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Research Article

A Single Center Prospective Observational Cohort Study on the Association of Asia Pacific Classification of Body Mass Index, Waist Circumference, Waist Hip Ratio with COVID-19 Outcomes and Severity in a Philippine Tertiary Hospital

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Abstract

Objective: This study aimed to determine the association between Asia-Pacific classification of body mass index, waist circumference and waist hip ratio and clinical outcomes of COVID-19 moderate & severe patients at the height of the COVID-19 pandemic.

Methods: This study involved adult patients diagnosed with COVID-19. 182 patients were analyzed and divided into 167 moderate and 15 severe COVID-19 patients. Primary outcomes (respiratory decompensation, septic shock and mortality) of patients were compared among Asia Pacific BMI groups.

Results: Among patients with moderate and severe COVID-19, 7 out of 10 patients were obese. Respiratory decompensation and sepsis were more frequently seen in obese patients. Obesity and waist circumference were significantly associated with the odds of respiratory decompensation (95% CI p=0.010 and p=0.002), however this association was not sustained upon adjustment for confounders. On univariate analysis, waist and hip circumferences were significantly associated with the odds of ICU admission (95% CI, p=.013 and p=.034), however after controlling for confounders, only hip ratio retained significant association. Among patients with severe COVID-19, there was insufficient evidence to support significant variations in distributions of outcomes of interest across Asia-Pacific Body Mass Index (BMI) groups.

Conclusion: Our study emphasized that although respiratory decompensation and sepsis were more frequently seen in obese patients. Progression of respiratory decompensation and mortality is not significantly associated with obesity as defined by the Asia Pacific BMI classification, warranting the need for larger prospective studies.

Keywords: Body Mass Index; Obesity; COVID-19

Introduction

Obesity has been postulated to aggravate the course of COVID-19 disease [1-6]. Few studies have focused on the association between COVID-19 infection and individual measures of visceral adiposity as measured by waist circumference and waist-hip ratio [3]. Visceral adiposity has been linked to cardiometabolic disorders and is known to be more metabolically active, secreting a variety of adipokines and pro-inflammatory cytokines, including tumor necrosis factor, C-reactive protein, Interleukin 6 (IL-6) and leptin [7]. Apart from insulin resistance and metabolic syndrome, elevated IL-6 levels are known to be related to airway diseases and recent studies report higher levels of IL-6 in COVID-19 non-survivors [7].

While previous studies have already identified overall obesity as a risk factor for severe courses of COVID-19, most studies only used body mass index [1-2,4,5]. There is no local data showing an association between body mass index, waist circumference and waist-hip ratio and how these different measures differ with one another in terms of which is more accurate or predictive of COVID-19 outcomes in Filipinos. Furthermore, it is expensive to obtain more accurate measures of visceral adiposity such as Computed Tomography (CT) based quantification of visceral adipose tissue [8].

Most studies on the association of Body Mass Index (BMI) and COVID-19 outcomes make use of the WHO classification and it has been a known fact that a BMI cut off of 30 kg/m^2 is associated with a greater risk of death from COVID-19 [1,2]. There is paucity of data on outcomes for those patients stratified in different Asia-Pacific classifications of body mass index, waist circumference and waist hip ratio with moderate and severe COVID-19 disease in terms of progression of severity in patients requiring critical care or progression to mortality.

Data on the association of Asia-Pacific classification of body mass index, waist circumference, waist-to-hip ratio and COVID-19 outcomes may contribute to further understanding the mortality risk of Filipinos, particularly the survival of patients with lower or higher body mass index, waist circumference and visceral adiposity. Our study attempts to explain how a patient's body mass index classification, waist circumference and waist-hip ratio affect COVID-19 outcomes in terms of severity requiring critical care or mortality, which is important both clinically and in public health. This study also aims to improve current practice in terms of the value of obtaining accurate anthropometric measurements in COVID-19 patients and in determining whether waist circumference and body mass index are associated with COVID-19 outcomes.

We hypothesize that patients with increased body mass index and visceral adiposity as measured by waist circumference and waist-hip ratio are at higher risk for developing severe outcomes from COVID-19. This prospective study aims to provide further insight into the risk stratification of patients with COVID-19 based on non-invasive measurements of height, weight, waist and hip circumference.

Material and Methods

Study Selection and Eligibility Criteria

This single-center prospective, analytical, observational cohort study included data from patients > 18 years old diagnosed with COVID-19 confirmed by nasopharyngeal swab Polymerase Chain Reaction (PCR) who were admitted at The Medical City from August 2021 to November 2021. A minimum sample size of 180 subjects was required for this study. The overall sample size provided was deemed to be sufficient to detect a significant relationship based on anticipated odds ratios and at 5% level of significance and 90% power.

