Clinical Characteristics and Predictors of Mortality in Minority Patients Hospitalized with COVID-19 Infection

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Abstract

Objectives To identify the early mortality predictors in minority patients hospitalized with coronavirus disease 2019 (COVID-19).

Design Demographics, presenting characteristics, admission laboratory data, ICU admission, and mortality data were collected from 200 consecutively hospitalized patients with COVID-19.

Results The mean (SD) age was 58.9 (15.1) years, 121(60.5%) were men, 143 (71.5%) were African Americans, and 33 (16.5%) were Latino. Common presenting symptoms were cough 130 (65.0%), shortness of breath 129 (64.5%), and fever 121 (60.5%). One or more comorbid illness occurred in 171 (85.5%) and common comorbidities were hypertension (130 (65.2%)), diabetes (100 (50.0%)) and chronic kidney disease (60 (30.0%)). Of the 200 patients, 71 (35.5%) were treated in the ICU, 47 (24.2%) received mechanical ventilation, 45 (22.5%) died, and 155(77.5%) patients discharged home alive. The non-survivors were significantly older and had elevated markers of inflammation, coagulation, and acute organ damage on presentation. Age $\geq$ 65 years (odds ratio (OR), 3.78; 95% CI, 1.74–8.22; $P = .001$), lactate dehydrogenase level > 400 IU/L (OR, 9.1; 95% CI, 2.97–28.1; $p < 0.001$), C-reactive protein > 20 mg/dl (OR, 5.56; 95%CI, 1.84–16.8; $p < 0.001$), ferritin > 2000 ng/ml (OR, 5.42; 95%CI, 1.63–17.9; $p = 0.006$), creatinine kinase > 1000 iu/l (OR, 3.57; 95% CI, 1.23 10.3; $p = 0.019$), procalcitonin > 2.5 ng/ml (OR, 4.21; 95% CI, 1.47–12.0; $p = 0.007$), D-dimer level > 3.0 µg/ml (OR,10.9; 95% CI, 3.33–36.2; $p = < 0.001$), creatinine > 2 mg/dl (OR, 4.5; 95% CI, 1.29–15.8; $P = 0.018$) at admission were associated independently with increases risk of in-hospital mortality.

Conclusion Patients of advanced age that present with elevated biomarkers of inflammation, coagulation, and end-organ damage were at higher risk of mortality.

Introduction

Coronavirus disease 2019 (COVID-19) has resulted in considerable morbidity and mortality. More than 1,270,000 worldwide and approximately 239,600 patients in the United States (US) have died since December 2019 [1]. Preliminary data indicate that minority populations such as African Americans (AA) and Latinos are contracting severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) at higher rates and are more likely to die, bearing a disproportionate burden in the US [2, 3]. For example, in the District of Colombia (DC), as of November 9, 2020, out of total of 18,173 COVID-19 cases and 657 deaths, 8850 cases and 490 deaths occurred in Black/AA race accounting for 48.7% of the cases and 74.6% of deaths despite AA composing only 46% of the district's population. The disproportionate impact of the coronavirus among AA and other minority populations meanwhile, is not limited to the District. Counties that are majority Black were reported to have three times the rate of infections and almost six times the rate of deaths as counties

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where white residents are in the majority [4]. A similar observation was noted in the District of Columbia ward level comparison data, with Ward 8 Black residents (92% Black) having the highest deaths (126 deaths) compared to Ward 3 majority White (81% White) residents having 34 deaths as of September 23, 2020 [5].

Multiple factors including patients' age and comorbidities have been recognized in increasing the risk of hospital admission and predicting worse outcomes [6–10]. However, data fully adjusted for comorbidities and laboratory markers to the reported differences in fatality rates among AA and other minority patients are limited. The early outcome predictors in those at high risk to be infected and to die if infected is not well-known. Our objective was to identify the early mortality predictors. In this study, we collected the demographics, baseline comorbidities, presenting clinical and laboratory data, and we report the clinical characteristics and the independent predictors of mortality of patients with COVID-19 hospitalized at an academic inner city hospital in Washington DC.

Methods

Study Design and Participants

The study was approved by the Howard University institutional review board as a minimal risk research, and the requirement for informed consent was waived. Consecutive adult patients admitted with COVID-19 between March 1 and May 30, 2020 were included. COVID-19 was confirmed with reverse-transcriptase–polymerase-chain-reaction assay (RT-PCR) of nasopharyngeal specimens.

Data Collection and Definitions

Demographics, comorbidities, clinical presentation, initial laboratory data, and inpatient treatments including invasive mechanical ventilation and new renal replacement therapy, intensive care unit (ICU) admission, discharge status, and survival status were extracted from electronic records manually. Obesity was defined as body mass index (BMI) ≥ 30 kg/m^2. Initial laboratory data was the first test results available, typically within 24 h of admission which included complete blood count, basic metabolic panel, ferritin, procalcitonin (PCT), C-reactive protein (CRP), lactate dehydrogenase (LDH), creatine phosphokinase (CPK), troponin, D-dimer, and interleukin-6 levels. Acute kidney injury (AKI) was defined as increase in serum creatinine of > 0.3 mg/dl from baseline present on admission. [11]

Outcomes

Primary outcome was in-hospital mortality. Secondary outcomes were need for intensive care unit (ICU) admission, mechanical ventilation, new renal replacement therapy (HD), and vasopressors.

