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Factors associated with survival in patients with COVID -19 admitted to a community hospital in New York City

Abstract

Introduction: COVID-19 has been associated with increased mortality in old age, hypertension and male gender. Higher prevalence of increased body mass index (BMI), mechanical ventilation and renal failure has been found in the patients admitted to our New York City community hospital; accordingly we aim to explore the association between these parameters and survival in our patients.

Methods: Retrospective review of patients admitted with the COVID-19 disease March 14 to April 30 of 2020. Analysis using Cox regression models, Log rank tests and Kaplan Meier curves was done for a total of 326 patients that met our criteria.

Results: The adjusted odds of death for those at least 75 years of age were higher than those within the age group of 18 to 44 years. The patients with over 92% oxygen saturation had lower adjusted odds of death than those with 88 to 92% oxygen saturation (Odds Ratio (OR)=0.2, 95% CI=0.06, 0.70), as well as lower adjusted hazard of dying (Hazard Ratio (HR)=0.4, 95% CI=0.21, 0.87). Intubation was associated with a higher adjusted odds ratio (OR=57.8, 95% CI=17.74, 188.30) and adjusted hazard ratio HR=5.4 (95% CI=2.59, 11.21) for death. After controlling for age and gender, neither levels of serum D-dimer nor creatinine were found to be significantly associated with mortality

The factors that comprise metabolic syndrome, i.e., elevated BMI, diabetes, hypertension, and hyperlipidemia, were found to have no significant association with the outcome of death after controlling for age and sex and they also had no significant association with the time until death.

Conclusions: In the study population, COVID-19 was associated with increased mortality in patients who required intubation, and in the elderly, which may be explained by changes in the immune system over time.

Elevated BMI, though not statistically significant, was present in the majority of our study population, which may have contributed to the group's high mortality.

Keywords: COVID-19, Corona virus, Pandemic, Outcomes, New York, NYC

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Abbreviations: COVID-19, corona virus disease 2019; BMI, body mass index; OR, odds ratio; VIF, variance inflation factors; HR, hazard ratio

Introduction

After the emergence of the disease in China in the latter part of 2019, severe acute respiratory syndrome virus -2 (SARS CoV-2) spread across the world. Twelve million people have been affected by this virus, with 0.56 million deaths globally.[1]

Although old age, hypertension, and male gender have been reported in association with increased mortality in patients with COVID-19,[2,3] body mass index (BMI), mechanical ventilation, and renal failure were highly prevalent in the patients admitted to our hospital with the disease[4]. Accordingly, we aimed to explore the association between BMI, mechanical ventilation, and renal failure with the survival of patients admitted with COVID-19 to a community hospital in New York City during the early period of the pandemic.

Methods

The data source for this study was the database designed for characterization of patients admitted to the hospital with COVID-19, and approved by the institutional review board. The study group was comprised of 326 patients who had been hospitalized from March 14th to April 30th of 2020 and discharged from the hospital or had died.

Univariate statistics were calculated for the non-missing observations of all the variables. All the continuous variables were categorized using the defined normal limits, and the frequencies and the percentages were computed.

Logistic regression models for metabolic syndrome, respiratory factors, and D-dimer were used to compute the unadjusted and adjusted associations between predictors and the outcome of death. Odds ratio (OR) were calculated. Fifth's logistic regression technique was applied to reduce sample bias and address low cell counts. Predictors were selected using a *priori* selection. Variance inflation factors (VIF) were calculated to assess multicollinearity (if VIF $\geq$ 2).

Log rank tests were used to assess the survival estimate equality for predictors, and Kaplan Meier curves were produced for the predictors that had significant differences in survival estimates. Cox regression models for the metabolic syndrome and respiratory factors, and plasma D-dimer levels were used to predict the hazard ratios (HR) for time until death. Efron's method was applied to account for the high number of ties in the study sample. All models were controlled for age and sex. The proportional hazards assumption was tested for all Cox regression models.

Results

The majority of patients, 67.5%, was men, had a high BMI, 76.3%, and the minority, 12%, and was older than 75 years (Table 1). Comorbidities included hypertension in 47% of the group, diabetes in 41 %, and hyperlipidemia in 28 %. The vital signs on admission were notable for tachypnea in 32% of the patients, with 12% being hypoxemic at the time of arrival, and 22 % requiring intubation during the hospitalization. However, the majority, 66%, was admitted with oxygen saturation greater than 92% (Table 1). Fifty-seven percent of the patients had an abnormal serum creatinine, and 76 % had a high plasma D-dimer level on admission.

