Role of body mass index in outcomes of patients hospitalized with COVID-19 illness

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Abstract

Background: Since the start of coronavirus disease 2019 (COVID-19) pandemic, several studies have linked obesity with severity of illness as well as mortality in patients with COVID-19. Outcomes of patients with overweight or obesity, who develop critical illness, have been studied extensively over the past decade where the studies have shown conflicting results. In this study, we aimed to assess the association between the body mass index (BMI) classes and outcomes among hospitalized patients with COVID-19.

Methods: This was a retrospective chart review of all adults admitted to our hospital with COVID-19 illness between 1 March 2020 and 30 June 2020. Patients were divided into four groups based on their BMI range as follows: patients with underweight (BMI < 18.5 kg/m²), patients with normal weight (BMI 18.5–24.9 kg/m²), patients with overweight (BMI 25–29.9 kg/m²), and patients with obesity (BMI ≥ 30 kg/m²).

Results: 1274 patients were admitted during the study period. There were 24 (1.9%) patients with underweight, 268 (21%) patients with normal weight, 445 (34.9%) patients with overweight, and 537 (42.2%) patients with obesity. Patients with obesity were younger (p < 0.001) and there were more females among patients with underweight and patients with obesity (54% and 48% respectively, p < 0.001). There were no differences in subgroup with regards to presence of hypertension, diabetes mellitus, coronary artery disease, congestive heart failure, and dyslipidemia. In a multivariate logistic regression model, patients with overweight and patients with obesity had higher odds of requiring mechanical ventilation. BMI class was not associated with difference in survival time in a multivariate analysis.

Conclusions: In our large single-center study of hospitalized patients with COVID-19, patients with overweight and obesity had higher need for mechanical ventilation but had similar mortality when compared to patients with normal weight and underweight.
1 | INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and remains a significant challenge worldwide to this date. Recently published data from World Health Organization (WHO) showed that during the week of 24–30 January 2022, over 22 million new cases and over 59,000 deaths were attributed to COVID-19.\(^1\) Many hospitalized patients with COVID-19 disease have comorbidities and several studies have shown that patients with obesity and underlying comorbidities have higher risk of severe COVID-19 illness.\(^2\)\(^-\)\(^6\) In a report published by Centers for Disease Control and Prevention of 148,494 U.S. adults in March 2021, patients with overweight and obesity had higher risk for invasive mechanical ventilation whereas only patients with obesity had higher risk of mortality.\(^7\) Outcomes of critically ill patients with overweight or obesity have been of significant debate in the pre-COVID era. A retrospective study of 504 mechanically ventilated patients with obesity showed that there was no difference in outcomes.\(^8\) Another study of 3902 patients admitted to 24 intensive care units (ICUs) found that patients with overweight and obesity had a reduced risk of ICU death.\(^9\)

More recent meta-analyses have also suggested lower mortality in septic patients with overweight whereas for septic patients with obesity mortality was similar to septic patients with normal weight.\(^10\) Another meta-analysis showed lower mortality in patients with obesity.\(^11\)

Body mass index (BMI) of $\geq 30$ kg/m\(^2\) has been shown to be associated with overall lower life expectancy.\(^12\)\(^-\)\(^13\) Association of BMI with outcomes in COVID-19 patients is of great significance due to its significant prognostic and therapeutic implications. While the data in COVID-19 largely points to association of higher BMI with adverse outcomes, the exact mechanisms behind this association is a matter of ongoing research. From an anatomical perspective, obesity causes reductions in functional residual capacity, expiratory reserve volume, respiratory system compliance, and impaired respiratory system mechanics that lead to a restrictive ventilatory defect.\(^14\) Adipose tissue is known to be metabolically active, and when present in excess, can be associated with a cluster of derangements referred to as metabolic syndrome. SARS-CoV-2 may also augment peri-organ fat inflammation and potentiate vital organ damage. It has been postulated that the proinflammatory milieu in individuals with metabolic syndrome is what drives the progression to severe COVID-19 disease.\(^15\)

