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African Americans Possessed High Prevalence of Comorbidities and Frequent Abdominal Symptoms, and Comprised A Disproportionate Share of Covid-19 Mortality among 9,873 Us-Hospitalized Patients Early in the Pandemic

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Abstract

Background and aim: Identifying clinical characteristics and outcomes of different ethnicities in the US may inform treatment for hospitalized COVID-19 patients. Aim of this study is to identify predictors of mortality among US races/ethnicities.

Design, Setting and participants: We retrospectively analyzed de-identified data from 9,873 COVID-19 patients who were hospitalized at 15 US hospital centers in 11 states (March 2020-November 2020). Main Outcomes and Measures: The primary outcome was to identify predictors of mortality in hospitalized COVID-19 patients.

Results: Among the 9,873 patients, there were 64.1% African Americans (AA), 19.8% Caucasians, 10.4% Hispanics, and 5.7% Asians, with 50.7% female. Males showed higher in-hospital mortality (20.9% vs. 15.3%, p=0.001). Non-survivors were significantly older (67 vs. 61 years) than survivors. Patients in New York had the highest in-hospital mortality (OR=3.54 (3.03 - 4.14)). AA patients possessed higher prevalence of comorbidities, had longer hospital stay, higher ICU admission rates, increased requirement for mechanical ventilation and higher in-hospital mortality compared to other races/ethnicities. Gastrointestinal symptoms (GI), particularly diarrhea, were more common among minority patients. Among GI symptoms and laboratory findings, abdominal pain (5.3%, p=0.03), elevated AST (n=2653, 50.2%, p=<0.001, OR=2.18), bilirubin (n=577, 12.9%, p=0.01) and low albumin levels (n=361, 19.1%, p=0.03) were associated with mortality. Multivariate analysis (adjusted for age, sex, race, geographic location) indicates that patients with asthma, COPD, cardiac disease, hypertension, diabetes mellitus, immunocompromised status, shortness of breath and cough possess higher odds of in-hospital mortality. Among laboratory parameters, patients with lymphocytopenia (OR2=2.50), lymphocytosis (OR2=1.41), and elevations of serum CRP (OR2=4.19), CPK (OR2=1.43), LDH (OR2=2.10), troponin (OR2=2.91), ferritin (OR2=1.88), AST (OR2=2.18), D-dimer (OR2=2.75) are more prone to death. Patients on glucocorticoids (OR2=1.49) and mechanical ventilation (OR2=9.78) have higher in-hospital mortality.

Conclusion: These findings suggest that older age, male sex, AA race, and hospitalization in New York were associated with higher in-hospital mortality rates from COVID-19 in early pandemic stages. Other predictors of mortality included the presence of comorbidities, shortness of breath, cough elevated serum inflammatory markers, altered lymphocyte count, elevated AST, and low serum albumin. AA patients comprised a disproportionate share of COVID-19 death in the US during 2020 relative to other races/ethnicities.

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Abbreviation list: C-Reactive Protein (CRP); Lactose dehydrogenase (LDH); Creatine Phosphokinase (CPK); Intensive Care Unit (ICU); Aspartate Transaminase (AST); Odds Ratio (OD).

Introduction

Coronavirus disease-2019 (COVID-19) was first recognized in December 2019 in China [1]. As of April 28th 2022, SARS CoV-2, the virus has infected more than 509 million people, including 6.2 million deaths [2]. More than 70 million cases have been confirmed in the US, with over 900,000 reported deaths [3]. Patients who acquire COVID-19 can experience a range of clinical manifestations, from no symptoms to severe critical illness to death. Available data suggest that older age groups, those with preexisting comorbid conditions and male sex are common predisposing risk factors for COVID-19 infection [4-7,8]. By March 2021, for each 100,000 Americans based on race/ethnicity, 180 African Americans (AA), 150 Caucasians, and 147 Hispanics had died from COVID-19. Nationwide, AA have died at 1.4 times the rate of White Americans [9,10]. To date where race is known, 15% of COVID-19 deaths in the US were African Americans [11]. People from racial/ethnic minority groups in Western countries experience undue socioeconomic and structural determinants of health burdens. These conditions resulted in inequalities and inequities in healthcare access and unsatisfactory health outcomes [8]. The present study aimed to examine hospitalized SARS-CoV-2-positive patients' racial/ethnic background, clinical manifestations including gastrointestinal symptoms, clinical inflammatory biomarkers, comorbidities, and disease severity to ascertain predictors of mortality from COVID-19 across 15 hospital centers in 11 states in US.

