ORIGINAL RESEARCH

Body Mass Index as a Major Prognostic Contributing Factor in COVID-19: A Multicentral Egyptian Study

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Background: Extreme body mass index (BMI) is an influential pathophysiological risk factor for serious illnesses following lower respiratory tract infection. The purpose of the current study was to examine how the BMI of Coronavirus disease-19 (COVID-19) patients affects their prognosis.

Methods: Two hundred patients with COVID-19 admitted to Al-Azhar, Qena, Aswan, and Sohag University hospitals in Egypt were included and categorized into four groups according to their BMI. The diagnosis was made according to a real-time reverse transcription-polymerase chain reaction (rRT-PCR) positive result for the SARS-CoV-2 nucleic acid in swabs from upper respiratory tract. A detailed history, clinical examination, and outcomes (disease severity and complications, hospital stay, ICU admission, mortality) were recorded for all patients. SPSS version 24 software was used for data analysis.

Results: Average age of participants (19–90 years old), 92 (46%) males and 108 females (54%). ICU admission was significantly higher among underweight patients (75%) and obese patients (78.6%). The majority of underweight (62.5%) and obese (57.1%) patients had critical disease. Invasive mechanical ventilation (MV) is frequently used in underweight (50%) and obese patients (42.9%) patients. Adult respiratory distress syndrome (ARDS), cardiac, neurological, and hematological complications, and incidence of myalgia and bed sores were most frequent among obese and overweight patients. Acute kidney injury was significantly higher among underweight patients (37.5%) and obese patients (28.6%) than among other classes (p=0.004). Frequency of endocrine complications was significantly higher in underweight patients than that in other classes (p=0.01). The majority of underweight (75%) and obese patients (50%) deteriorated and died, whereas the majority of normal-weight patients (90.3%) and overweight patients (75.8%) improved and were discharged (p<0.001).

Conclusion: Body mass index is a major contributing factor to the outcome of patients with COVID-19, and patients with extreme of body mass index were associated with the worst prognosis.

Keywords: body mass index, COVID-19, obese, underweight, intensive care unit

Introduction

In December 2019, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) first appeared. It spread quickly over the world. Wide-ranging symptoms of the coronavirus disease 2019 (COVID-19) can progress to more serious presentations such pneumonia and a number of non-respiratory consequences. Recently obesity has been linked to increased vulnerability to

5985

COVID-19 hospitalization and mortality. This is due to associated physiological disturbances in obese persons including low grade inflammation (with increased pro-inflammatory cytokines), dysregulated innate and adaptive immunologic, cardiovascular, neurologic, and endocrine systems.^{1–4} Additionally, the high adipose tissue expression of angiotensin- converting enzyme- 2(ACE-2) that used by SARS-CoV-2 for cell entry, making it acts as a reservoir for the virus.⁵

Increased risk of hospitalization and death from COVID-19 also being linked to underweight (BMI<18.5 kg/m²) due to the associated poor nutritional status, reduced muscle mass and associated hypoalbuminemia.^{5,6}

In Egypt, obesity is a serious epidemic issue. According to reports, 35.3% of Egyptian adults are obese.⁷ Obesity has serious mechanical damaging effects on respiratory system via altered pulmonary biomechanics, enhancing and worsening the airway hyperresponsiveness (AHR), narrowing and resistance, especially when lower respiratory tract infections are present.⁸

Obesity seems to increase the likelihood of respiratory complications, ICU hospitalization, and the need for mechanical ventilation.⁹ It is possible for COVID-19 to expose the airways in danger produce adult respiratory distress syndrome (ARDS), and lead to respiratory failure.^{10,11} As researches on the effect of BMI on COVID19 were controversial with few studies regarding Egyptian patients with COVID-19, so the purpose of this study was to look at how COVID-19 patients' BMI affected their clinical characteristics and prognosis among sample of Egyptian population.

Patients and Methods

Study Design and Participants

This observational study was conducted in Al-Azhar, Qena, Aswan, and Sohag University hospitals, Egypt, during the study period from November 2021 to May 2022. The study was approved by the local Ethics Committees of Faculties of Medicine, Al-Azhar, Qena, Aswan, and Sohag Universities (Ethical approval codes: MSR/ AZ.AST/ CHT019 18 218 4 2023; SVU-MED-GIT023-4-23-5-637) and was carried out in conformity with the principles outlined in the Helsinki Declaration. Clinically stable patients or the family members of critically ill patients provided written informed consent.

In total, 200 COVID-19 patients were included in this study. Depending on their BMI, the patients were categorized into four groups:¹² the underweight group (patients with a BMI < 18.5 kg/m²), normal group (patients with a BMI ranging between 18.5 and 24.9 kg/m²), overweight group (patients with a BMI between 25 and 29.9 kg/m²), and the obese group (patients with a BMI > 30 kg/m²).

Inclusion criteria: Patients of all ages were enrolled with laboratory-confirmed COVID-19; Positive result on the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) real-time reverse-transcriptase polymerase chain reaction (RT-PCR) assay of nasal and pharyngeal swab specimens served as the basis for laboratory confirmation.¹³ Patients with available clinical and initial CT findings at admission.

Exclusion criteria: Patients without clinical or CT records at admission.

Clinical Assessments

Demographic and clinical data of the patients involved in the study were recorded including history, comorbidities, age, body mass index (BMI), vital signs, clinical findings of chest, heart and abdominal examinations, therapeutic modalities, and outcomes.

The WHO—China Joint Mission on COVID-19 used an assessment of disease severity upon admission.¹⁴ In order to categorize COVID-19 patients, four categories were used: mild (laboratory-confirmed, without pneumonia), moderate (laboratory-confirmed, with pneumonia), severe (oxygen saturation \leq 93% at rest; dyspnea with a respiratory rate \geq 30 breaths/min and/or lung infiltrates \geq 50% of the pulmonary field within 24–48 h) and critical (respiratory failure requiring mechanical ventilation, shock, or other organ failure that requires intensive care.

Nutrition ratio index: Nutrition risk score (NRS) 2002,¹⁵ which formed of two parts. The first part (impaired nutritional status, which is determined by evaluating weight loss and BMI. The same remains true for the proportion of food consumed last week relative to needs. The rating scale ranges from 0 to 3, with 0 representing no degradation in health and 3 representing a serious decline in health). Second, patients may obtain 0–3 points for their disease severity (an increase in nutritional requirements), where 0 represents normal nutritional needs and 3 represents severe disease.