Table 1 Characteristics of COVID-positive patients at metropolitan hospital who died in hospital or were discharged alive (n=326)

Demographics		
	N	**%**
Total	326	
Age in years		
18-44	96	29.45
45-54	59	18.1
55-64	77	23.62
65-74	55	16.87
≥75	39	11.96
Gender		
Male	220	67.48
Female	106	32.52
Hypertension	154	47.24
Hyperlipidemia	91	28
Diabetes Mellitus	134	41.1
Body Mass Index		
Underweight (<18.5)	5	1.71
Normal (18.5-<25)	64	21.92
Elevated (≥25)	223	76.37
Respiratory Rate		
≤ 20rpm (Normal)	217	68.03
>20rpm (Abnormal)	102	31.97

Table Continues...

Demographics		
	N	**%**
Percent Oxygen Saturation on Presentation		
<88%	39	11.96
88-92%	72	22.09
>92%	215	65.95
pCO_2		
Low (<35 mmHg)	52	21.31
Normal (35-48 mmHg)	156	63.93
High (>48 mmHg)	36	14.75
pH		
Low (<7.3)	28	11.48
Normal (7.3-7.4)	116	47.54
High (>7.4)	100	40.98
Intubation	71	21.78
D-dimer level		
Normal (<230 ng/dL)	57	23.55
Abnormal (≥230 ng/dL)	185	76.45
Serum Creatinine level		
Normal (<0.9 mg/dL)	140	43.08
Abnormal (≥0.9 mg/dL)	185	56.92

Note: Some frequencies do not add up to the total 326 due to missing observations.

Diabetes, hypertension, and hyperlipidemia were associated with an increase in the odds of death and hazard ratio in the unadjusted multivariable logistic regression model (Table 2) and the unadjusted Cox regression model (Table 3), respectively. The factors that comprise the metabolic syndrome, i.e., elevated BMI, diabetes, hypertension, and hyperlipidemia, were found to have no significant association with the outcome of death after controlling for age and sex and also had no significant association with the time until death.

The adjusted odds of death for those at least 75 years of age were higher than those within the age group of 18 to 44 years, 15.6 (95% confidence interval (CI)=4.60, 53.08). The adjusted odds of death for those within the age group of 65 to 74 years were higher than those with age within 18 to 44 years, 6.3 (95% CI=2.16, 18.39) as well. The hazard ratio of death for the patients aged 75 or older was 6.8 (95% CI=2.27, 20.47) times the hazard of death for the patients between the ages of 18 to 44 years, and those aged between 65 to 74 years

had 3.6 (95% CI=1.28, 10.06) times the hazard of death as compared to those within the age group of 18 to 44years. The proportional hazards assumption was met by the data in the model (Global Test Chi-Square=13.06, p=0.220), signifying that the trends in each hazard group were proportional and that the Cox proportional hazard was an appropriate test to be used.

Table 2 Logistic regression: metabolic syndrome (Firth's Logistic Regression)

	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Age, in years				
18 to 44	1 (ref)		1 (ref)	
45 to 54	1.45 (0.48, 4.37)	0.509	(1.47 (0.46, 4.72)	0.513
55 to 64	2.96 (1.14, 7.50)	0.022*	2.49 (0.85, 7.28)	0.095
65 to 74	8.63 (3.46, 21.54)	<0.001*	6.30 (2.16, 18.39)	0.001*
>75	18.86 (7.08, 50.24)	<0.001*	15.62 (4.60, 53.08)	<0.001*
Sex				
Male	1.20 (0.69, 2.09)	0.523	1.30 (0.67, 2.53)	0.433
Female	1 (ref)		1 (ref)	
BMI				
Underweight BMI	0.90 (0.13, 6.22)	0.919	0.39 (0.05, 3.36)	0.395
Normal BMI	1 (ref)		1 (ref)	
Elevated BMI	0.77 (0.41, 1.45)	0.42	1.11 (0.52, 2.36)	0.783
Diabetes Mellitus	2.04 (1.21, 3.43)	0.007*	1.00 (0.52, 1.93)	0.993
Hypertension	4.15 (2.36, 7.31)	<0.001*	1.40 (0.67, 2.94)	0.373
Hyperlipidemia	2.47 (1.44, 4.25)	<0.001*	1.38 (0.68, 2.79)	0.372

