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The Effect of Obesity on COVID-19 Course

Obezitenin COVID-19 Seyrine Etkisi

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Abstract

Objectives: Clinical features and risk factors are highly variable for Coronavirus disease-2019 (COVID-19). Researchers investigate for the prediction of people who have high risk of developing severe illness and dying. The aim of this study is to examine the effect of obesity on the course of COVID-19.

Materials and Methods: Patients with laboratory confirmed COVID-19 were retrospectively screened between March 11 and April 30. Anthropometric measures including standing height and body weight were measured at admission. Body mass index (BMI) was calculated and patients were classified into three groups as BMI<25, BMI 25-29.99, and BMI≥30 according to the guidelines for the diagnosis and treatment of obesity in Turkey.

Results: A statistically significant correlation was found between BMI and disease severity and intensive care unit admission (p<0.001and p<0.001 respectively). A significant relationship was found between the BMI and support of invasive mechanical ventilation (p=0.007). Mortality rates of the patients were also significantly different in BMI groups (p=0.030). The mortality rate was 1.1% in patients with a BMI <25 and 1.3% in patients with a BMI 25-29.99. However, mortality rate was 8.6% in patients with a BMI ≥30.

Conclusion: The relationship between infectious diseases and obesity has not been established yet. Immune system deficiency, obesity-related comorbidities and respiratory tract abnormalities may cause poor prognosis of infectious diseases. So early detection and aggressive treatment for obese patient with COVID-19 is very important.

Key Words: Obesity, COVID-19, Infection Diseases

Öz

Amaç: Klinik özellikler ve risk faktörleri, Koronavirüs hastalığı-2019 (COVID-19) için oldukça değişkendir. Ağır hastalığa yakalanma ve ölme riski yüksek olan kişileri öngörmek için çeşitli araştırmalar yapılıyor. Bu çalışmanın amacı obezitenin COVID-19 seyrine etkisini incelemektir.

Gereç ve Yöntem: Laboratuvarca doğrulanmış COVID-19'u olan hastalar, 11 Mart ile 30 Nisan tarihleri arasında retrospektif olarak tarandı. Yatışta antropometrik ölçümlerden boy ve vücut ağırlığı ölçüldü. Vücut kitle indeksi (VKİ) hesaplandı ve hastalar Türkiye obezite tanı ve tedavi kılavuzlarına göre VKİ<25, VKİ 25-29,99 ve VKİ≥30 olmak üzere üç gruba ayrıldı.

Bulgular: VKİ ile hastalık şiddeti ve yoğun bakım ünitesine yatış arasında istatistiksel olarak anlamlı bir ilişki bulundu (sırasıyla p<0,001 ve p<0,001). VKİ ile invazif mekanik ventilasyon desteği arasında anlamlı bir ilişki bulundu (p=0,007). Hastaların ölüm oranları da VKİ gruplarında anlamlı olarak farklıydı (p=0,030). Ölüm oranı VKİ <25 olan hastalarda %1,1, VKİ 25-29,99 olan hastalarda %1,3 idi. Ancak VKİ 30 olan hastalarda ölüm oranı %8,6 olarak saptandı.

Sonuç: Enfeksiyon hastalıkları ile obezite arasındaki ilişki net bir şekilde kurulamamıştır. Bağışıklık sistemi yetersizliği, obezite ile ilişkili komorbiditeler ve solunum yolu anormallikleri bulaşıcı hastalıkların kötü prognozuna neden olabilir. Bu nedenle COVID-19 ile izlenen obez hasta için erken teşhis ve agresif tedavi çok önemlidir.