Laboratory Investigations

- (A) The diagnosis of COVID-19 disease in the included patients was made according to a real-time reverse transcription-polymerase chain reaction (rRT-PCR) positive result for the SARS-CoV-2 nucleic acid in nasal and pharyngeal swabs from upper respiratory tract using PCR-fluorescence probe diagnostic kit with catalog number S3102E supplied by Sansure Biotech Inc., China.
- (B) Blood samples were collected from patients and the following hematological and biochemical laboratory parameters were measured: Complete blood counts (CBC) using Cell Dyne-Ruby purchased from Abbott diagnostics, USA. Fasting blood glucose levels (using colorimetric assay kits) and HbA1c levels (Cobas c311, Hitachi device, Roche Diagnostics, Germany). The kidney (serum urea and creatinine) and liver [alanine aminotransferase (ALT), aspartate aminotransferase (AST), serum total bilirubin, and serum albumin] profiles were measured using an autoanalyzer (Dialab 450 system).C-reactive protein (using a semi-quantitative latex agglutination test), D-dimer (using an automated blood coagulation analyzer CS-1600, Japan), and ferritin [using a microplate ELISA reader (EMR-500, Labomed Inc., USA) using a commercially available ELISA assay kit]. Erythrocyte sedimentation rate (ESR): using ESR STAT 6 Sed Rate Analyzer from HemaTechnologies, USA. Lipid profiles, in the form of total cholesterol and triglycerides, were determined using enzymatic colorimetric techniques. Serum electrolytes in the form of sodium and potassium were measured using inductively coupled plasma mass spectrometry (ICP-MS; Thermo Scientific X-SERIES 2).

Radiological Assessments

Using chest X-ray and CT on each patient, each of the five lung lobes was visually rated from 0 to 5 as follows: No involvement (0), < 5% involvement (1), 25% involvement (2), between 26% and 49% involvement (3), between 50% and 75% involvement (4), and (5) if involvement over 75%.¹⁶

Statistical Analysis

The Statistical Package for Social Sciences (SPSS) version 24 software for Windows was used for data analysis. Numerical data are described in terms of means and standard deviations if normally distributed. The Kolmogorov–Smirnov test was used to test the normality of the distribution of the numerical variables. The chi-square test was used to test the association between categorical variables. Fisher's exact test was used when assumptions were violated. ANOVA test followed by post-hoc analysis was used to test the difference between different groups concerning parametric numerical variables. Predictors of mortality were determined by logistic regression analysis. P was set at p < 0.05.

Results

The current research has been conducted on 200 patients with COVID-19. Their age ranged between 19 and 90 years old with a mean of 59.73 ± 13.74 years old. More than half of included patients (54% of included patients, 108 patients) were females. Based on body mass index category, 16 (8%), 62 (31%), 66 (33%), and 56 (28%) patients were underweight, normal weight, overweight, and obese, respectively. Most of these patients were alive (69%), and 62 (31%) had deteriorated and died.

Patients with a normal BMI had a significantly lower mean age (53.39 years) than those in the other groups. The majority of patients in all BMI classes were male, with the exception of the majority (89.3%) of obese patients, who were female. In addition, underweight patients had a significantly higher frequency of smoking (37.5%) than other classes. Hypertension, diabetes mellitus, and liver disease were significantly frequent among obese patients (75%, 50%, and 17.9% respectively), whereas underweight patients had a significantly higher frequency of ischemic heart disease (37.5%) than other BMI classes. The incidence of chest diseases was significantly higher among underweight (37.5%) and obese patients (37.5%) (Table 1).

This study found that underweight and obese patients had significantly higher leukocyte (p=0.006), C-reactive protein (P=0.006), erythrocyte sedimentation rate (p=0.001), creatinine (p=0.002), glycosylated hemoglobin (P=0.002), and fasting blood sugar (p=0.002) levels than normal and overweight, (Table 2).

Table I Baseline Data of the Studied Patients Based on Body Mass Index

*Variables		Class of Body		**P value	***Subgroup	
	Underweight (n= 16)	Normal (n= 62)	Overweight (n= 66)	Obese (n= 56)		Analysis
Age (years)	68.13 ± 11.29	53.29 ± 15.12	62.06 ± 13.45	61.71 ± 9.97	< 0.001	P1< 0.001 P2=0.11 P3=0.09 P4=0.03 P5=0.04 P6=0.87
Sex (No.,%) • Male • Female	8 (50%) 8 (50%)	38 (61.3%) 24 (38.7%)	40 (60.6%) 26 (39.4%)	6 (10.7%) 50 (89.3%)	< 0.001	P1=0.11 P2=0.08 P3< 0.001 P4=0.09 P5< 0.001 P6< 0.001
Residence (No.,%) • Rural • Urban	12 (75%) 4 (25%)	30 (48.4%) 32 (51.6%)	32 (48.5%) 34 (51.5%)	40 (71.4%) 16 (28.6%)	0.01	P1=0.03 P2=0.03 P3= 0.34 P4=0.87 P5=0.04 P6=0.04
Smoking (No.,%)	6 (37.5%)	18 (29%)	18 (27.3%)	6 (10.7%)	0.04	P1=0.19 P2=0.22 P3= 0.04 P4=0.98 P5=0.01 P6=0.02
Diabetes mellitus (No.,%)	4 (25%)	14 (22.6%)	25 (37.5%)	28 (50%)	0.01	P1=0.76 P2=0.34 P3= 0.01 P4=0.38 P5=0.01 P6=0.06
Hypertension (No.,%)	6 (37.5%)	6 (9.7%)	24 (36.4%)	42 (75%)	< 0.001	P1< 0.001 P2= 0.18 P3< 0.001 P4=0.01 P5< 0.001 P6= 0.02
Chest diseases (No.,%)	6 (37.5%)	19 (30.6%)	21 (31.8%)	21 (37.5%)	< 0.001	P1=0.12 P2=0.09 P3= 0.65 P4=0.10 P5=0.12 P6=0.09

Table I (Continued).