Patients and Methods

Patient selection: In this retrospective cross-sectional study we collected de-identified information and reviewed demographics, clinical manifestations, laboratory tests and outcomes of COVID-19 patients hospitalized in 15 US hospital representing 11 states between March 2020 and November 2020. We received approval from the Howard University Institutional Review Board (IRB) and individual participating hospitals. As this study includes the de-identified patient data, we were granted an exemption of informed consent from the IRB. An excel file template was shared with our collaborators to standardize the process of data collection and database construction. The total number of patients included in this study was 9,873; however, the total number for each variable in the overall analysis varies due to some missing values. Inclusion and exclusion criteria: The following inclusion criteria were used: confirmed SARS-CoV-2 RT-PCR and hospitalization for COVID-19, without distinction on sex, age, treatment regimen, clinical manifestations, comorbidities, or outcomes. Individuals involved in studies that did not include AA or Hispanic patients, studies from outside of the US, cases that were not confirmed by RT-PCR, cases with incomplete symptoms and comorbidities, and cases with overlapping data were excluded.

Statistical analysis: Patient demographics, symptoms, underlying comorbidities, treatment, and outcomes were compared among AA, Caucasian, Hispanic, and other ethnic groups. Predictors of hospital mortality were evaluated by using logistic and/or multiple logistic regression employing four models to assess the effect of each risk factor: OR1: no adjustment; OR2: adjusted for gender, age, ethnicity, and center; OR3: the OR2 model further adjusted for comorbidities; and OR4: the OR3 model further adjusted for disease severity. In each analysis, odds ratios (ORs) and associated 95% confidence intervals were calculated. The 95% confidence interval was investigated to see if it contained unity. Confidence intervals that included one were considered not statistically significant.

Results

COVID-19 hospitalized patient characteristics: There are 9,873 patients from 15 US hospitals across 11 states in the United States (Table 1). The mean age was 60.2 years. Males (n=4511, 49.3%) and females (n=4640, 50.7) distribution was balanced. Of the total cohort there were, 5591 (64.1%) AA, 1729 (19.8%) Caucasian, 903 (10.4%) Hispanic, and 498 (5.7%) Asian. The average hospital stay was 8.9 days, with length of stay significantly higher in non-survivors than in survivors (15.3 vs 6.07 days, p=0.03). A majority of patients were obese (n=3262, 46.5%). Hypertension (n=5101, 60.2%), diabetes mellitus (n=3046, 35.3%), and chronic kidney disease (n=1156, 18.1%) were the most common comorbidities (Table 2). The overall mortality was 18.10% (n=1654).

Our study includes patients from the North and Midwest, East and South geographical regions of the US (Table 1). Patients above 65 years were more likely to die from COVID-19 compared to <65 years. A large proportion of patients were from Michigan (n=3,674, 37.2%) and New York (n=2,505, 25.4%) (Table 1). Michigan had the highest number of African Americans, Caucasians, and Asians in this cohort. In comparison, New York had the highest number

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of Hispanic patients. The mean length of hospital stay was higher among COVID-19 non-survivors in Michigan (15.6 days) (Table 1). More patients in Louisiana and Texas were obese (Table 1). There were higher rates of ICU admission in Maryland (n= 60, 42%) and New York (n=663, 41.3%). COVID-19 patients requiring mechanical ventilation were more prevalent in Maryland (n=49, 33.7%). Mortality was significantly higher in New York (n=774, 31%, p= 0.001) (Table 1, eFigure 1).