Similarly, COVID-19 patients with underweight have also shown to have varied response. A retrospective study showed the patients with underweight are at risk of mechanical ventilation and death from COVID-19\(^16\) whereas another study did not show any association of patients with underweight and severity of illness.\(^17\) A more recent study showed that patients with underweight, overweight, and grade 3 obesity were at higher risk of COVID-19 related mortality compared to patients with grade I or grade II obesity.\(^18\) On the other hand a French study of 1461 critically ill patients with COVID-19 showed mortality was higher in patients with obesity class III (BMI $\geq 40$ kg/m\(^2\)).\(^19\)

In this study, we examined the association between the BMI classes (patients with underweight [BMI $< 18.5$ kg/m\(^2\)], patients with normal weight [BMI 18.5–24.9 kg/m\(^2\)], patients with overweight [BMI 25–29.9 kg/m\(^2\)], and patients with obesity [BMI $\geq 30$ kg/m\(^2\)]) and outcomes among patients hospitalized with COVID-19 in our inner-city patient population.

2 | SUBJECTS, MATERIALS, AND METHODS

We conducted this study at Bronx Care Health System, which is a large not-for-profit health system in the Bronx borough of New York City. We conducted a retrospective chart review of all adults admitted with COVID-19 illness between 1 March 2020 and 30 June 2020 using data extraction form. COVID-19 was diagnosed based on positive polymerase chain reaction (PCR) analysis of nasopharyngeal swab at any point during their hospitalization. Patients were divided into four groups based on their BMI range as follows: patients with underweight (BMI under 18.5 kg/m\(^2\)), patients with normal weight (BMI 18.5–24.9 kg/m\(^2\)), patients with overweight (BMI 25–29.9 kg/m\(^2\)), and patients with obesity (BMI $\geq 30$ kg/m\(^2\)). Need for consent was waived due to retrospective nature of the study. The study was approved by the institutional review board at Bronx Care Health System, Bronx, New York (IRB#09102005).

3 | PARTICIPANTS AND ELIGIBILITY CRITERIA

Our study included adult patients (aged 18 and above) who were hospitalized with COVID-19 illness. During the study period, an inpatient guide for the management of COVID-19 was developed by the Department of Medicine. Our patients received supportive and therapeutic modalities based on individual physician's clinical discretion, our inpatient guide and best available evidence at that time. Data extraction was done from the electronic medical records. The data obtained included patients' demographics, comorbidities, self-reported symptoms at presentation; admission labs, therapeutic modalities received during hospitalization, baseline laboratory findings, and final disposition. Study outcomes were need for mechanical ventilation and hospital survival.
Continuous normally distributed variables were reported using means and standard deviation. They were compared between the groups using t-test. If the normality was not met the rank Kruskal-Wallis test was applied instead. Equality of variances was tested using Levene’s test. Continuous not normally distributed variables were reported using median, first and third quartile (Q1 and Q3). Normality was assessed using Shapiro-Wilk test. Categorical variables were compared using Chi-squared test. We studied total survival time and the need of mechanical ventilation. These two outcomes were first compared between four BMI groups using log-rank test and univariate logistic regression model. Then multivariate models were built for each outcome, Cox for the hazard of death and the multivariate logistic regression model for the mechanical ventilation binary response. For the logistic regression the receiver operator curve (ROC) was plotted and the area under the curve was calculated in order to assess the prediction ability of the model. Final models were obtained using stepwise backward procedure with p-value for removal >0.1. Only the results significant at 0.05 levels are interpreted. The proportion-hazard assumption in a Cox final model was tested using Schoenfeld residuals.