*Variables		Class of Body	Mass Index		**P value	***Subgroup	
	Underweight (n= 16)	Normal (n= 62)	Overweight (n= 66)	Obese (n= 56)		Analysis	
Ischemic heart disease (No.,%)	6 (37.5%)	2 (3.2%)	5 (7.6%)	12 (21.4%)	< 0.001	P1 < 0.001 P2 < 0.001 P3 = 0.04 P4 = 0.45 P5 = 0.04 P6 = 0.05	
Chronic kidney disease (No.,%)	2 (12.5%)	2 (3.2%)	2 (3%)	6 (10.7%)	0.15	P1=0.45 P2=0.19 P3= 0.09 P4=0.10 P5=0.06 P6=0.07	
Liver disease (No.,%)	0	2 (3.2%)	3 (4.5%)	10 (17.9%)	< 0.001	P1=0.19 P2=0.22 P3= 0.04 P4=0.12 P5=0.05 P6=0.45	
Malignant lesions (No.,%)	0	2 (3.2%)	4 (6.1%)	2 (3.6%)	0.67	P1=0.19 P2=0.10 P3= 0.19 P4=0.98 P5=0.65 P6=0.09	
No comorbidities (No.,%)	2 (12.5%)	22 (35.5%)	14 (21.2%)	2 (3.6%)	< 0.001	P1< 0.001 P2=0.09 P3= 0.45 P4=0.04 P5=0.20 P6=0.04	

Notes: *Data expressed as frequency (percentage), mean (SD). **P value was significant if < 0.05 and indicates significance between the different groups. ***P1 compares between underweight and normal weight groups, P2 compares between underweight groups, P3 compares between underweight and obsess groups, P4 compares between normal and overweight groups, P5 compares between normal and obses groups, P6 compare between overweight and obses groups.

	Table 2	Clinical	and	Laboratory	Data	of	the	Studied	Patients	Based	on	Body	Mass	Index
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*Variables		Class of Boo	**P value	***Subgroup		
	Underweight (n= 16)	Normal (n= 62)	Overweight (n= 66)	Obese (n= 56)		Analysis
Cough	16 (100%)	56 (90.3%)	60 (90.9%)	54 (96.4%)	0.34	P1=0.09 P2=0.34 P3= 0.22 P4=0.45 P5=0.34 P6=0.40

Table 2 (Continued).

*Variables		Class of Bod		**P value	***Subgroup	
	Underweight (n= 16)	Normal (n= 62)	Overweight (n= 66)	Obese (n= 56)		Analysis
Dyspnea	16 (100%)	62 (100%)	64 (100%)	54 (96.4%)	0.44	P1=- P2=- P3=0.70 P4=- P5=0.70 P6=0.70
Sore throat	0	24 (38.7%)	22 (33.3%)	12 (21.4%)	0.009	PI < 0.001 P2=0.01 P3=0.03 P4=0.45 P5=0.09 P6=0.28
Fever	12 (75%)	50 (80.6%)	48 (72.7%)	38 (67.9%)	0.46	P1=0.13 P2=0.07 P3=0.34 P4=0.11 P5=0.14 P6=0.08
Diarrhea	2 (12.5%)	22 (35.5%)	14 (21.2%)	8 (14.3%)	0.03	P1=0.03 P2=0.13 P3=0.56 P4=0.06 P5=0.04 P6=0.18
Leucocytes (10/ul ³)	12.80 ± 7.26	8.35 ± 4.68	10.63 ± 6.21	11.15 ± 4.59	0.006	PI < 0.001 P2=0.13 P3=0.34 P4=0.10 P5=0.36 P6=0.08
Neutrophils (10/ul ³)	7.89 ± 5.67	5.55 ± 3.22	6.09 ± 2.39	7.87 ± 2.19	0.50	P1=0.22 P2=0.23 P3=0.44 P4=0.08 P5=0.09 P6=0.18
Lymphocytes (10/ul ³)	1.20 ± 0.14	0.89 ± 0.33	1.08 ± 0.09	1.11 ± 0.29	0.16	P1=0.20 P2=0.10 P3=0.45 P4=0.35 P5=0.22 P6=0.40

*Variables		Class of Bod		**P value	***Subgroup	
	Underweight (n= 16)	Normal (n= 62)	Overweight (n= 66)	Obese (n= 56)		Analysis
Hemoglobin (g/dl)	12.23 ± 2.08	11.93 ± 1.64	12.42 ± 2.63	11.95 ± 2.09	0.54	P1=0.10 P2=0.09 P3=0.99 P4=0.25 P5=0.56 P6=0.77
Platelets (10/ul ³)	241.12 ± 115.20	216.80 ± 93.30	229.90 ± 110.50	245.89 ± 109.34	0.50	P1=0.50 P2=0.55 P3=0.35 P4=0.23 P5=0.33 P6=0.12
C-reactive protein (mg/dl)	46.68 ± 34.13	29.07 ± 17.65	39.28 ± 22.34	55.85 ± 21.87	0.006	PI < 0.001 P2=0.09 P3=0.06 P4=0.06 P5< 0.001 P6=0.07
Erythrocyte sedimentation rate (mL/h)	60.87 ± 33.46	39.03 ± 26.85	51.96 ± 30.51	65.82 ± 29.54	0.001	P1 < 0.001 P2=0.44 P3 < 0.001 P4=0.09 P5 < 0.001 P6=0.04
Ferritin (ng/dl)	568.76 ± 399.29	514.27 ± 434.87	497.85 ± 444.56	648.98 ± 508.56	0.34	P1=0.67 P2=0.09 P3=0.87 P4=0.12 P5=0.22 P6=0.87
D-dimer (ng/mL)	2.67 ± 2.21	6.58 ± 2.45	2.11 ± 1.96	2.98 ± 2.10	0.29	P1=0.10 P2=0.20 P3=0.08 P4=0.56 P5=0.43 P6=0.21
Alanine transmarine (U/L)	27.87 ± 8.83	46.61 ± 39.41	47.30 ± 15.66	64.89 ± 17.45	0.57	P1=0.10 P2=0.09 P3=0.22 P4=0.08 P5=0.19 P6=0.06