Race/ethnicity specific patient demographics, clinical characteristics, and outcomes: There were significant differences in age and sex distribution across racial/ethnic groups (Table 3). The mean age, in years, was 60.7 for AA, 62.1 for Caucasians, 53.9 for Hispanics, and 56.8 for Asians. Most obese patients were AA. Hypertension (AA: 67.7%, Caucasian:50.1%, Hispanic: 46.9% and Asian: 45.7%) and diabetes mellitus (AA: 29.3%, Caucasian: 26.5%, Hispanic: 35.7%, and Asian: 31%) are the most common comorbidities (Table 3). Shortness of breath (45.4%) followed by cough (42.8%) and fever (42.5%) were the most common presenting symptoms for all participants in the cohort. CRP, LDH, ferritin and D-dimer were the most elevated inflammatory markers for all races/ethnicities (Table 4). African Americans had higher ICU admission rates (AA: 39.8%, Caucasian: 22.9%, Hispanic: 15.1% and Asian: 26.2%). Similarly, AAs had highest rates of mechanical ventilation (17.1%). The mortality rate was significantly higher in the AA (19.1%) compared to Caucasians (17.6%), Hispanics (16.2%), and Asians (14.1%) (Table 4).

Gastrointestinal manifestations were most common among hospitalized Hispanics and minorities: Diarrhea (12.8%) was the most common gastrointestinal (GI) symptom (Table 2). GI symptoms were most seen among Hispanics (44.5%, n=182) followed by AAs (14.5%, n=688), when compared to Caucasians (6%, n=120), and Asians (5%, n=21) (Table 4). Symptoms of abdominal pain (5.3%, p=0.03), anosmia (n=130, 2.3%, p=0.001)), and ageusia (n=100, 3.8%, p=0.001), as well as the presence of chronic liver disease (n=622, 16.3%, p=0.001), splenomegaly (n=142, 31.6%, p=0.01), elevated AST (n= 2653, 50.2%,

Table 1: Demographics and Disease severity of COVID-19 across the 11 states in the United States.

	DC	GA	IN	KY	LA	MD	MI	NJ	NY	RI	TX
Mean Age (Years) Survivors Non-Survivors	54.2 68.6	60.3 69.5	57.2 75.3	56.1 65.6	58.8 68.7	54.1 68.9	56.4 75.4	57.8 73.1	61.2 69.1	38.6 -	52.3 69.7
Mean LOS (Days) Survivors Non-Survivors	8.8 12.39	6.5 10.2	7.2 9.1	7.6 10.1	10 11.2	-	5.2 15.6	4.3 6.7	9.5 8.7	5.4 -	5.1 8.7
	DC n (%)	**GA** n (%)	**IN** n (%)	**KY** n (%)	**LA** n (%)	**MD** n (%)	**MI** n (%)	**NJ** n (%)	**NY** n (%)	**RI** n (%)	**TX** n (%)
Male Sex	236 (51)	400 (56.2)	72 (51.4)	384 (54.9)	406 (52.3)	82 (56.2)	1972 (53.7)	317 (56.2)	1355 (54.1)	77 (73.3)	50 (56.8)
Race AA Caucasian Latin American Asian	309(5.3) 27(1.3) 111(12.3) 9(1.5)	594(10.2) 108(4.8) - 16(2.7)	90(1.5) 37(1.8) 7(0.8) 5(0.8)	220(3.8) 383(18.1) - 97(16.3)	581(10) 99(4.7) - 96(16.1)	97(1.7) 27(1.3) 13(1.4) 8(1.3)	2040(35.1) 1172(55.5) 14(1.5) 237(39.8)	191(3.3) 74(3.5) 139(15.4) 72(12.1)	1694(29.1) 191 (9) 434 (48.1) 56 (9.4)	105(11.6)	82(9.1)
BMI	158 (37.7)	-	75 (27.3)	181 (26)	409 (52.5)	59 (41.5)	1772 (51.8)	179 (31.7)	976 (43.3)	-	47 (52.4)
ICU	104 (23.2)	189 (26.5)	-	85 (34)	271 (34.9)	60 (42)	492 (13.4)	94 (16.7)	663 (41.3)	-	22 (25)
Mechanical Ventilation	62 (13.6)	138 (19.4)	-	-	187 (24.1)	49 (33.7)	398 (10.8)	80 (14.2)	271 (28.5)	-	12 (13.6)
Death	71 (15.4)	116 (16.3)	22 (15.7)	105 (17)	140 (18.1)	11 (7.5)	407 (11.1)	98 (17.4)	774 (31)	0	15 (17)

