). Obesity is now recognized as a pro-inflammatory state where cytokines such as IL-6 have been shown to contribute to the chronic low-grade inflammation (Eder et al., 2009). Therefore, it is believed that the pro-inflammatory state of obesity is worsened upon SARS-CoV-2 infection. Conversely, there is also data suggesting that obesity, due to its chronic inflammatory status and constant immune activation, may be protective in instances such as pneumonia. This has been named the “obesity paradox” (Nie et al., 2014). However, the association between COVID-19 and obesity remains relatively unknown. In a study in Italy, 21% of 482 patients with COVID-19 were classified as obese with a BMI > 30 kg/m². High BMI of 30–34.9 kg/m² was associated with increased risk of respiratory failure and admission to Intensive Care Unit (ICU). Moreover, a BMI > 35 kg/m² was associated with increased death rates (Rottoli et al., 2020).

In the United Arab Emirates (UAE), obesity is a common health concern especially among young males. 27% and 30% of Emirati men are classified as overweight and obese, respectively compared to 23% and 10% among women (Regmi et al., 2020). With the quick lifestyle changes that have occurred in the last 30 years, the overweight/obesity rates have reached over 30%. Therefore, it would be of interest to see the association of obesity and COVID-19 outcomes among the infected population in the UAE. Although anecdotally there seems to be a correlation between obesity and death in the region, there are, to our knowledge, no studies in the Middle East which have assessed the outcomes of COVID-19 in relation to obesity. Therefore, this study aimed to study the effect of BMI on COVID-19 outcomes in infected patients in the UAE.

2. Methods

2.1. Study participants

Clinical data from 417 patients were collected retrospectively from the Al Kuwait Hospital, Ministry of Health and Prevention (MOHAP), Dubai, UAE, who were admitted between March and June 2020. The study was approved by the MOHAP Research Ethics Committee; approval number (MOHAP/DXB-REC / MMM/ NO.44/2020). Inclusion criteria: patients over the age of 18 years with confirmed COVID-19 by positive reverse transcriptase polymerase chain reaction (RT-PCR) of nasopharyngeal swabs. Exclusion criteria: patients without available BMI. The final number of analyzed patients was 334 patients (Fig. 1). Complete medical history was obtained from patients. The database incorporated all presenting symptoms (fever, cough, sore throat, shortness of breath, fatigue, myalgias, headache, rhinorrhea, vomiting, diarrhea, nausea), major co-morbidities (chronic lung disease, cardiovascular disease, cancer, chronic kidney disease, diabetes mellitus, hypertension), blood counts (WCC count, neutrophil, lymphocyte, platelet, and

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**Fig. 1.** Flowchart of the study design.
Hemoglobin (Hb)), urea, creatinine, alanine transaminase (ALT), aspartate aminotransferase (AST), albumin, C-reactive protein (CRP), lactate dehydrogenase (LDH), procalcitonin, ferritin, troponin, D-dimer, COVID-19 severity, intensive care unit (ICU) admission, death, ventilation, acute respiratory distress syndrome (ARDS), septic shock. Chronic medical history (Table 1) was defined as presence of at least one chronic medical condition.

2.2. Patient classification

Patients were initially divided into 3 groups according to their BMI: lean (BMI 18.5–24.9 kg/m²) (n = 60), overweight (BMI 25–29.9 kg/m²) (n = 159), obese (BMI 30.0 kg/m² and above) (n = 115). The patients were then further divided into the different classes of obesity, according to the Center for Disease Control (CDC)