*Variables		Class of Bod	Class of Body Mass Index							
	Underweight (n= 16)	Normal (n= 62)	Overweight (n= 66)	Obese (n= 56)		Analysis				
Aspartate transmarine (U/L)	36.37 ± 20.51	43.77 ± 20.76	41.22 ± 25.44	47.57 ± 15.98	0.83	P1=0.22 P2=0.45 P3=0.68 P4=0.19 P5=0.39 P6=0.65				
Bilirubin (mmol/l)	1.11 ± 0.51	1.03 ± 0.59	1.11 ± 0.95	1.17 ± 0.73	0.74	P1=0.09 P2=0.39 P3=0.19 P4=0.35 P5=0.98 P6=0.88				
Albumin (mg/dl)	3.35 ± 0.47	3.32 ± 0.49	3.11 ± 0.52	3.20 ± 0.57	0.39	P1=0.20 P2=0.39 P3=0.98 P4=0.10 P5=0.39 P6=0.54				
Creatinine (mg/dl)	2.31 ± 1.75	1.31 ± 0.63	1.50 ± 0.89	1.95 ± 0.83	0.002	PI< 0.001 P2< 0.001 P3=0.89 P4=0.90 P5=0.65 P6=0.32				
Urea (mg/dl)	62.12 ± 17.04	50.48 ± 33.37	51.34 ± 29.55	55.85 ± 34.76	0.50	P1=0.09 P2=0.39 P3=0.11 P4=0.76 P5=0.69 P6=0.08				
Glycosylated hemoglobin (%)	7.06 ± 2.89	6.36 ± 1.87	6.87 ± 2.27	8.04 ± 2.84	0.002	P1=0.11 P2=0.45 P3=0.08 P4=0.22 P5=0.003 P6=0.04				
Fasting blood sugar (mg/dl)	143.13 ± 67.74	116.58 ± 50.11	130.30 ± 52.02	161.03 ± 83.74	0.002	PI< 0.001 P2=0.13 P3=0.09 P4=0.07 P5< 0.001 P6=0.04				

Table	2	(Continued).
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*Variables	es Class of Body Mass Index							
	Underweight (n= 16)	Normal (n= 62)	Overweight (n= 66)	Obese (n= 56)		Analysis		
Cholesterol (mg/dl)	234.98 ± 34.56	223.76 ± 43.86	229.87 ± 29.08	235.55 ± 45.54	0.11	P1=0.18 P2=0.07 P3=0.45 P4=0.22 P5=0.07 P6=0.19		
Triglyceride (mg/dl)	145.76 ± 22.34	141.34 ± 32.45	144.87 ± 24.87	140.09 ± 23.23	0.45	P1=0.11 P2=0.12 P3=0.09 P4=0.19 P5=0.08 P6=0.18		
Sodium (mmol/l)	133.45 ± 0.45	131.13 ± 0.89	134.98 ± 1.80	132.34 ± 0.23	0.23	P1=0.26 P2=0.89 P3=0.09 P4=0.08 P5=0.57 P6=0.57		
Potassium (mmol/I)	4.61 ± 0.55	4.44 ± 0.32	4.65 ± 0.28	4.49 ± 0.21	0.09	P1=0.20 P2=0.49 P3=0.19 P4=0.18 P5=0.08 P6=0.12		

Notes: *Data expressed as frequency (percentage), mean (SD). **P value was significant if < 0.05 and indicates significance between the different groups. ***PI compares between underweight and normal weight groups, P2 compares between underweight groups, P3 compares between underweight and obsess groups, P4 compares between normal and overweight groups, P5 compares between normal and obese groups, P6 compare between overweight and obese groups.

There was a significant difference between BMI classes and plain radiographic findings. Normal radiographs were frequently found in those with a normal BMI (12.9%). Ground-glass opacity was frequently observed in underweight (75%), overweight (78.8%), and obese (100%) patients. Crazy paving was frequently observed in underweight (75%) and obese (60.7%) patients. In contrast, consolidation was frequently detected in patients with a normal BMI (51.6%). Regarding the CT score, a score-3 was frequently found in underweight patients (37.5%) and overweight patients (36.4%), a score-2 was frequently found in patients with normal BMI (35.5%) a score-5 was frequently detected in obese patients (28.6%). The nutrition ratio index did not significantly differ between the patients in terms of their BMI class (p > 0.05), (Table 3).

ICU admission was significantly higher among underweight (75%) and obese (78.6%) patients. Additionally, there was a significant disparity in disease severity and BMI groups, where the majority of underweight (62.5%) and obese (57.1%) patients had critical disease, whereas the majority of normal-weight (48.4%) and overweight (57.6%) patients had severe disease. The majority of underweight patients (75%) and obese patients (50%) deteriorated and died, whereas the majority of normal-weight patients (75.8%) improved and were discharged (Table 4).

There were significant differences in the frequency of complications between the different complications with the exception of acute hepatitis (p = 0.35). ARDS was significantly more frequent in obese (39.3%) and overweight (12.1%) patients. Acute myocardial injury, atrial fibrillation, heart failure, and uncontrolled HTN were present in 6 (10.7%), 2

Table 3 Radiological Findings and Nutrition Ratio Index in Studied Patients Based on Body Mass Index

*Variables	Class of Body	Mass Index			**P value	***Subgroup				
	Underweight (n= 16)	Normal (n= 62)	Overweight (n= 66)	Obese (n= 56)		Analysis				
Plain-radiograph				·						
• Normal	0	8 (12.9%)	6 (9.1%)	2 (3.6%)	0.01	P1=0.89				
Unilateral mild opacity	0	4 (6.5%)	2 (3%)	0		P2=0.40				
Unilateral moderate opacity	0	2 (3%)	0	0		P3=0.01				
Bilateral mild opacity	8 (50%)	30 (48.4%)	34 (36.4%)	18 (32.1%)		P4=0.19				
Bilateral moderate opacity	4 (25%)	14 (22.6%)	26 (39.4%)	20 (35.7%)		P5=0.34				
Bilateral severe opacity	4 (25%)	4 (6.5%)	8 (12.1%)	16 (28.6%)		P6=0.59				
CT findings										
• Ground glass opacity	12 (75%)	36 (58.1%)	52 (78.8%)	56 (100%)	< 0.001	P1=0.01 P2=0.56 P3=0.01 P4=0.19 P5< 0.001 P6=0.19				
• Crazy paving	12 (75%)	8 (12.9%)	26 (39.4%)	34 (60.7%)	< 0.001	P1< 0.001 P2< 0.001 P3=0.13 P4= 0.05 P5< 0.001 P6=0.12				
Consolidation	4 (25%)	32 (51.6%)	19 (28.8%)	19 (32.1%)	0.02	P1=0.01 P2= 0.15 P3=0.19 P4= 0.06 P5=0.22 P6=0.07				
Cardiomegaly	0	0	0	2 (3.6%)	0.15	P1= P2= P3=0.65 P4= P5=0.65 P6=0.65				
• Pleural effusion	0	0	0	2 (3.6%)	0.15	P1= P2= P3=0.65 P4= P5=0.65 P6=0.65				