Statistical Analysis

Explanatory analysis using Pearson's Chi Square test, Student's t test, and Fischer's exact test were performed as appropriate. Categorical variables were shown by frequencies and percentages. Continuous variables were shown as mean ± standard deviation (SD) or transformed into ordered categorical variables. Continuous variables were transformed into ordered categorical variable to enable the assessment of linearity of association in the regression analysis. Ordered categorization of these continuous variables was based on clinical significance and distribution of respective range of values. Initial laboratory values were categorized into 3 groups viz. serum creatinine (Scr) < 1, 1–2, > 2 mg/dl; blood urea nitrogen (BUN) < 25, 25–35, > 35 mg/dl; CPK < 250, 250–1000, > 1000 iu/l; troponin < 0.05, 0.05–0.10, > 0.10 ng/ml; procalcitonin < 0.5, 0.5–2.5, > 2.5 ng/ml; LDH < 300, 300–400, > 400 iu/l; CRP < 10, 10–20, > 20 mg/dl;D-dimer < 1, 1–3, > 3 μg/ml and ferritin < 500, 500–2000, > 2000 ng/ml. Lactic acid level was categorized into 2 groups of < 2.2 and > 2.2 mm/l. Multivariable logistic regression models were performed to identify independent factors associated with inpatient mortality. Variables with significant association in the univariable analysis were included in the multivariable analysis. A base multivariable regression model was performed with variables identified to be statistically significant among patients' demographics and baseline comorbid conditions in the univariable analysis. To avoid overfitting, we rerun the base model with each of the laboratory/inflammatory markers each at a time to determine the independence of each laboratory/inflammatory maker as a predictor of mortality. We also created receiver operating characteristics (ROC) curves to compare mortality prediction among the various initial inflammatory markers, which were summarized by area under the curve (AUC) estimates among the various models. The analysis was performed using STATA statistical software version 14.1 (Statacorp, College Station, Texas). Statistical significance was accepted at P value < 0.05.

Results

Demographics and Patient Characteristics

A total of 200 patients were admitted to hospital during the study period. The mean (SD) age was 58.9 (15.1) years, 121

(60.5%) were men, 143 (71.5%) were Black/AA, and 33 (16.5%) were Latino patients. One or more underlying comorbid illness occurred in 171 (85.5%) of the patients. Most common comorbidities were hypertension (HTN) 130 (65.0%), diabetes mellitus (DM) 100 (50.0%), chronic kidney disease (CKD) 60 (30.0%), and cardiovascular diseases 56 (28.5%) as shown in Table 1.

Common presenting symptoms were cough 130 (65.0%), fever 121 (60.5%), and shortness of breath (SOB) 129 (64.5%) shown in Table 2. Admission laboratory data showed lymphopenia (lymphocyte count, 1.1×10^9 per L [mean 0.65×10^9 per L)], elevated markers of inflammation, coagulation, and acute organ damage as shown in Table 2.

Outcomes and Predictors for Mortality

In-hospital mortality occurred in 45 (22.5%) patients. Compared with survivor group, non-survivors were older (67.1 ± 13.7 vs. 58 ± 14.9 years; $P < 0.001$). Comorbidities, such as HTN (77.8% vs. 61.3%; $P = 0.04$), CKD (42.2% vs 26.5%; $P = 0.04$), CAD (26.7% vs. 13.6%; $p = 04$) were higher in those deceased when compared to those discharged alive respectively (Table 1). The non-survivor group had higher markers of inflammation, including a higher serum CRP (17.1 ± 8.8 vs. 11.6 ± 8.2 mg/dl; $p < 0.001$), ferritin (1592 ± 2259 vs. 839 ± 1079 ng/ml, $p = 0.003$), LDH (561 ± 330 vs. 352 ± 177 iu/l, $p < 0.001$), procalcitonin (2.52 ± 3.04 vs. 0.70 ± 1.20 ng/ml; $p = 0.003$), and D-dimer [(3.68 ± 5.09 vs. 2.40 ± 3.43 μg/ml; $p = 0.063$), as shown in Table 2.

Unadjusted mortality rates were highest in patients with initial level of LDH > 400 iu/l (38.5%), CRP > 20 mg/dl (38.2%), procalcitonin > 2.5 ng/dl (50%), ferritin > 2000 ng/ml (37.5%), CPK > 1000 iu/l (38.2%), Scr level in non-hemodialysis dependent > 2 mg/dl (48.4%), highest in-hospital D-dimer level > 6 μg/dl (53.8%), and age > 65 years (38.5%) Fig. 1.

Secondary outcomes namely need for ICU admission, mechanical ventilation, new renal replacement therapy (HD), and vasopressors were met by 71 (35.5%), 47 (24.2%), 12 (6.1%), and 25 (12.5%) respectively. Inpatient mortality occurred in 39 out of 71 (54.9%) who required ICU care, 9 out of 12 (75%) who required new HD, 22 out of 25 (88%) who needed vasopressors, and 31 out of 47 (83.7.5%) who needed mechanical ventilation as shown in Supplemental Table 1.

Univariate regression analysis identified age, hypertension, chronic kidney disease, coronary artery disease, dyslipidemia, and history of stroke as important demographics/baseline comorbidities associated with death as summarized in Table 3. Age was an independent predictor of mortality in our base multivariable regression model and in subsequent models. Independent of the demographics and baseline comorbidities, initial BUN and Scr (in non-hemodialysis dependent), CPK,