Table 3 Cox regression: metabolic syndrome

	aHR	95% CI	p-value
Age, in years			
18 to 44	1 (ref)		
45 to 54	2.18	(0.69, 6.89)	0.184
55 to 64	2.76	(0.96, 7.91)	0.059
65 to 74	3.59	(1.28, 10.06)	0.015*
>75	6.82	(2.27, 20.47)	0.001*
Sex			
Male	0.88	(0.51, 1.51)	0.631
Female	1 (ref)		
BMI			
Underweight BMI	0.26	(0.03, 2.02)	0.197
Normal BMI	1 (ref)		
Elevated BMI	0.71	(0.38, 1.34)	0.295
Diabetes Mellitus	0.77	(0.42, 1.41)	0.399
Hypertension	1.64	(0.83, 3.24)	0.155
Hyperlipidemia	1.07	(0.59, 1.92)	0.827

The patients with over 92% oxygen saturation had 80% lower odds of death than those with 88 to 92% oxygen saturation, with an OR=0.2, 95% CI=0.06, 0.70, as well as 58% lower hazard of dying ((HR)=0.4, 95% CI=0.21, 0.87)) after adjusting for other covariables. Intubation was associated with a higher odds of death (OR=57.8, 95% CI=17.74, 188.30), as well as a higher hazard of death (HR=5.4 (95% CI=2.59, 11.21) as compared to the patients who did not require intubation after adjusting for other covariables (Tables 4 & 5).

Table 4 Logistic regression: respiratory status (Firth's Logistic Regression)

	Unadjusted	p-value	Adjusted	p-value
	OR (95% CI)		OR (95% CI)	
Age				
18 to 44	1 (ref)		1 (ref)	
45 to 54	1.45 (0.48, 4.37)	0.509	0.97 (0.13, 6.91)	0.972
55 to 64	2.96 (1.14, 7.50)	0.022*	3.97 (0.90, 17.59)	0.069
65 to 74	8.63 (3.46, 21.54)	<0.001*	7.17 (1.43, 35.85)	0.017*
>75	18.86 (7.08, 50.24)	<0.001*	93.27 (15.67. 555.09)	<0.001*
Sex				
Male	1.20 (0.69, 2.09)	0.523	1.88 (0.62, 5.72)	0.268
Female	1 (ref)		1 (ref)	
Respiratory Rate				
< 20rpm	1 (ref)		1 (ref)	
>20rpm	2.18 (1.27, 3.73)	0.005*	1.29 (0.46, 3.60)	0.628
Percent Oxygen Saturation on Presentation				
<88%	5.28 (2.27, 12.28)	<0.001*	1.76 (0.37, 8.23)	0.475
88-92%	1 (ref)		1 (ref)	
>92%	0.27 (0.15, 0.47)	<0.001*	0.20 (0.06, 0.70)	0.012*
pCO2				
Low (<35mmHg)	1.79 (0.92, 3.49)	0.086	0.89 (0.25, 3.11)	0.852
Normal (35-48mmHg)	1 (ref)		1 (ref)	
High (>48mmHg)	1.57 (0.73, 3.40)	0.252	0.83 (0.21, 3.30)	0.793
pH				
<7.3	3.64 (1.57, 8.46)	0.003*	2.71 (0.63, 11.72)	0.182
7.3-7.4	1 (ref)		1 (ref)	
>7.4	0.54 (0.28, 1.02)	0.057	0.59 (0.18, 1.91)	0.383
Intubation	38.64 (18.98, 78.69)	<0.001*	57.80 (17.74, 188.30)	<0.001*

Table 5 Cox regression: respiratory status

	aHR	95% CI	p-value
Age			
18 to 44	1 (ref)		
45 to 54	2.18	(0.69, 6.87)	0.183
55 to 64	2.26	(0.87, 5.91)	0.094
65 to 74	2.06	(0.83, 5.15)	0.12
>75	11.46	(4.37, 30.06)	<0.001*
Sex			
Male	1.86	(1.01, 3.44)	0.048*
Female	1 (ref)		
Respiratory Rate			
< 20 rpm	1 (ref)		
>20 rpm	0.96	(0.55, 1.69)	0.899
Percent Oxygen Saturation on Presentation			
<88%	1.09	(0.48, 2.50)	0.831
88-92%	1 (ref)		
>92%	0.42	(0.21, 0.87)	0.019*
pCO2			
Low (<35 mmHg)	0.81	(0.39, 1.68)	0.573
Normal (35-48 mmHg)	1 (ref)		
High (>48 mmHg)	0.91	(0.40, 2.07)	0.818
pH			
<7.3	3.27	(1.45, 7.38)	0.004*
7.3-7.4	1 (ref)		
>7.4	0.6	(0.30, 1.24)	0.169
Intubation	5.39	(2.59, 11.21)	<0.001*

After controlling for age and gender, neither plasma levels of D-dimer nor serum creatinine were found to be significantly associated with mortality (Tables 6 & 7).