*Variables	Class of Body	Mass Index			**P value	***Subgroup	
	Underweight (n= 16)	Normal (n= 62)	Overweight (n= 66)	Obese (n= 56)		Analysis	
CT score					< 0.001	P1=0.01	
• Score –I	2 (12.5%)	22 (35.5%)	8 (12.1%)	6 (10.7%)		P2=0.44	
• Score -2	4 (25%)	26 (41.9%)	22 (33.3%)	12 (21.4%)	-	P3=0.09	
• Score –3	6 (37.5%)	8 (12.9%)	24 (36.4%)	14 (25%)		P4=0.01	
• Score -4	0	2 (3.2%)	8 (12.1%)	8 (14.3%)		P5=0.67	
• Score-5	4 (25%)	4 (6.5%)	4 (6.1%)	16 (28.6%)		P6=0.53	
Nutrition ratio index					0.74	P1=0.56	
• < 3	3 (18.8%)	8 (12.9%)	8 (12.1%)	5 (8.9%)		P2=0.09	
• ≥ 3	13 (81.3%)	54 (87.1%)	58 (87.9%)	51 (91.1%)		P3=0.11 P4=0.57 P5=0.09 P6=0.11	

Table 3 (Continued).

Notes: *Data expressed as frequency (percentage). **P value was significant if < 0.05 and indicates significance between the different groups. ***PI compares between underweight and normal weight groups, P2 compares between underweight groups, P3 compares between underweight groups, P4 compares between normal and overweight groups, P6 compares between overweight and obese groups.

*Variables		Class of Body		**P value	***Subgroup Analysis	
	Underweight (n= 16)	Normal (n= 62)	Overweight (n= 66)	Obese (n= 56)		
Hospital stay (days)	11.75 ± 3.82	10.51 ± 3.83	11.12 ± 5.43	9.82 ± 4.12	0.30	P1=0.11 P2=0.56 P3=0.09 P4=0.22 P5=0.87 P6=0.10
Admission to intensive care unit (days)	12 (75%)	22 (35.5%)	38 (57.6%)	44 (78.6%)	< 0.001	P1< 0.001 P2=0.05 P3=0.11 P4=0.05 P5< 0.001 P6=0.01
Severity • Mild • Moderate • Severe • Critical	0 0 6 (37.5%) 10 (62.5%)	18 (29%) 6 (9.7%) 30 (48.4%) 8 (12.9%)	4 (6.1%) 2 (35) 38 (57.6%) 22 (33.3%)	0 4 (7.1%) 20 (35.7%) 32 (57.1%)	< 0.001	PI < 0.001 P2=0.05 P3=0.88 P4=0.03 P5< 0.001 P6< 0.001

 Table 4 Hospital Stay, Severity and Outcome in Studied Patients Based on Body Mass Index

Table 4 (Continued).

*Variables	Class of Body Mass Index				**P value	***Subgroup Analysis
	Underweight (n= 16)	Normal (n= 62)	Overweight (n= 66)	Obese (n= 56)		
Alive	4 (25%)	56 (90.3%)	50 (75.8%)	28 (50%)	0.01	P1< 0.001
Died	12 (75%)	6 (9.7%)	16 (24.2%)	28 (50%)		P2< 0.001 P3=0.11 P4=0.05 P5=0.01 P6=0.04

Notes: *Data expressed as mean (SD), frequency (percentage). **P value was significant if < 0.05 and indicates significance between the different groups. ***PI compares between underweight and normal weight groups, P2 compares between underweight groups, P3 compares between underweight and obsess groups, P4 compares between normal and overweight groups, P5 compares between normal and obese groups, P6 compare between overweight and obese groups.

(3.6%), 10 (17.9%), and 21 (21.4%) obese patients, respectively, whereas 4 (6.1%), 2 (3%), 4 (6.1%), 2 (3%), and 2 (3%) obese patients developed acute myocardial injury, atrial fibrillation, sinus tachycardia, heart failure, and uncontrolled HTN, respectively. Only two patients with normal BMI developed heart failure. Thrombocytopenia occurred in two (3.2%), two (3%), and eight (14.3%) normal-weight, overweight, and obese patients, respectively. Myalgia occurred in two (3.2%), two (3%), and eight (14.3%) normal-weight, overweight, and obese patients, respectively. DM developed in only two patients and all of whom had a normal BMI, while subacute thyroiditis occurred in 2 (12.5%) underweight patients and 2 (3.6%) obese patients. Bed sores occurred in four (25%), two (3.2%), two (3%), and 18 (32.1%) underweight, normal-weight, overweight, respectively (Table 5).

Underweight patients, patients with diabetes mellitus, or underlying chest or liver diseases were significant predictors of mortality among the included patients using logistic regression analysis (Table 6).

*Variables	Class of body mass index				**P value	***Subgroup Analysis
	Underweight (n= 16)	Normal (n= 62)	Overweight (n= 66)	Obese (n= 56)		
Respiratory complications					< 0.001	P1=0.22
Alveolar hemorrhage	0	0	2 (3%)	2 (3.6%)		P2=0.09
• ARDS	2 (12.5%)	4 (6.5%)	8 (12.1%)	22 (39.3%)		P3< 0.001
Severe asthma	0	0	2 (3%)	4 (7.1%)		P4=0.34
Pulmonary embolism	0	0	2 (3%)	0		P5< 0.001
						P6=0.04
Cardiovascular complications					< 0.001	PI< 0.001
• Acute myocardial injury	4 (25%)	0	4 (6.1%)	6 (10.7%)		P2=0.13
Atrial fibrillation	0	0	2 (3%)	2 (3.6%)		P3=0.05
• Sinus tachycardia	0	0	4 (6.1%)	0		P4=0.09
• Heart failure	0	2 (3.2%)	2 (3%)	10 (17.9%)		P5=0.44
• Uncontrolled hypertension	2 (12.5%)	0	2 (3%)	12 (21.4%)		P6=0.04
Neurological complications					< 0.001	P1=0.01
Seizures	2 (12.5%)	0	0	2 (3.6%)		P2=0.02
• Stroke	0	4 (6.4%)	2 (3%)	2 (3.6%)		P3=0.03
						P4=0.98
						P5=0.09
						P6=0.33

Table 5 Different Complications in Studied Patients Based on Body Mass Index

Table 5 (Continued).

