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OBESITY AS A RISK FACTOR OF MORE SEVERE COURSE OF COVID-19 IN UZBEKISTAN

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Original Research

Abstract: Background: According to some studies, patients with obesity seem to be more prone to have severe COVID-19 symptoms, than non-obese people. The association between obesity and an increased risk of hospitalization, critical conditions, or even death as a result of COVID-19 in Uzbekistan is currently under research. The aim of the study was to evaluate the impact of obesity on the severity and course of disease of COVID-19.

Design and methods: The design of the study is an observational cohort study. The patients were followed over 30 days, after COVID-19 disease to examine short-term outcomes. Among patients seeking medical treatment or receiving the initial medical communication in distribution centers in Tashkent, Uzbekistan, we selected 4675 consecutive patients, who had proven SARS-CoV-2 PCR-positive test results. By using a t-test to continuous data related with an increased risk of hospitalization, critical conditions, or even mortality owing to COVID-19 in Uzbekistan, we compared individuals with obesity and those who did not have obesity. Furthermore, we chose to evaluate data from databases like as PubMED, Elsevier, Cochrane, Lancet, World Obesity, Science, and World Health Organization guidelines through to the end of the ear 2021, as well as data from existing databases. In addition, we investigated a number of scientific online sites, including karger.com, Medscape, CDC.gov, and Google scholar to find the association between COVID-19 and obesity.

Results: In the whole cohort, 1280 out of 4675 (27.35%) patients had obesity. All-cause mortality in 30 days was 112 (2.39%). Mortality in patients without obesity was 18 (0.53%) whereas this rate in obese patients were significantly higher and was 94 (7.34%) ($p<0.001$). There was a significant association between obesity and all-cause mortality in 30 days due to COVID-19, $\chi^2(1) = 184.549$, $p < 0.001$. During the course of COVID-19 disease, 951 out of 4675 patients (20.34%) were required at least one day hospitalization in hospital unit. Patients with obesity had the highest hospitalization rate with 602 out of 1280 (47%) than those without obesity with 349 out of 3395 (10.27%), $\chi^2(1)=774.800$, $p < 0.001$. After adjusting all confounders, unavailable and multivariable logistic regression analysis revealed that obesity significantly increased odds of all-cause mortality in 30 days (OR = 3.62, 95%CI [1.46–7.25], $p< 0.001$).

Conclusion: This study showed that obesity had detrimental impact worthening the course of COVID-19 including increasing hospitalization, ICU admission and mortality. The prevalence of patients with obesity in the Uzbekistan cohort was nearly 30%. This indicates an importance for preventive measures to decrease obesity as a risk factor e.g. COVID-19.

Key words: Obesity, Covid-19, Risk factor, Mechanism.

Introduction

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Study design

The design of the study is an observational cohort study. The patients were followed over 30 days, after COVID-19 disease to examine short-term outcomes. Among patients seeking medical treatment or receiving the initial medical communication in distribution centers in Tashkent, Uzbekistan, we selected 4675 consecutive patients, who had proven SARS-CoV-2 PCR-positive test results. By using a t-test to continuous data related with an increased risk of hospitalization, critical conditions, or even mortality owing to COVID-19 in Uzbekistan, we compared individuals with obesity and those who did not have obesity. Furthermore, we chose to evaluate data from databases like as PubMED, Elsevier, Cochrane, Lancet, World Obesity, Science, and World Health Organization guidelines through to the end of the ear 2021, as well as data from existing databases. In addition, we investigated a number of scientific online sites, including karger.com, Medscape, CDC.gov, and Google scholar to find the association between COVID-19 and obesity.

Study patients

The study population consisted of 4675 patients with confirmed covid-19. Overall, 95 percent of patients had first medical contact within three days of onset of symptoms.