5 | RESULTS

A total of 1274 patients were admitted to the hospital during the study period. Of these 24 (1.9%) patients had underweight, 268 (21%) patients had normal weight, 445 (34.9%) patients had overweight, and 537 (42.2%) had obesity (Table 1). Patients with obesity were younger (median age 60) compared to patients with underweight (median age 68), normal weight (median age 68), and overweight (median age 66; p = <0.001). Patients with underweight and obesity had higher percentage of females (54% and 48%, respectively) compared to patients with normal weight (36%) and overweight (30%). There were no differences in subgroups regarding presence of hypertension, diabetes mellitus, coronary artery disease, congestive heart failure, and dyslipidemia. Patients with underweight had higher prevalence of obstructive airway disease (OAD; 33% vs. 21% in patients with normal weight; 15% in patients with overweight; and 23% in patients with obesity; p = 0.008) and infection with human immunodeficiency virus (HIV; 33% vs. 11% in patients with normal weight, 6% in patients with overweight, and 4% in patients with obesity; p = 0.008), hepatitis B infection (HBV; 8% vs. 0% in patients with normal weight, 0.2% in patients with overweight, and 0.5% in patients with obesity; p = 0.008), and hepatitis C infection (HCV; 16% vs. 5% in patients with normal weight, 5% in patients with overweight, and 2% in patients with obesity; p = 0.008). There were more patients with obesity and overweight who never smoked (74% patients with obesity, 73% patients with overweight, 65% patients with normal weight, and 63% patients with underweight; p = 0.028). Regarding presenting symptoms, patients with overweight and obesity were more likely to present with fever, cough, and shortness of breath whereas abdominal discomfort/pain was a more common presenting symptom in patients with underweight. When comparing the admission laboratory findings, there was no difference in the four groups when comparing white blood cell count, absolute neutrophil count (ANC), serum lactate dehydrogenase (LDH) level, C-reactive protein (CRP) levels, and hemoglobin A1C levels. Serum creatinine levels were highest in patients with underweight (1.4 mg/dl, inter-quartile range [IQR] 0.95–4.22) compared to patients with normal weight (1.3 mg/dl, IQR 0.9–2.2), patients with overweight (1.1 mg/dl, IQR 0.9–1.9), and patients with obesity (1.1 mg/dl, IQR 0.8–1.7; p = 0.002). Absolute lymphocyte count (ALC) was lower and ANC/ALC ratio was higher in patients with underweight (ratios in median: 11.6 in patients with underweight, 7.83 in patients with normal weight, 7.27 in patients with overweight, and 6.37 in patients with obesity; p = <0.001). Similarly, D-dimer levels were higher in patients with underweight (798 ng/ml, IQR 622.5–2384.5) compared to patients with normal weight (745 ng/ml, IQR 339.3–2129.5), patients with overweight (493.5 ng/ml, IQR 283–1235.3), and patients with obesity (478 ng/ml, IQR 288–977; p < 0.001). There were no statistically significant differences between the groups with regards to therapeutic interventions including systemic steroids, anti-coagulation, remdesivir, convalescent plasma, tocilizumab, hydroxychloroquine, antiretrovirals, antibiotics, oseltamivir, and mechanical ventilation use.

6 | NEED FOR MECHANICAL VENTILATION

In a univariate logistic regression model for mechanical ventilation with the BMI groups, patients with overweight had higher odds of mechanical ventilation compared to the patients with underweight (odds ratio [OR] 3.968, 95% confidence interval [CI] 1.1656–13.5097, p = 0.027; Table 2). Similarly, patients with obesity also had higher odds of mechanical ventilation compared to patients with underweight (OR 3.77, 95% CI 1.1103–12.8061, p = 0.033). This outcome was not statistically different when patients with normal weight and patients with underweight were compared with each other. In a multivariate logistic regression model, patients with overweight (OR 1.811, 95% CI 1.1632–2.8195, p = 0.009) and patients with obesity (OR 1.7459, 95% CI 1.1425–2.6678, p = 0.01) had higher odds of mechanical ventilation (Table 3). Among the comorbid conditions, diabetes mellitus (OR 2.1378, 95% CI 1.5563–2.9366, p-value = 0.000) and end-stage renal disease (OR 2.0661, 95% CI 1.1337–3.7652, p-value 0.018) were associated with need for mechanical ventilation. Among the laboratory parameters, higher CRP levels (OR 1.0036, p-value 0.000, 95% CI 1.002–1.0051), higher serum LDH levels (OR 1.0008, p-value 0.000, 95% CI 1.0004–1.0013), and lower ALC levels (OR 0.6191, p-value 0.003, 95% CI 0.4494–0.8528) were associated with need for mechanical ventilation. Odds for requiring mechanical ventilation were also higher in patients using systemic steroids, anticoagulation, hydroxychloroquine, and were lower in patients who received tocilizumab. ROC for final logistic regression was 0.7925.
TABLE 1 Baseline demographic, clinical, and laboratory variables comparison with respect to BMI groups

