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Body Mass Index as a Predictor of Symptom Duration in COVID-19 Outpatients

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Abstract

Background: Obesity is a risk factor for various diseases and can affect the disease course. Studies have shown detrimental effects of obesity on patients affected with SARS-CoV-2 including increased hospitalization and more severe disease. This study aims to investigate the effects of obesity on symptom duration in patients with COVID-19, and also explore the possibility of using BMI as a predictor of symptom duration in outpatient settings.
Methods: Patients diagnosed with COVID-19 between June and October 2020, who had no other comorbidities, and were planned to receive treatment in the outpatient setting were enrolled in the study. Duration of the symptoms was determined based on participants' self-report of their symptoms. Linear regression was used to create predictive models based on participants' BMI, age, sex, disease presentation, and their self-reported symptom duration.
Results: A total of 210 patients were included in the final analysis. Patients with higher BMI had significantly longer symptom duration. Linear regression models showed highest correlation between BMI and symptom duration compared to other covariates.
Conclusion: Low error in predictions and high coverage of data variability showed BMI can be used as a predictive factor for symptom duration in COVID-19 patients treated in outpatient settings.

Introduction

An outbreak with a novel coronavirus, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) started in late 2019 in China and rapidly spread among other countries and territories, resulting in the Coronavirus Disease of 2019 (COVID-19) pandemic. Primarily, fever and respiratory manifestations such as dry cough and dyspnea were recognized as the hallmark symptoms of the disease caused by SARS-CoV-2, COVID-19.[1] However, the list of symptoms expanded to include a range of manifestations from mild constitutional symptoms to life-threatening conditions such as multi-organ failure.[2] Several studies have focused on the factors that determine the duration of the symptoms, outcome of the disease, and its transmission rate. Pre-existing conditions and comorbidities play a major role in determining the outcome of COVID-19.[3] Among the comorbidities studied, hypertension, cardiovascular diseases (CVD), and diabetes mellitus are more emphasized as factors worsening the outcome of COVID-19 patients.[4] Obesity, as a disease coming hand-in-hand with aforementioned preexisting conditions, has been studied regarding its effects on different aspects of infection with SARS-CoV-2, including severity of symptoms, duration of hospitalization, and outcome of the disease. Herein, the effects of obesity on symptom duration in COVID-19 outpatients is studied.

Methods

This is a cross-sectional study of patients with symptoms suggestive of COVID-19 who presented to the emergency department of Khatam Hospital in Salmas, Northwest Iran, between June 15 to October 15, 2020. This was shortly after a surge in the disease cases was controlled in the study area by restrictions to employ social distancing. Inclusion criteria were age > 18 years old, positive SARS-CoV-2 real-time polymerase chain reaction (RT-PCR) or lung involvement in chest computed tomography (CT) scans, and symptoms suggestive of COVID-19 disease including respiratory symptoms (cough or dyspnea), constitutional symptoms (fever, myalgia, malaise, anorexia, fatigue, or headache), gastrointestinal (GI) symptoms (nausea, vomiting, heart burn, or diarrhea), and symptoms mimicking myocardial infarction (MI) if patients had no history of CVD, and their evaluation, including physical examination and diagnostic

workup, as well as laboratory tests and electrocardiograms, were not confirming diagnosis of MI. Exclusion criteria were hospital admission either in the primary visit or anytime during the course of follow-up, patients with symptoms of MI with risk factors for CVD (with the exception of obesity as the mere risk factor) or further evaluation suggestive of MI, and chronic comorbidities including chronic respiratory disorders, diabetes, hypertension, cancer, or use of immunosuppressive drugs. The rationales behind these exclusion criteria were to limit the confounding factors, as chronic diseases have been shown to worsen the outcome of disease in patients with COVID-19. Furthermore, by excluding patients that were hospitalized at any point, it was attempted to include cases with comparable disease severity. This allowed comparing participants' symptom duration based on their age, sex, BMI, and disease presentation.

The 3 main variables defined in this study were: (1) body mass index (BMI): calculated as participant's weight (kg) divided by the square of their height (m^2), measured during the emergency department visit, (2) symptom group: defined as constitutional symptoms, GI symptoms, respiratory symptoms, or a combination of these symptoms, and (3) symptom duration in days: defined as the day patient reported the start of the symptoms until the day symptoms were resolved during telemedicine follow up. Follow up was performed at weekly intervals by the emergency department's physician first visiting the participant through phone calls, and if necessary, through in-person visits. All participants were comparable in terms of treatment and medications received in the outpatient setting, which included use of vitamin C, vitamin D, zinc supplements, and antipyretics as needed.

