COVID-19 in Northeast Bosnia and Herzegovina and patients length of hospitalization

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Abstract

Background Since outbreak of COVID-19 pandemic clinical data from various parts of the world have been reported, until now there has been no provide data from Bosnia and Herzegovina (B&H) about COVID-19. Aim was to report on the first cohort of patients from B&H and to analyze clinical factors of COVID-19 patients that influence the length of hospitalization.

Methods Retrospective cohort study conducted at UKC Tuzla. The study included 25 COVID-19 positive patients that were hospitalized between March 28th and April 27th 2020. The LOH was measured from the time of admission to discharge. Hospitalization greater than 10 days was considered as prolonged. Factors analyzed induced age, BMI, comorbidities, serum creatinine and oxygen saturation upon admission.

Results The mean age was 52.92±19.15 years and BMI 28.80±4.22. LOH for patients with normal BMI was 9±SE2.646 days (CI 95% 3.814-14.816) vs 14.182 ±SE .937 (CI 95% 12.346-16.018; $p<0.05$) for ≥25 BMI. Patients without underlying diseases had a LOH of 11.70 ±SE1.075 (CI 95% 9.592-13.808), while those with comorbidities 14.8 ±SE1.303 (CI95% 12.247-17.353; $p<0.05$).

Conclusion LOH varied among COVID-19 patients and was prolonged when clinical characteristics such as elevated BMI, comorbidities, elevated creatinine and low oxygen saturation levels were taken into consideration. Furthermore, risk factors for COVID-19 patients in B&H do not deviate from data reported in other countries.

Introduction

In December 2019, a novel β-coronavirus emerged in the Wuhan region of China, causing pneumonia-like illness. Later this virus was identified as the severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV2), this virus caused a widespread flu-like respiratory disease, which was named the Coronavirus Disease 2019 (COVID-19) (1, 2). Shortly after that, as the virus was spreading worldwide at an alarming rate, the World Health Organization (WHO) declared COVID-19 to be a global pandemic on March 11th, 2020. The reported mortality rate varied from country to country, from 7.2% in Italy to 2.3% that has been reported in China (3, 4). Until April 28th, 2020 the total number of people who have been infected globally reached more than 3 million, with more than 200 thousand fatalities. On the same date, Bosnia and Herzegovina (B&H) reported 1,585 individuals with COVID-19, of which 63 people had passed away (5). The first COVID-19 positive case in B&H was documented on March 17th, however, in the region of Tuzla (population 477,000) the first case to be registered positive was on March 28th, 2020. This is comparably late for the first discovered infection and comparing to other nations in Europe, which had earlier detection of COVID-19 infection. Interestingly, this coincided with the near end of the flu season and was 14th days after lockdown measures were activated in this part of B&H (social distancing measures due to COVID-19 were imposed on 14th of May). This is the first article that has analyzed hospitalized patient with COVID-19 in B&H as of yet and can provide insight into the nature of COVID-19 in this part of Europe (6–8)

SARS-CoV2 is an RNA virus, from the family of the coronaviruses. Coronaviruses were first identified in the 1960s, and since that time, seven of the coronaviruses are known to infect humans (9). Usually, coronaviruses cause mild flu-like symptoms and these viruses are transmitted when infected droplets come in contact with the mucous membranes of a susceptible human host, this can be either directly through person to person contact, or indirectly when one touches a contaminated surface and then touches their own face. Conjunctival tears, saliva, urine and stool are also being considered as possible pathways of infection of COVID-19 (10)

The process of virulence with COVID-19 is initiated when SARS-CoV2 viruses latch on receptors of the Angiotensin-Converting Enzyme 2 (ACE2). Different levels of ACE2 among population groups were speculated as a reason behind the

range of severity of inflammation. Individuals who develop pneumonia due to COVID-19 infection experience infiltration of polymorphonuclear cells and macrophages in the interalveolar space, with further formation of hyaline membrane that increases the thickness of the alveolar wall, consequently reducing oxygen uptake in the lungs (10).