|                          | All patients N = 1274 | Patients with overweight N = 445 | Patients with normal weight N = 268 | Patients with underweight N = 24 | p-value |
|--------------------------|-----------------------|---------------------------------|------------------------------------|----------------------------------|---------|
| Age median (IQR)         | 64 (53–73)            | 68 (57–78)                      | 66 (56–75)                         | 60 (48–70)                       | <0.001  |
| Sex (females) N (%)      | 502 (39%)             | 13 (54%)                        | 97 (36%)                           | 135 (30%)                        | <0.001  |
| Race/ethnicity N (%)     |                       |                                 |                                    |                                  |         |
| Black                    | 354 (28%)             | 12 (50%)                        | 84 (31%)                           | 101 (23%)                        | 0.030   |
| White                    | 20 (2%)               | 0                               | 4 (1%)                             | 4 (1%)                           |         |
| Asian                    | 2 (0.3%)              | 0                               | 0                                  | 2 (0.4%)                         |         |
| Hispanics                | 779 (60%)             | 11 (46%)                        | 150 (56%)                          | 298 (67%)                        |         |
| Others                   | 119 (9%)              | 1 (4%)                          | 30 (11%)                           | 42 (9%)                          |         |
| BMI median (IQR)         | 28.7 (25.16–33.5)     | 17.6 (16.7–18.1)                | 22.66 (21.11–23.94)                | 27.41 (26.18–28.5)               | <0.001  |
| Baseline comorbidities N (%) |                    |                                 |                                    |                                  |         |
| Hypertension             | 790 (62%)             | 17 (71%)                        | 174 (65%)                          | 257 (58%)                        | 0.166   |
| Diabetes mellitus        | 585 (46%)             | 6 (25%)                         | 125 (47%)                          | 204 (46%)                        | 0.367   |
| Hyperlipidemia           | 561 (44%)             | 12 (50%)                        | 130 (49%)                          | 194 (43%)                        | 0.314   |
| Obstructive airway disease | 259 (20%)           | 8 (33%)                         | 57 (21%)                           | 69 (15%)                         | 0.008   |
| Congestive heart failure | 124 (10%)             | 0                               | 27 (10%)                           | 35 (8%)                          | 0.099   |
| Coronary artery disease  | 137 (11%)             | 1 (4%)                          | 28 (10%)                           | 49 (11%)                         | 0.753   |
| HIV infection            | 86 (7%)               | 8 (33%)                         | 30 (11%)                           | 26 (6%)                          | <0.001  |
| Hepatitis B infection    | 6 (0.5%)              | 2 (8%)                          | 0                                  | 1 (0.2%)                         | <0.001  |
| Hepatitis C infection    | 56 (4%)               | 4 (16%)                         | 15 (5%)                            | 25 (5%)                          | 0.001   |
| End stage renal disease  | 84 (6%)               | 2 (8%)                          | 30 (11%)                           | 20 (4%)                          | 0.005   |
| Tobacco                  |                       |                                 |                                    |                                  |         |
| Never                    | 831 (72%)             | 12 (63%)                        | 154 (65%)                          | 296 (73%)                        | 0.028   |
| Active                   | 157 (13%)             | 4 (21%)                         | 47 (20%)                           | 42 (10%)                         |         |
| Past                     | 171 (15%)             | 3 (16%)                         | 36 (15%)                           | 65 (16%)                         |         |
| Presenting symptoms N (%) |                    |                                 |                                    |                                  |         |
| Fever                    | 775 (61%)             | 9 (37%)                         | 146 (54%)                          | 271 (61%)                        | 0.003   |
| Cough                    | 799 (63%)             | 11 (46%)                        | 139 (52%)                          | 282 (63%)                        | <0.001  |
| Shortness of breath      | 843 (66%)             | 14 (58%)                        | 160 (60%)                          | 293 (66%)                        | 0.026   |
| Abdominal discomfort/pain| 399 (31%)             | 10 (42%)                        | 86 (32%)                           | 156 (35%)                        | 0.045   |
| Diarrhea                 | 163 (13%)             | 2 (8%)                          | 26 (10%)                           | 57 (13%)                         | 0.249   |
| Baseline labs median (IQR) |                |                                 |                                    |                                  |         |
| White blood cell count (K/μl) | 7.7 (5.6–10.3) | 8.15 (5.8–8.77)                | 7.8 (5.4–11.2)                     | 7.5 (5.5–10.2)                   | 0.171   |
| Absolute neutrophil count (K/μl) | 6.1 (4.1–8.5) | 6.9 (4.57–17.3)                | 6.1 (4–9.4)                        | 6.1 (3.8–8.5)                    | 0.137   |
| Absolute lymphocyte count (K/μl) | 0.9 (0.6–1.2) | 0.8 (0.42–1.1)                 | 0.8 (0.5–1.2)                      | 0.8 (0.5–1.1)                    | <0.001  |