Inclusion criteria for the present study were:

Patients with confirmed covid-19 by RT-PCR test;

Height and weight data available;

Exclusion criteria for the present study were:

Age <40 ears;

Age >88 ears;

Pregnancy;

Missing data on height or weight;

Body mass index was calculated as weight in kilograms divided by squared height in meters (kg/m2) and defined overweight as ≥25 kg/m2, class one obesity as ≥30 kg/m2, class two obesity as ≥35 kg/m2, and class three obesity as ≥40 kg/m2, respectively. Body mass index between 18 and 25 kg/m2 was used as the reference throughout the study.

Study setting

The strengths of the study is that all cohort consecutive COVID-19 patients' data with no loss of thirty days follow-up. Furthermore we estimated impact of comorbidities such as type two diabetes mellitus, myocardial infarction, hypertension, coronary artery disease on the severity of the disease and course of COVID-19 cases, outcomes, as well as thirty days of all-cause mortality. Our this cohort study's one of the main strength is that it documents variety of aspects of medical care and medication use across in hospital settings. This in turn, allowed us to construct a comprehensive database with complete capture of prior taken medications and increased capture of short term outcomes within a set of time.

SARS-CoV2 diagnostics

All included patients had been diagnosed with COVID-19 for SARS-CoV-2 using real-time reverse transcriptase-polymerase chain reaction (PCR) assays and validated by clinical and instrumental data. The clinical classification of was based on Local Guidelines for the Management of Patients Infected with COVID-19 (7th ed.) developed by the local experts in the field validated by the Ministry of Health of Uzbekistan, adopted from the temporary guidelines of the WHO. Clinical classification of the COVID-19 course was the following: 1) mild clinical symptoms; 2) moderately severe patients who had not signs of severe COVID-19; 3) severe course with signs of respiratory distress; 4) critically severe if intensive care treatment was required.

Data acquisition

The active surveillance and follow-up data system had been established on the basis of outpatient clinics to monitor patients' conditions daily until symptoms resolved for outpatients and within at least one month after discharge from distribution centers or hospitals. COVID-19 patients management in inpatient clinics, distribution centres, and outpatient clinics, including testing, exams, and medications had been completely free of charge for people and fully covered by the government.

Outcomes

In order to investigate the importance of high body mass index/weight and waist circumference for outcomes reflecting severe covid-19 in both survivors and non survivors, we estimated the possible association between body mass index and the composite of death within 1 months after diagnosed covid-19. We also estimated influence of high body mass index in outcomes separately. Furthermore, we estimated association of body mass index and severity of the course of disease of covid-19. Other comorbidities and concomitant disease separately evaluated together with body mass index.

Statistical analysis

Statistical analysis was performed by using SPSS software (v27, IBM, Chicago, IL, USA). Descriptive data was presented as mean (standard deviation [SD]) for continuous variables and n(%) for dichotomous variables. Student's t test was used to compare means and chi-square test for frequencies. Binomial test had been used in order to test number of men and women. Logistic regression models had been used in order to estimate associations between variables. Outcome and the exposure (body mass index as a continuous variable) were dependent variables whereas covariates were independent variables, and they were presented as odds ratios (ORs) with ninety five percent confidence intervals (95% CI).This model had been adjusted for covariates gender, age, presence of any of the comorbidities or concomitant disease (such as CVD, hypertension, T2DM, liver disease, kidney disease etc.).Linear regression model was used with the similar modelling for the length of stay as

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continuous outcome. On-linear relations had been estimated by inclusion of a quadratic term for body mass index. P value was referred as statistically significant if it was <0.05.