*Variables	Class of body mass index				**P value	***Subgroup Analysis
	Underweight (n= 16)	Normal (n= 62)	Overweight (n= 66)	Obese (n= 56)		
Acute kidney injury	6 (37.5%)	4 (6.5%)	18 (27.3%)	16 (28.6%)	0.004	PI < 0.001 P2=0.09 P3=0.22 P4=0.06 P5=0.05 P6=0.20
Acute hepatitis	0	10 (16.1%)	8 (12.1%)	6 (10.7%)	0.35	P1=0.12 P2=0.09 P3=0.19 P4=0.29 P5=0.47 P6=0.08
Haematological complications • DVT • Pancytopenia • Thrombocytopenia	0 0 0	4 (6.5%) 0 2 (3.2%)	0 2 (3%) 4 (6.1%)	0 0 6 (10.7%)	0.04	P1=0.13 P2=0.30 P3=0.09 P4=0.12 P5=0.06 P6=0.90
Myalgia and bone pain	0	2 (3.2%)	2 (3%)	8 (14.3%)	0.02	P1=0.12 P2=0.56 P3=0.04 P4=0.19 P5=0.08 P6=0.07
Endocrine complicationsDiabetes mellitusSubacute thyroiditis	0 2 (12.5%)	2 (3.2%) 0	0 0	0 2 (3.6%)	0.01	P1=0.01 P2=0.11 P3=0.98 P4=0.05 P5=0.56 P6=0.18
Bed sores	4 (25%)	2 (3.2%)	2 (3%)	18 (32.1%)	0.001	PI= 0.02 P2=0.01 P3=0.06 P4=0.09 P5=0.01 P6< 0.001

Notes: *Data expressed as frequency (percentage). **P value was significant if < 0.05 and indicates significance between the different groups. ***PI compares between underweight and normal weight groups, P2 compares between underweight groups, P3 compares between underweight groups, P4 compares between normal and overweight groups, P6 compares between normal and obese groups.

Discussion

This study explored the possible role of BMI in the characteristics, complications, and outcomes of patients with COVID-19 from multiple tertiary care centers in Egypt during the COVID-19 pandemic. The overall findings of the current work revealed that the included underweight and obese patients with COVID-19 have more comorbidities and/or alterations in biochemical tests, and a worse prognosis.

	OR	95% CI	P value			
Age (years)	1.01	0.45–2.34	0.19			
Male sex	0.90	0.33-1.80	0.11			
Body mass index (kg/m²)						
Normal weight	Ret					
Underweight	2.11	1.33-4.34	0.03			
Overweight	0.87	0.22–1.66	0.11			
• Obese	1.01	0.76–2.19	0.34			
Diabetes mellitus	3.22	2.90–7.11	< 0.001			
Hypertension	0.87	0.22–1.90	0.10			
Chest disease	4.34	3.40-12.39	< 0.001			
Ischemic heart disease	0.40	0.11-0.90	0.19			
Chronic kidney disease	1.09	1.01–2.18	0.06			
Liver disease	2.11	1.22–5.10	0.03			
Malignant lesions	1.34	1.31–2.98	0.65			

Table 6 Multivariate Regression for Predictors of Mortality

In the present study 8% were underweight, 33% were overweight, and 28% were obese. According to Mehanna et al¹⁷ 62% of patients with COVID-19 included in their study were obese, 25% were overweight, and 13% were of normal weight (obesity group OR=1.61; 95% CI 1.17–2.23). Schaalan et al¹⁸ showed that 37.2% of participants had an overweight BMI, reflecting the association role of obesity with infection.

In the present study, the mortality rate was 31%. Wu et al¹⁹ and Zhou et al²⁰ both exhibited death rates of 21.9% and 28.3%, respectively. In contrast to Almazeedi et al²¹ and Guan et al²² who reported fatality rates of 1.7% and 1.4%, respectively, the mortality rate in our study was greater.

The current study found that patients with a normal BMI had a significantly lower mean age than those in the other groups. Underweight patients had the highest mean age. Additionally, the majority of the included obese patients were females, while in other BMI classes there was male predominance. Our results are in accordance with those of Soeroto et al⁸ reported that male patients are less affected by obesity. According to Khamiss et al²³ 52.3% of the sample was male and 47.7% female. Hendren et al²⁴ reported that higher BMI categories were associated with a younger age.

In addition, the present study revealed that underweight patients had a significantly higher frequency of smoking than the other classes (P=0.04). According to Gao et al⁵ reported that among those without a recorded BMI measurement, a higher proportion of people had a smoking status (288 780 (23.5%)) than among those with available BMI measurements. In contrast, according to Cai et al²⁵ those with a BMI \geq 24 were more likely to have smoked in the past.

Our findings showed that, compared to other categories, obese patients had significantly higher rates of diabetes mellitus, hypertension, and liver disorders. Compared to other BMI classes, underweight patients had a significantly increased frequency of ischemic heart disease. Compared with normal and overweight individuals, chest diseases were considerably more common among underweight and obese patients. This was in line with the findings of Mehanna et al¹⁷ who reported higher frequency of comorbidities (diabetes, hypertension, elevated glucose levels, dyslipidemia, and hypertension) among obese group compared to the overweight and normal-weight groups. Age, diabetes type 2, and hypertension were found to be inversely correlated with the effects of increased BMI and obesity on associated negative outcomes, according to Soeroto et al.⁸ In addition, Espiritu et al²⁶ reported that underweight patients had greater proportions of concurrent HIV/AIDS and chronic kidney disease, which may be related to the detrimental impact that

these diseases have on weight and muscle mass.²⁷ According to Cai et al^{25} patients with BMI \ge 24 had acute/chronic liver injury, ARDS, and were of the severe/critical form.