procalcitonin, LDH, CRP, and ferritin level were all independent predictors of mortality. After adjustment for important variables (variables in the base model), patients with initial LDH level > 400 IU/l vs. with < 300 IU/l had a 9-fold greater risk of inpatient mortality (OR, 9.1,;95% CI − 2.97 to 28.1; $p < 0.001$), and initial CRP > 20 mg/dl had 6-fold greater risk for mortality than CRP < 10 mg/dl (OR, − 5.56; 95% CI, − 1.84 to 16.8; $p < 0.001$). The same linear trend was noted for initial ferritin, CPK, BUN, creatinine, and procalcitonin levels, with initial ferritin > 2000 ng/ml conferring a 5-fold greater risk than level < 500 ng/ml (OR 5.4; 95% CI, − 1.63 to 17.9; $p = 0.006$) and CPK > 1000iu/l conferring 3.6-fold greater risk than those within the normal reference range (OR, 3.57; 95% CI, − 1.23 to 10.3; $p = 0.019$) Table 3. Kidney function at the time of presentation was also an important independent predictor of mortality, patients with initial creatinine level > 2 mg/dl in non-dialysis dependent patients was associated with 4.5-fold greater risk of mortality compared with < 1 mg/dl creatinine level (OR, 4.5; 95% CI 1.29 = 15.8; $p = 0,018$). The patient group with initial procalcitonin level of 2.5 ng/ml had 4-fold mortality risk compared with procalcitonin < 0.5 ng/dl (OR, 4.21; 95% CI, 1.47–12.0; $p = 0.007$). Initial D-dimer level was not found to be an independent predictor of mortality; however, rapid increase in D-dimer level and peak D-dimer during hospitalization was the strongest independent predictor of mortality. A peak D-dimer level > 3.0 μg/ml conferred 11-fold and > 6.0 μg/ml conferred 24-fold mortality risk compared with peak D-dimer level < 3.0 μg/ml.

Both initial LDH and CRP were identified as independent predictor of unfavorable outcomes for both ICU admission and inpatient mortality. Area under the curve (AUC) estimates among the different models (Fig. 2), identified initial LDH (AUC 0.84), followed by initial CRP (AUC 0.79) as the two most important laboratory/inflammatory markers to predict unfavorable outcomes in our study. LDH appeared to be a better prognosticator of inpatient mortality among the laboratory markers with mortality rates ranging 9.8% in patients with initial LDH < 300 iu/l to 38.4% in patients with initial LDH > 400 iu/l (Fig. 1). Two-thirds of all inpatient mortality in our study population occurred in patients with initial LDH of 400 iu/l and above. A ROC curve for in-hospital mortality had an estimated AUC of 0.74 for LDH alone followed by 0.69 for CRP alone.

Discussion

This retrospective cohort study identified older age, elevated biomarkers of inflammation, rising coagulation marker, and markers of acute organ damage at presentation were associated with higher odds of in-hospital mortality.

Table 1 Baseline characteristics of hospitalized patients with COVID-19 by survival status

Characteristics	All (N=200)	Non-survivors (n=45)	Survivors (n=155)	p value
Age mean, (SD), yr.	58.9 (15.1)	67.1 (13.7)	58 (14.9)	<0.001
Age group, no. (%)				
<65 yr	122 (61.0)	15 (33.3)	107 (69.0)	<0.001
≥65 yr	78 (39.0)	30 (66.7)	48 (31.0)	
Gender, no. (%)				
Male	121 (60.5)	29 (64.4)	92 (59.4)	0.540
Female	79 (39.5)	16 (35.6)	63 (40.6)	
Race, no. (%)				
African American	143 (71.5)	35 (77.8)	108 (69.7)	0.500
Hispanic/Latino	33 (16.5)	5 (11.1)	28 (18.1)	
White	15 (7.5)	3 (6.7)	12 (7.7)	
Others	9 (4.5)	2 (4.4)	7 (4.5)	
Insurance, no. (%)				
Medicare	21 (10.5)	5 (11.1)	16 (10.3)	
Medicaid alone	24 (12.0)	4 (8.9)	20 (12.9)	
Medicaid and other [a]	79 (39.5)	27 (60.0)	52 (33.6)	0.020
Private	59 (29.5)	8 (17.8)	51 (32.9)	
Uninsured	17 (8.5)	1 (2.2)	16 (10.3)	
Referral, no. (%)				
Community	137 (68.5)	24 (53.3)	113 (72.9)	0.009
Nursing home residents	46 (23.0)	19 (42.2)	27 (17.4)	0.001
Homelessness	17 (8.5)	2 (4.4)	15 (9.7)	0.270
Body mass index, no. (%)				
18.5–24.9, kg/m^2	45 (22.5%)	11 (24.4%)	34 (21.9%)	
25–29.9, kg/m^2	64 (32.0%)	16 (35.6%)	48 (31%)	0.490
≥30, kg/m^2	74 (37.0%)	14 (31.1%)	60 (38.7%)	
Body mass index, kg/m^2, mean, (SD)	30 (9)	28.3 (8.3)	30.6 (9.2)	0.14
Comorbidities, no. (%)				
Diabetes mellitus	100 (50.0)	26 (57.8)	74 (47.7)	0.240
HbA1C, mean (SD)	7.7 (2.6)	7.3 (2.5)	7.8 (2.6)	0.32
Hypertension	130 (65.0)	35 (77.8)	95 (61.3)	0.04
Coronary artery disease	33 (16.5)	12 (26.7)	21 (13.6)	0.04
Congestive heart failure	26 (13.0)	4 (8.9)	22 (14.2)	0.35
Cardiovascular diseases [b]	56 (28.0)	15 (33.3)	41 (26.5)	0.36
Dyslipidemia	69 (34.5)	24 (53.3)	45 (29.0)	0.003
Chronic kidney disease	60 (30.0)	19 (42.2)	41 (26.5)	0.04
ESRD on dialysis	27 (13.5)	4 (8.9)	23 (14.8)	0.30
History of stroke	22 (11.0)	9 (20.0)	13 (8.4)	0.03
COPD	19 (9.5)	7 (15.6)	12 (7.7)	0.11
Asthma	20 (10.0)	3 (6.7)	17 (11)	0.39
Chronic lung disease [c]	41 (20.5%)	9 (20%)	32 (20.7%)	0.93
Comorbidities, no. (%)				
Hepatitis B	3 (1.5)	0 (0.0)	3 (1.9)	0.34
Hepatitis C	5 (2.5)	2 (4.4)	3 (1.9)	0.34
HIV	14 (7.0)	4 (8.9)	10 (6.5)	0.57
Malignancy[d]	13 (6.5)	3 (6.7%)	10 (6.5)	0.95
Dementia	24 (12.0)	10 (22.2)	14 (9.0)	0.01