Inclusion criteria included hospitalized, ambulatory, patients >18 years with COVID-19 confirmed by reverse transcription-polymerase chain reaction testing. The study participants belonged to the World Health Organization (WHO) clinical progression scales 4, 5 and 6, namely those who were hospitalized with no oxygen therapy, hospitalized with oxygen therapy through nasal prongs or mask and hospitalized who utilized non-invasive ventilation, respectively. Exclusion criteria excluded any patient who was unable to stand upright and/or have his/her waist and hip circumference measurements obtained, any patients who was pregnant as confirmed by history, patients with a "do not resuscitate/intubate" order, patients who dropped out or withdrew from the study before the 30 days from the time of admission or upon discharge, bedridden patients, patients classified as 7, 8, 9 and 10 according to the WHO clinical progression scale, namely, those who were intubated and mechanically ventilated with $p0_2/Fi0_2$ >150 or $Sp02/Fi0_2$ >200, those who were mechanically ventilated with $p0_2/Fi0_2$ ratio of <150 ($Sp0_2/Fi0_2$ <200) or on vasopressors, those who were mechanically ventilated with $p0^2/Fi0^2$ ratio of <150 and on vasopressors, on dialysis or on Extracorporeal Membrane Oxygenation (ECMO) and patients who expired, respectively. Patients who were unable to ambulate or stand up because of dementia, osteoarthritis, amputations and any physical disability were also excluded from the study. The selection process is shown in Fig. 1.

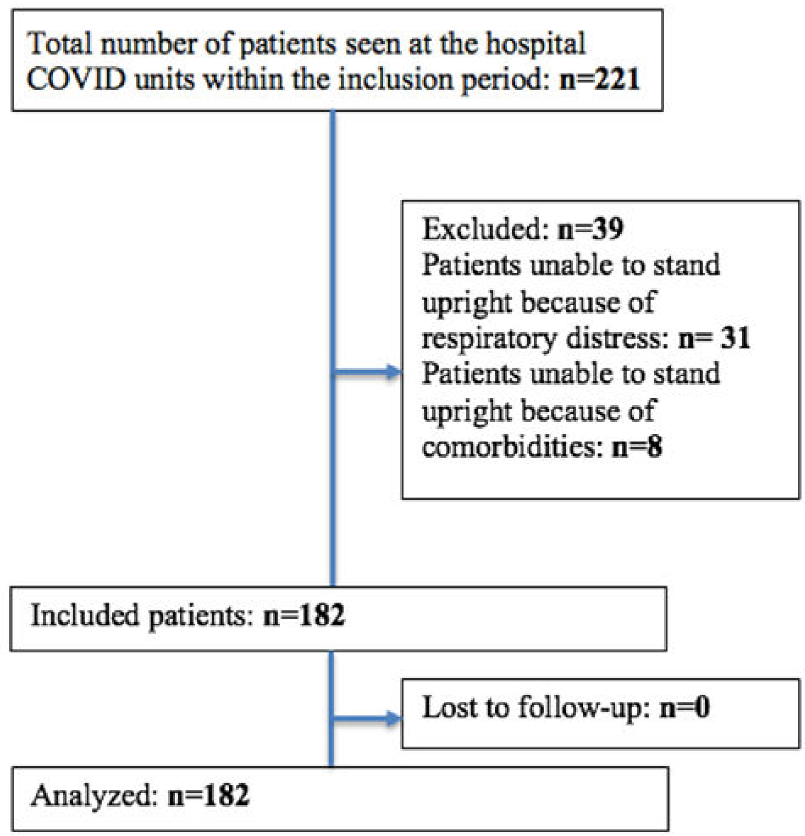

Figure 1: Patient enrolment and inclusion.

Study Procedures

This study was approved by the Institutional Review Board (IRB) and was made under the specifications and mandates of the IRB and Clinical and Translational Research Institute (CTRI) of The Medical City. This study adheres to the ethical considerations and ethical principles set out in relevant guidelines, including the Declaration of Helsinki, WHO guidelines, International Conference on Harmonization-Good Clinical Practice, Data Privacy Act of 2012 and the National Ethics Guidelines for Health Research 2017. The height, weight waist and hip circumference measurements were obtained. Laboratory and imaging data were obtained from the electronic medical records. Data elements included the following pertinent laboratory tests: hemoglobin (g/dL), absolute lymphocyte count, creatinine (g/dL), blood urea nitrogen (mg/dL), creatinine (mg/dL), estimated glomerular filtration rate (ml/min/1.73m^2), alanine aminotransferase (U/L), alkaline phosphatase (U/L) CRP (mg/L), LDH (U/L), ferritin (ng/mL), sodium (mEq/L), potassium (mEq/L), chloride (mEq/L) and magnesium (mEq/L).

Primary Outcomes of Interest

The primary outcomes of interest were respiratory decompensation (progression to invasive or non-invasive ventilation from the time of admission up to any point within the 30-day follow-up period), sepsis, septic shock and hospital mortality. Secondary outcomes included a diagnosis of Acute Respiratory Distress Syndrome (ARDS) using the Berlin Criteria, Intensive Care Unit (ICU) admission, length of hospital stay and severity of COVID-19 defined by the World Health Organization (WHO) clinical progression scale. The primary outcomes and the secondary outcomes of patients with moderate and severe COVID-19 infection were compared among Asia Pacific BMI groups. Subgroup comparisons were performed to study the association of COVID-19 severity, visceral adiposity indicators namely waist circumference, hip circumference and waist-hip ratio with respiratory decompensation, ICU admission and mortality.