(Continues)
TABLE 1 (Continued)

| Variable                                | All patients N = 1274 | Patients with overweight N = 35 | p-value |
|-----------------------------------------|-----------------------|---------------------------------|---------|
| ANC/ALC ratio                           | 6.92 (4.33–12)        | 7.10 (4.5–14.5)                 | 0.001   |
| Serum creatinine (mg/dl)                | 1.2 (0.9–2)           | 1.3 (0.9–2)                     | 0.002   |
| D-dimer (ng/ml)                         | 527 (297.8–1329)      | 745 (339.3–2129.5)              | <0.001  |
| Serum LDH (μ/L)                         | 484 (343–702)         | 487 (332.5–653.75)              | 0.808   |
| C-reactive protein (mg/L)               | 112 (57.17–190.47)    | 107.8 (50.6–184.45)             | 0.894   |
| Serum ferritin (ng/ml)                  | 756.05 (367.2–1420.5) | 880.95 (493.75–1596)            | <0.001  |
| Hemoglobin A1c (%)                      | 6.6 (5.8–8.55)        | 6.3 (5.6–9.2)                   | 0.277   |

Therapeutics and interventions

| Hydroxychloroquine                       | 957 (75%)             | 198 (74%)                       | 0.643   |
| Anti-HIV                                 | 114 (9%)              | 26 (10%)                       | 0.880   |
| Antibiotics                              | 1209 (95%)            | 260 (97%)                      | 0.238   |
| Oseltamivir                              | 1137 (89%)            | 237 (88%)                      | 0.250   |
| Remdesivir                               | 11 (1%)               | 3 (1%)                         | 0.890   |
| Convalescent plasma                      | 32 (2%)               | 3 (1%)                         | 0.302   |
| Systemic steroids                        | 488 (38%)             | 88 (33%)                       | 0.137   |
| Anticoagulation                          | 777 (61%)             | 151 (56%)                      | 0.338   |
| Tocilizumab                              | 112 (9%)              | 17 (6%)                        | 0.106   |
| Needs for mechanical ventilation         | 435 (34%)             | 83 (31%)                       | 0.066   |

Abbreviations: ALC, absolute lymphocyte count; ANC, absolute neutrophil count; HIV, human immunodeficiency virus; IQR, interquartile range; LDH, lactate dehydrogenase; SE, standard error.