COPD, chronic obstructive lung disease; ERSD, end-stage renal disease; HIV, human immunodeficiency virus; HbA1c, hemoglobin A1c

[a] Insurance status of Medicaid and others is combination of Medicaid with any other insurance

[b] Cardiovascular Diseases (cardiovascular diseases variable is combined CAD, CHF, atrial fibrillation, and PAD)

[c] Chronic lung diseases (combination of COPD, asthma, and obstructive sleep apnea)

[d] Malignancy both active and in remission

Specifically, age ≥ 65 years, elevated admission serum levels of LDH, CRP, ferritin, PCT, CPK, troponin, BUN and Scr, and rising D-dimer level all had an independent increased risk of in-hospital mortality. Elevated admission serum LDH and CRP levels were also independent predictors for ICU admission. These biomarkers can help in the early identification of patients that progress rapidly to severe acute respiratory distress syndrome (ARDS), multi-organ failure, and death.

Among the biomarkers, elevated serum LDH level at admission had a better predictive ability. Serum LDH > 400 IU/l was associated with a 9-fold increase in odds of hospital mortality. A finding similar to a study that performed a pooled analysis from studies [12, 13] with a total of 514 patients [14]

Table 2 Presenting symptoms and admission laboratory results of hospitalized patients with COVID-19 by survival status

| Characteristics	All, $N=200$	Non-survivors ($n=45$)	Survivors ($n=155$)	p value
Presenting symptoms, no. (%)				
Fever	121 (60.5)	20 (44.4)	101 (65.2)	0.01
Shortness of breath	129 (64.5)	28 (62.2)	101 (65.2)	0.71
Cough	130 (65.0)	24 (53.3)	106 (68.4)	0.06
Chest pain	19 (11.1)	0 (0.0)	19 (13.9)	0.02
Myalgia	90 (45.0)	14 (31.1)	76 (49.0)	0.03
Altered mental status	32 (19.5)	11 (24.4)	21 (13.5)	0.07
Headache	20 (11.6)	0 (0.0)	20 (12.9)	0.01
Diarrhea	23 (11.5)	6 (13.3)	17 (11.0)	0.66
Vomiting	26 (13.0)	6 (13.3)	20 (12.9)	0.94
Loss of appetite	48 (24.1)	13 (28.9)	35 (22.6)	0.38
Abdominal pain	21 (12.2)	4 (8.9)	17 (11.0)	0.69
Initial vital signs, no. (%)[a]				
Hypotension (SBP <90 mmHg)	9 (4.5)	2 (4.4)	7 (4.5)	0.98
Tachycardia (HR ≥100 beats per minute)	68 (34.0)	18 (40.0)	50 (32.2)	0.33
Tachypnea (RR >20 per minute)	38 (17)	13 (28.9)	25 (16.1)	0.06
Fever (T >38.0 °C)	55 (27.5)	7 (15.6)	48 (31)	0.05
Need for supplemental oxygen	67 (36.6)	20 (44.4)	47 (30.3)	0.08
AKI on presentation	65 (32.5)	27 (60.0)	38 (24.7)	<0.001
Admission laboratory results, mean (SD)				
White blood cell, $\times 10^9$ per L	7.8 (4.1)	8.8 (4.2)	7.5 (4.0)	0.06
Hemoglobin, g/dL	12.4 (2.4)	12.7 (2.0)	12.3 (2.6)	0.33
Platelets, μl/L, $\times 10^9$ per L	217 (90)	200 (74)	222 (94)	0.14
Absolute neutrophil count, $\times 10^9$ per L	5.9 (3.9)	6.8 (4.20)	5.6 (3.8)	0.06
Absolute lymphocyte count, $\times 10^9$ per L	1.15 (0.65)	1.1 (0.70)	1.16 (0.64)	0.55
Complete metabolic panel, mean (SD)				
Admission BUN, mg/dL[b]	28.0.9 (29.4)	41.9 (29.3)	23.7 (28.1)	<0.001
Admission creatinine, mg/dL[c]	1.60 (1.91)	2.16 (1.60)	1.42 (1.97)	0.03
Albumin, g/dl	3.5 (5.4)	3.3 (5.2)	3.5 (5.3)	0.007
Alkaline phosphatase, IU/L	86.2 (94.0)	122 (176)	75 (42)	0.003
AST, IU/L	74.0 (235.0)	108 (258.0)	64 (228.0)	0.27
ALT, IU/L	51.8 (187.0)	51 (79.0)	51 (209.0)	0.99
Total bilirubin, mg/dl	0.64 (0.67)	0.70 (0.72)	0.63 (0.66)	0.50
Marker of inflammation/tissue damage, mean (SD)				
Admission CPK, IU/L	1111.6 (6699.3)	3107 (13150)	439 (857)	0.024
Admission troponin, ng/ml	0.14 (0.77)	0.11 (0.22)	0.08 (0.260)	0.427
Admission procalcitonin, ng/ml	2.74 (11.3)	2.69 (4.8)	1.90 (9.14)	<0.001
Admission lactic acid, mm/l	1.50 (0.82)	1.79 (1.02)	1.41 (0.73)	0.006
Admission LDH, IU/L	397 (234.3)	561 (330.0)	352 (177.0)	<0.001
Admission CRP, mg/dl	12.8 (8.6)	17.1 (8.8)	11.6 (8.2)	<0.001
Admission D-dimer, μg/ml	2.68 (3.87)	3.68 (5.09)	2.40 (3.43)	0.063
Admission ferritin, ng/ml	1004 (1461)	1592 (2259)	839 (1097)	0.003
IL-6, pg/ml	189.9 (373.1)	372.8 (575.3)	127 (251)	0.007
Highest D-dimer, μg/ml	4.67 (5.72)	9.83 (7.54)	3.19 (4.0)	<0.001
Highest ferritin, ng/ml	1317 (1994)	2219 (3037)	1062 (1499)	<0.001
Highest troponin, ng/ml	0.38 (1.51)	0.82 (2.28)	0.24 (1.15)	0.030