Statistical Analysis

STATA 15.0 (StataCorp SE, College Station, TX, USA) was used for data analysis. Descriptive statistics were used to summarize the general and clinical characteristics of the participants. Frequency and proportion were used for categorical variables. Shapiro-Wilk test was used to determine the normality distribution of continuous variables. Continuous quantitative data that met the normality assumption was summarized using mean and Standard Deviation (SD). Continuous variables which were normally distributed were compared using the Independent t-test. Otherwise, the non-parametric Mann-Whitney U test was used. For categorical variables, Chi-square test was used to compare the outcomes. If the expected percentages in the cells were less than 5%, Fisher's Exact test was used instead. One-way ANOVA, Kruskal-Wallis test and Fisher's Exact test were used to determine the difference of mean, median and frequency, respectively. Odds ratio and the corresponding 95% confidence intervals from binary logistic regression were computed to determine the association of BMI and visceral adiposity with clinical outcomes. All valid data were included in the analysis. Null hypothesis was rejected at 0.05α-level of significance.

Ethical Statement

This study was made under the specifications and mandates of the Institutional Review Board (IRB) and Clinical and Translational Research Institute (CTRI) of The Medical City. This study adheres to the ethical considerations and ethical principles set out in relevant guidelines, including the Declaration of Helsinki, WHO guidelines, International Conference on Harmonization-Good Clinical Practice, Data Privacy Act of 2012 and the National Ethics Guidelines for Health Research 2017.

Results

Study Characteristics

There were a total of 182 adult subjects, divided into 167 moderate and 15 severe COVID-19 patients (Table 1), with median age was 54.5 (range 20-86) years. 54% were male. Seven in 10 were obese by Asia-Pacific BMI classification. The mean (±SD) waist circumference, hip circumference and waist-hip ratio were 101.75 ± 14.27 cm, 102.65 ± 13.06 cm and 0.99 ± 0.07, respectively. The most common comorbidities of patients were hypertension (58%) and type 2 diabetes (52%) and more than a fourth (27%) were active smokers.

Patients were seen at a median of 7 (range 1-17) days since onset of illness, with 51% not yet receiving any dose of COVID-19 vaccine and 10% being partially vaccinated. The top presenting features were fever (57%), cough (86%) and difficulty of breathing (73%). Blood tests revealed elevated median levels of CRP (84.14 mg/L), LDH (367 U/L) and ferritin (1020 ng/mL). The most frequently utilized therapeutics were steroids (91%), remdesivir (87%) and tocilizumab (48%).

Severe COVID-19 patients had higher median days of illness on admission, ALT, LDH, ferritin and chloride compared to moderate COVID-19 patients ($p < .05$). The severe COVID-19 group had a higher proportion of patients that have the following medical interventions: vasopressors; nutritional support; endotracheal intubation; tracheostomy; NMBA; hemoperfusion; and tocilizumab.

	All (n=182)	Moderate (n=167)	Severe (n=15)	*P*
	Mean ± SD; Median (Range); Frequency (%)			
Age, years	54.5 (20-86)	54 (20-86)	59 (39-82)	.396*
Sex				.999†
Male	98 (53.85)	90 (53.89)	8 (53.33)	
Female	84 (46.15)	77 (46.11)	7 (46.67)	
BMI, kg/m^2				.999†
<18.5 (underweight)	2 (1.1)	2 (1.2)	0	
18.5-22.9 (normal)	26 (14.29)	24 (14.37)	2 (13.33)	
23.0-24.9 (overweight)	26 (14.29)	24 (14.37)	2 (13.33)	
≥25.0 (obese)	128 (70.33)	117 (70.06)	11 (73.33)	
Waist circumference, cm	101.75 ± 14.27	101.84 ± 14.39	100.69 ± 13.31	.765‡
Hip circumference, cm	102.62 ± 13.06	102.86 ± 13.16	99.98 ± 12.03	.415‡
Waist-hip ratio	0.99 ± 0.07	0.99 ± 0.08	1.00 ± 0.04	.285‡
Low-risk	12 (6.59)	12 (7.19)	0	.603†
High-risk	170 (93.41)	155 (92.81)	15 (100)	
Co-morbidities				

	All (n=182)	Moderate (n=167)	Severe (n=15)	*P*
	Mean ± SD; Median (Range); Frequency (%)			
Neurologic				
Stroke or TIA	12 (6.59)	9 (5.39)	3 (20)	.064†
Brain tumor	1 (0.55)	1 (0.6)	0	.918†
Cardiac				
Hypertension	106 (58.24)	97 (58.08)	9 (60)	.999†
Coronary disease	17 (9.34)	14 (8.38)	3 (20)	.152†
Heart failure	2 (1.1)	2 (1.2)	0	.999†
Pulmonary				
Asthma	24 (13.19)	24 (14.37)	0	.226†
COPD	7 (3.85)	6 (3.59)	1 (6.67)	.458†
Pulmonary TB	4 (2.2)	4 (2.4)	0	.999†
Renal				
CKD	2 (1.1)	1 (0.6)	1 (6.67)	.158†
Liver				
Chronic liver disease	0	0	0	-
Liver cirrhosis	0	0	0	-
Chronic hepatitis	1 (0.55)	1 (0.60)	0	.999†
Hematologic disease				
Anemia	4 (2.2)	4 (2.4)	0	.999†
Coagulopathy disorder	0	0	0	-
Endocrine				
Type 1 DM	1 (0.55)	1 (0.60)	0	.999†
Type 2 DM	95 (52.2)	87 (52.1)	8 (53.33)	.999†
Thyroid disease	10 (5.49)	9 (5.39)	1 (6.67)	.587†
Active smoking status	50 (27.47)	47 (28.14)	3 (20)	.763†
Smoking exposure, pack years	[N=50] 10 (1-50)	[N=47] 10 (1-50)	[N=3] 30 (2-35)	.324†
Presenting symptoms				
Fever	156 (85.71)	142 (85.03)	14 (93.33)	.699†
Cough	159 (87.36)	145 (86.83)	14 (93.33)	.697†
Colds	75 (41.21)	67 (40.12)	8 (53.33)	.413†
Difficulty breathing	132 (72.53)	118 (70.66)	14 (93.33)	.072†
Sore throat	78 (42.86)	69 (41.32)	9 (60)	.182†
Watery stool	63 (34.62)	56 (33.53)	7 (46.67)	.396†
Vomiting	9 (4.95)	9 (5.39)	0	.999†
Seizure	1 (0.55)	1 (0.60)	0	.999†
Muscle pain	50 (27.47)	43 (25.75)	7 (46.67)	.126†
Loss of smell	89 (48.9)	80 (47.9)	9 (60)	.427†
Loss of taste	90 (49.45)	80 (47.9)	10 (66.67)	.187†
Day of illness on admission	7 (1-17)	7 (1-16)	8 (4-17)	**.014**
COVID-19 vaccination				.070†
None	93 (51.1)	81 (48.5)	12 (80)	
First dose	18 (9.89)	18 (10.78)	0 (0)	
Second dose	71 (39.01)	68 (40.72)	3 (20)	
ECG finding				.099†
Ischemia	5 (2.79)	4 (2.44)	1 (6.67)	