DC: District of Columbia, GA: Georgia, IN: Indiana, KY: Kentucky, LA: Louisiana, MD: Maryland, MI: Michigan, NJ: New Jersey, NY: New York, RI: Rhode Island, TX: Texas. LOS: Length of Hospital Stay, AA: African Americans, BMI: Body Mass Index, ICU: Intensive care unit.

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Table 2: Baseline demographics and clinical characteristics of Covid-19 hospitalized patients.

	All patients	Survivor	Non-survivor	p-Values
	n/N (%)	n/N (%)	n/N (%)	
Characteristics (N: Total no of patients)				
Age (N=9873)	60.2 ± 17.6	61 ± 14	67 ± 12	<0.001
Length of stay in hospital (days)	8.9 ± 6.9	6.07 ± 8.5	15.3 ± 7.5	0.02
Sex (N=9151)				
Male	4511(49.3)	3569 (79.1)	942 (20.9)	<0.001
Female	4640 (50.7)	3931 (84.7)	709 (15.3)	
Race (N=8721)				
African American	5591(64.1)	4524(80.9)	1069(19.1)	< 0.009
Caucasian	1729(19.8)	1425(82.4)	304(17.6)	
Hispanic	903(10.4)	757(83.8)	146(16.2)	
Asian	498(5.7)	428(85.9)	70(14.1)	
BMI (N=7016)				
Normal	1746(24.9)	1356(77.7)	210 (22.3)	<0.001
Overweight	2008(28.6)	1607(801)	390(20)	
Obese	3262(46.5)	2748(84.2)	67.5(15.8)	
Comorbidities				
COPD	715/ 7449(9.6)	507(70.9)	208(29.1)	<0.001
Chronic Kidney Disease	1156/6370(18.1)	852(73.7)	304(26.3)	<0.001
Hypertension	5101/8472(60.2)	4041(79.2)	1060(20.8)	<0.001
Diabetes Mellitus	3046/8616(35.3)	2345(77)	701(23)	<0.001
Malignancy	596/6498(9.2)	438(73.5)	158(26.5)	<0.001
Cardiac Disease	1218/7732(15.7)	880(72.2)	338(27.8)	<0.001
Chronic Liver Disease	622/3812(16.3)	429(69)	193(31)	<0.001
Asthma	1250/7742(16.1)	921(73.7)	329(26.3)	<0.001
Immunocompromised	288/4481(6.4)	200(69.4)	88(30.6)	0.01
Smoking	1291/7725(16.7)	1014(78.5)	277(21.5)	<0.001
Symptoms				
Fever	3487/8441 (41.3)	2862(82.1)	625(17.9)	<0.001
Shortness of Breath	3127/7115 (43.9)	2524 (80.7)	603 (19.3)	<0.001
Headache	639/ 6903(9.21)	480 (75.1)	159(24.9)	<0.001
Cough	3648/8853 (41.2)	2911(79.8)	737(20.2)	<0.001
Chest Pain	552/6555(8.4)	485(87.9)	67(12.8)	0.103
Fatigue	976/6433(15.2)	814(83.4)	162(16.6)	0.03
Altered Mental Status	201/1105(18.2)	139(69.1)	62(30.9)	<0.001
Myalgia	765/6332(12.1)	640(83.7)	125(16.3)	<0.045
Loss of Smell	130/5548(2.3)	127(97.7)	3(2.3)	<0.001
Loss of Taste	100/2599(3.8)	97(9.7)	3(3)	<0.001
Abdominal Pain	375/7030(5.3)	331(82.3)	44(17.7)	0.034
Diarrhea	910/7112(12.8)	744(81.7)	166(18.3)	0.314
Nausea	746/7334(10.2)	649(87)	89(13)	0.062