Anahtar Kelimeler: Obezite, COVID-19, Enfeksiyon Hastalıkları

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Introduction

On February 11, 2020, the World Health Organization (WHO) named the pneumonia with unknown etiology as Coronavirus disease-2019 (COVID-19). Clinical features and risk factors are highly variable for COVID-19. COVID-19 can be asymptomatic, mild or severe forms. So researchers investigate for prediction of people who have high risk of developing severe illness and dying. Chronic conditions such as diabetes mellitus (DM), hypertension (HT), chronic lung diseases (CLD) and cardiovascular diseases, increase the risk for severe COVID-19 (1,2). Recent study have linked obesity to more severe COVID-19 illness and mortality (3,4). Obesity leads to dysregulated immune response. This is very important for infection diseases. The aim of this study is to examine the effect of obesity on COVID-19 course.

Materials and Methods

Patients with laboratory confirmed COVID-19 who were admitted to the main pandemia hospital in Turkey, between March 11 and April 30, were retrospectively screened. Patients with COVID-19 were confirmed by a positive result from real-time reverse transcriptase-polymerase chain reaction assay with nasal and pharyngeal swab specimens for severe acute respiratory syndrome causing Coronavirus-2 RNA. The clinical data of 335 patients have been obtained. Patients who were under the age of 18, underweight [body mass index (BMI)<18.5], pregnant, using steroid therapy and who had malignancy were excluded. A total of 229 patients were included in the final analysis. Cases were diagnosed on the basis of interim guidance of WHO (5). Patients were classified into three groups as mild disease, pneumonia and severe pneumonia (Table 1). Clinical symptoms, signs and laboratory data were obtained from medical records of hospital. Anthropometric measures including standing body weight and height were measured at admission, with no shoes and light indoor clothing. Weight was measured to the nearest 0.1 kg and height was measured to the nearest 0.1 cm and BMI was calculated as weight divided by height, expressed as kilogram per square meter. Patients were classified into three groups as BMI <25, BMI 25-29.99 and BMI ≥30 according to Turkey obesity diagnosis and treatment guidelines. This study was approved by Locals Ethics Committee (date: 21.05.2020, number: E1-20-623) and by Ministry of Health (number: 2020-05-07T08_51_26.xml).

Statistical Analysis

Statistical analysis of the data was performed using Statistical Package for the Social Sciences (Version 22, SPSS Inc., Chicago, IL, USA) package program. The normal distribution of the data was tested with the Shapiro-Wilk test. Descriptive statistics of categorical variables were reported as number and percentage (%). Descriptive statistics of continuous variables were reported as mean ± standard deviation or median ± interquartile range (minimum-maximum) according to data normality distribution. Relationships between BMI level and socio-demographic characteristics, smoking, symptoms, comorbidity, disease severity, need for intensive care, need for mechanical ventilation, and mortality were investigated using the chi-square test or Fisher's exact test, depending on the number of data in the crosstab cells. Relationships between continuous variables were evaluated with the Pearson correlation coefficient. Hospitalization durations of the patients between 3 different BMI groups were compared using the One-Way ANOVA test. Post-hoc pairwise comparison tests with Bonferroni correction were used to determine which groups caused the difference. Covariance analysis (ANCOVA) was used to compare the length of hospital stay by statistically controlling the effect of patient ages among the BMI groups. Since the data was not normally distributed between two different BMI groups, the length of ICU stay was compared with the Mann-Whitney U test. Statistical significance level was accepted as p<0.05.

Results

Two hundred and twenty-nine patients were included in the study. One hundred and twenty-two (53.3%) of patients were female and 107 (46.7%) were male. The mean age of the patients was 45.16±16.19 (18-86). The seventy-six (33.2%) patients were BMI <25.95 (41.5) patients were BMI 25-29.99

Table 1: Study groups

Mild disease	- Positive results of RT-PCR for SARS-CoV-2 - Uncomplicated upper respiratory tract viral infection symptoms of COVID-19 such as fever, fatigue, cough, anorexia, muscle pain, headache and sore throat. Patients may also experience diarrhea, nausea and vomiting. - No typical computed tomography (CT) image abnormalities of viral pneumonia
Pneumonia	- Positive results of RT-PCR for SARS-CoV-2 - Fever or fatigue, cough (with or without sputum production), anorexia, malaise, muscle pain, sore throat, dyspnea, nasal congestion, headache, diarrhea, nausea, and vomiting - Typical CT image abnormalities of viral pneumonia.
Severe pneumonia	- Shortness of breath, respiratory rate (RR) ≥30 times/min. - Oxygen saturation (resting state) ≤93% on room air