	All (n=182)	Moderate (n=167)	Severe (n=15)	*P*
	Mean ± SD; Median (Range); Frequency (%)			
Tachyarrhythmia	48 (26.82)	42 (25.61)	6 (40)	
Bradyarrhythmia	12 (6.7)	10 (6.1)	2 (13.33)	
Normal sinus rhythm	114 (63.69)	108 (65.85)	6 (40)	
CO-RADS classification				.999†
0 (not interpretable)	1 (1.49)	1 (1.59)	0	
1 (very low)	0	0	0	
2 (low)	0	0	0	
3 (equivocal)	0	0	0	
4 (high)	0	0	0	
5 (very high)	1 (1.49)	1 (1.59)	0	
6 (PCR+)	65 (97.01)	61 (96.83)	4 (100)	
Blood tests				
Hematology				
Hemoglobin, g/dL	[N=182] 13.65 (8-17.9)	[N=167] 13.6 (8-17.9)	[N=15] 14.1 (10.4-15.9)	.945*
ALC, x10^9/L	[N=181] 6.7 (1-32.1)	[N=166] 6.7 (2.8-32.1)	[N=15] 9.1 (1-25.3)	.087*
Renal markers				
Creatinine, mg/dL	[N=182] 0.86 (0.35-9.82)	[N=167] 0.85 (0.35-9.82)	[N=15] 0.88 (0.55-1.3)	.541*
BUN, mg/dL	[N=127] 12.04 (2.7-93)	[N=113] 12.04 (2.7-93)	[N=14] 17.65 (9.8-36.13)	.609*
Liver markers				
ALT, U/L	[N=175] 38 (8-405)	[N=160] 37.5 (8-405)	[N=15] 41 (23-340)	**.025***
Alkaline phosphatase, U/L	[N=22] 63.5 (17.6-242)	[N=19] 58 (17.6-242)	[N=3] 87 (43-106)	.702*
Inflammatory markers				
CRP, mg/L	[N=180] 84.14 (0.59-757)	[N=165] 82.23 (0.59-757)	[N=15] 145.7 (42-258.5)	.128*
LDH, U/L	[N=178] 367 (120-3229)	[N=163] 352 (120-3229)	[N=15] 712 (279-1448)	**.002***
Ferritin, ng/mL	[N=181] 1020 (0.58-17780)	[N=166] 941 (0.58-17400)	[N=15] 2533 (157-17780)	**.002***
Electrolytes				
Sodium, mEq/L	[N=180] 135 (103-145)	[N=165] 135 (103-144)	[N=15] 134 (117-145)	.614*
Potassium, mEq/L	[N=179] 4 (2.9-5.5)	[N=164] 4 (2.9-5.5)	[N=15] 4.1 (3.2-5.2)	.257*
Chloride, mEq/L	[N=31] 100 (73-114)	[N=25] 100 (73-114)	[N=6] 102 (88-112)	.900*
Magnesium, mEq/L	[N=69] 1.95 (1.46-3.16)	[N=59] 1.95 (1.46-3.16)	[N=10] 2.095 (1.95-2.43)	**.032***
Medical interventions				
Vasopressor or inotrope	25 (13.74)	17 (10.18)	8 (53.33)	**<.001†**
Nutritional support	31 (17.03)	22 (13.17)	9 (60)	**<.001†**
Endotracheal intubation	22 (12.09)	13 (7.78)	9 (60)	**<.001†**

	All (n=182)	Moderate (n=167)	Severe (n=15)	*P*
	Mean ± SD; Median (Range); Frequency (%)			
Tracheostomy	5 (2.75)	0	5 (33.33)	**<.001†**
Prone positioning	133 (73.08)	122 (73.05)	11 (73.33)	.999†
NMBA	19 (10.44)	11 (6.59)	8 (53.33)	**<.001†**
Hemoperfusion	15 (8.24)	7 (4.19)	8 (53.33)	**<.001†**
CPT	0	0	0	-
Steroids	165 (90.66)	151 (90.42)	14 (93.33)	.999†
Remdesivir	159 (87.36)	145 (86.83)	14 (93.33)	.697†
Tocilizumab	88 (48.35)	75 (44.91)	13 (86.67)	**.002†**
ALC: Absolute Lymphocyte Count; CO-RADS: COVID-19 Reporting and Data System; CPT: Convalescent Plasma Therapy; NMBA: Neuromuscular Blocking Agent. Statistical tests used: * - Mann-Whitney U test; † - Fisher's Exact test; ‡ - Independent t-test				

Table 1: Clinical profiles and interventions, by COVID-19 severity.