Table 6 Logistic regression: D-dimer and serum creatinine (Firth's Logistic Regression)

	Unadjusted	p-value	Adjusted	p-value
	OR (95% CI)		OR (95% CI)	
Age				
18 to 44	1 (ref)		1 (ref)	
45 to 54	1.45 (0.48, 4.37)	0.509	1.14 (0.32, 4.13)	0.838
55 to 64	2.96 (1.14, 7.50)	0.022*	2.13 (0.74, 6.14)	0.162
65 to 74	8.63 (3.46, 21.54)	<0.001*	4.53 (1.56, 13.15)	0.006*
>75	18.86 (7.08, 50.24)	<0.001*	8.47 (2.78, 25.85)	<0.001*
Sex				
Male	1.20 (0.69, 2.09)	0.523	1.49 (0.72, 3.09)	0.284
Female	1 (ref)			
D-dimer level				
Normal (<230 ng/dL)	1 (ref)		1 (ref)	
Abnormal (>230 ng/dL)	4.80 (1.74, 13.22)	<0.001*	2.77 (0.95, 8.06)	0.062
Serum Creatinine level				
Normal (<0.9 mg/dL)	1 (ref)		1 (ref)	
Abnormal (>0.9 mg/dL)	4.31 (2.31, 8.04)	<0.001*	1.55 (0.71, 3.39)	0.27

Table 7 Cox regression: anticoagulation and D-dimer

	aHR	95% CI	p-value
Age			
18 to 44	1 (ref)		
45 to 54	1.25	(0.35, 4.46)	0.735
55 to 64	1.84	(0.66, 5.14)	0.242
65 to 74	2.13	(0.76, 5.96)	0.15
>75	4.2	(1.54, 11.46)	0.005*
Sex			
Male	1.29	(0.70, 2.37)	0.418
Female	1 (ref)		
D-dimer level			
Normal (<230 ng/dL)	1 (ref)		
Abnormal (>230 ng/dL)	2.21	(0.67, 7.29)	0.195
Serum creatinine level			
Normal (<0.9 mg/dL)	1 (ref)		
Abnormal (>0.9 mg/dL)	1.4	(0.68, 2.87)	0.365

The overall median survival for the patients in our study was 17 days. Kaplan-Meier curves for the survival estimates for the overall survival, age, BMI, diabetes, percentage of oxygen saturation on arrival, and intubation are shown in Figures 1-6, respectively.

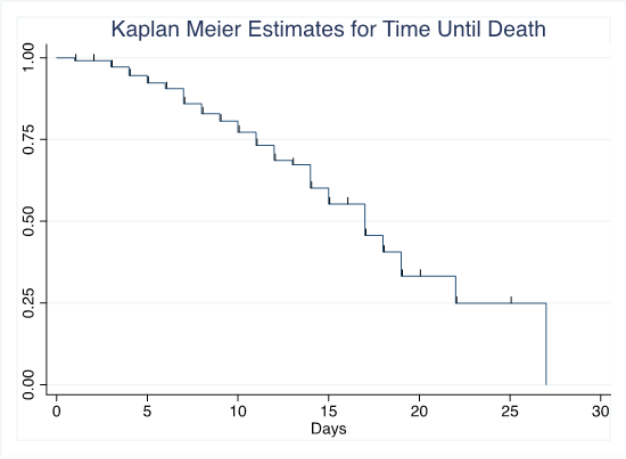

Figure 1 Kaplan Meier estimates for time until death.

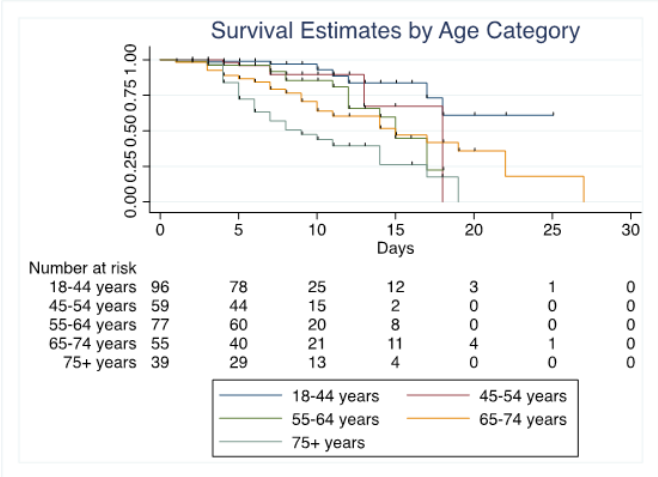

Figure 2 Survival estimates by BMI category.

