Bangladesh Journal of Medicine (BJM)
ISSN : 1023 - 1986
eISSN : 2408 - 8366

ORIGINAL ARTICLE

THE RELATIONSHIP BETWEEN BMI AND NEUTROPHIL/LYMPHOCYTE RATIO IN NON-CRITICAL HOSPITALIZED PATIENTS WITH CORONAVIRUS DISEASE 2019

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Abstract

Background: *People with obesity may be adversely affected by Coronavirusdisease 2019 (COVID-19). The objective of the study was to assess the clinical and biochemical characteristics of non-critical hospitalized patients of COVID-19 with obesity.* ***Methods:*** *This cross-sectional observational study was done among 88 non-critical hospitalized patients of COVID-19 [age: 50.0 (33.50-60.0) years, median (IQR); m/f: 36/52). The severity of COVID-19 at diagnosis was determined by WHO interim guidance on COVID-19, 2000, and obesity was defined by a body mass index of 25 kg/m^2. Clinical and biochemical information at diagnosis were collected in a data sheet.* ***Results:*** *Around 34% of the patients had obesity. Baseline characteristics and clinical features were statistically similar between obese and non-obese patients (NS for all). Among biochemical features, only total leukocytes (p=0.007), absolute neutrophils count (p=0.001), and neutrophils/ lymphocytes ratio (p=0.002) were significantly lower in obese patients than non-obese patients. Body mass index (BMI) had significant negative correlations with total leukocytes (r=-0.318, p=0.005), absolute neutrophil count (r=-370, p=0.001) and neutrophils/lymphocytes ratio (r=-0.349, p=0.002) in the study population.* ***Conclusion:*** *BMI had inverse associations with total leukocytes, absolute neutrophil count, and neutrophil/lymphocyte ratio among non-critical hospitalized patients with COVID-19.*

Keywords: *Coronavirus disease 2019, body mass index, obesity, neutrophil/lymphocyte ratio*

Received: 08.11.2022 *Accepted: 12.12.2022*

DOI: https://doi.org/10.3329/bjm.v34i1.63425

Citation: *Morshed MS, Banu H, Sultana N, Hasanat MA, Arafat SM. The relationship between BMI and neutrophil/lymphocyte ratio in non-critical hospitalized patients with coronavirus disease 2019. Bangladesh J Medicine 2023; 34: 36-42.*

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Introduction:

Coronavirus disease 2019 (COVID-19) is one of the greatest disasters in the history of mankind. As a pandemic, it has also affected Bangladesh with more than 02 million confirmed cases with nearly 30 thousand deaths (up to 06 August, 2022)[1]. Among several risk factors, obesity is one of the important risk factors for COVID-19 in several aspects. Overweight and obesity are associated with increased hospitalization for COVID-19 as well as increased need for intensive care unit (ICU) admission, mechanical ventilation, and mortality from COVID-19[2]. It may be associated with reduced response to vaccination also[3]. Increased COVID-19 hazards are linked to a number of factors in obese individuals. These include immune system impairments, adipose tissue inflammation, metabolic dysfunctions, co-morbidities linked to obesity, and mechanical pulmonary impairments[4].

Although obesity is the second most common COVID-19-associated co-morbidity worldwide but rarely reported in Asian countries, especially Bangladesh[5]. Twenty percent of Bangladeshi adults are overweight and 5.4% are obese, while seven out of ten persons are at an increased risk of obesity, with females being more than six times as likely to be affected.[6] Prevalence of overweight population has increased during COVID-19 in Bangladesh. The pandemic-associated stress, unemployment, and sedentary lifestyle are the main contributing factors[7].

Most of the studies focused on the outcomes of COVID-19 patients with obesity. Moreover, the results were mostly described in severe, critical patients requiring ICU support. However, most of the COVID-19 patients are noncritical in whom the associations of body mass index (BMI) with different clinical and biochemical manifestations are rarely described in the literature. With this view, the aim of the study was to see the associations of obesity with different characteristics of hospitalized noncritical COVID-19 patients.