AST, aspartate aminotransferase; *ALT*, alanine aminotransferase; *CRP*, c-reactive protein; *CPK*, creatine phosphokinase; *HR*, heart rate; *IL-6*, interleukin-6; *LDH*, lactate dehydrogenase; *RR*, respiratory rate; *SBP*, systolic blood pressure

[a] Hypotension was defined as systolic blood pressure <90 mmHg. Tachycardia was defined as heart rate >100/min and tachypnea was defined as respiratory rate >20/min

[b,c] Values excluding ESRD patients

and others that reported, LDH to be associated with worse outcomes in patients severe COVID-19 [15] and other viral pneumonia [16]. Studies from the USA that included AA patients [7, 17, 18] reported, LDH to be associated with disease severity but none of these studies showed its independent association with mortality. Except, a study with no race ethnicity information from the DC [19], where AA accounted for 74% of COVID-19-related mortality, showed an 8-fold increased odds of death occurred when the LDH level was greater than 1200 units/l, a finding similar to our study. LDH is present in lung tissue (isozyme 3) and patients with severe COVID-19 infections can have elevated LDH in the circulation. Additionally, LDH levels can be elevated in patients from cytokine mediated multiple organ injury [14, 20].
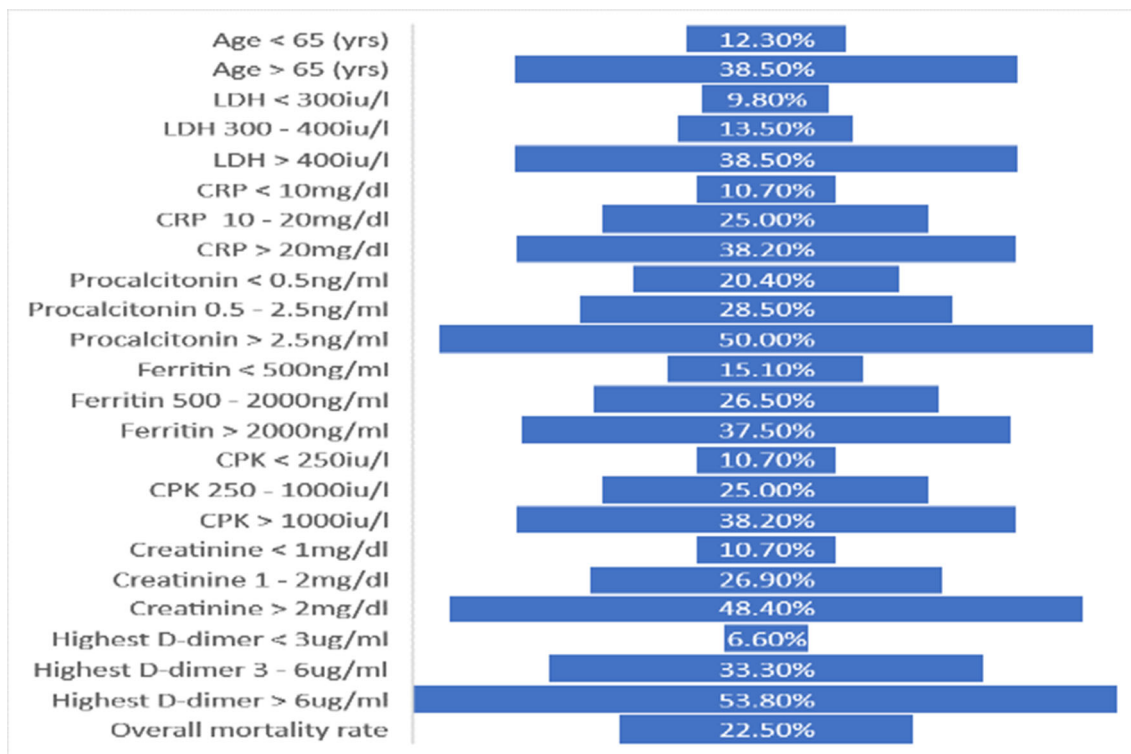
Abbreviation; LDH = lactate dehydrogenase; CRP = c-reactive protein; CPK = creatine phosphokinase

Fig. 1 Unadjusted mortality rates across different sub-groups

In addition, markers of acute cardiac injury using an elevated troponin and CPK and acute kidney injury (AKI) using admission sScr and BUN were independent predictors of mortality in this study. These findings are similar to previous studies that reported myocardial injury as indicated by elevated troponin with severe COVID-19 and the association with higher mortality [21–23]. Scr > 2 mg/dl had a 4-fold increased risk and BUN > 35 mg/dl close to 5-fold increase in odds of mortality in this study. Acute kidney injury was reported in critically ill COVID-19 in studies from the USA [7], China [24], and Italy [25], and was associated with a higher risk of mortality [26, 27]. SARS-CoV-2 might cause organ injury through direct and indirect pathogenic pathways such as immune activation, dehydration, hypoxemia, and acid-base imbalances [25]. In addition, most COVID-19 patients are older and have comorbidities such as HTN and DM, well-known factors for both cardiac and renal vulnerability [28].