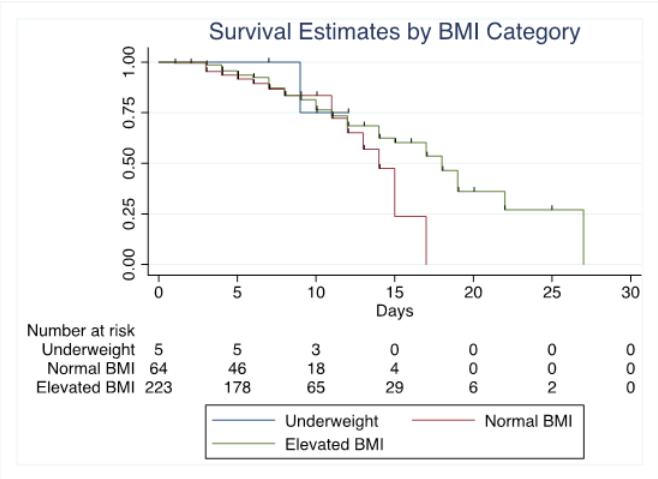

Figure 3 Survival estimates by intubation status.

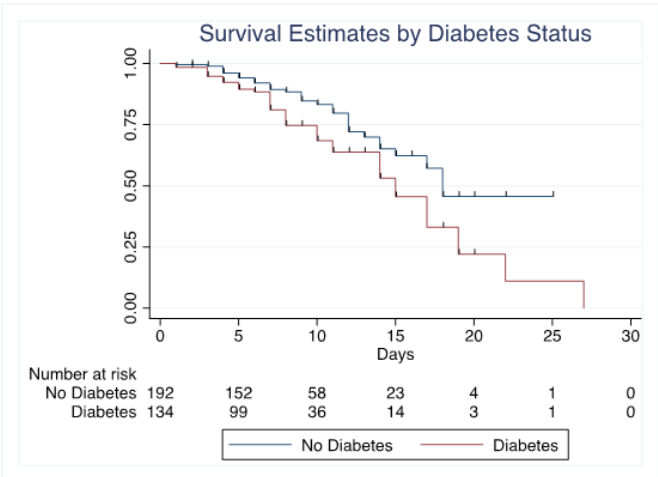

Figure 4 Survival estimates by age category.

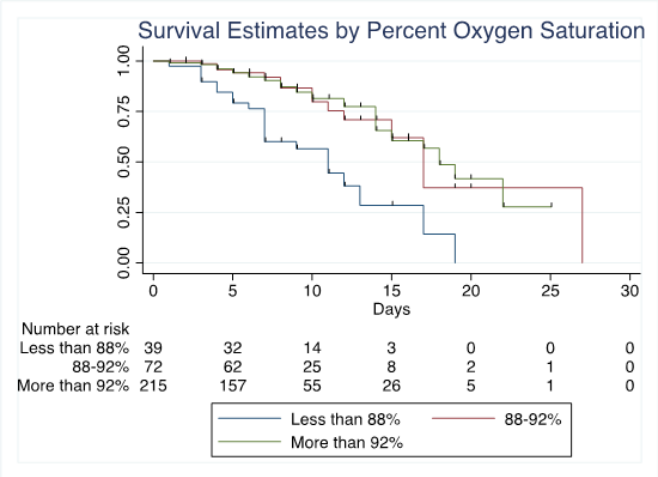

Figure 5 Survival estimates by diabetes status.

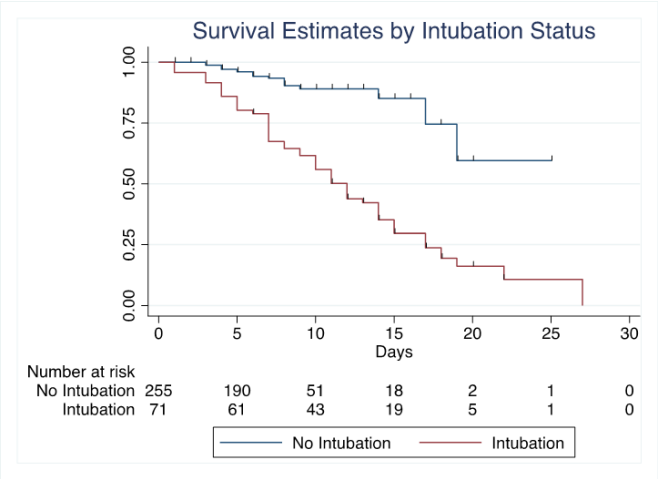

Figure 6 Survival estimates by percent oxygen saturation.