RT-PCR: Reverse transcriptase-polymerase chain reaction, SARS-CoV-2: Severe acute respiratory syndrome causing Coronavirus-2, COVID-19: Coronavirus Disease-2019, min: Minute and 58 (25.3%) patients were BMI ≥30. Female and male ratios were similar between BMI groups (p=0.074) (Table 2). Patient ages were statistically significantly different between BMI groups (p<0.001).

In the BMI groups, the gender distribution, smoking rates, and symptom rates were similar (p=0.074, p=0.707, p=0.112, respectively) (Table 2), and the rates of comorbidity were significantly different (p=0.032). The distributions of coronary artery, CLD and kidney disease were similar (p=0.581, p=0.412, p=0.091, respectively). The distribution of DM and HT was significantly different between BMI groups (p=0.027, p=0.047, respectively).

A statistically significant correlation was found between BMI and disease severity (p<0.001, Table 3). A significant correlation was found between the BMI and intensive care unit (ICU) admission (p<0.001), (Table 3). A significant relationship was found between the BMI and support of invasive mechanical ventilation (p=0.007) (Table 3). While the support of mechanical ventilation was required in 1.3% of the patients with a BMI <25 and in 1.1% of the patients with a BMI 25-29.99, support of mechanical ventilation was required in 10.3% of the patients with a BMI ≥30. Mortality rates of the patients were also significantly different in BMI groups (p=0.030) (Table 3). Since the mean age of the patients in the BMI groups was statistically significantly different, the patients were divided into two groups as under 60 and over 60 and a statistically significant relationship was found between BMI level and disease severity in both age groups (age<60: p<0.001; age≥60: p=0.026) (Table 4). In patients under the age of 60: Mild disease was observed in 44.4% of patients with a BMI<25, while 24.3% of patients with a BMI 25-30 and 21.6% of patients with a BMI≥30 had mild disease. In patients aged 60 and above, mild disease was observed in 50% of those with a BMI <25, while 12% of patients with a BMI 25-29.99 and 9.5% of patients with a BMI≥30 had mild diseases.

The comparison of hospital stay times between research groups is given in Table 5. The length of stay in hospital was statistically significantly different between the groups (p=0.001). The post-hoc double comparison test was performed to determine the groups where the difference

Table 2: Comparison of gender, smoking, symptom and comorbidity distributions of patients between BMI groups

		BMI Groups				
		<25 (n=76)	25-30 (n=95)	>30 (n=58)	Total (n=229)	p-values
Gender	**Female**	35 (46.1%)	49 (51.6%)	38 (65.5%)	122 (53.3%)	0.074[a]
	Male	41 (53.9%)	46 (48.4%)	20 (34.5%)	107 (46.7%)	
Smoking		9 (11.8%)	9 (9.5%)	8 (13.8%)	26 (11.4%)	0.707[a]
Symptoms		69 (90.8%)	93 (97.9%)	54 (93.1%)	216 (94.3%)	0.112b
Comorbidity		15 (19.7%)	32 (33.7%)	23 (39.7%)	70 (30.6%)	**0.032[a]**
Coronary artery		2 (2.6%)	6 (6.3%)	3 (5.2%)	11 (4.8%)	0.581[b]
HT		5 (6.6%)	17 (17.9%)	13 (22.4%)	35 (15.3%)	**0.027[a]**
DM		5 (6.6%)	8 (8.4%)	11 (19.0%)	24 (10.5%)	**0.047[a]**
CLD		4 (5.3%)	5 (5.3%)	6 (10.3%)	15 (6.6%)	0.412[b]
Kidney disease		0 (0%)	4 (4.2%)	0 (0%)	4 (1.7%)	0.091[b]