Table 1 represents the distribution of patients with COVID-19 divided into three groups according to body mass index metrics. From the Table 1 we can see that mean age gradually increases with the increasing of body mass index. Advanced aged population with covid-19 tended to have increased weight than younger ones. When it comes to gender differences, female tended to be more frequent in obese patients than counterparts were. When we analyzed course of disease, presented patients with lower body mass index inclined to have mild to moderate course of covid-19 cases whilst patients with obesity tented ta have more severe course of disease. Among comorbidities, diabetes mellitus positively associated with the increased level of body mass index (1.5 (1.2-2.2) CI 95 %, P<0.05). When we analyzed outcomes of the COVID-19 in terms of the presence of the obesity, patients with increased body mass index prone to stay hospital prolonged period than those normal level of it (P<0.05). Besides, hospitalization rate due to COVID-19 were significantly higher in obese patients than non-obese ones (P<0.05). In addition to this, obesity directly influence on the stay in the intensive care unit due to COVID-19 as patients with increased body mass index admitted ICU frequently and stayed longer than those patients with lower level of body mass index (P<0.05). When we analyzed all-cause mortality, obesity has influenced directly on this index that is patients with obesity tended to have poor adverse events accounted by death due to COVID-19 (P<0.05). Overall baseline characteristics of patients were presented in Table 2.

Table 1.

Baseline characteristics of COVID-19 patients with the 30 days outcome. Body mass index was classified according to WHO classification.

	BMI 18-25 kg/m2 N=1812	BMI 25-30 kg/m2 N=934	BMI 30-35 kg/m2 N=796	BMI 30-40 kg/m2\ N=638	BMI<40 kg/m2 N=495
Age (years) mean±SD	42.2±14.8	48.35±14.25	57.12±12.2	63.12±14.2	61.6±11.0
Age >65 ears	65	98	215	385	327
Sex, n (%)					
Male	906 (50%)	505 (54%)	382 (48%)	293 (46%)	231 (47%)
Female	906 (50)	429 (46%)	414 (52%)	345 (54%)	264 (53%)
Course of COVID-19 disease					
Mild (%)	50.7	42.6	29.1	12	6
Moderate (%)	41.3	44.4	34.9	27	10
Severe (%)	6	9	22	26	37

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Critical (%)	2	4	12	35	47
Comorbidities					
History of myocardial infarction	24	68	154	128	119
Kidney disease	12	34	46	42	57
Diabetes	82	158	201	227	238
Liver disease	45	36	145	214	186
Outcomes					
Duration of COVID-19, days	8.6±6.0	9.0±6.3	11.0±12.0	17.2±14.6	24.6±18.2
Hospitalization (%)	4.6	8.2	21.6	30.8	34.8
Stay in hospital, days	114	232	186	205	214
Stay in ICU, days	2	7	26	38	56
All-cause mortality, 30 days	1	8	24	35	44

Data are n (%), where n is the number of participants with non-missing data, or mean ± SD. Baseline characteristics were calculated for the participants at the first outpatient exam. COVID-19 symptoms onset to recovery or symptoms onset to death. BMI – body mass index. CI = confidence interval. ICU = intensive care unit.

Distribution of patients with COVID-19 by having diabetes mellitus (DM) along with the presence or absence of obesity.

In the whole cohort, diabetes mellitus were in 906 out of 4675 patients (19.37%). Concomitant diabetes mellitus was significantly higher in obese patients than those without obesity infected with COVID-19. There was a significant association between obesity and concomitant diabetes mellitus presented with COVID-19, $\chi^2(1) = 294.870$, $p < 0.001$ (Table 2).

Distribution of patients with COVID-19 by having myocardial infarction in history along with the presence or absence of obesity.

In our cohort, 493 out of 4675 patients (10.54%) had comorbid myocardial infarction. When we analyzed association with the myocardial infarction with obesity, there were significant association between them in patients infected with COVID-19, $\chi^2(1) = 54.324$, $p < 0.001$ (Table 2).

Distribution of patients with COVID-19 by coronary artery disease (CAD) along with the presence or absence of obesity.

In the entire cohort, 496 out of 4675 (10.60%) patients with COVID-19 had coronary artery disease. CAD were 8.54% in patients without obesity, whereas 16.1% patients had CAD in patients with obesity admitted due to COVID-19. There was a significant association between obesity and CAD in COVID-19 patients, $\chi^2(1) = 55.895$, $p < 0.001$ (Table 2).