In addition to the biomarkers of acute organ damage, a rising D-dimer was also associated with increased odds death in this study. Elevated D-dimer, an indirect marker of coagulation activation, has been reported to be associated with severity of illness and mortality among hospitalized patients with COVID-19 [29, 30]. In this study, we found those who died had 3-fold increased D-dimer levels than those who survived which is similar to an observation by Tang et al. [31] that reported, D-dimer values were nearly 3.5-fold higher in those who died than in those who survived. Similarly, a study

that included 138 patients [32], D-dimer values were nearly 2.5-fold higher in COVID-19 patients with severe disease than in those without. We found the rising D-dimer had the largest increase in odds of mortality. A peak D-dimer between 3 and 6 μg/ml was associated with 11-fold increased risk and D-Dimer> 6 μg/ml having 24-fold increased risk of mortality suggesting a dynamic measurement of D-dimer might reveal more information [33, 34]. Similar observation was reported by others, that D-dimer and rising D-dimer linked to mortality [31]. The observed elevation of D-dimer might be due to direct viral-related endothelial injury [35] and other known thrombosis risk factors [36–38]. Additionally, the D-dimer elevation can be seen in some patients due to sepsis-induced coagulopathy [39]. These findings all together suggest D-dimer elevation is associated with poor outcomes and the consideration of anticoagulation in hospitalized patients with COVID-19 [40, 41].

With respect to inflammatory biomarkers, significantly increased levels of CRP, IL-6, ferritin, and PCT were observed at admission in the non-survivors. A similar observation was reported by several studies [12, 17, 42, 43]. In multivariate analysis, CRP, PCT, and high ferritin were also independent predictors of mortality. A CRP level > 20 mg/dl had 6-fold higher odds of in-hospital mortality which was also reported by others [19]. A 4-fold higher risk of mortality occurred for patients who had elevated PCT in this study, which is similar to a study [44], that reported PCT associated with a nearly 5-

Table 3 Univariate and multivariate analysis of mortality predictors hospitalized patients with coronavirus disease 2019

Variable	N (%)	Univariable			Multivariable		
		OR	95% CI	P value	OR	95% CI	P value
Age ≥65 yrs. vs <65 yrs	78 (39)	4.45	2.19–9.04	<0.001	3.78	1.74–8.22	**0.001**
Female gender	79 (39.5)	0.81	0.40–1.60	0.54			
Race–Black	143 (71.5)	1.52	0.69–3.32	0.29			
Current or ex-smoker	50 (25)	1.71	0.83–3.54	0.14			
Body mass index, kg/m^2							
18.5–24.9	45 (22.5)	Ref.					
25–29.9	64 (32)	0.89	0.39–2.03	0.79			
≥30	74 (37)	0.61	0.27–1.38	0.24			
Hypertension	130 (65)	2.21	1.02–4.79	0.04	0.89	0.34–2.32	0.81
Diabetes mellitus	100 (50)	1.49	0.77–2.93	0.23			
Coronary artery disease	33 (16.5)	2.32	1.04–5.19	0.04	1.11	0.43–2.85	0.82
Heart failure	26 (13)	0.59	0.19–1.81	0.36			
Dyslipidemia	69 (34.5)	2.79	1.41–5.51	0.003	2.12	0.94–4.77	0.07
Lung diseases	37 (18.5)	1.13	0.49–2.61	0.79			
Chronic kidney disease	60 (30)	2.03	1.02–4.05	0.04	1.25	0.56–3.01	0.54
Chronic hemodialysis	27 (13.5)	0.56	0.18–1.71	0.31			
History of stroke	22 (11.0)	2.73	1.08–6.88	0.03	1.34	0.45–4.02	0.59
Vital signs on presentation							
Systolic BP, mmHg	200 (100)	0.99	0.98–1.01	0.70			
Diastolic BP, mmHg	200 (100)	0.98	0.97–1.01	0.37			
Heart rate, b/m	200 (100)	1.00	0.98–1.02	0.78			
Respiratory rate, b/m	200 (100)	1.06	0.98–1.15	0.10			
Oxygen saturation (%)	200 (100)	0.89	0.82–0.97	0.01	0.84	0.76–0.93	**0.001**
Admission laboratory variable							
Creatinine, mg/dl [a]*							
<1	75 (43.4)	Ref.			Ref.		
1–2	67 (38.7)	3.07	1.23–7.64	0.016	2.45	0.91–6.55	**0.074**
>2	31 (17.9)	7.85	2.84–21.7	<0.001	4.51	1.29–15.8	**0.018**
BUN, mg/dl [b]*							
<25	117 (67.6)	Ref.			Ref.		
25–35	21 (12.1)	4.2	1.48–11.8	0.007	3.71	1.12–12.2	**0.031**
>35	35 (20.3)	7.2	3.06–16.9	<0.0001	4.73	1.63–13.6	**0.004**
CPK, IU/L*							
<250	95 (55.9)	Ref.			Ref.		
250–1000	51 (30.0)	4.06	1.81–9.16	0.001	3.49	1.47–8.25	**0.004**
> 1000	24 (14.1)	4.51	1.66–12.2	0.003	3.57	1.23–10.3	**0.019**
Troponin, ng/ml*							
<0.05	122 (69.7)	Ref.			Ref.		
0.05–0.10	30 (17.1)	2.95	1.22–7.14	0.016	1.92	0.69–5.32	**0.20**
> 0.10	23 (13.2)	5.56	2.15–14.4	0.001	2.92	0.98–8.70	**0.06**
Procalcitonin, ng/ml*							
<0.5	93 (58.9)	Ref.			Ref.		
0.5–2.5	35 (22.2)	1.55	0.68–3.79	0.329	1.74	0.63–4.81	**0.28**
>2.5	30 (18.9)	3.89	1.62–9.34	0.002	4.21	1.47–12.0	**0.007**
Lactic acid, mm/l*							
<2.2	153 (82.7)	Ref.			Ref.		
> 2.2	32 (17.3)	2.69	1.20–6.04	0.016	1.97	0.80–4.82	0.13