[a]Chi-square test, [b]Fisher's exact test
DM: Diabetes mellitus, HT: Hypertension, CLD: Chronic lung disease, BMI: Body mass index

Table 3: Comparison of disease severity, intensive care need, mechanical ventilation need and patient conditions among BMI groups

		BMI groups				
		<25 (n=76)	25-30 (n=95)	>30 (n=58)	Total (n=229)	p-values
Disease severity	**Mild disease**	34 (44.7%)	20 (21.1%)	10 (17.2%)	64 (27.9%)	**<0.001[a]**
	Pneumonia	41 (53.9%)	64 (67.4%)	27 (46.6%)	132 (57.6%)	
	Severe pneumonia	1 (1.3%)	11 (11.6%)	21 (36.2%)	33 (14.4%)	
Need for intensive care		1 (1.3%)	6 (6.3%)	14 (24.1%)	21 (9.2%)	**<0.001[a]**
Need for mechanical ventilation		1 (1.3%)	1 (1.1%)	6 (10.3%)	8 (3.5%)	**0.007[b]**
Mortality rate		1 (1.3%)	1 (1.1%)	5 (8.6%)	7 (3.1%)	**0.030[b]**

[a]Chi-square test, [b]Fisher's exact test
BMI: Body mass index

Table 4: Comparison of COVID-19 disease severity at different ages between BMI groups

Age group	Disease severity	BMI Groups <25	25 - 30	>30	Total	p-values
<60	Mild disease	32 (44.4%)	17 (24.3%)	8 (21.6%)	57 (31.8%)	<0.001[a]
	Pneumonia	39 (54.2%)	48 (68.6%)	20 (54.1%)	107 (59.8%)	
	Severe pneumonia	1 (1.4%)	5 (7.1%)	9 (24.3%)	15 (8.4%)	
	Total	72	70	37	179	
≥60	Mild disease	2 (50%)	3 (12%)	2 (9.5%)	7 (14%)	0.026[b]
	Pneumonia	2 (50%)	16 (64%)	7 (33.3%)	25 (50%)	
	Severe pneumonia	0 (0%)	6 (24%)	12 (57.1%)	18 (36%)	
	Total	4	25	21	50	

[a]Chi-square test, [b]Fisher's exact test
COVID-19: Coronavirus disease-2019, BMI: Body mass index

Table 5: Comparison of the length of stay in the hospital between BMI groups

Length of hospital stay	BMI Groups <25 (1) (n=76)	25-30 (2) (n=95)	>30 (3) (n=58)	p-values	Post-hoc p-values with Bonferroni corrections
One-Way ANOVA	9.76±4.15 (8.81-10.71)	12.32±5.36 (11.22-13.41)	12.28±6.95 (10.45-14.10)	0.001[a]	1-2: 0.002 1-3: 0.019 2-3: 1.000
ANCOVA	10.35±5.51 (9.11-11.6)	12.18±5.34 (11.1-13.26)	11.73±5.45 (10.32-13.14)	0.094[b]	-

[a]One-Way ANOVA test with mean ± standard deviation (95% confidence interval for mean)
[b]ANCOVA test with mean ± standard deviation (95% confidence interval for mean)
BMI: Body mass index, ANOVA: Analysis of variance, ANCOVA: Analysis of covariance

originated. The length of stay in hospital of the patients with a BMI 25-29.99 was 11±5 (4-38), BMI≥30 was 11±5 (2-52) and BMI <25 was 9±5 (2-26). The length of stay in hospital of the patients with a BMI 25-29.99 and BMI≥30 were significantly higher than BMI<25 (respectively, p=0.002, p=0.019) (Table 5, Figure 1). The mean age of the patients in the BMI groups was statistically significantly different (p<0.001) and there was a weakly significant linear relationship between age and length of hospital stay (r=0.282, p<0.001). Therefore, keeping the age of the patients under control with ANCOVA among the BMI groups, the hospitalization periods of the patients were compared. In the model, the effect of age on the length of stay in hospital was significant (p<0.001). After controlling for patient ages (The mean age in all groups was evaluated as 45.16), no significant difference was found between the length of hospital stay between BMI groups (p=0.094), (Table 5).