Discussion

In this study, age older than 75 years was associated with higher mortality than in the other age groups. An oxygen saturation of at least 92% at presentation, although consistent with hypoxemia, was associated with increased odds of survival, in contrast to intubation, which was associated with a significantly decreased odds of survival. We did not find any significant association between the plasma concentration of D -dimer or serum creatinine with mortality when adjusted for age and gender.

COVID-19 is associated with adverse outcomes in the elderly population, as documented in other conditions like bacterial or viral pneumonia; this may be related to the presence of comorbidities or a decrease in the competency of the immune system.[5,6] Decreased clearance of oral secretions, mucociliary function, and elastic recoil of the lungs are factors that put the elderly at an increased risk for complications from pneumonia.[6] However, the waning immunity with aging has been challenged by the senescent remodeling theory of the immune system,[7] which proposes the preservation or enhancement of innate immunity with increasing age and the existence of specific immune phenotypes that may put a person at an increased risk for

infection, which results from complex changes in both the adaptive and innate immunity as a person ages. Nevertheless, aging has been statistically related to worse outcomes in patients with viral and bacterial pneumonia, evidenced by the inclusion of age as a common variable in different models predicting the severity of the disease, e.g., CURB-65, PSI, A-DROP.[8–10] Elderly patients may also exhibit atypical symptoms of various infectious diseases including, pneumonia, urinary tract infections, and meningitis. Similarly, elderly patients with COVID-19 may present with diarrhea and delirium more frequently than patients in other age groups; hence, there may be a delay in seeking treatment, making a diagnosis, and providing subsequent specific management of the patients.[10,11]

Insulin resistance or the presence of conditions that comprise the metabolic syndrome have been considered to be associated with increased morbidity and mortality in patients with COVID-19.[12–14] However, there was no statistically significant increased risk of death associated with the presence of metabolic syndrome after it was adjusted for age and gender in our study. One explanation for this finding is that the majority of the patients, more than three-fourths, in our study group, had an elevated BMI; hence, the patients with normal BMI were underrepresented, making the comparison insignificant. In this context, a limitation of our study is the predominance of patients with high BMI, which has limited our ability to assess the effect of COVID-19 in patients with normal BMI.

Intubation was needed for 25% of the patients, which is higher than the 2-17% reported in other publications.[15–17] Intubation itself, in our study, was associated with a five time increase risk of dying as compared to the patients who did not require intubation. The increased need for intubation in our study may have been due to the high prevalence of obesity in the study population, as a high BMI is associated with poor respiratory function.[18–20] ARDS, a complication of COVID-19,[21,22] was present in 30% of the patients. One of the mechanisms proposed in the development of this complication is diffuse alveolar damage associated with the development of micro-thrombosis and endothelial cell damage. Furthermore, increased angiogenesis, specifically intussusceptive angiogenesis[23], where a new vessel is formed by developing a pillar within the lumen of the vessel compared to sprouting angiogenesis wherein new channels bud from the existing vessels, has been observed more frequently in the patients with COVID-19.[21] In addition, a recent study has suggested that pulmonary vascular dilatation contributes to development of hypoxemia in patients with COVID-19 pneumonia.[24]

Increased odds of mortality and critical illness with an elevated serum creatinine level in patients with COVID-19 have been reported in other studies.[25–27] Elevated serum creatinine was found in more than 50% of the patients in our study on admission. It was found to be a significant indicator of mortality on its own, but, when adjusted for age it was insignificant. This points towards the importance of increased age as a determinant of mortality in patients with COVID-19.

Conclusion

In conclusion, COVID-19 was associated with increased mortality in patients who required intubation, which reflects the severity of pneumonia, and in the elderly, which may be explained by changes in the immune system from aging. Elevated BMI, though not statistically significant, was present in the majority of our study population, which may have contributed to the group's high mortality; this finding may reflect a baseline inflammatory state propitiated by obesity itself and worsened by a devastating infection such as that from SARS-CoV-2.[28]

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Conflicts of interest

Author declares there are no conflicts of interest.

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