To study the effects of BMI on symptom duration, participants were categorized into 4 BMI categories: underweight (< 18.5 kg/m^2), normal weight (>= 18.5 and < 24.9 kg/m^2), overweight (>= 24.9 and < 29.9 kg/m^2), and obese (>= 29.0 kg/m^2) (www.cdc.gov). Mann-Whitney U test and Student's t-test were used to compare the duration of symptoms among the 4 BMI groups. In an additional analysis to assess BMI as a predictor of symptom duration in COVID-19 outpatients, 4 general linear models (GLM) were used. In Model A, numeric values of BMI were used to predict symptoms duration. Model B used numeric values of BMI along with participants' age, sex, and symptom groups (as mentioned earlier). In both models, 70% of data were used to train the model and 30 percent of the data was used to test accuracy of the model. Significance level of alpha was 0.05 for all analyses. All analyses were performed in R 4.0.5 (R Foundation for Statistical Computing, Vienna, Austria).[5] This study was exempted by the Institutional Review Board of Salmas Health Network.

Results

During the duration of the study, a total of 210 participants were enrolled. Age of participants ranged between 18 and 67 years (mean: 44.5 ± 15.03). Participants' BMI ranged between 16.87 and 38.26 (mean: 25.16 ± 4.67). Further information regarding the recruited participants is summarized in Table 1.

Using Mann-Whitney U test, it was found that underweight participants had significantly shorter symptom duration when compared to overweight participants, however, their symptom duration was not significantly different from that of normal weight or obese participants (Table 2A). Student's t test showed significant difference between normal, overweight, and obese participants (Table 2A).

To find how BMI could be used to predict symptom duration in participants, 2 linear regression models were used. In Model A, BMI had a correlation coefficient of 0.67 ($P\ value < 0.01$), an adjusted R-squared of 0.67, and a root mean square error (RMSE) of 1.436516e-16. In Model B, of the covariates included, BMI had the largest correlation coefficient (0.64, $P\ value < 0.01$) followed by symptom category (0.19, $P\ value = 0.09$), participants' age (0.02, $P\ value = 0.06$) and their sex (- 0.02, $P\ value = 0.9$). Adjusted R-squared for Model B was 0.68 ($P\ value < 0.01$) and RMSE for this model was 1.023553e-15. As the predictive models showed, and as depicted in Figure 1, BMI showed a linear correlation with participants' disease duration, which supports the hypothesis of BMI affecting disease duration in COVID-19 outpatients.

Discussion

Obesity is a risk factor or an exacerbating factor for many diseases such as CVD, diabetes, various cancers, depression, kidney and liver diseases, and osteoarthritis.[6] Expectedly, several studies have investigated the effects of obesity on the outcome of COVID-19 patients, as reviewed in the study of Zhang *et al.*[7] These studies are of importance as they can help with management of healthcare services, especially in inpatient settings where providing healthcare has become challenging due to limited resources. Thus far, obesity is found to be a risk factor for increased hospital admissions, especially among younger populations,[8,9] as well as for increased severity of diseases and rates of mortality among hospitalized patients.[10,11]

Factors determining the course of the disease are not merely important for resource management in inpatient settings. Estimating when an individual treated in outpatient settings can return to normal life is also important for both the affected individual and resource management in other industries. In addition, when COVID-19 patients will be symptom-free can also affect isolation periods and viral shedding, however, these require further investigation. Even though several studies have been dedicated to finding factors that can affect the duration and course of the disease in COVID-19 hospitalized patients, few studies have focused on factors determining the symptom duration in outpatients.[12,13] Of these studies, only a few have focused on the effects of BMI on duration of the disease[12,13] with such research being mostly focused on obese individuals.[12]

This study suggests BMI as an important factor in determining the duration of self-reported symptoms and based on the coefficients of the variables included in the study, its role in predicting duration of symptoms is more prominent than other covariates in the absence of other comorbidities. In addition, the significant difference between symptom duration of overweight and obese participants shows that effects of BMI are directly associated with symptom duration. A relatively recent study found that patients with high BMI and obesity can benefit from Metformin in outpatient settings,[14] which denotes the importance of considering obesity in patient management in outpatient settings. Furthermore, the COVID-19 pandemic has had detrimental effects on individuals' BMI and obesity trends worldwide[15] which need to be addressed, not only as a risk factor for COVID-19, but also for other chronic diseases. These require holistic preventive approaches in fighting against COVID-19, which are not limited to physical distancing, isolation, vaccination, and intensive care for severely affected cases.