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Vomiting	555/6921(8)	461(83.1)	94(16.9)	0.911
Laboratory Parameters				
Sodium (Low)	1251/3210(39)	1051(84)	200(16)	<0.001
Potassium (Low)	594/3024(18.5)	517(87.1)	77(12.9)	<0.001
Chloride (Low)	886/3209(27.6)	730(82.4)	92(17.6)	<0.001
WBC				
Low	716/2756(26)	568(79.3)	101(20.7)	0.001
High	321/2756(11.6)	220(68.5)	148(31.5)	0.001
Lymphocyte count				
Low	3029/6063(50)	2454(81)	575(19)	0.001
High	650/6063(10.7)	460(70.8)	190(29.2)	0.001
Hemoglobin (Low)	1968/3516(56)	1635(83.1)	333(16.9)	0.59
BUN (elevated)	1566/3446(45.4)	1138(72.7)	428(27.3)	<0.001
Creatinine (elevated)	2616/6576(40.6)	1605(61.3)	765(38.7)	<0.001
Blood Glucose				
Low	10/3127(0.3)	5(50)	5(50)	0.001
High	1086/3127(34.7)	810(74.6)	276(25.4)	<0.001
ProBNP (elevated)	363/804(45.1)	257(70.8)	106(29.2)	0.01
CPK (elevated)	1091/2305(47.3)	870(79.7)	221(20.3)	0.003
Troponin (elevated)	1558/5513(28.3%)	1027(65.9)	531(34.1)	0.001
Ferritin (elevated)	3126/4717(67)	2497(79.9)	665(20.1)	<0.001
ALT (elevated)	595/4204(14.2)	464(78)	131(28)	0.051
AST (elevated)	2653/5227(50.8)	1995(75.2)	658(24.8)	<0.001
ALP (elevated)	111/987(11.2)	87(78.4)	24(21.6)	0.18
Albumin (low)	361/2040(17.7)	216(59.8)	145(40.2)	0.03
Total Bilirubin (elevated)	439/3807(11.5)	321(73.1)	118(26.9)	<0.001
Procalcitonin (elevated)	1535/3558(43.1)	1027(66.9)	508(33.1)	<0.001
LDH (elevated)	2176/2741(79.4)	1595(73.3)	581(26.7)	<0.001
CRP (elevated)	4625/5095(90.8)	3626(78.4)	999(21.6)	<0.001
D-dimer (elevated)	3584/4426(81)	2828(78.9)	756(21.1)	<0.001
Diagnostic Imaging				
Chest X-ray (Abnormal)	2356/2752(85.6)	1787(75.8)	569(24.1)	<0.001
Splenomegaly on CT-Chest	142/450(31.6)	96(67.6)	46(32.4)	<0.01

p=<0.001, OR=2.18), bilirubin (n=577, 12.9%, p=0.01) and low albumin (n=361, 19.1%, p=0.03) were significantly associated with death (Table 2-5).