According to this study, obese and underweight individuals had considerably higher levels of leukocytes, C-reactive protein, erythrocyte sedimentation rate, creatinine, glycosylated hemoglobin, and fasting blood sugar than normal-weight and overweight individuals did. Our findings concur with those of Mehanna et al¹⁶ who noted that the obese group had greater levels of acute-phase reactants (eg C-reactive protein, ferritin, lactate dehydrogenase, ESR, and D-dimer) than the overweight and normal weight groups, which indicate how severe the inflammation is. According to Cai et al²⁵ patients with a BMI \geq 24 showed greater levels of hemoglobin, liver enzymes, total bilirubin, serum creatinine, CK, LDH, glucose, and CRP than patients with a BMI \leq 24.

According to the results of the present study, the most frequent finding in underweight and normal-weight patients was bilateral mild opacity, whereas the most common finding in overweight and obese patients was bilateral moderate opacity. According to Cai et al²⁵ radiological data showed that bilateral pneumonia was the most prevalent condition in the two groups (BMI \geq 24 and BMI < 24), which was correlated with poor imaging results over the course of the disease. Additionally, it was noted that people with a BMI \geq 24 had a higher prevalence of bilateral pneumonia, numerous mottlings, and ground-glass opacity; however, the difference was not statistically significant. According to the registry, obese individuals had a greater prevalence of hypoxemia and radiographic abnormalities on chest X-rays, according to Hendren et al.²⁴

Regarding the CT score in the current study, a score-3 was frequently detected in underweight and overweight patients, and a score-5 was frequently observed in obese patients. Blokhin et al²⁸ concluded that body mass index does not affect chest standard-dose and low-dose computed tomography interpretation in COVID-19, using the visual semiquantitative CT 0–4 grading system. According to Lu et al²⁹ at the time of admission and at 5-month intervals, CT scans of obese individuals revealed more severe pneumonia lesions. The acute phase revealed substantial differences in lung lesions (LV), ground-glass opacity (GV), lung lesion percentages (PLV), and ground-glass opacity volume percentages (PGV) across the three groups, which was in line with a prior study.³⁰ As the primary imaging characteristic in COVID-19 patients, the GGO is frequently superimposed with a crazy-paving pattern and can be caused by pulmonary disease which impacts both the interstitial and airspace compartments. It can also appear throughout the entire course of the COVID-19 lung lesions.¹⁶ The peak stage of COVID-19 pneumonia is identified by consolidation on chest CT images, which occurs more frequently in patients who are most severely ill.³¹ According to Lu et al 's findings, obese and overweight people had more severe acute LV, GV, PLV, and PGV results than people of normal weight.²⁹ However, it was delight that the CV and PCV in fat and overweight patients did not significantly increase in their study at the acute stage.

We found different groups had insignificant difference as regard nutrition ratio index among underweight, normal weight, overweight and obese patients included in the present research. This agrees with Haraj et al³² reported that there was no statistically significant difference between BMI and Mini Nutritional Assessment (MNA) score. According to a study by Kim et al³³ just 2.2% of adult patients had malnutrition based on BMI, using the WHO-recommended cut-off point. However, another study showed that 52.7% of elderly patients admitted with COVID-19 has malnutrition using MNA approach.³⁴ This could be explained by the presence of comorbidities, anorexia, the inflammatory consequences, and the gastrointestinal manifestations associated with the infection.³⁵ According to Huh et al³⁶ women who are overweight patients had a more rapid progression of the disease and a higher mortality risk. Patients with higher NRS scores had more severe COVID-19, according to a retrospective analysis of 63 COVID-19 patients who were hospitalized in China.³⁷

Our findings showed that there were no significant differences between patient groups based on BMI classes in terms of length of hospital stay. This result was consistent with other observations that suggested that obesity did not significantly shorten hospital stay.^{38,39} On the other hand, Sawadogo et al⁴⁰ found that obese and extremely obese COVID-19 patients at higher risk of hospital admission and death than overweight persons.

In our study, the proportion of obese and underweight patients admitted to the ICU was significantly higher. According to Mehanna et al¹⁷ there were twice as many obese COVID-19 patients admitted to ICUs (84 versus 43, respectively) as there were overweight or normal-weight patients. Numerous studies have found findings that are similar to ours regarding the likelihood that obese COVID-19 patients may need specialized treatment and ICU admission.^{41–43}

Additionally, this study found a significant association between BMI and disease severity. While the majority of underweight and obese patients had critical diseases, the majority of normal-weight and overweight patients had severe

diseases. In COVID-19 adult patients, Soeroto et al⁸ demonstrated that both higher BMI and obesity were associated with worse outcomes (severe COVID-19). According to a retrospective study by Rao et al,⁴⁴ individuals with severe illnesses had considerably higher BMIs and were more likely to be overweight. Additionally, those who were overweight had a higher risk of developing severe pneumonia than those with normal weight.

Our study found a significant difference between the groups of patients based on BMI and mode of mechanical ventilation. SIMV is frequently used in obese patients. Invasive mechanical ventilation (IMV) was frequently used for underweight and obese patients. This agrees with Soeroto et al⁸ who reported that adult COVID-19 patients with higher BMIs and obesity had worse results (requiring mechanical ventilation). This is also in agreement with Simonnet et al⁴³ who showed that the need for IMV gradually increased with higher BMI and reach up to 90% with MBI \geq 35. Similarly, Palaiodimos et al⁴⁵ demonstrated an independent relationship between increased oxygen demand, intubation, and a BMI of 35 kg/m2 or above. In contrast, Kooistra et al⁴⁶ reported that BMI was not related to unfavorable respiratory mechanics.

The current study revealed significant differences between different BMI classes with regard to the frequency of different complications, including respiratory, cardiovascular, neurological, hematological, and endocrine complications, as well as acute kidney injury, myalgia, and bedsores. Caussy et al⁴⁷ observed that COVID-19 patients with obesity were more likely to have major health problems, which is consistent with our findings. It is widely acknowledged that COVID-19 patients' immune systems are disrupted by disorders including diabetes, hypertension, hyperglycemia, and dyslipidemia. Additionally, Schaalan et al¹⁸ observed that there was an increased risk factor of 1.509 times greater for post-COVID-19 symptoms in obese patients.