Methods:

This cross-sectional observational study was done in the COVID-19 unit of a University hospital during the period of September 2021-February 2022. Hospitalized patients with RT-PCR confirmed noncritical COVID-19 patients were included consecutively. Socio-demographic history, clinical features, and COVID-19-related investigation findings were directly obtained by the data collector. The study was conducted according to the Helsinki declaration. Ethical clearance was taken from the institutional review board of the University. Informed written consent was taken from each participant.

Oxygen saturation and pulse were measured by a pulse oximeter. Respiratory rate was observed over one minute. Blood pressure was measured in a supine position with maintaining standard procedure. Height (cm) was measured by a wall-mounted stadiometer and weight (kg) by a calibrated bathroom scale. BMI was calculated from the following formula: BMI= weight in kg ÷ (height in meter)^2. All the COVID-19-related investigation findings [complete blood count (CBC), electrolytes (sodium and potassium), alanine aminotransferase (ALT), creatinine, C-reactive protein (CRP), D-dimer, ferritin] at admission were recorded.

Diagnosis of COVID-19 and its severity was done by the world health organization's (WHO) guideline[8]. We used a BMI cut-off of 25 kg/m^2 (Asian population criteria) to define obesity[9].

We used SPSS software version 22.0 to analyze our data. Data were expressed in median (inter-quartile range, IQR) for quantitative and frequency (percent, %) for qualitative values. Comparison between groups was done by Mann-Whitney U test or Pearson's chi-square/Fisher's exact test as appropriate. Correlations of BMI with clinical and biochemical variables were done by Spearman's correlation test. There were many missing data. Available numbers were mentioned appropriately and analyses were done within the available data. P values below 0.05 were considered statistically significant.

Results:

Among 88 noncritical hospitalized COVID-19 patients, 30 (34.09%) had obesity. Among non-obese people, 09 (10.2%) had under-nutrition (<18.5 kg/m^2), 32 (36.4%) had optimal BMI (18.5 – 22.99 kg/m^2) and 17 (19.3%) had overweight (23 – 24.99 kg/m^2). The median age of the study population was 50.0 (33.50-60.0, IQR; min: 18, max: 65) years with a predominance of females (52, 59.1%). The demographic characteristics of the study population showed that there were no statistically significant differences in age, sex, marital status, or comorbidities between patients with or without obesity (NS for all) (Table I).

Table-I

Baseline characteristics of hospitalized noncritical COVID-19 patients with obesity (N=88)

Variables	Characteristics	Obese	Non-obese	p
Number (%)		30 (34.1)	58 (65.9)	
Age, years	48.50 (30.25-57.25)	53.0 (35.0-62.50)	0.208	
Sex	Male	9 (30.0)	27 (46.6)	0.172
	Female	21 (70.0)	31 (53.4)	
Maritalstatus	Married	28 (93.3)	47 (81.0)	0.204
	Unmarried	2 (6.7)	11 (19.0)	
Co-morbidities	Hypertension	15 (50.0)	23 (39.7)	0.373
	DM	16 (53.3)	21 (36.2)	0.172
	OLD	6 (20.0)	7 (12.1)	0.353
	Hypothyroidism	2 (6.7)	2 (3.4)	0.603

DM (diabetes mellitus); OLD (obstructive lung disease)
Within parenthesis are percentages over column total for qualitative variables
Data were expressed in median (IQR) or frequency (%)
Mann-Whitney U test or Pearson's chi-square/Fisher's exact test was done

The first ten common symptoms, vital signs, and severity of illness were shown in Table II. Fatigue, cough, fever, and dyspnea were the predominant symptoms. The frequency of all the symptoms was statistically similar between the study groups (NS for all). Less common symptoms were sore throat (16.7% vs. 15.5%, p=1.00); nausea (13.3% vs. 13.8%, p=1.00); nasal stuffiness (10.0% vs. 10.3%, p=1.00); dysgeusia (6.7% vs. 5.2%, p=1.00) etc. Similar to symptoms, the frequencies of vital signs and severity of illness were also statistically similar (NS for all).