Obesity and high body mass index (BMI) association with more serious clinical presentation and outcome in COVID-19 infected patients is currently being investigated. The risk of mortality in obese patients was recognized before COVID-19, where in the previous influenza pandemics of H1N1 and H1N5, patients with a higher BMI were more likely to die (11, 12). In Shenzhen, China, 32% from 383 patients with COVID-19 were overweight, and 10.7% were obese. Those who were obese had 2.42 higher odds of their disease progressing to severe pneumonia (13). Moreover, a more extensive study from New York that included 4,103 COVID-19 positive patients assessed factors that were mostly correlated with the need for hospital admission and these were first being 65 years and older, followed by having a BMI above 40, and third, having a history of heart failure. In a retrospective cohort from France which included 124 patients admitted in the ICU, most of the patients who required invasive mechanical ventilation were obese with a BMI above 35 (85.7%), and they concluded obesity to be a risk factor for severity (14).

According to the CDC, older age groups and any age group with underlying medical comorbidity were found to have a higher risk of developing severe illness from a SARS-CoV2 infection. Medical comorbidities found in patients who had a more serious form of COVID-19 were moderate or severe asthma, chronic lung conditions, diabetes, serious heart disease, kidney disease undergoing dialysis, chronic liver disease, cancer or being immunocompromised, as well as obesity (15). In China, a summary report of 72,314 cases from the Chinese Center for Disease Control and Prevention found that the highest death rates were among those with cardiovascular disease, then by people with diabetes, followed by those who have had a chronic respiratory disease, hypertension, and cancer (16). As people age, they are more likely to suffer from a noncommunicable health condition, making them more likely to have the aforementioned health conditions (17).

This report aims to analyze the sample of 25 patients who tested positive for COVID-19 and whose condition required admission to Tuzla University Clinical Center, Bosnia and Herzegovina and to see the impact of different factors on the length of hospitalization (LOH). Additionally, the correlation between BMI and disease severity will be included. These patients were followed from admission to discharge. Further exploration of their clinical characteristics will be elaborated as a full understanding of the disease is still limited.

Methods/patients

Patients studied in this retrospective cohort study were admitted to the Infections Diseases Clinic, Tuzla University Clinical Center, Bosnia and Herzegovina in the period 28th of March 2020 until the 27th of April 2020, when the last patient in this study was discharged. The diagnosis was established based on positive oropharyngeal swab using reverse transcription polymerase chain reaction (RT-PCR) diagnostic test for COVID-19. Criteria for discharge were being afebrile for three consecutive days, improvement of respiratory symptoms, oxygen saturation > 94%, no need for oxygen support, as well as two consecutive COVID-19 negative tests with 48 hours in-between two tests. Twenty-five patients were admitted to the hospital due to their clinical severity (n = 25). Data was collected from the patients' history and discharge reports, as well as from laboratory results of the investigations that were collected upon admission of the patient to hospital care. Data included duration of hospitalization, the eventual outcome of care, age, Body Mass Index (BMI), creatinine, as well as any presence existing comorbidities. Ethical approval was granted from ethical committee of Tuzla University Clinical Center, Tuzla.

Statistical analysis

Data is represented as mean ± standard deviation if not indicated otherwise. Kaplan-Meier survival analysis was used for analyzing the duration of hospitalization until discharge, and the difference between two groups was analyzed using the log-rank; any $p < 0.05$ was reported as significant. The statistical analysis and graph creation were conducted using SPSS v.25 (IBM Corp., Armonk, NY, USA).

Results

Out of the 25 patients, 60% were male (n = 15) and 40% female (n = 10) The mortality rate in this study was 0%. In respect to underlying health conditions 60% had one or more while 40% had no known underlying condition. The mean age of patients upon hospitalization was 52.92 ± 19.46, when divided by gender mean age of females was 51.4 ± 17.43 while males was 53.93 ± 20.75. Seven patients in this group were 65 and over, with the eldest 85 years of age and youngest being 2 years old. One or more comorbidities were reported in 60% (n = 15) patients while 40% did not have any. Duration of hospitalization for all patients was in days 13.56 ± SE 0.93 (CI 95% 11.74- 15.381;).

When length of hospitalization was compared based on BMI the mean duration of hospitalization for patients with normal BMI was 9 ± SE 2.646 (CI 95% 3.814–14.816) while patients with equal or higher BMI than 25 had 14.182 ± SE .937 (CI 95% 12.346–16.018; p = 0.040) length of hospitalization (survival curve 1).