| Patients Characteristics | Normal (n = 50) | Overweight (n = 134) | Class I (n = 66) | Class II (n = 18) | Class III (n = 18) | Pearson Chi Square |
|--------------------------|----------------|----------------------|-----------------|-----------------|-------------------|-------------------|
| **Demography**           |               |                      |                 |                 |                   |                   |
| Sex                      | F 14 28%      | 25 19%               | 20 30%          | 6 33%           | 13 72%            | <0.001            |
|                          | M 36 72%      | 109 81%              | 46 70%          | 12 67%          | 5 28%             |                   |
| **Presentation**         |               |                      |                 |                 |                   |                   |
| Fever                    | No 18 36%     | 51 38%               | 25 38%          | 8 44%           | 6 33%             | ns                |
|                          | Yes 32 64%    | 83 62%               | 41 62%          | 10 56%          | 12 67%            |                   |
| Headache                 | No 46 92%     | 125 93%              | 63 96%          | 16 89%          | 14 78%            | ns                |
|                          | Yes 4 8%      | 9 7%                 | 3 5%            | 2 11%           | 4 22%             |                   |
| Fatigue                  | No 48 96%     | 122 91%              | 61 92%          | 18 100%         | 16 89%            | ns                |
|                          | Yes 2 4%      | 12 9%                | 5 8%            | 0 0%            | 2 11%             |                   |
| Myalgia                  | No 43 86%     | 116 87%              | 61 92%          | 17 94%          | 15 83%            | ns                |
|                          | Yes 7 14%     | 18 13%               | 5 8%            | 1 6%            | 3 17%             |                   |
| Sore throat              | No 44 88%     | 118 88%              | 60 91%          | 18 100%         | 16 89%            | ns                |
|                          | Yes 6 12%     | 16 12%               | 6 9%            | 0 0%            | 2 11%             |                   |
| **On Admission**         |               |                      |                 |                 |                   |                   |
| **Radiological**         |               |                      |                 |                 |                   |                   |
| Admission CXR bil airspace consolidation | 0 22 44% | 54 40% | 27 41% | 5 28% | 7 39% | ns |
|                          | 1 24 48%     | 69 52%               | 36 55%          | 11 61%          | 11 61%            |                   |
| CT chest bilateral peripheral ground glass opacities | 4 8% | 4 8% | 4 8% | 4 8% | 4 8% | 0.001 |
| Illness severity Critical | No 49 98%    | 120 90%              | 58 88%          | 15 83%          | 17 94%            | ns                |
|                          | Yes 1 2%      | 14 10%               | 8 12%           | 3 17%           | 1 6%              |                   |
| Illness severity Med to Moderate | No 29 58% | 72 54% | 39 59% | 9 50% | 9 50% | ns |
|                          | Yes 21 42%    | 62 46%               | 27 41%          | 9 50%           | 9 50%             |                   |
| Illness severity Severe  | No 22 44%     | 76 57%               | 53 55%          | 12 67%          | 10 56%            | ns                |
|                          | Yes 28 56%    | 58 43%               | 31 47%          | 6 33%           | 8 44%             |                   |
| ARDS                     | No 49 98%     | 116 87%              | 57 86%          | 16 89%          | 17 94%            | ns                |
|                          | Yes 1 2%      | 18 13%               | 9 14%           | 2 11%           | 1 6%              |                   |
| **COVID-19 Severity and complications** |               |                      |                 |                 |                   |                   |
| Admission to intensive care unit | No 48 96% | 121 90% | 56 85% | 14 78% | 17 94% | ns |
|                          | Yes 2 4%      | 13 10%               | 10 15%          | 4 22%           | 1 6%              |                   |
| Ventilated              | No 50 100%    | 130 97%              | 61 92%          | 17 94%          | 18 100%           | ns                |
|                          | Yes 0 0%      | 4 3%                 | 5 8%            | 1 6%            | 0 0%              |                   |

Patients were initially divided into 3 groups according to their BMI: lean (BMI 18.5–24.9 kg/m²) (n = 60), overweight (BMI 25–29.9 kg/m²) (n = 159), obese (BMI 30.0 kg/m² and above) (n = 115). The patients were then further divided into the different classes of obesity, according to the Center for Disease Control (CDC)
classification: class I (BMI of 30–34.9 kg/m²), class II (BMI of 35–39.9 kg/m²), class III (BMI of 40 kg/m² or higher) (CIDCa, 2020). Moreover, the average BMI for this study population was 29.39 kg/m², which was used as a cutoff value when comparing patients with and without co-morbidities.