Table-II

Clinical features of hospitalized noncritical COVID-19 patients with obesity (N=88)

Variables	Characteristics	Obese	Non-obese	p
Symptoms	Fatigue	23 (76.7)	46 (79.3)	0.790
	Cough	21 (70.0)	44 (75.9)	0.613
	Fever	20 (66.7)	41 (70.7)	0.808
	Dyspnea	15 (50.0)	38 (65.5)	0.175
	Headache	12 (40.0)	24 (41.4)	1.00
	Sleep disturbance	9 (30.0)	22 (37.9)	0.491
	Dizziness	13 (43.3)	14 (24.1)	0.088
	Vomiting	8 (26.7)	12 (20.7)	0.595
	Palpitation	6 (20.0)	14 (24.1)	0791
	Chest pain	4 (13.3)	15 (25.9)	0.274
Signs	Pulse, bpm	88.0 (80.0-102.50)	88.0 (80.0-101.25)	0850
	Respiratory rate	14.0 (12.0-14.0)	14.0 (12.0-18.0)	0.059
	Systolic BP	123.50 (112.25-140.50) [26]	120.0 (110.0-135.25) [54]	0.514
	Diastolic BP	80.0 (70.0-90.0) [26]	78.0 (70.0-84.0) [54]	0.467
Severity of illness	Mild	21 (70.0)	33 (56.9)	0.368
	Moderate	5 (16.7)	18 (31.0)	
	Severe	4 (13.3)	7 (12.1)	

Data were expressed in frequency (%). [Available number]
Pearson's chi-square/Fisher's exact test was done

Table- III

Investigation profile in hospitalized noncritical COVID-19 patients with obesity

Investigations	Available no.	Obese	Available no.	Non-obese	p
Hemoglobin, gm/dL		11.25 (9.87-12.10)	26	11.45 (10.20-12.60)	50	0.443
Total leukocytes, $\times10^3$ /µL		7.09 (6.34-925)		10.15 (7.83-13.25)		**0.007**
Neutrophils, $\times10^3$ /µL		5.60 (3.39-6.20)		7.38 (5.40-11.15)		**0.001**
Lymphocytes, $\times10^3$ /µL	76	1.94 (1.40-2.75)		1.55 (1.19-2.32)		0.244
Platelets count, $\times10^3$ /µL		219.0 (166.50-267.0)		223.50 (149.75-298.50)		0.865
Neutrophils/lymphocytes		2.41 (1.55-4.62)		4.13 (2.49-9.15)		**0.002**
Platelets/lymphocytes		128.09 (83.36-164.28)		127.70 (92.84-240.08)		0.346
Serum Na^+, mmol/L	56	135.0 (131.50-136.0)	21	134.0 (131.0-139.0)	35	0.932
Serum K^+, mmol/L		4.0 (3.86-4.55)		3.90 (3.20-4.40)		0.090
ALT, U/L	29	61.0 (19.50-71.50)	10	380 (24.0-59.0)	19	0.512
Serum creatinine, mg/dL	51	0.95 (0.70-1.24)	18	0.86 (0.68-1.23)	33	0.454
CRP, mg/L	48	23.30 (5.44-60.50)	15	28.0 (11.0-89.45)	33	0.266
Ferritin, ng/dL	36	214.90 (51.26-517.83)	14	491.50 (189.50-862.45)	22	0.071
D-dimer, mg/L	56	0.54 (0.11-2.80)	20	0.74 (0.34-2.91)	36	0.521

Data were expressed in median (IQR).
Mann-Whitney U test was done

All the investigation findings were statistically similar between obese and non-obese patients except for total leukocytes (p=0.007), absolute neutrophils count (p=0.001), and neutrophils/lymphocytes ratio (p=0.002) which were significantly lower in obese patients than non-obese patients (Table III).

BMI had significant negative correlations with total leukocytes (r=-0.318, p=0.005), absolute neutrophil count (r=-370, p=0.001), and neutrophils/lymphocytes ratio (r=-0.349, p=0.002) in the whole study population (Table IV).