Patients without underlying diseases had a mean duration of hospitalization 11.700 ± SE1.075 (CI 95% 9.592–13.808), while those with comorbidities had mean 14.8 ± SE1.303 (CI 95% 12.247–17.353; p = 0.029) (survival curve 2). Patients with elevated creatinine levels had longer length of hospitalization 19.667 ± SE3.180 (CI95% 9.582 to 13.808; p = 0.049) when compared to group of patients that have had normal levels of creatinine on admission 12.727 ± 0.846 (CI95% 11.070 to 14.385; $p < 0.05$) (survival curve 4). Mean duration of patients with normal levels of oxygen ≥ 95% saturation had length of hospitalization 11.000 ± SE1.397 (CI95% 8.261 to 13.739; p = 0.046), on the other side LOH for ≤ 94% was 14.471 ± SE1.167(CI95% 12.184 to 16.757 p = 0.042)

Discussion

This retrospective cohort followed 25 COVID-19 positive patients who were admitted to UKC Tuzla hospital between 28 March and 27 April, 2020. All patients in the hospital ward were included. All patients recovered and were discharged in stable condition. Even though the mortality rate due to infection of COVID-19 all around the world ranged of 2% up to 7.2%, the mortality rate in the region of Tuzla was 0% (3). The possible reasons for lack of lethal cases could be explained by the younger age of patients in our study compared to the mean age in other studies; also, a high proportion of patients in this study group did not have an underlying health condition (40%; this could have had a significant effect on overall mortality). Furthermore, delayed screening at the beginning of the pandemic could have influenced the official count of deaths due to COVID-19. Also, the study takes place in late March, which coincided with the end of the flu-season and warmer climate which possibly reduced the speed of transmission of the virus. In addition, the COVID-19 virus has not been detected in elderly homes in Tuzla thereby circumventing the group that has the highest risk for mortality due to COVID-19 infection. Another favourable factor would be that the region of Tuzla has a population of 470,000 with a population density of 168 /km2, which is considered low when compared to Lombardy in Italy or New York in the United States, this in turn could lead to slower spread of the COVID-19 virus among the people in the region of Tuzla.

The length of stay in our sample was affected by certain factors; patients who had comorbidities, a higher BMI, elevated creatinine and CRP level had a longer length stay. These factors could be used as predictive measures in planning patient care, and may in turn aim to exhaust hospital resources to a lesser extent. The effect BMI had on the length of hospitalization was significant, where patients who were categorised as overweight or obese had a longer stay as

compared to patients of normal BMI, 9 vs 14.18 days on average ($p < 0.05$). Even though our study had no mortality, it conforms with previous studies on how BMI impacts disease severity and can be used as an morbidity predictor (13, 14, 16, 18)Our study has also demonstrated that there is a significant reduction in hospitalization between the group who had elevated BMI and the group who had had normal BMI values ($p < 0.05$). This suggests that we can evaluate the duration of the patient's hospitalization and make more accurate predictions of occupancy of hospital beds and sorting patients upon admission. As described by Stefan et al, the mechanism on how obesity correlates to more severe outcomes could be explained by the substantial respiratory system compromise as obese patients have increased airway resistance, impaired gas exchange, a lower lung volume and weaker muscle strength. Obese patients are also more likely to suffer from health conditions such as cardiovascular disease, insulin resistance and metabolic imbalances, all these facts place obese patients at risk of a more severe COVID-19 course .

Patients with extensive pneumonia due to COVID-19 tend to have decreased levels of oxygen saturation and on admission these levels could be deranged. COVID-19 patients exhibit diffuse alveolar damage with mononuclear cells, and macrophages infiltrating the alveolar area as well as the development of hyaline membranes and consequential thickening of the alveolar wall. This alveolar damage in severe cases is bilateral, compromising the functionality of the lungs and their ability to facilitate the transfer of oxygen thus leading to hypoxia (12). As mentioned above the nature of COVID-19 infection affects the ability of normal transfusion of oxygen. Patients with levels of O2 saturation levels $\leq$ 94% showed longer hospitals stay when compared to those with normal levels.

COVID-19 patients who have had comorbidities on admission to hospital or critical care had higher mortality rates, as well as severe clinical manifestation. Individuals who have underlying health issues are more inclined to be of poorer health with reduced capacity to withstand COVID-19 infection (17). When patients in our sample were divided into two groups, one with known comorbidities and second without any comorbidities; there was a statistical difference in the duration of hospitalization. Patients without a known underlying condition had hospitalization 11.700 ± SE1.075 days (CI 95% 9.592–13.808) compared to 14.8 ± SE1.303 (CI 95% 12.247–17.353; $p < 0.05$).