The comparison of the length of the stay in ICU between the study groups is given in Table 5. There was only 1 patient in the group with a BMI<25 who was admitted to intensive care so the BMI groups were combined. The length of stay in the ICU was similar between the patient groups with BMI<30 and BMI≥30 (p=0.636), (Table 5,6, Figure 2).

Since there was no significant relationship between patient ages and the length of stay in ICU (p=0.623), the effect of age was not taken into account when comparing intensive care hospitalization periods.

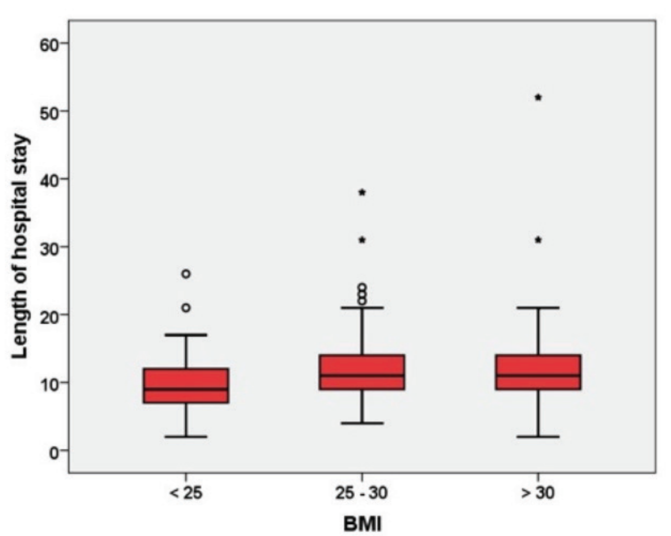

Figure 1: Length of hospital stay
BMI: Body mass index

Table 6: Comparison of the length of stay in the intensive care unit between BMI groups

	BMI groups		
	≤30 (n=7)	>30 (n=14)	p-values
Length of ICU stay	11±8 (3-25)	8.5±12 (1-30)	0.636

Mann-Whitney U test with median ± interquartile range (minimum-maximum)
BMI: Body mass index, ICU: Intensive care unit