TABLE 2 Univariate logistic regression model for mechanical ventilation with the BMI group (group 1 = patients with underweight, group 2 = patients with normal weight, group 3 = patients with overweight, group 4 = patients with obesity)

| Variable                                | OR        | SE        | p-value | 95% CI |
|-----------------------------------------|-----------|-----------|---------|--------|
| Group 2 versus 1                         | 3.1405    | 1.9822    | 0.070   | 0.9114–10.8212 |
| Group 3 versus 1                         | 3.968     | 2.4803    | 0.027   | 1.1656–13.5097 |
| Group 4 versus 1                         | 3.7707    | 2.352     | 0.033   | 1.1103–12.8061 |
| Constant                                 | 0.1428    | 0.0881    | 0.002   | 0.0426–0.47893 |

Abbreviations: OR, odds ratio; SE, standard error.

7 | SURVIVAL ANALYSIS

Kaplan–Meier survival estimates were obtained by the BMI groups, which showed no statistically significant difference between the groups (p = 0.7746; Figure 1). In the multivariate cox model for total survival time, BMI class was not associated with difference in survival time. HIV was the only comorbid condition that was associated with increased risk of death (hazard ratio [HR] 1.5304, p = 0.03, 95% CI 1.0417–2.2483; Table 4). Among the laboratory parameters, higher ANC/ALC ratio (HR 1.014, p = 0.002, 95% CI 1.0051–1.0231), higher serum LDH (HR 1.0002, p = 0.003, 95% CI 1.0001–1.0002), higher serum creatinine (HR 1.0375, p = 0.015, 95% CI 1.0072–1.0688), and higher D-dimer levels (HR 1.00001, p = 0.002, 95% CI 1.0001–1.0002) were associated with increased risk of death. With regards to the therapeutic interventions, systemic steroids (HR 0.4583, p = 0.000, 95% CI 0.353–0.595), convalescent plasma (HR 0.3723, p = 0.002, 95% CI 0.1969–0.7038), anticoagulation (HR 0.6482, p = 0.002, 95% CI 0.4916–0.8546), antiretrovirals (HR 0.6016, p = 0.016, 95% CI 0.3973–0.9109), and antibiotics use (HR 0.4449, p = 0.013, 95% CI 0.2339–0.8546) were associated with lower risk of death whereas remdesivir use was associated with higher risk of death (HR 2.3803, p = 0.036, 95% CI 1.0575–5.3577). Patients requiring mechanical ventilation also had higher risk of death (HR 7.2546, p < 0.001, 95% CI 5.4257–9.7002).
We performed additional Kaplan–Meier survival analyses among the subgroup of patients with obesity. When we compared the survival estimates for patients with BMI ≥ 30–39.9 (class I and II obesity) with patients BMI ≥ 40 (class III obesity), there was no statistically significant difference in this outcome (log-rank p = 0.6586; Figure 2). We also compared survival in patients with BMI ≥ 30–34.9 (class I obesity) to patients with BMI ≥ 40 (class III obesity) and there was no significant difference in this outcome between the two groups (log-rank p = 0.7331; Figure 3).

**TABLE 3** Estimates from logistic regression for need of mechanical ventilation

| Variable                        | OR  | SE  | p-value | 95% CI          |
|---------------------------------|-----|-----|---------|-----------------|
| Patients with overweight       | 1.811 | 0.4090 | 0.009  | 1.1632–2.8195  |
| Patients with obesity          | 1.7459 | 0.3776 | 0.01   | 1.1425–2.6678  |
| Diabetes mellitus              | 2.1378 | 0.3462 | 0.000  | 1.5563–2.9366  |
| Tobacco use                    | 1.9147 | 0.4477 | 0.005  | 1.2107–3.0281  |
| End-stage renal disease        | 2.0661 | 0.6326 | 0.018  | 1.1337–3.7652  |
| C-reactive protein             | 1.0036 | 0.0007 | 0.000  | 1.002–1.0051   |
| Lactate dehydrogenase          | 1.0008 | 0.0002 | 0.000  | 1.0004–1.0013  |
| Absolute lymphocyte count      | 0.6191 | 0.1011 | 0.003  | 0.4494–0.8528  |
| Systemic steroids              | 3.8527 | 0.6749 | 0.000  | 2.733–5.4311   |
| Therapeutic anticoagulation    | 1.7956 | 0.3282 | 0.001  | 1.2549–2.5693  |
| Tocilizumab                    | 0.414 | 0.1086 | 0.001  | 0.2476–0.6924  |
| Hydroxychloroquine             | 2.5671 | 0.5856 | 0.000  | 1.6414–4.0146  |
| Constant                       | 0.0231 | 0.0091 | 0.000  | 0.0107–0.0499  |