Creatinine levels show the overall function of the kidney-urinary system; elevated levels could point to decrease in function or kidney injury. Patients with acute kidney injury in COVID-19 patients showed higher levels of hospital deaths than those with normal levels. Elevated levels of creatinine were recorded in this study. When the length of hospitalization was divided based on levels of creatinine, patients with elevated creatinine levels showed longer duration of hospitalization 19.67 ± 3.18 (CI95% 13.434–25.899) days, higher than those with normal levels 12.727 ± 0.85; CI95% 11.07- 14.385; $p < 0.05$) (19). Longer hospitalization length was also observed when patients were divided in age groups, one below 50 years of age and the other above. Longer hospitalization was significantly higher in the older group ($p < 0.05$). These results implicate that we can potentially evaluate the duration of the patient hospitalization and make validated predictions of occupancy of hospital beds and of sorting patients upon admission.

Conclusion

In conclusion, the planning of hospitalization of COVID-19 is one of the crucial aspects of this pandemic. In areas where hospital capacity and resources may be limited, predicting the length of hospitalizations of COVID-19 could provide insight and could lessen the overwhelm on the system. Factors that were associated with a longer hospital stay were having a high BMI, having a comorbidity, and elevated Creatinine and CRP levels. Despite the absence of mortality in our sample, considering patient clinical characteristics upon admission and their laboratory findings could aid in better patient care and outcomes. This is the first study regarding COVID-19 pandemic that has been written about clinical characteristics of patients from B&H and biochemical derangements noticed. Results in this study would add to the current information about the COVID-19 pandemic in Europe. Furthermore, it provides additional information on risk factors attributed to longer hospitalization. However, this study involved a fraction of COVID-19 patients and

encompassed only a part of the B&H experience. Moreover, not all biochemical and inflammatory markers that are routinely ordered to monitor patients with COVID-19 were analyzed or taken from our patients, such as d-dimer; hence, they were not included in this study. Also, a larger sample of patients with COVID-19 is needed to make further conclusions on the nature of the pandemic in B&H. Inclusion of all the infected patients with COVID-19 in B&H along with other biochemical markers could provide a more in-depth insight into the extent of the infection and more accurately predict the duration of the hospitalization.

Declarations

Competing Interest Statement

The authors have declared no competing interest

Funding Statement

This study was retrospective and was based on medical records; no funding was needed

Authors deceleration

All relevant ethical guidelines have been followed; approval for data was obtained from ethical committee of Tuzla University Clinical Center

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Table

Table 1
Clinical data of the hospitalized COVID-19 patients (n = 25)

	Overall	BMI*		Comorbidities*		Creatinine*		O_2 %†	
		BMI < 25	BMI ≥ 25	Without	With	Normal	Elevated	≤ 94% O_2	≥ 95% O_2
BMI	28.80 ± 4.22	22.67 ± 2.30	29.64 ± 3.71	26.10 ± 1.91	30.60 ± 4.42	28.64 ± 4.41	30.00 ± 2.651	30.06 ± 4.13	25.57 ± 2.99
Age (years)	52.92 ± 19.15	29.67 ± 28.1	56.10 ± 15.99	41.90 ± 9.63	60.27 ± 20.60	50.59 ± 19.01	70.00 ± 10	42.57 ± 20.14	57.29 ± 18.18
Male/ female	15/10	1/2	14/8	5/5	5/10	13/9	2/1	8/9	6/1
Comorbidities (yes/no)	15/10	null	14/8	n = 10	n = 15	12/10	3/0	12/5	3/4
Creatinine (µmol/L)	81.96 ± 24.89	57.33 ± 15.89	85.32 ± 24.19	77.30 ± 17.58	85.07 ± 28.94	75.82 ± 17.66	127.00 ±26.46	86.86 ± 37.74	80.35 ± 19.46
Oxygen saturation (mean % pO_2)	92.19 ± 3.99	94.40 ± 2.15	91.43 ± 4.13	94.43 ± 2.87	90.85 ± 4.04	92.17 ± 4.38	89.25 ± 1.34	90.82 ± 3.70	95.51 ± 2.53
LOH (days)	13.56	9.0	14.18	11.70	14.8	12.73	19.67	14.47	11.00