According to Gao et al⁴⁸ obesity has been linked with an increased risk of serious health problems. In our study, ARDS was most frequent among obese patients, followed by overweight patients, compared with other classes. This result is in accordance with Soeroto et al⁸ who demonstrated that in COVID-19 adult patients, both higher BMI and obesity were linked to adverse clinical outcomes (ARDS). Ritter et al⁴⁹ demonstrated a link between obesity and a dysregulated immune response that causes persistent systemic inflammation, this could be a risk factor for ARDS and poor outcomes in individuals with obesity who have COVID-19.

Obesity seems to increase the likelihood of respiratory complications, ICU hospitalization, and the need for mechanical ventilation.^{50,51} The possibility for ARDS, and respiratory failure from COVID-19 exist.⁵² The current study reported that majority of underweight and obese patients were deteriorated and died while majority of normal weight patients and overweight patients were improved and discharged. This was in line with the findings of Hussain et al⁵³ who showed that obese patients infected with COVID-19 had a higher mortality rate. According to Mehanna et al¹¹ obese COVID-19 patients had a significantly higher mortality rate and case-fatality ratio (26, 18.3%) than those who were overweight (4, 6.89%) or normal weight (1, 3.33%). These variations demonstrate that obese individuals are more likely to experience difficulties and require urgent care and ICU admission. In COVID-19 adult patients, Soeroto et al⁸ shown that both higher BMI and obesity were associated with adverse outcomes (hospital admission and mortality). In contrast, Kooistra et al⁴⁶ reported that BMI was not related to a different immunological response, unfavorable respiratory mechanics, or impaired outcome. Sawadogo et al⁴⁰ reported significant association of overweight with hospital admission, ICU, and IMV, but not death among general population.

The incidence of cardiac complications (acute myocardial injury, atrial fibrillation, heart failure, and uncontrolled HTN) was significantly higher among obese and overweight patients than among other classes. This is consistent with the findings of Heubel et al⁵⁴ that demonstrated worse endothelial function during acute COVID-19 in individuals with obesity and/or higher BMI. This finding supports earlier theories that endothelial dysfunction might account, at least in part, for one of the processes through which obesity increases the risk of severe COVID-19.

Obesity has been linked in a retrospective study,²⁴ to a high risk of venous thromboembolism in addition to and elevated risk of in-hospital mortality. Similar evidence was discovered in a retrospective cohort of 609 COVID-19 hospitalized patients,⁵⁵ where patients who were obese in the class I and class III subgroups had significantly higher risk-adjusted probabilities of venous thromboembolism than those who were not obese.

Numerous symptoms can be included in the COVID-19 neurological presentation, and rapid clinical decline may be linked to the emergence of neurological disease.⁵⁶ Incidence of neurological complications in our study was significantly

higher among obese and overweight patients than among other classes. This was in line with the findings of Espiritu et al²⁶ who demonstrated that, among COVID-19 patients with an acute neurologic presentation or condition at admission, obesity may be an independent predictor of poor neurologic recovery. According to Yanover et al⁵⁷ neurological diseases are a risk factor for individuals over 65 years of age, while obesity is a risk factor for patients aged 18 to 50 years.

We found that the occurrence of acute kidney injury was significantly higher in underweight and obese patients than in those of other classes. According to Yanover et al⁵⁶ obesity is a risk factor for patients aged 18–50 years, whereas chronic renal disease is a risk factor for patients aged 50–65 years. AKI rates were higher in obese COVID-19 patients, making the infection more severe. AKI predisposes patients to severe pneumonia, acute respiratory distress syndrome (ARDS), and the use of invasive mechanical ventilation.⁵⁸ Additionally, inflammatory mediators linked to obesity may harm kidney function.⁵⁹

The current research demonstrated that compared to other classes of patients, obese and overweight patients had a significantly greater frequency of haematological problems. According to a French study, patients with COVID-19 who had abnormal BMI had a 7-fold higher likelihood of being admitted to hospitals for ICU support than patients who were not fat.⁶⁰ Obesity has been identified as a significant factor contributing to a more severe clinical course in COVID-19 patients because of its associations with pulmonary dysfunction, hypercoagulability, and an increased risk of thrombosis.⁶¹ The lowest mean of MCV and MCH were found in overweight people, according to Augusto et al.⁶² According to Ghizlane et al's study, there was no discernible difference between the groups with and without lymphopenia in terms of the median BMI.⁶³

Our results revealed that the incidence of myalgia was significantly higher among obese and overweight patients than among other classes. The findings of Cai et al⁶⁴ were consistent with this finding, who discovered that severe/critical patients had a considerably greater rate of myalgia and exhaustion, which may be caused by an increased body burden from excess fat.

The incidence of endocrine complications in this study was significantly higher in underweight patients than that in other classes. DM developed in only two patients and all of whom had a normal BMI, while subacute thyroiditis occurred in 2 underweight patients and 2 obese patients. Male, overweight, and elderly patients who are most susceptible to severe COVID-19 have lower GH levels. This may imply that GH is involved in halting COVID-19's evolution.⁶⁵ The most significant endocrine dysfunctions that adversely affect COVID-19 patients' prognoses are diabetes mellitus and obesity.⁶⁶ Additionally, COVID-19 commonly exhibits metabolic abnormalities, such as dyslipidemia and elevated leptin.⁶⁷

Our study showed that the incidence of bedsores was significantly higher among obese and overweight patients than among the other classes. This was in line with Hyun et al⁶⁸ who reported that the incidence of pressure ulcers was 8.6%, 5.5%, 2.8%, and 9.9% in the underweight, normal-weight, obese, and extremely obese groups, respectively. Extreme obesity increased the risk of developing a pressure ulcer by almost two-fold compared with normal-weight patients when both the Braden scale score and body mass index were predictive of ulcers. In contrast to research showing that BMI affects the risk profile,^{69,70} Challoner et al⁷¹ revealed that risk factors including BMI were not relevant in the development of pressure ulcers.

Conclusion

The majority of critically ill overweight or obese patients were hospitalized, mechanically ventilated, and had acute renal injuries. The majority of underweight and obese patients worsened and died, while the majority of normal-weight and overweight patients who improved and were discharged. Extremes of BMI (underweight and obese) could have a significant prognostic adverse factor in patients with COVID-19.

Limitations of the Study

Relatively small sample size and the lack of inclusion of pediatric population were the main study's limitations.

Data Sharing Statement

The corresponding author will provide the datasets used and/or analyzed during the current work upon reasonable request.

Author Contributions

All authors made a significant contribution to the work reported, whether in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas, took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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