Table 3 (continued)

Variable	N (%)	Univariable			Multivariable		
		OR	95% CI	P value	OR	95% CI	P value
LDH, IU/L*							
<300	61 (34.3)	Ref.			Ref.		
300–400	52 (29.2)	1.42	0.45–4.54	0.549	1.34	0.38–4.74	**0.64**
>400	65 (36.5)	5.72	2.15–15.3	<0.001	9.14	2.97–28.1	**<0.001**
CRP, mg/dl*							
<10	75 (42.4)	Ref.			Ref.		
10–20	68 (38.4)	2.79	1.11–6.79	0.028	2.57	0.96–6.89	**0.060**
>20	34 (19.2)	5.18	1.89–14.2	0.001	5.56	1.84–16.8	**0.002**
Initial D-dimer, µg/ml*							
<1	75 (40.8)	Ref.			Ref.		
1–3	68 (36.9)	3.06	1.27–7.29	0.012	1.88	0.72–4.90	0.195
> 3	41 (22.3)	3.03	1.15–7.99	0.025	2.12	0.73–6.13	0.164
Ferritin, ng/ml*							
<500	99 (52.9)	Ref.			Ref.		
500–2000	64 (34.2)	2.02	0.92–4.42	0.076	2.74	1.11–6.70	**0.027**
>2000	24 (12.8)	3.36	1.24–9.06	0.017	5.42	1.63–17.9	**0.006**
Highest D-dimer, µg/ml *							
<3	104 (57.5)	Ref.			Ref.		
3–6	33 (20.4)	10.7	3.48–32.9	<0.001	10.9	3.33–36.2	**<0.001**
> 6	44 (22.1)	21.9	7.34–65.2	<0.001	23.7	7.33–76.7	**<0.001**

BP, blood pressure; *BUN*, blood urea nitrogen; *CRP*, c-reactive protein; *CPK*, creatine phosphokinase; *CI*, confidence interval; *LDH*, lactate dehydrogenase; *OR*, odds ration

[a,b] Values excluding ESRD patients

*Data was not available for all patients

fold higher risk of severe disease. Elevated PCT level indicates superimposed bacterial infection, and might help in guiding antibiotic use in critically ill patients.

About 15–20% of the COVID-19 patients require hospitalization [32]. Some of those admitted progress rapidly into a severe ARDS and multi-organ failure and death [45]. Why some individuals become critically ill, while others do not is not fully understood. In addition to viremia-induced cell damage, another mechanism leading to disease severity, complications, and death might be an aberrant inflammatory response [46]. An observation that was reported in other severe viral pneumonias, such as highly pathogenic avian influenza [47], SARS, and pandemic and seasonal influenza [48]. Our findings appear to corroborate that the inflammatory indices are independently associated with patients becoming critically ill, requiring ventilatory support and dying. It remains unclear whether these inflammatory indicators are biologic markers of disease or mediators of the hypothesized "cytokine storm," in which excessive cytokine release results in hyperinflammation and multi-organ disease.

In the present study, the deceased group (67 ± 13.7 years) were close to one decade older than those who survived (58 ± 14.9 years) and had significantly higher comorbidities which is consistent with the observations of earlier studies [6, 7, 17, 49, 50]. Compared to those aged < 65 years, the odds of dying for patients aged ≥ 65 years was 3.78. This implies that the elderly population needs to be especially protected from contracting this virus, as they are about 4 times more likely to die independent of their comorbidities. As to why the elderly are dying? Previous studies in macaques inoculated with SARS-CoV found that older macaques had stronger host innate responses to virus infection than younger adults, with an increase in differential expression of genes associated with inflammation [51]. The age-dependent defects in T cell and B cell function and the excess production of type 2 cytokines could lead to a deficiency in control of viral replication and more prolonged proinflammatory responses, potentially leading to poor outcome in the elderly [52].