Note: Statistical difference between group is marked with the sign (*)
† levels of oxygen saturation for one patient were not available in medical records

Figures

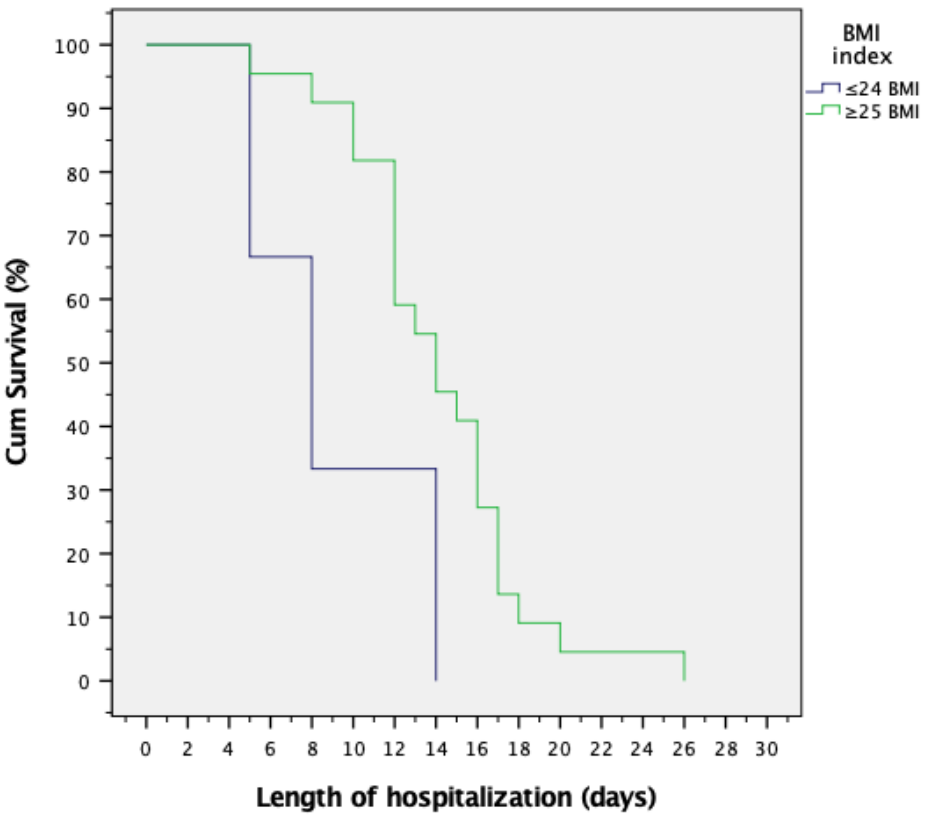

Figure 1

Survival curve 1. Duration of hospitalization based upon BMI. The terminal event was considered the discharge from the hospital. The blue line represents patients who have had BMI lower or equal to 24, while the green line represents the patients who had had BMI equal or larger than 25. The mean duration of hospitalization was for group 1 was 9 ± SE 2.646 (CI 95% 3.814-14.816) while for the group 2 was 14.182 ± SE .937 (CI 95% 12.346-16.018; p=0.04)