Asia Pacific Classification of Body Mass Index and Clinical Outcomes

Among patients with moderate COVID-19, there was insufficient evidence to support significant variations in the incidences of septic shock, ICU admission, need for vasopressor and mortality across Asia-Pacific BMI groups. Respiratory decompensation and sepsis were more frequently seen in obese patients than in the other three BMI classes, but pairwise comparisons were unable to reveal statistical significance (Table 2).

Measured Outcome	All (n=167)	Underweight (n=2)	Normal (n=24)	Overweight (n=24)	Obese (n=117)	*p*
	Frequency (%)					
Respiratory decompensation	100 (59.88)	1 (50)	10 (41.67)	10 (41.67)	79 (67.52)	.013*
Sepsis	31 (18.56)	0	0	1 (4.17)	30 (25.64)	.001*
Septic shock	18 (10.78)	0	1 (4.17)	0	17 (14.53)	.118
ICU admission	18 (10.78)	0	1 (4.17)	0	17 (14.53)	.118
Need for vasopressor	17 (10.18)	0	1 (4.17)	0	16 (13.68)	.145
Mortality	14 (8.38)	0	1 (4.17)	1 (4.17)	12 (10.26)	.680
Statistical test used: Fisher's exact test. *Not significant on Bonferroni-adjusted pairwise comparisons.						

Table 2: Clinical outcomes in moderate COVID-19, by BMI class (n=167).

Among patients with severe COVID-19, there was insufficient evidence to support significant variations in distributions of outcomes of interest across Asia-Pacific BMI groups (Table 3).

Measured outcome	All (n=15)	Normal (n=2)	Overweight (n=2)	Obese (n=11)	*p*
	Frequency (%)				
Respiratory decompensation	13 (86.67)	1 (50)	2 (100)	10 (90.91)	.476
Sepsis	8 (53.33)	1 (50)	2 (100)	5 (45.45)	.713
Septic shock	8 (53.33)	1 (50)	2 (100)	5 (45.45)	.713
ICU admission	9 (60)	1 (50)	2 (100)	6 (54.55)	.736
Need for vasopressor	8 (53.33)	1 (50)	2 (100)	5 (45.45)	.713
Mortality	9 (60)	1 (50)	2 (100)	6 (54.55)	.736
Statistical test used: Fisher's exact test.					

Table 3: Clinical outcomes in severe COVID-19, by BMI class (n=15).

Univariate and Multivariate Analyses

Respiratory Decompensation

On univariable analysis, obesity and waist circumference were significantly associated with the odds of respiratory decompensation. However, this association was not sustained upon adjustment for comorbidities, smoking, COVID-19 vaccination history, day of illness on admission and use of investigational drugs (Table 4).

	Crude Odds Ratio (95% CI)	***p***	**Adjusted Odds Ratio* (95% CI)**	***p***
BMI category				
Normal	Reference	-	Reference	-
Underweight	1.36 (0.08-24.27)	.833	4.03 (0.16-100.36)	.396
Overweight	1.17 (0.39-3.50)	.780	0.64 (0.14-2.90)	.567
Obese	**3.11 (1.31-7.39)**	**.010**	1.15 (0.36-3.67)	.810
Waist circumference, cm	**1.04 (1.01-1.06)**	**.002**	1.02 (0.98-1.05)	.345
Hip circumference, cm	1.02 (1.00-1.04)	.099	1.01 (0.97-1.04)	.679
Waist-hip ratio**				
Low risk	Reference	-	Reference	-
High risk	2.44 (0.74-8.01)	.142	1.36 (0.31-6.03)	.685
*Adjusted for the following variables: comorbidities, smoking status, COVID-19 vaccination history, day of illness on admission and investigational drugs (e.g., tocilizumab, remdesivir). **Low risk is ≤0.85 in females and ≤0.90 in males.				

Table 4: Association of visceral adiposity indicators with respiratory decompensation.

ICU Admission

On univariable analysis, waist and hip circumferences were both significantly associated with the odds of ICU admission. After controlling for potential confounders, only hip circumference retained significant association, with odds for the outcome increased by 5% (95% CI 1-10%) with every additional centimeter in hip circumference (Table 5).

	Crude Odds Ratio (95% CI)	***p***	**Adjusted Odds Ratio* (95% CI)**	***p***
BMI category				
Normal	Reference	-	Reference	-
Underweight	-		-	-
Overweight	1.00 (0.13-7.69)	.999	0.67 (0.05-8.83)	.759
Obese	2.63 (0.58-11.92)	.210	1.23 (0.17-8.62)	.837
Waist circumference, cm	**1.04 (1.01-1.07)**	**.013**	1.04 (1.00-1.08)	.076
Hip circumference, cm	**1.03 (1.003-1.07)**	**.034**	**1.05 (1.01-1.10)**	**.029**
Waist-hip ratio				
Low risk**	Reference	-	Reference	-
High risk	1.99 (0.25-16.05)	.520	0.62 (0.05-7.09)	.698
*Adjusted for the following variables: comorbidities, smoking status, COVID-19 vaccination history, day of illness on admission and investigational drugs (e.g., tocilizumab, remdesivir). **Low risk is ≤0.85 in females and ≤0.90 in males.				