The majority of patients hospitalized with COVID-19 in this study were Black/AA followed by Latino. This findings are in line with the District COVID-19 data and
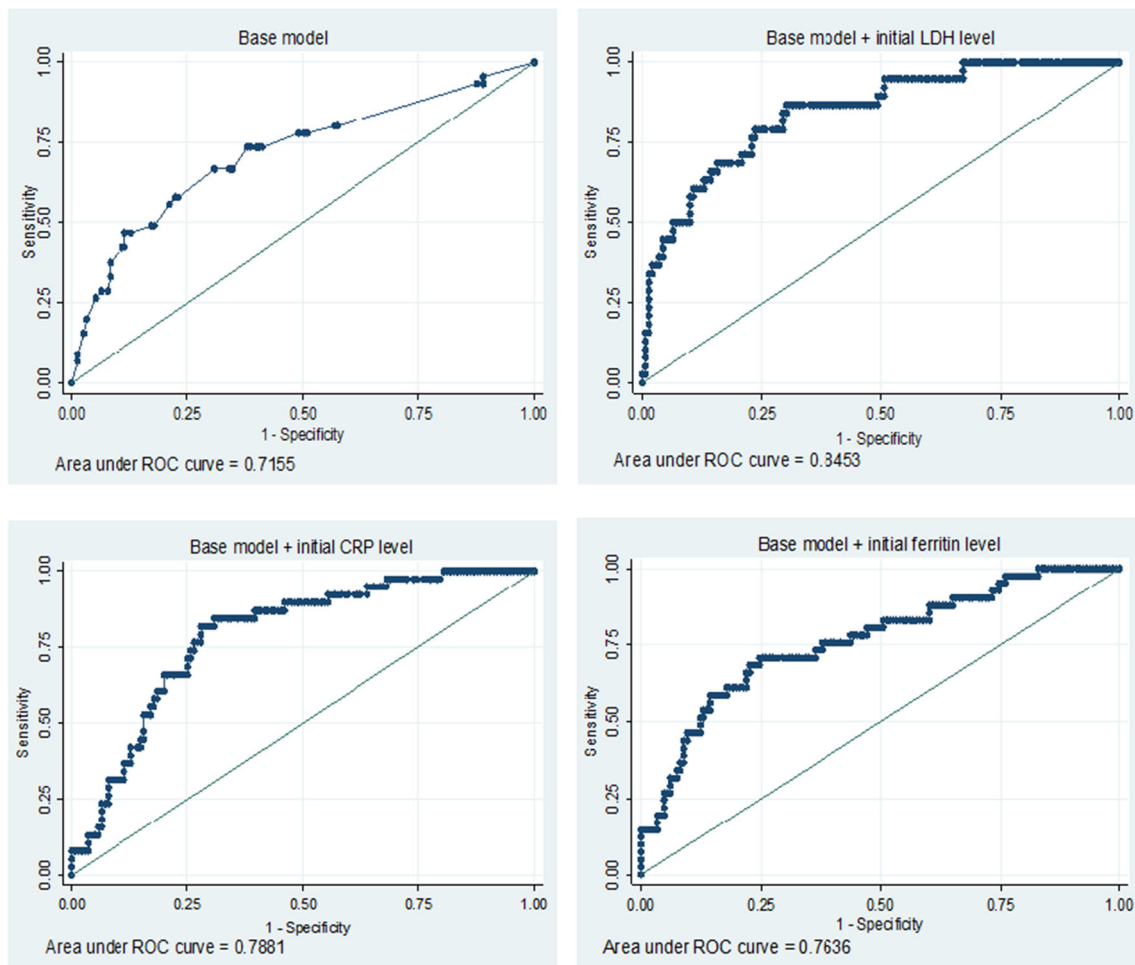
Fig. 2 Area under the curve (AUC) estimates among the different models. **A.** AUC of base model, made of variables including age, hypertension, coronary artery disease, dyslipidemia, chronic renal disease, and history of stroke; **B** AUC of the variables in the base model and initial LDH level; **C** AUC of the variables in the base model and initial CRP level; **D** AUC of the variables in the base model and initial ferritin level

other's that reported AA and other minority groups experiencing infection and death rates from COVID-19 that are disproportionately high for their share of the total population in the USA [2]. In Washington DC, as of September 23, 2020, AA race accounted for 51.2% of the cases and 74.4% of deaths despite AA composing only 46% of the districts population. Possible explanations are intersecting forces of racial disparities, underlying conditions, and poverty that affect how the virus spreads are some of contributing factors [2].

Our study aimed to identify an early mortality risk markers in those who are at high risk to be infected and to die if infected. In-hospital mortality occurred in 45 (22%) patients in this study. This rate is higher than that observed in Italy (7.2%) and is substantially higher than in China (2.3%) [53] but similar to that reported in the USA [7, 19, 54]. The observed differences between countries could be due to the age distribution of the population, distribution of cases in different

continents, the capacity of the health care system, and how COVID-19-related death is defined. Not surprisingly, patients admitted to the ICU had higher need of invasive mechanical ventilation, acute kidney injury requiring dialysis (HD), shock, and mortality in this study. Similar findings from a study in minority patients reported 58% who required HD, 69% who needed vasoactive pressor, and 73% who needed mechanical ventilation had inpatient mortality [54]. In one of the early studies by Yang et al., among patients admitted to ICU, 28-day mortality was 61.5% [24]. Also a retrospective study from China reported 97% of patients who were intubated and 100% of those who received renal replacement therapy died during hospitalization [12]. A study from New York City reported 88% who received mechanical ventilation and 96% who received kidney replacement therapy died [7]. The association of mortality in those admitted to ICU reflected the degree of organ damage involved and hence risk of mortality.

Strengths and Limitations

These strengths of the study are a comprehensive data from a decent number with outcomes ascertained in all patients. However, our study is retrospective from a single center, majority are African American patients; hence, might have selection bias. Further studies should build on our findings and seek to better understand the reasons for the observed high mortality. This will give prudence to the development of prevention, early diagnosis, and optimal timing of targeted approaches in therapies in minority populations who are among the highest risk of death from COVID-19 infection.

Conclusion

We identified independent of demographics and baseline comorbidities, age ≥ 65 years, biomarkers of inflammation (CRP, ferritin, IL6, PCT), marker of coagulation(D-dimer), and acute organ damage (BUN, creatinine, CK, LDH, and troponin) as independent predictors of mortality in minority patients hospitalized with COVID-19. These biomarkers can help clinicians identify patients early who are at a high risk for clinical deterioration.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40615-020-00961-x.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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