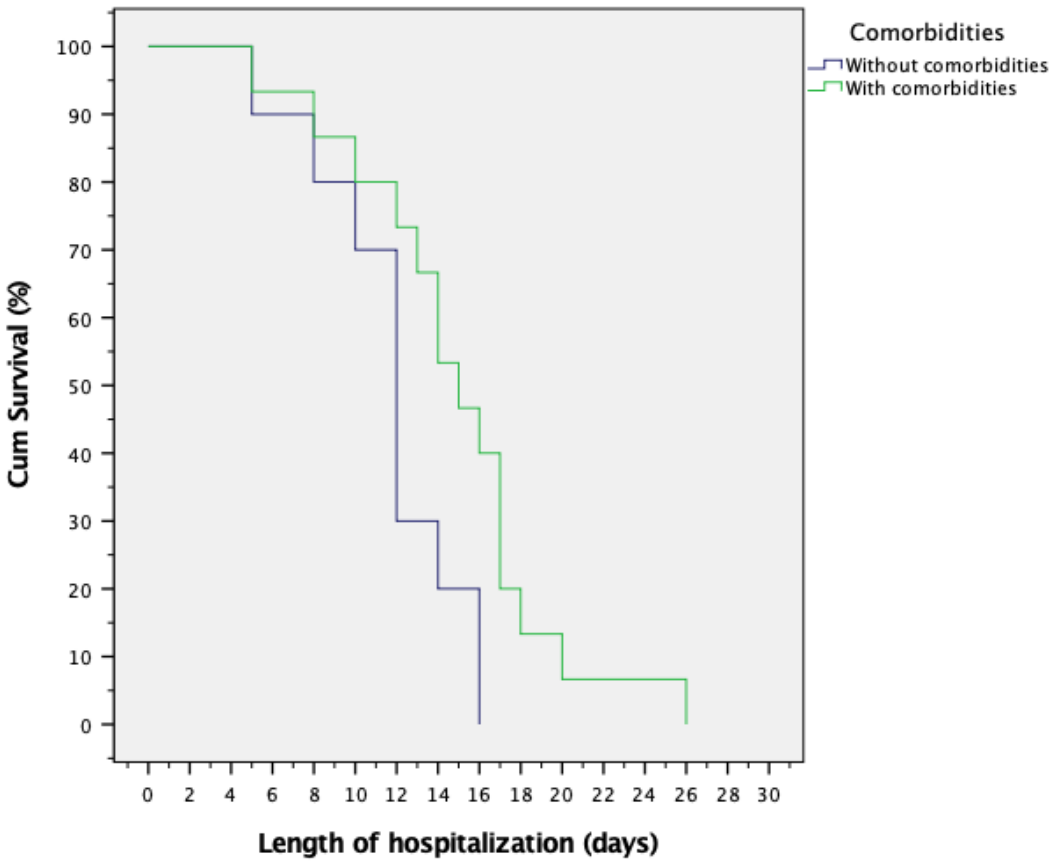

Figure 2

Survival curve 2. Duration of hospital admission based on underlying health conditions. The purple line indicates group 1 (patients without underlying diseases) had a mean duration of hospitalization 11.700± SE1.075 (CI 95% 9.592-13.808) while the group 2 (with comorbidities) had mean 14.8± SE1.303 (CI 95% 12.247-17.353; p=0.029) ODDS radio