2.3 Blood test

Laboratory tests analyses include the following parameters: (1) complete blood count, including white cell count; WCC (normal range; NR: 4–11 x10³/µL), neutrophil count (NR: 2–7 x10³/µL), lymphocyte count (NR: 1–3 x10³/µL), Hb (NR: 12–15 gm/dL), and platelets count (NR:150–450 x10³/µL), (2) renal function tests, including urea (NR: 2.5–6.5 mmol/L) and creatinine (NR: 53–88 umol/L), (3) liver function tests, including ALT (NR: 16–63 IU/L), AST (NR: 15–37 IU/L), and albumin (NR: 34–50g/L), (4) inflammatory markers, including CRP (NR: 0–3 mg/L), D-dimers (NR:<55 mg/L), LDH (NR: 85–227 IU/L), procalcitonin (NR: < 0.1 ng/mL) and ferritin (8–388 mg/L). For risk of severe cases, the presence of lymphopenia, neutrophilia, high ALT and/or AST, high LDH, high CRP, high ferritin, high D-dimer, and high procalcitonin, above the age and gender-matched references were used as indicators of risk. Admission chest X-Ray (presence of bilateral air consolidation), and computerized tomography (CT) scan (presence of bilateral peripheral ground-glass opacities) were documented.

2.4 Statistical analysis

For all statistical analyses and tests, SPSS was used (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp). The Chi-Square Test of Independence was used to examine the association between categorical variables.

3. Results

3.1 Obese COVID-19 patients are older and have more comorbidities and WCC compared to the non-obese

After excluding the records with outlier or missing medical results, COVID-19 patients (n = 286) were categorized according to their corresponding BMI with a total average BMI of 29 ± 6.2 kg/m². While dividing patients into normal and overweight/obese (BMI ≥ 25 kg/m²) showed that 83% of the cohort are obese (Tables 1 and 2). Stratification of COVID-19 patients according to their BMI showed that the majority were overweight (n = 134/286 [46.85%], BMI = 26.8 ± 1.5 kg/m²), followed by obese class I (n = 66/286 [23.07%], BMI = 31.5 ± 1.3 kg/m²), normal (n = 50/286 [17.48%], BMI = 22.5 ± 1.8 kg/m²), obese class II (n = 18/286 [6.29%], BMI = 36.4 ± 1.5 kg/m²) and obese class III (n = 18/286 [6.29%], BMI = 46.7 ± 6.2 kg/m²).

Interestingly, in relation to gender classification, class III obese patients were mostly female (n = 13/18, 72%) compared to other BMI classes; normal (n = 14/50, 28%), overweight (n = 25/134, 19%), obese class I (n = 20/66, 30%), and obese class II (n = 6/18, 33%) (p < 0.001).

Although the difference in the age of the groups did not reach statistical difference, there was a trend showing that COVID-19 patients with normal BMI were younger (42.4 ± 15.3 years) compared to obese groups (p = 0.071). There was no difference between the groups in their presenting symptoms but there was significant difference in the presence of comorbidities among different groups. Class III obese patients had more lung disease (n = 3/18, 17%) compared to the other BMI classes normal (n = 2/50, 4%), overweight (n = 5/134, 4%), obese class I (n = 1/66, 1.5%), and obese class II (n = 0/18, 0%), p = 0.046. On the other hand, class II obese patients had more comorbidities such as cardiovascular disease (CVD), hypertension (HTN), diabetes mellitus (DM), cancer, and chronic kidney disease (CKD), (n = 14/18, 78%) compared to the other BMI classes: obese class III (n = 13/18, 72%), obese class I (n = 36/66, 55%), overweight (n = 66/134, 49%) and normal (n = 20/50, 40%), p = 0.024.