Abbreviations: OR, odds ratio; SE, standard error.

**FIGURE 1** Kaplan–Meier survival estimates by BMI class (p = 0.7746). X-axis depicts time in days. Y-axis depicts survival probability.

**8** | **DISCUSSION**

In our inner-city patient population, which consists primarily of ethnic minority patients, our study showed that patients with overweight and obesity who developed COVID-19 illness were more likely to require mechanical ventilation whereas there was no difference between the various BMI subclasses with regards to survival. Similarly, there was no difference in survival between subclasses of patients with obesity. Our survival data is in contrast with most of the published data associating various BMI subclasses with survival...
This page contains statistical data and graphs that illustrate the relationship between BMI and survival in COVID-19 patients. The Kaplan-Meier survival curve shows survival probability over time for different BMI categories. The table presents a multivariate Cox model for total survival time, listing variables such as HIV status, ANC/ALC ratio, and serum creatinine, along with their hazard ratios, standard errors, p-values, and 95% confidence intervals. Furthermore, it discusses the implications of obesity in COVID-19 patients, highlighting the hyperinflammatory cascade associated with obesity and its potential impact on clinical outcomes.

**TABLE 4 Multivariate Cox model for total survival time**

| Variable          | HR    | SE   | p-value | 95% CI             |
|-------------------|-------|------|---------|--------------------|
| Ethnicity-F       | 4.8324| 3.6005| 0.034   | 1.1219–20.8150     |
| HIV               | 1.5304| 0.3003| 0.03    | 1.0417–2.2483      |
| ANC/ALC ratio     | 1.014 | 0.0045| 0.002   | 1.0051–1.0231      |
| Serum LDH         | 1.0002| 0.0001| 0.003   | 1.0001–1.0002      |
| Serum creatinine  | 1.0375| 0.0156| 0.015   | 1.0072–1.0688      |
| D-dimer levels    | 1.00001| 4.29 \times 10^6| 0.002   | 1.0001–1.0002      |
| Systemic steroids | 0.4583| 0.061 | 0.000   | 0.353–0.595        |
| Convalescent plasma | 0.3723| 0.1209| 0.002   | 0.1969–0.7038      |
| Anticoagulation   | 0.6482| 0.0914| 0.002   | 0.4916–0.8546      |
| Antiretroviral use| 0.6016| 0.1273| 0.016   | 0.3973–0.9109      |
| Remdesivir        | 2.3803| 0.9853| 0.036   | 1.0575–5.3577      |
| Antibiotics       | 0.4449| 0.1458| 0.013   | 0.2339–0.8546      |
| Mechanical ventilation | 7.2546| 1.0752| <0.001  | 5.4257–9.7002      |

**FIGURE 2** Kaplan-Meier survival curve by between patients with BMI ≥ 30–39.9 and patients BMI ≥ 40 BMI (p = 0.6586). X-axis depicts time in days. Y-axis depicts survival probability.

**FIGURE 3** Kaplan-Meier survival curve by between patients with BMI ≥ 30–34.9 and patients with BMI ≥ 40 BMI (p = 0.7331). X-axis depicts time in days. Y-axis depicts survival probability.