Table-IV

Correlation of BMI with characteristics of hospitalized noncritical COVID-19 patients with obesity

Determinants of 'r'	No.	r	p
Age, years	88	-0.011	0.918
Systolic BP, mm-Hg	80	0.184	0.102
Diastolic BP, mm-Hg		0.104	0.357
Hb, gm/dL	76	-0.114	0.325
Total leukocytes, $\times10^3$ /µL		-0.318	**0.005**
Neutrophils, $\times10^3$ /µL		-0.370	**0.001**
Lymphocytes, $\times10^3$ /µL		0.153	0.186
Platelets count, $\times10^3$ /µL		0.027	0.819
Neutrophils/lymphocytes		-0.349	**0.002**
Platelets/lymphocytes		-0.066	0.569
Serum Na^+, mmol/L	56	0.012	0.927
Serum K^+, mmol/L		0.136	0.319
Serum ALT, U/L	29	0.037	0.848
Serum creatinine, mg/dL	51	0.129	0.368
Serum CRP, mg/L	48	-0.136	0.355
Serum ferritin, ng/dL	36	-0.247	0.146
Serum D-dimer, mg/L	56	-0.093	0.496

Spearman's correlation test was done

Discussion:

In this study, we found that around 34% of noncritical hospitalized patients had obesity. Obese patients had similar characteristics in comparison to non-obese hospitalized non-critical patients with COVID-19 except for lower total leukocytes, absolute neutrophil count and neutrophils/lymphocytes count. Moreover, these variables significantly and negatively correlated with BMI in the study group.

With a BMI cut-off of 25 kg/m^2, almost one-third of our study population was obese. Using a cut-off of 27 kg/m^2, earlier research discovered that 24.4% had obesity[10]. A previous study found higher BMI in the severe group without a significant association between them[11].We did not find a significant association between obesity with disease severity.

We did not find any significant association of any clinical features with the BMI category. A previous study from Bangladesh did not find any significant association between different BMI categories with patients categorized based on symptoms[12].

Neutrophilia along with lymphopenia which is the elevated neutrophils/lymphocytes ratio is one of the independent risk factors of severe COVID-19 and poor outcome[12,13]. Around 75% of deceased Bangladeshi hospitalized COVID-19 patients had also high NLR (e"5)[14]. So, the expected association of BMI with NLR is in a positive direction. However, we found a negative association between them. A study conducted in Turkey among hospitalized patients for physiotherapy also showed a similar association[15]. Furthermore, National Health and Nutrition Examination Survey (1999-2016) conducted among more than 48,000 adults also found a significant and independent negative association between BMI with NLR[16]. We did not find any study describing their association with COVID-19 patients.

The association between BMI with leukocytes in our study was mainly due to the significant association with the neutrophil count. However, previously reported Bangladeshi studies found an association of severity of COVID-19 only with lymphopenia but not with neutrophilia in critical patients[17,18]. A previous study found a significant correlation of neutrophils with lymphocytes only in severe and critical patients but not in non-severe patients[19]. We found the association with only neutrophils rather than lymphocytes. NLR is also able to distinguish severe cases from mild-moderate cases of COVID-19[20]. The majority of the participants in our research had mild symptoms of COVID-19, and 70% of the obese patients had mild cases as well. In the initial stages during hospitalization, total leukocyte count might be similar to healthy controls which further increased in the later days of the disease course. Even some studies found initial leukopenia upon admission[21].Another key element is the age dependence of leukocyte counts, with older persons having greater counts than younger ones[22]. Similarly, our obese patients were younger than our non-obese patients.Furthermore, males had higher NLR than females, and in our study, the number of men in the obese group was lower than in the non-obese group[23].These factors, when combined, most likely affected our findings.

Most critical COVID-19 patients who are obese suffer from it[2]. Probably, for this reason, we did not identify any significant link between the severity of disease in noncritical patients and obesity. However, we could not able to include critical patients as measuring BMI was difficult in these patients. The sample size was small with very few cases of severe disease. There were many missing data also. The main strength of this study was that we were able to collect data directly from patients rather than in previously described retrospective studies.

Conclusion:

Obesity was found in more than 30% of Bangladeshi noncritical hospitalized COVID-19 patients. BMI, demonstrated an inverse relationship with total leukocytes, absolute neutrophil count, and neutrophil/lymphocyte ratio. Further large-scale studies are needed to clarify this paradoxical association in COVID-19 patients.

Acknowledgment:

We are grateful to the Department of Microbiology and Immunology, BSMMU for laboratory support.

Conflict of interest:

None of the authors has any conflict of interest to declare.

Ethical approval:

The research protocol was approved by Institutional Review Board, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.

Funding statement:

We obtained a grant from Research and Development, BSMMU

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