Distribution of patients with COVID-19 by taking aspirin and statins along with the presence or absence of obesity.

When it comes to medications where patients had being taken up to being infected with COVID-19, aspirin in 496 out of 4675 (10.61%) and statins in 494 out of 4675 (10.56%) had been common in obese patients than those ones without obesity ($\chi^2(1) = 55.895$, $p < 0.001$ for aspirin, and $\chi^2(1) = 53.798$, $p < 0.001$ for statin;(Table 2).

Distribution of patients with COVID-19 according to blood pressure level together with the presence of obesity.

We also separately analyzed patients with COVID-19 according to the blood pressure levels in terms of the presence or absence of the obesity. The study revealed that blood pressure level slightly correlated with the obesity in patients with COVID-19. Main part of the patients with normal blood pressure had not have obesity. The prevalence of the stage-1 untreated hypertension were 410 out of 4675 (8.77%), stage-2 untreated hypertension were 226 out of 4675 (4.83%) and the prevalence of the stage-1 treated hypertension were 696 out of 4675 (14.88%), stage-2 treated hypertension were 865 out of 4675 (18.50%). As long as blood pressure continued to rise, number of patients with obesity increased ($p<0.001$). Especially, the trend was obvious in stage 2 untreated hypertensive patients (Table 2).

Mortality rate of patients with COVID-19 due to the presence of obesity or not.

In the whole cohort, all-cause mortality in 30 days was 2.39%. Mortality in patients without obesity was 0.53% whereas this rate in obese patients were significantly higher and was 7.34% ($P<0.001$). There was a significant association between obesity and all-cause mortality in 30 days due to COVID-19, $\chi^2(1)=184.549$, $p < 0.001$ (Table 2).

Hospitalization rate of patients with COVID-19 according to the presence of obesity.

During the course of COVID-19 951 out of 4675 patients (20.34%) were required at least one day hospitalization in hospital unit. Patients with obesity had the highest hospitalization rate with 602 out of 1280 (47%) than those without obesity with 349 out of 3395 (10.27%), $\chi^2(1)=774.800$, $p < 0.001$ (Table 2).

Distribution of patients with COVID-19 by blood pressure level according to the presence of obesity.

Of the entire cohort, 2359 out of 4675 (50.45%) patients had either controlled or uncontrolled hypertension. Among them, 1268 out of 2359 (53.75%) controlled hypertension (BP>140/90 mmHg), whilst 1091 out of 2359 (46.25%) had uncontrolled hypertension (BP<140/90 mmHg). Patients with obesity were significantly higher in both controlled and uncontrolled hypertension group than non-hypertension group, $p< 0.001$ (Table 2).

Distribution of patients by gender according to the presence or absence of obesity.

In the whole cohort, 2269 out of 4675 (48.53%) were male, whereas 2406 out of 4675 (51.47%) were female. Female patients tended to havemore frequent obesity than counterparts, $\chi^2(1)=3.197$, p = 0.074 (Table 2).

Distribution of intensive care unit admissions in patients with COVID-19.

In our cohort, 129 out of 4675 (2.76%) patients required at least one day of stay in intensive care unit. There was a significant association between the staying in intensive care unit weather or not having obesity, $\chi^2(1)=183.654$, p < 0.001 (Table 2).

After adjusting all confounders, unavailable and multivariable logistic regression analysis revealed that obesity significantly increased odds of all-cause mortality in 30 days (OR = 3.62, 95%CI [1.46–7.25], p< 0.001).