Abbreviations: ALC, absolute lymphocyte count; ANC, absolute neutrophil count; F, female; HR, hazard ratio; HIV, human immunodeficiency virus; LDH, lactate dehydrogenase; SE, standard error.
COVID-19 in England, patients with BMI of more than 23 kg/m² had increased risk of severe disease leading to hospital admission and death. A Korean study also reported that patients with BMI < 18.5 and with BMI 25 and above had high risk of COVID-19 related fatal illness. Our study findings are in contrast with these observations.

Another significant finding of our study is the presence of co-morbid conditions among different BMI subgroups. As opposed to the common association of obesity with diabetes mellitus and cardiac abnormalities, in our study population, there were no differences in BMI subgroups with regards to presence of hypertension, diabetes mellitus, coronary artery disease, congestive heart failure, and dyslipidemia. Obesity is a risk factor for asthma, but in our study underweight patients had higher incidence of OAD. HIV incidence was higher in patients with BMI < 30 kg/m² and similar observations have been identified in prior literature. Our study also noted a higher incidence of HBV and HCV infections in patients with overweight who developed COVID-19, a finding that has not been widely reported in the literature.

Among the laboratory parameters, a notable finding was incidence of higher serum creatinine in patients with overweight. Similar observation was reported by Jayanama and colleagues in their study of 147 patients with COVID-19 stratified by BMI. However, contrary to Jayanama study, the serum creatinine levels were lower in patients with obesity in our study. Acute kidney injury in patients with COVID-19 has been proposed to be multifactorial including direct injury from the virus, pre-renal azotemia, tubular injury, and thrombotic microangiopathy. We also observed that patients with underweight who had lower ALC levels, higher ANC/ALC ratio, and higher D-dimer levels were at increased risk of adverse outcomes. These parameters have been previously linked with adverse outcomes in patients with COVID-19.

Our study data linking use of systemic steroids with improved survival is in line with RECOVERY trial data. Similarly, our study also noted an improved survival with use of tocilizumab which is also similar to the RECOVERY trial data. Contrary to recently published data from CONCOR-1 trial, our study patients also showed improved survival with use of convalescent plasma. Other COVID-specific treatment related notable findings were association of increased survival with anticoagulation use and of decreased survival with use of remdesivir.

Our study has several limitations. Our findings have limited generalizability due to specific patient population in our study. While we noted higher use of mechanical ventilation in patients overweight and obesity, this could be due to clinical bias toward earlier intervention in this subgroup and not just related to the severity of COVID-19. While we collected information about therapeutic interventions including mechanical ventilation, we did not collect information about use of supplemental oxygen, high flow oxygen, and non-invasive positive pressure ventilation. This could limit the ability to stratify the severity of illness and subsequent adjustment in the multivariate analysis.

9 CONCLUSION

In our large single-center study of hospitalized COVID-19 patients, patients with overweight and obesity had higher need for mechanical ventilation when compared to patients with normal weight and underweight. Patients with underweight were more likely to have higher serum creatinine and should be closely watched for development of acute kidney injury.

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CONFLICT OF INTEREST

We have no conflict of interest to disclose.

INFORMED CONSENT STATEMENT

Patient consent was waived due to retrospective nature of the study. No identifiable patient information is presented in this study.

AUTHOR CONTRIBUTIONS

Maleeha Zahid, Vivien Leung, and Sridhar Chilimuri designed the study. Maleeha Zahid, Nikitha Mantri, Haozhe Sun, and Sudharsan Gongati collected the data. Maleeha Zahid, Vivien Leung, Suresh Kumar Nayudu, Sneha Galiveeti, Vijaya Perugu, and Sridhar Chilimuri analyzed the data and wrote the manuscript. Maleeha Zahid, Vivien Leung, Suresh Kumar Nayudu, Sneha Galiveeti, Nikitha Mantri, Haozhe Sun, Sudharsan Gongati, Vijaya Perugu, and Sridhar Chilimuri revised the manuscript. All authors reviewed and approved the final version of the manuscript.

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