Table 5: Association of visceral adiposity indicators with ICU admission.

Mortality

BMI, waist circumference, hip circumference or WHR were not found to be significantly associated COVID-19 mortality, whether on univariable nor multivariable analysis (Table 6).

	Crude Odds Ratio (95% CI)	*P*	Adjusted Odds Ratio* (95% CI)	*p*
BMI category				
Normal	Reference	-	Reference	-
Underweight	-	-	-	-
Overweight	1.57 (0.24-10.24)	.640	0.57 (0.05-6.44)	.646
Obese	1.96 (0.43-9.03)	.386	0.44 (0.06-3.38)	.428
Waist circumference, cm	1.02 (0.99-1.05)	.195	1.02 (0.98-1.06)	.437
Hip circumference, cm	1.01 (0.97-1.04)	.637	1.01 (0.96-1.06)	.653
Waist-hip ratio				
Low risk**	Reference	-	Reference	-
High risk	3.98 (0.23-69.55)	.344	2.55 (0.12-52.39)	.543

*Adjusted for the following variables: comorbidities, smoking status, COVID-19 vaccination history, day of illness on admission and investigational drugs (e.g., tocilizumab, remdesivir).
**Low risk is ≤0.85 in females and ≤0.90 in males.

Table 6: Association of visceral adiposity indicators with mortality.

Discussion

This is the first prospective observational cohort to investigate the influence of Asia-Pacific classification of Body Mass Index and visceral adiposity assessed by waist circumference and waist hip ratio on COVID-19 outcomes. According to the Asia Pacific classification, BMI is classified into four groups: underweight (<18.5 kg/m^2), normal weight (18.5-22.9 kg/m^2), overweight (23-24.9 kg/m^2) and obese (> 25 kg/m^2).

In our study involving 182 adult patients hospitalized with COVID-19, 127 or 70% of the patients were obese (BMI >25 kg/m^2) by Asia-Pacific BMI classification. The mean waist circumference, hip circumference and waist-hip ratio were 101.75 ± 14.27 cm, 102.65 ± 13.06 cm and 0.99 ± 0.07, respectively. This proportion is consistent with a Philippine-based retrospective cohort study in 2017 examining the individual features of metabolic syndrome among 1367 subjects in a Philippine tertiary hospital [11]. In this study, 66.2% of the patients were obese and the mean BMI was 28.2 kg/m^2 [11]. The mean waist circumference was documented at 96.8 cm [11].

Of the 182 patients, 167 presented with moderate COVID-19 and 15 patients had severe COVID-19. The incidence of severe COVID-19 infection in middle-aged patients was similar to that in older populations, which meant that the attributable risk may be similar in both groups. Our study findings show that in the obese group, most were male. There were no deaths recorded in the underweight group, although there were only two patients in this group. The mortality rate was lowest among those with normal BMI (7.69%).

On univariable analysis, waist and hip circumferences were both significantly associated with the odds of ICU admission. However, upon controlling for potential confounders, only hip circumference retained significant association with ICU admission. In particular, for every additional centimeter increase in hip circumference, the odds for the outcome of ICU admission increased by 5% (95% CI, p-value <0.05). In contrast, an observational study done in Ukraine determining mortality risks in 367 in-patients with COVID-19 found that only waist circumference (>105 centimeters) is an independent risk factor for severe COVID-19 outcomes particularly mortality [12]. Our hospital cohort of COVID-19 patients found no significant association between waist circumference and respiratory decompensation and mortality. To date, there are no studies showing the association of hip circumference alone with respiratory decompensation and mortality from COVID-19. While waist-hip ratio is based on the values of waist circumference and hip circumference, it provides a different measurement and perhaps may not always follow the trend of hip and waist circumference. For instance, a higher hip or waist circumference might not always indicate a higher waist-hip ratio.

Furthermore, our study found that BMI, waist circumference, hip circumference or waist-hip ratio were not found to be significantly associated COVID-19 mortality, whether on univariable or multivariable analysis. Several studies have investigated the association between COVID-19 and obesity, body mass index, waist circumference and waist-hip ratio, yet the mechanistic associations in Asians and in Filipinos remain unclear. Respiratory decompensation and sepsis were more frequently seen in obese patients (BMI > 25 kg/m²) than in the other three BMI classes. A possible explanation for the increased risk of developing respiratory decompensation and mortality among patients with higher BMI include difficulties in lung expansion, difficulties in ventilation and proning, which may complicate recovery time [13]. However, adjusting for confounders attenuated the significance of the association.

Our results show that visceral adiposity measured by waist and hip circumference, may be related to respiratory decompensation in COVID-19 (Table 6). Univariate analysis showed that obesity and waist circumference were significantly associated with the odds of respiratory decompensation or progression to more invasive ventilation and progression to mortality. A study by van Velst explains that visceral adiposity and respiratory failure are associated given that increased intraabdominal pressure due to local fat deposition may lead to mechanical obstruction and impaired ventilation of the lower lung regions [3]. However, this association was unable to retain its significance upon adjustment for confounders.