Even though this study suggests an association between high BMI and longer duration of self-reported symptoms, there were limitations that need to be addressed. The number of patients with low BMI based on classification of the Center for Disease Control

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Table 1. Participants' demographics

BMI group	Weight (mean ± SD)	Age (mean ± SD	Sex (M = male, F = female)	Respiratory symptoms (N)	GI symptoms (N)	Constitutional symptoms (N)	Combination* (N)	Duration (mean±SD)
Underweight	46.42 ± 4.03	24.42 ± 6.99	1 M, 6 F	0	0	7	0	5.7 ± 11.11
Normal	63.62 ± 8.38	44.01±15.73	54 M, 47 F	5	12	62	22	6.97±1.6
Overweight	78.7±8.91	46.07±13.58	25 M, 44 F	8	1	26	34	11.94±2.86
obese	96.09±14.21	46.87±14.15	16 M, 17 F	2	0	5	26	14.57±2.94
total	73.1 ±15.87	44.49 ±15.03	96 M, 114 F	15	13	100	82	9.75±3.84

N, Number; SD, standard deviation; combination, patients having a combination of respiratory, GI, or constitutional symptoms

Table 2. Mann-Whitney U test and Student's t test to compare the duration of disease in COVID-19 outpatients. Upper panels show p values and lower panels show calculated W and t values. Significant differences are marked by asterisk

BMI Category	Normal	Underweight	Overweight	Obese
Normal		$P = 0.04357$	$P < 2.2e\text{-}16$	$P < 2.2e\text{-}16$
Underweight	W = 512.5		$P = 2.329e\text{-}05$	$P = 3.925e\text{-}05$
Overweight	t = 13.068*	W = 476*		$P = 7.168e\text{-}05$
Obese	t = 14.153*	W = 231	t = 4.2578*	

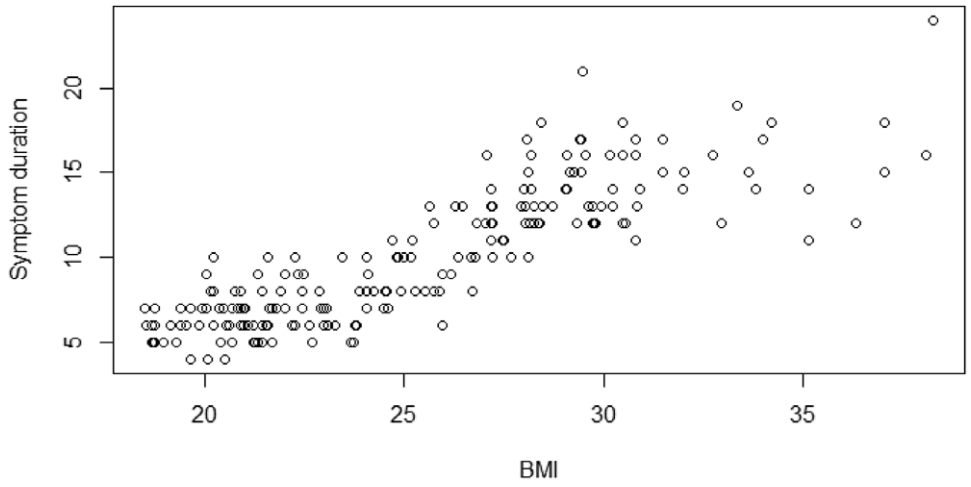

Figure 1. Patients' BMI is correlated with duration of symptoms in outpatient COVID-19 patients.

and Prevention was small, and BMI of these patients were above the World Health Organization cut off for moderate and severe thinness (BMI < 17 kg/m^2). Therefore, this study cannot reveal if very low BMI indicating severe thinness can be a risk factor for longer disease on its own. Furthermore, this study tried to eliminate any confounding factor that can prolong the disease due to limitations posed by the geographical area. Effects of BMI need to be studied in patients with other comorbidities as well. Furthermore, the exact statistics of the geographic area in which this study was performed was not available, which could affect the interpretation of the results from this study. Even though the findings of this study are in concert with other studies regarding the effects of higher BMI on the COVID-19 course,[7–14] these findings need to be verified by studies with larger sample sizes which also focus on other aspects of the disease such as duration of viral shedding, duration of seropositivity for anti-SARS-CoV-2 antibodies, and when the patients test negative for SARS-CoV-2 RT-PCR.

Conclusion

Obesity is a risk factor as well as an exacerbating factor for many chronic and acute diseases. Many studies have found detrimental effects of obesity on COVID-19 patients, including increased severity and longer hospital stays. In this study, it was suggested that obesity plays an important role in the duration of the disease and can be used as a predictive factor for symptom duration in COVID-19 patients.

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the manuscript; Saied Ebrahimi: critical review of the manuscript, writing of the manuscript; and Nima Rezaei: critical review of the manuscript, design of the research.

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