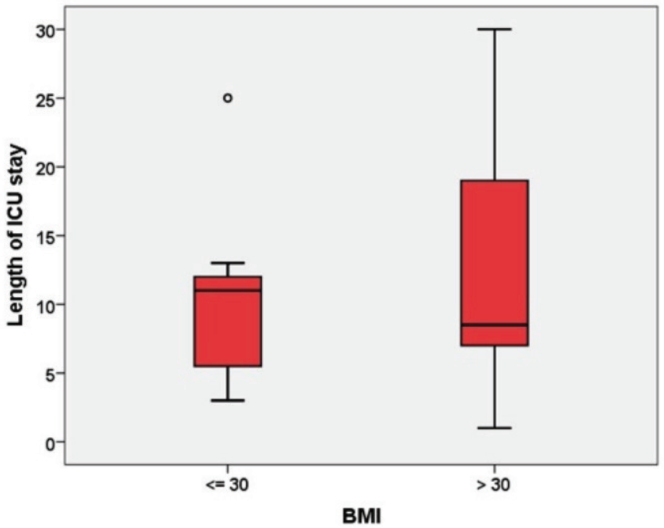

Figure 2: Length of intensive care unit (ICU) stay
BMI: Body mass index

Discussion

Obesity, which is accepted as a multifactorial and complex disease negatively affects health. It is the second most important cause of preventable deaths after smoking today. Interest in the interactions between infections and obesity has been prompted by the influenza H1N1 pandemic. A global study conducted by WHO included 70,000 laboratory confirmed cases with H1N1 indicated a clear association between obesity and poor outcome in H1N1 (6). Some of reports have linked obesity is associated with severe COVID-19 illness and death (7). In our study, the rates of BMI levels of the patients in the mild disease, pneumonia and severe pneumonia groups were significantly different (p<0.001). Severe disease was observed in 1.3% of patients with a BMI <25, while 11.6% of patients with a BMI 25-29.99 and 36.2% of patients with a BMI ≥30 had severe disease. Disease severity was correlated with the increase in BMI. In our study, the mean age of the patients between BMI groups was statistically significantly different (p<0.001). Older age was associated with increased risk of severe disease. In our study, after adjustment for age increased BMI was also correlated with disease severity but older age was associated with length of stay in hospital. A study from New York including 3615 objects, patients with a BMI <30 and BMI between 30-34.9 were compared. Patients with a BMI between 30-34.9 were 2.0 and 1.8 times more admitted to ICU (3). The risk for mechanical ventilation in patients with COVID-19 in ICU was more than seven-fold higher for those with BMI>35 compared with BMI <25 kg/m^2 (4). In our study, consistently with the literature a significant correlation was found between the BMI and ICU admission and mechanical ventilation support (p<0.001 and p=0.007 respectively) (Table 3).

The relationship between infectious diseases and obesity has not been established yet. Immune system deficiency, respiratory tract abnormalities, and obesity-related comorbidities may cause poor prognosis of infectious diseases (8). Obesity causes reduced expiratory reserve volume, functional residual capacity and ventilation/perfusion abnormalities. Sleep apnea syndromes is commonly associated with obesity too (9). Obesity has various effects on the immune system (10). Adipocytes and immune system cells show similarities in function and structure of various inflammatory mediators (10). The differentiation of macrophages has been shown to be affected by the presence of obesity and complex interactions take place between immune and metabolic system cells (8). Obesity disrupt the well-balanced system of adipocytes and immune system cells. This leads to dysregulated immune response, impaired chemotaxis and altered macrophage differentiation. Leptin plays a key role in linking nutritional status with T-cell function. As a result of the increase in leptin, CD 8+ T-cells, natural killer cells activity and antigen presentation of dendritic cells decrease (8). Adiponectin has been used to predict mortality in critically ill patients upon admission to the ICU (11). Obesity is strongly associated with circulating levels of C-reactive protein (CRP) and fibrinogen. High levels of CRP and fibrinogen cause chronic inflammation. It is explaining the increased risk of atherosclerotic disease associated with obesity (12). Serum angiotensin converting enzyme-2 (ACE-2) plays important role in the course of COVID-19. ACE-2 enzyme is expressed in adipose tissue (13). Therefore, as the amount of adipose tissue increases, ACE-2 expression also increases.

Obesity is a confirmed cause of DM and cardiovascular disease, leading to higher overall mortality (14). DM was associated with a higher mortality rate, severe COVID-19 and acute respiratory distress syndrome (15). In our study, DM and HT was significantly different between BMI groups (p=0.027 and p=0.047, respectively).

Study Limitations

Our study has some limitations. The number of patients was not equal among the study groups. And our study sample size was small.

Conclusion

In conclusion, the risk of severe diseases is high in obese patients. So early detection and aggressive treatment for obese patient is very important. In our study sample size was small. Further studies are needed to understand the impact of obesity on COVID-19 severity and the mechanisms behind this with larger patients groups.

Ethics

Ethics Committee Approval: The study protocol was approved by Ankara City Hospital Clinical Researchs Locals Ethics Committee (date: 21.05.2020, number: E1-20-623) and by Ministry of Health (number: 2020-05-07T08_51_26.xml).

Informed Consent: Patients were retrospectively screened.

Peer-reviewed: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: B.C., M.A., E.M.S., A.A.A., B.K., R.G., İ.H., A.K.K., F.E., E.A., Concept: B.C., R.G., Design: B.C., R.G., Data Collection or Processing: Y.A.B., B.Ö., B.C., M.A., E.M.S., Analysis or Interpretation: B.C., M.A., E.M.S., Literature Search: B.C., Writing: B.C., M.A.

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