In our study, we stratified our analysis of COVID-19 outcomes with measures of visceral adiposity since previous studies conclude that obesity and increased waist circumference are associated with severe COVID-19 outcomes and overall mortality [1,2,5,14]. Our study dealt with a smaller sample population compared to the earlier studies hence the possibility of selection bias due to the inclusion criteria. There were also significantly more obese patients (70% of the study population) and more moderate than severe COVID-19 patients (91.75% or 167 patients, vs 8.25% or 15 patients) which proved investigating significant differences between the two groups and their COVID-19 outcomes across the BMI classifications to be challenging. The associations were difficult to establish due to the uneven distribution of the subjects in each category, specifically because there were more patients analyzed in the moderate group versus severe and majority of the patients were obese. Thus, the interpretation of results should be viewed carefully. These factors may account for the association not retaining its significance upon adjustment for comorbidities, smoking, COVID-19 vaccination history, day of illness on admission and use of investigational drugs such as remdesivir and tocilizumab.

Our study attempted to examine the risk associated with unit increases in Asia Pacific classification of Body Mass Index, however we found that in patients afflicted with moderate and severe COVID-19, there were no significant variations in distributions of outcomes of interest (respiratory decompensation, sepsis, septic shock and mortality) across Asia-Pacific BMI groups. A large population-based study, of which a large population had a BMI lower than 30 kg/m², found that having a Body Mass Index (BMI) of 30 kg/m² or higher was associated with a slightly greater risk of death from COVID-19 than a BMI of less than 30 kg/m² [2]. A community-based prospective cohort study found a significant positive linear association between increasing BMI and admission to hospital and to ICU due to COVID-19, with significantly higher risk for every BMI unit increase, with each unit increase in BMI above 23 kg/m² associated with increased risk of hospital admission and death due to COVID-19 particularly among people aged 20-39 years [1]. In another study, they found that risks for hospitalization, ICU admission and death were lowest among patients with BMIs of 24.2 kg/m², 25.9 kg/m² and 23.7 kg/m², respectively and that the risk increased with increasing body mass index [4]. A plausible explanation for not finding a significant interaction between COVID-19 outcomes and BMI groups in our study is that a large proportion (70%) of the study population are obese or have a BMI higher than 25 kg/m².

Limitations

Due to the nature of the study and the inclusion criteria, the study population was limited to patients who belonged in the WHO severity scales 4, 5 and 6 and this population may not be representative of severity of risk in the general population. Another limitation of our study was that we did not include prevalence rates of individual features of metabolic syndrome, such as elevated triglyceride levels, low high density lipoprotein levels, elevated fasting blood sugar and incidence of diabetes and hypertension in the assessment and these may be valuable to include in larger studies to further characterize the risk profile of Filipinos. Furthermore, the level of control of co-morbidities of the study population was not analyzed, which would account as an important confounder. There was bias in measurement of the waist-hip circumference, since the patients are supposed to be measured in an upright position. Therefore, patients who were unable to stand at admission due to dyspnea or respiratory distress had to be excluded from analysis, hence introducing selection bias. Due to the number of patients to whom this applied (39 out of 221), the influence on the results may be substantial. The limitations may also be explained by difficulty in completing parameters during the pandemic in the local setting. Our final limitation is that our data collection was done during the height of the COVID-19 surge involving the Delta variant and the results may not be representative of the patients afflicted by the other variants such as the Omicron variant.

Conclusion

Our findings from this single center prospective cohort emphasize that although the COVID-19 mortality rate was lowest among those with normal BMI (7.69%), progression severity and respiratory decompensation were not significantly associated with obesity as defined by the Asia Pacific BMI classification. This finding warrants confirmation in future studies with a representative sample size in each Asia pacific body mass index category. Further evaluation with larger prospective cohorts would prove to be useful, since body mass index is an important modifiable risk factor that may guide national health policy creation in terms of prioritization of populations for risk reduction and vaccination against COVID-19 infection. Although still unproven, interventions that reduce weight and visceral adiposity (waist circumference, waist-hip ratio) may reduce the risk of severe COVID-19 outcomes in Filipinos.

Clinical pearls for endocrinologists and clinicians should include the information that a non-invasive measurement of height, weight, waist and hip circumference on patients afflicted with COVID-19 may help in the acquisition of more robust data sets which may help shed light on further implications of the Asia Pacific classification of body mass index and measures of visceral adiposity on the outcomes of COVID-19 infection in Filipinos.

Consent for Publication

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Authors' Contributions

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Supplemental Tables

	Under weight (n=2)	Normal (n=26)	Over weight (n=26)	Obese (n=128)	*p*
	Frequency (%)				
Co-morbidities					
Neurologic					
Stroke or TIA	0	1 (3.85)	3 (11.54)	8 (6.25)	.671
Brain tumor	0	0	0	1 (0.78)	.999
Cardiac					
Hypertension	1 (50)	16 (61.54)	12 (46.15)	77 (60.16)	.569
Coronary disease	0	3 (11.54)	0	14 (10.94)	.358
Heart failure	0	0	0	2 (1.56)	.999
Pulmonary					
Asthma	0	2 (7.69)	4 (15.38)	18 (14.06)	.772
COPD	0	2 (7.69)	1 (3.85)	4 (3.13)	.524
Pulmonary TB	0	2 (7.69)	0	2 (1.56)	.233
Renal					
CKD	0	0	0	2 (1.56)	.999
Liver					
Chronic liver disease	0	0	0	0	-
Liver cirrhosis	0	0	0	0	-
Chronic hepatitis	0	0	1 (3.85)	0	.297
Hematologic disease					
Anemia	0	1 (3.85)	0	3 (2.34)	.759
Coagulopathy disorder	0	0	0	0	-
Endocrine					
Type 1 DM	0	0	0	1 (0.78)	.999
Type 2 DM	2 (100)	9 (34.62)	12 (46.15)	72 (56.25)	.088
Thyroid disease	0	2 (7.69)	1 (3.85)	7 (5.47)	.887