Table 2. n (%)

		Total	Obesity		Total number of patients
			No	Yes	
Diabetes	No	3769(80.6)	2944 (78.1)	825 (21.9)	4675
	Yes	906(19.4)	451 (49.8)	455 (50.2)	
MI	No	4182 (89.5)	3106 (74.3)	1076 (25.7)	4675
	Yes	493 (10.5)	289 (58.6)	204 (41.4)	
CAD_syptomatic	0	4179 (89.4)	3105 (74.3)	1074 (25.7)	4675
	1	496 (10.6)	290 (58.5)	206 (41.5)	
Aspirin	0	4179 (89.4)	3105 (74.3)	1074 (25.7)	4675
	1	496 (10.6)	290 (58.5)	206 (41.5)	
Statin	0	4181 (89.4)	3105 (74.3)	1076 (25.7)	4675
	1	494 (10.6)	290 (58.7)	204 (41.3)	
Mortality_30d	No	4563 (97.6)	3377 (74)	1186 (26)	4675
	Yes	112 (2.4)	18 (16)	94 (84)	
Hospitalization presence	No	3724 (79.7)	3046 (81.8)	678 (18.2)	4675
	Yes	951 (20.3)	349 (36.7)	602 (63.3)	
ICU_presence	No	4546 (97.2)	3369 (74.1)	1177 (25.9)	4675
	Yes	129 (2.8)	26 (21.2)	103 (79.8)	
Gender	Male	2269 (48.5)	1675 (73.8)	594 (26.2)	4675
	Female	2406 (51.5)	1720 (71.5)	686 (28.5)	
	No	2316 (49.5)	1987 (85.8)	329 (14.2)	

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Hypertension	Controlled	1268 (27.1)	789 (62.2)	479 (37.8)	4675
	Uncontrolled bp 140/90+	1091 (23.4)	619 (56.7)	472 (43.3)	
Hypertension_group	Normal	2135 (45.7)	1827 (85.6)	308 (14.4)	4675
	Elevated	343 (7.3)	236 (68.8)	107 (31.2)	
	1 stage untreated	410 (8.8)	263 (64.1)	147 (35.9)	
	1 stage treated	696 (14.9)	450 (64.7)	246 (35.3)	
	2 stage untreated	226 (4.8)	104 (46)	122 (54)	
	2 stage treated	865 (18.5)	515 (59.5)	350 (40.5)	

Discussion

In our study, obesity increased either mortality or stay of intensive care unit. After adjusting sex, gender, comorbidities like coronary artery disease, type two diabetes mellitus, hypertension as well as medications like aspirin and statins, obesity had statistically significant effect on all-cause mortality in 30 days. These effects were more pronounced with high level of body mass index than those with low level of it were. Thirty days after the onset of the first symptoms, 112 out of 4675 (2.39%) patients were died from COVID-19. Mortality was significantly higher in obese patients presented with COVID-19 than without obesity 94 out of 1280 (7.34%) vs 18 out of 3395 (0.53%), p<0.001). Besides, increased body mass index directly influenced on hospitalization rate and day of hospitalizations in patients with COVID-19, and these effects had been statistically significant (p< 0.001). A total of 951 patients (20.34%) had to be hospitalized. Hospitalization rate were significantly higher in obese patients than non-obese ones (p< 0.001). Hospitalization rate were significantly higher after adjustment of age, sex, comorbidities, medications (p<0.001). The reason of high hospitalization and high mortality rate are unclear. Perhaps, inflammatory interleukins play an important role for the course of disease and increased number of mortality and hospitalization (Emiliano Lopez Barrera et al, 2018). Our study results are in line with several studies in terms of severe course of disease of COVID-19 in patients with obesity (Sarah-Jeanne Salvy, 2022; Dennis Freuer 2021; Antonia Petersen, 2020). Furthermore, the study results regarding the association of obesity and length of hospital stay agrees with the results of Ahmed Abdalazim Dafallah Albashir conducted on 2020 (Ahmed Abdalazim Dafallah Albashir et al, 2020). Besides, we have demonstrated that all-cause mortality is high in patients with obesity with COVID-19 than those without obesity patients. This is might be due to systemic inflammation of the organism in obesity as adipocytes overworks as a result variety of interleukins and inflammatory cytokines are released by the cells, which in turn exaggerates immune response to viral infection (Lovisa Sjögren et al, 2020). Our results confirm all existing data regarding the direct impact of obesity on the severe course of disease, hospital stays, intensive care unit stays as well as all-cause mortality in patients with COVID-19.