Not surprisingly, hypertension was the most significant comorbidity associated with obesity in COVID-19 patients. Obese patients of class II and III showed the highest percentage of HTN (n = 8/18 and n = 8/18; 44% and 44%, respectively) compared to other groups, obese class I (n = 23/66, 35%), overweight (n = 31/134, 23%), and normal (n = 4/50, 8%), p = 0.001. White cell count (WCC) was the only laboratory marker that showed a trend of difference between the BMI groups. Class I and II obese patients showed higher levels of WCC (8.3 ± 4.1, 9.3 ± 5.5) compared to normal (7.4 ± 2.6), overweight (7.9 ± 3.5) and class III (6.4 ± 1.7).
3.2 Obese COVID-19 patients with comorbidities developed more ARDS, required ICU and ventilation and had higher mortality rate

As it was obvious from the patients’ characteristics that normal BMI COVID-19 patients were different from patients with BMI higher than 29 kg/m² (the average BMI for this study population) in terms of comorbidities, gender and age we sought to compare the clinical outcomes between both groups during the course of the disease. We have designated all patients below 29 kg/m² as category A and patients ≥ 29 kg/m² as category B. Compared to category A COVID-19 with comorbidities, category B patients with comorbidities required more admission to ICU (n = 13/60, 21.7% Vs. n = 8/76, 10.53%), p = 0.07, needed to be ventilated (n = 5/60, 8.3% Vs. n = 1/76, 1.3%), p = 0.05, and with higher mortality (n = 6/60, 10% Vs. n = 1/76, 1.3%) p = 0.02 (Table 3).

4. Discussion

Our results present the association between BMI and outcomes of COVID-19 in the UAE. To our knowledge, this is the first study of its kind in the Middle East and North Africa (MENA) region to examine this association. Previous studies have either examined BMI or co-morbidities as risk factors. However, our study has looked at the effect of both BMI and co-morbidities in parallel on clinical outcomes of COVID-19. Our data suggests that presence of underlying co-morbidities and high BMI work synergistically in COVID-19 resulting in more clinical complications.

Obesity has emerged as one of the most significant risk factors for complications associated with COVID-19. Many countries around the world have reported that BMI ≥ 30 kg/m² predisposes individuals to severe outcomes in response to SARS-CoV-2 infection. In a study in Italy, patients with BMI between 30 and 34.9 kg/m² were at significantly increased risk of respiratory failure and of admission to ICU whereas risk of death was seen in patients with BMI ≥ 35 kg/m² (Rottoli et al., 2020).

In our study, the patients examined were at high risk of severe outcomes of COVID-19 at lower BMI than reported in the previous studies. Moreover, our COVID-19 patients with BMI over 29 kg/m² (which was the average BMI) and presence of co-morbidities, such as CVD, HTN, DM, cancer, and CKD which have been associated with COVID-19 were at increased risk of developing ARDS, admission to ICU, need for ventilation as well as death compared to patients with co-morbidities and BMI less than 29 kg/m². Therefore, the presence of comorbidities and obesity together are strongly associated with COVID-19 outcomes whereas the co-morbidities alone in patients with BMI less than 29 kg/m² are not associated with COVID-19 outcomes. This is interesting as other studies in centers across the globe have shown that risk factors such as diabetes and HTN have been shown to associate with COVID-19 outcomes, without adjustment carried out for the BMI as a confounder. In a study on 5700 patients in New York City, 56.6% of patients had hypertension whereas 33.8% of them had diabetes (Richardson et al., 2020). However, it is important to note that 41.7% of patients had a BMI over 30 kg/m². Diabetes and HTN were not assessed in relation to BMI. Our study is added to previous findings that describe BMI as an independent risk factor in COVID-19 outcomes.

The same cohort of patients also showed that class I and class II obesity were associated with higher WCC compared to other groups and class III obesity. A previous study has shown that patients with higher WCC are more likely to be admitted to the ICU, require ventilation and have underlying chronic illnesses and have higher mortality rates (Zhao et al., 2020). In fact, our study shows that class II obese patients had higher percentage of overall chronic disease compared to normal, overweight, classes I and III obese patients. Interestingly, the class III obese patients were mostly female whereas in the other groups a majority of the patients were male. In a study by Jin et al, it was shown that male COVID-19 patients are at increased risk of developing severe complications due to SARS-CoV-2 infection compared to female patients (Jin et al., 2020). It has been suggested that the distribution of fat in women may explain why obesity is not an independent risk factor in female patients. This was shown in a retrospective cohort study in a large integrated healthcare organization in Southern California where female COVID-19 patients had no increased risk of death in association with BMI (Tarfof et al., 2020). Moreover, a study on the distribution of fat in relation to COVID-19 severity showed that visceral adipose tissue and upper abdominal circumference significantly increase the severity of COVID-19 (Petersen et al., 2020).