	Under weight (n=2)	Normal (n=26)	Over weight (n=26)	Obese (n=128)	*p*
	Frequency (%)				
Presenting symptoms					
Fever	2 (100)	18 (69.23)	20 (76.92)	116 (90.63)	**.016**
Cough	1 (50)	18 (69.23)	21 (80.77)	119 (92.97)	**.001**
Colds	2 (100)	8 (30.77)	10 (38.46)	55 (42.97)	.271
Difficulty breathing	2 (100)	13 (50)	16 (61.54)	101 (78.91)	**.008**
Sore throat	2 (100)	4 (15.38)	7 (26.92)	65 (50.78)	**<.001**
Watery stool	0	5 (19.23)	3 (11.54)	55 (42.97)	**.002**
Vomiting	0	1 (3.85)	1 (3.85)	7 (5.47)	.429
Seizure	0	1 (3.85)	0	0	.297
Muscle pain	0	4 (15.38)	10 (38.46)	36 (28.13)	.259
Loss of smell	2 (100)	8 (30.77)	11 (42.31)	68 (53.13)	.065
Loss of taste	2 (100)	10 (38.46)	12 (46.15)	66 (51.56)	.363

Table 1: Comorbidities and presenting symptoms by BMI class.

	All (n=182)	Under weight (n=2)	Normal (n=26)	Over weight (n=26)	Obese (n=128)	*p*
	Frequency (%)					
Respiratory decompensation	113 (62.09)	1 (50)	11 (42.31)	12 (46.15)	89 (69.53)	**.009**
Sepsis	39 (21.43)	0	1 (3.85)	3 (11.54)	35 (27.34)	**.016**
Septic shock	26 (14.29)	0	2 (7.69)	2 (7.69)	22 (17.19)	.509
ICU admission	27 (14.84)	0	2 (7.69)	2 (7.69)	23 (17.97)	.441
Need for vasopressor	25 (13.74)	0	2 (7.69)	2 (7.69)	21 (16.41)	.573
Mortality	23 (12.64)	0	2 (7.69)	3 (11.54)	18 (14.06)	.689
Statistical test used: Fisher's exact test.						

Table 2: Clinical outcomes by BMI class.

	All (n=93)	Normal (n=14)	Overweight (n=16)	Obese (n=63)	*p*
	Frequency (%)				
Respiratory decompensation	61 (65.59)	6 (42.86)	7 (43.75)	48 (76.19)	**.008**
Sepsis	24 (25.81)	0	3 (18.75)	21 (33.33)	**.020**
Septic shock	18 (19.35)	0	2 (12.50)	16 (25.40)	.069
ICU admission	19 (20.43)	0	2 (12.50)	17 (26.98)	**.042**
Need for vasopressor	18 (19.35)	0	2 (12.50)	16 (25.40)	.069
Mortality	18 (19.35)	0	3 (18.75)	15 (23.81)	.106
Statistical test used: Fisher's exact test.					

Table 3: Clinical outcomes in unvaccinated COVID-19 patients by BMI class (n=93).

	All (n=18)	Overweight (n=2)	Obese (n=16)	*p*
	Frequency (%)			
Respiratory decompensation	12 (6.67)	2 (100)	10 (62.50)	.529
Sepsis	2 (11.11)	0	2 (12.50)	.999
Septic shock	2 (11.11)	0	2 (12.50)	.999
ICU admission	2 (11.11)	0	2 (12.50)	.999
Need for vasopressor	2 (11.11)	0	2 (12.50)	.999
Mortality	1 (5.56)	0	1 (6.25)	.999
Statistical test used: Fisher's exact test.				

Table 4: Clinical outcomes in partially vaccinated COVID-19 patients by BMI class (n=18).

	All (n=71)	Underweight (n=2)	Normal (n=12)	Overweight (n=8)	Obese (n=49)	*p*
	Frequency (%)					
Respiratory decompensation	40 (56.34)	1 (50)	5 (41.67)	3 (37.50)	31 (63.27)	.333
Sepsis	13 (18.31)	0	1 (8.33)	0	12 (24.49)	.342
Septic shock	6 (8.45)	0	2 (16.67)	0	4 (8.16)	.592
ICU admission	6 (8.45)	0	2 (16.67)	0	4 (8.16)	.592

	All (n=71)	**Underweight (n=2)**	**Normal (n=12)**	**Overweight (n=8)**	**Obese (n=49)**	***p***
	Frequency (%)					
Need for vasopressor	5 (7.04)	0	2 (16.67)	0	3 (6.12)	.392
Mortality						
Statistical test used: Fisher's exact test.						

Table 5: Clinical outcomes in fully vaccinated COVID-19 patients by BMI class (n=71).