The strengths of the study is that all cohort consecutive COVID-19 patients' data with no loss of thirty days follow-up. Furthermore, we estimated impact of comorbidities such as type two diabetes mellitus, myocardial infarction, hypertension, coronary artery disease on the severity of the disease and course of COVID-19 cases, outcomes, as well as thirty days of all-cause mortality. This cohort study's one of the main strengths is that it documents variety of aspects of medical care and medication use across in hospital settings. This in turn, allowed us to construct a comprehensive database with complete capture of prior taken medications and increased capture of short-term outcomes within a set of time.

Obesity appears to be associated with worse outcomes and an increased likelihood of having more severe course of disease in patients with COVID-19 developing acute respiratory distress syndrome, prolonged hospitalized, staying in an intensive care unit and even requiring intensive medical treatment. Furthermore, obesity appears to be associated with poor outcomes in terms of all-cause mortality in thirty days from the index hospitalization. These two major indexes were obvious even after adjustment of cofounders and other existing risk factors. These results directly influence on physicians' management strategy as every clinician easily can measure of patients' body mass index and evaluate likelihood of the possible severity course of disease. While defining body mass index and other risk factors clinicians easily can stratify patients into several category and manage more accurately. In the other hand obesity, negatively influence on comorbidities such as type two diabetes mellitus and cardiovascular disease, which in turn exaggerates this concomitant disease and increases likelihood of complications related with those disorders. These are all chronic disease – increase COVID-19 related complications and exaggerates course of disease of COVID-19. There are several explanations that obesity can increase risk of COVID-19. Firstly, the risk partially may be associated with confounding by age. From the results of the study, we have noticed that overweight patients inclined to be older than those without obesity. Compelling data suggest that old age is considered risk for the COVID-19. However, after adjustment of age, obesity still had significant impact of the course of disease of COVID-19. Secondly, from the evidence-based data we can assume that obese patients inclined to viral infectious disease than non-obese patients. However, exact mechanisms to explain of the phenomenon is scarce and still debated. On other hand, obesity considered as chronic inflammatory disease and inflammation may exaggerate viral infectious disease. Thirdly, obesity directly can change lungs and chest muscles mechanical properties, which in turn may lead to respiratory impairments and making patients more susceptible to the various infectious disease. However, it is unclear whether these changes lead to COVID-19 or increase the risk of course of disease with COVID-19. Fourthly, obesity directly may lead to high blood pressure or diabetes mellitus which are associated with increased risk of COVID-19 and poor adverse outcomes. Thus, the association of obesity with severe course of disease of COVID-19 mediated partially by the other chronic diseases. We consider that premature use of increased body mass index as a screening indicator in order to decide whether to accommodate or not of patients in intensive care unit where ICU beds are limited might be appropriate way to reduce the burden on healthcare and to improve patient's outcomes with COVID-19.

Even though, treatment of patients with obesity can be challenging, last longing, in the longer term and prospective, our efforts should be based on to work on reducing body mass, and lead healthy life in a population level. Such measurements and interventions except risk of COVID-19, undoubtedly will lower the likelihood of type two diabetes mellitus, hypertension and coronary artery disease which will be continued throughout and after the pandemic and existing burden on healthcare. Along with COVID-19 pandemic, our efforts should focus on combatting the existing pandemic and urgency to reduce mortality and morbidity concerned with obesity.

Conclusion

Overall, significant number of patients were in our cohort. In the whole cohort, patients with obesity had worse outcomes compared to those without obesity presented with COVID-19. The study results revealed that obesity directly correlated with the severity of the course of disease of COVID-19. Furthermore, admitted patients with COVID-19 who have obesity had prolonged hospital stays in intensive care unit. The data obtained in the results of the study will help us to understand novel insights behind pandemic concerned with obesity.

Data sharing

Additional File

Ethics and consent

Funding information

Competing Interests

Author Contributions

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