However, when our COVID-19 patients were categorized into overweight, normal, overweight, obese class I, class II and class III, we noted that most COVID-19 patients were in the overweight

| Table 3 |
| --- |
| Clinical outcomes of COVID-19 patients with and without comorbidities. Patients were divided according to the average BMI among the cohort (29 kg/m²). Category A patients have a BMI < 29 kg/m² and category B patients ≥ 29 kg/m². Abbreviation: ARDS: Acute respiratory distress syndrome. |
| Illness severity | Chronic medical history |  |
| --- | --- | --- |
| No | Category A (BMI < 29 kg/m²) | Category B (BMI ≥ 29 kg/m²) | Pearson Chi Square | Yes | Category A (BMI < 29 kg/m²) | Category B (BMI ≥ 29 kg/m²) | Pearson Chi Square |
| Count | % | Count | % |  |
| Mild to Moderate | No | 48 | 6.50 | 21 | 44.70 | 0.19 |  |
| | Yes | 37 | 43.50 | 26 | 55.30 | 0.32 |  |
| Severe | No | 43 | 50.00 | 28 | 59.60 | 0.52 |  |
| | Yes | 42 | 49.40 | 19 | 40.40 | 0.32 |  |
| Critical | No | 79 | 92.90 | 45 | 95.70 | 0.52 |  |
| | Yes | 7 | 7.10 | 2 | 3.30 | 0.02 |  |
| Admission to intensive care unit | No | 79 | 92.90 | 44 | 93.60 | 0.88 |  |
| | Yes | 7 | 7.10 | 3 | 0.60 | 0.23 |  |
| Ventilated | No | 83 | 97.65 | 45 | 95.74 | 0.45 |  |
| | Yes | 2 | 2.35 | 1 | 0.25 | 0.005 |  |
| ARDS | No | 78 | 91.76 | 45 | 95.74 | 0.38 |  |
| | Yes | 7 | 8.24 | 2 | 4.26 | 0.02 |  |
| Death | No | 84 | 98.82 | 45 | 95.74 | 0.25 |  |
| | Yes | 1 | 1.18 | 2 | 4.26 | 0.005 |  |
category. Although there was no significant difference between COVID-19 outcomes and BMI, there was trend towards an increase in ARDS risk among overweight, class I and class II obese patients. It is for that reason that we further classified the patients in relation to the average BMI which is close to the cutoff for obesity. This is an interesting finding as being overweight is not classified as obese although often the terms are used interchangeably. It would seem that among the UAE patients most patients were overweight which follows the trend of the general population where 43% of expatriates are classified as overweight compared to 32% which are classified as obese (Sulaiman et al., 2017). In fact, in the context of ARDS, it has been shown that obesity and morbid obesity are associated with lower mortality (Ni et al., 2017). Our data show that class III obese patients are not at increased risk of developing ARDS. Due to this, it has been questioned whether the “obesity paradox” may be validated (or invalidated) in COVID-19 where ARDS. Due to this, it has been questioned whether the “obesity paradox” may be validated (or invalidated) in COVID-19 where obese individuals, due to the chronic inflammation which may confer a protective environment, may be protected against severe outcomes of the disease (Jose and Manuel, 2019). Further investigations need to be done to conclude this theory.

5. Conclusion

The absence of an association between BMI and parameters such as severity, admission to ICU and death highlight the importance of other factors such as the presence of co-morbidities in infected patients in the UAE. Interestingly, this study sheds light on the association between overweight/obese category and co-morbidities and emphasizes the need to monitor these patients although most attention has been focused on the obese and morbidly obese patients. Moreover, it is the first study on the association between BMI/co-morbidities in the MENA region. A limitation of this study is that only hospitalized patients were included, and it would be of interest to evaluate the association between BMI and hospitalization risk and outcomes in outpatients.

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Author contribution

All authors contributed equally to the data collection, analysis, manuscript preparation.

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