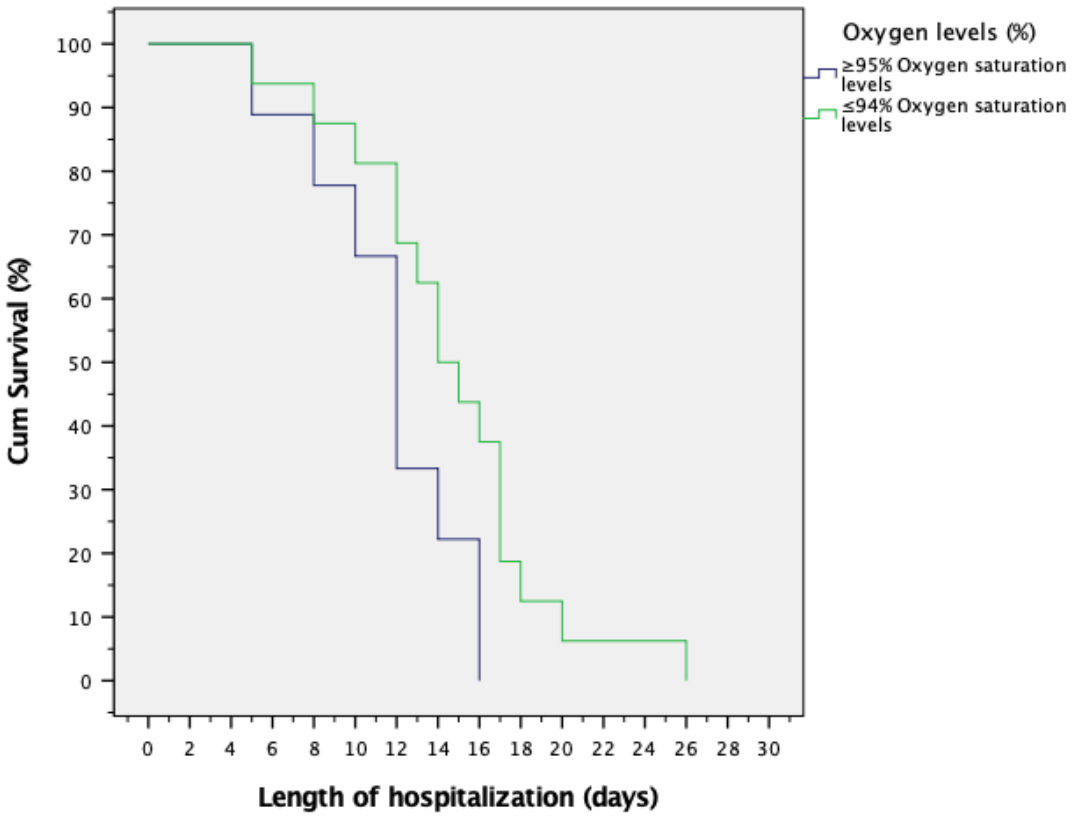

Figure 3

Survival curve 3. Effect of oxygen saturation upon admission, on length of hospitalization of COVID-19 patients (LOH). The levels of oxygen equal or below 94% (green line) has resulted in increased duration of hospitalization 11.667 ±SE1.202 (CI 95% 9.311- 14.022) while normal oxygen levels (purple line) results in decreased length of hospitalization 14.625± SE1.231 (CI 95% 12.212- 17.038; p=0.046)

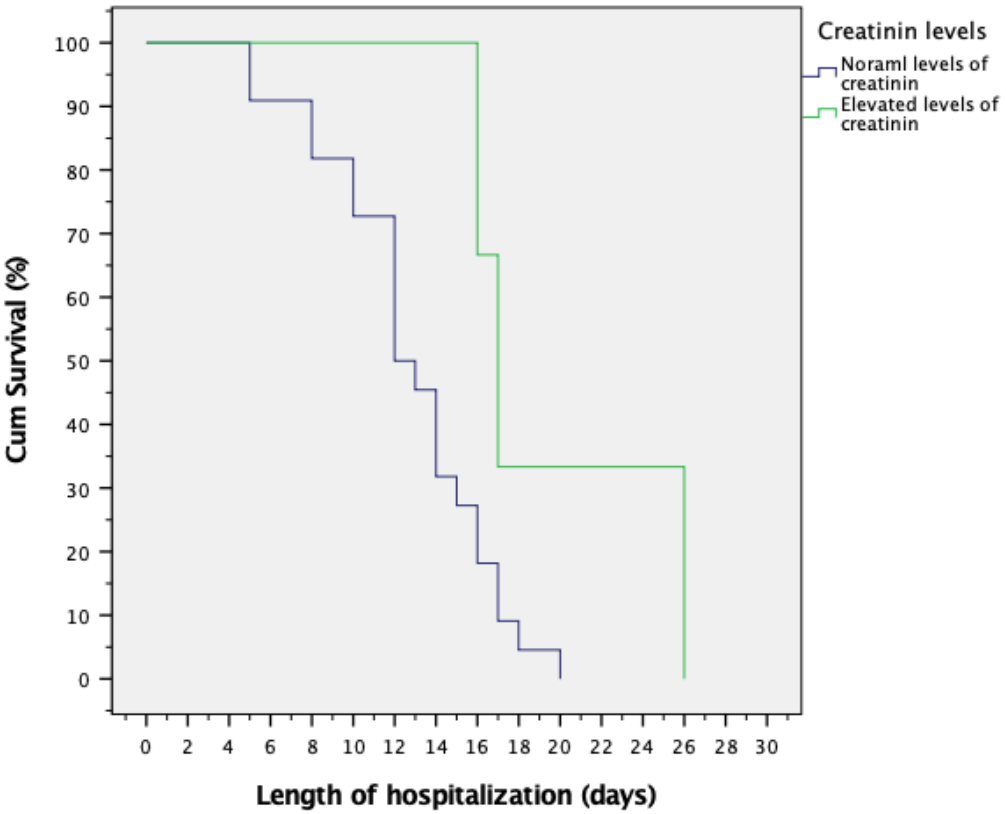

Figure 4

Survival chart 4. Impact of elevated levels of creatinine on length of hospitalization. The patient with elevated creatinine levels (green line) had longer length of hospitalization when compared to group of patients that have had normal levels of creatinine (purple line) on