Predictors of mortality on multivariable modeling for the study cohort: Age was a significant predictor of mortality from COVID-19 (Table 5). Compared to individuals < 35 years of age, those who were >= 75 years were at substantially higher risk of death with an OR1 (95% CI) of 9.24 (6.24-15.0). This association remained strong after adjustment for comorbidities, with OR3 (95% CI) of 8.43 (4.98-10.84). Other demographic predictors of mortality were male sex (p= 0.001, OR=1.46, 1.31-1.62) and AA race (p=0.009). New York state had significantly higher mortality even after adjusting for demographics (p=<0.001, OR2: 3.51) (Fig 1). Michigan, Indiana, Rhode Island, and Maryland had significantly lower death rates (Table 5 and Supplemental Figure 1).

Several comorbidities were associated with increased risk of death, including presence of asthma (p=0.001, OR2=1.42), COPD (p=<0.001, OR2=1.45), diabetes mellitus (p=0.001,

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Table 3: Demographics and comorbidities of covid-19 patients based on individual races

	African American	Caucasian	Latin American	Asian
Mean Age (N=9429)	60.7 (5816)	62.1 (2112)	53.9 (905)	56.80 (596)
Length of hospital stay (mean, days)	7.86	6.46	7.8	6.05
	n (%)	**n (%)**	**n (%)**	**n (%)**
Sex (n=9421)				
Female (n=4318)	3061 (52.7)	1083 (51.3)	403 (44.6)	271 (45.5)
Male (n=4603)	2749 (47.3)	1029 (48.7)	500 (55.5)	325 (54.5)
BMI				
Normal (N=2017)	1022 (23.6)	644 (35.6)	190 (24.8)	161 (36.2)
Overweight (N=2059)	1151 (26.6)	491(27.1)	264(34.4)	153(34.??)
Obese (N=3270)	2152(49.8)	674(37.3)	313(40.8)	131(29.4)
Co-Morbidities				
COPD (N=7725)				
Yes (793)	447(10)	273(13.7)	54(6.8)	20(4.1)
No (6932)	4011(90)	1713(86.3)	739(93.2)	469(95.8)
CKD (N=6060)				
Yes (1113)	764(21.4)	227(15)	88(13.9)	34(11.2)
No (4932)	2840(78.6)	1279(84.5)	544(86.1)	269(88.8)
Cardiac Disease (N=8026)				
Yes (1323)	821(17.2)	339(17)	121(15.8)	42(8.8)
No (6703)	3963(82.8)	1658(83)	644(84.2)	438(91.3)
Hypertension (N=8768)				
Yes (5266)	3567(67.7)	1037(50.1)	402(46.9)	260(45.7)
No (3502)	1705(32.3)	1032(49.9)	456(53.1)	309(54.3)
Diabetes Mellitus N=8911)				
Yes (3155)	2110(29.3)	555(26.5)	311(35.7)	179(31)
No (5756)	3257(60.7)	1541(73.5)	560(64.3)	398(69)
Asthma (N=8027)				
Yes (1273)	932(19.2)	175(8.7)	113(19.3)	53(9.3)
No (6754)	3919(80.8)	1844(91.3)	473(80.7)	518(90.7)
Malignancy (N=6800)				
Yes (611)	343(9)	202(10.4)	49(8.2)	17(3.8)
No (6189)	3467(91)	1741 (89.6)	546(91.8)	435 (96.2)
Chronic Liver Disease (N=4318)				
Yes (598)	322(12.8)	80(10.1)	180(22.9)	16(7.2)
No (3720)	2191(87.2)	716(89.9)	606(77.1)	207(92.8)
Immunocompromised (N=5056)				
Yes (310)	210(6.2)	49(5.9)	43(7.3)	8(3)
No (4746)	3153(93.8)	785(94.1)	548(92.7)	260(97)

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OR2=1.58), hypertension (p=0.001, OR2=1.20), cardiac disease (p=0.01, OR2=1.32), malignancy (p=<0.001, OR2=1.50) and immunosuppression (p=0.01, OR2=1.46). Patients with BMI >30 was more than twice as likely to die from COVID-19 than normal BMI patients (OR1: 2.65), this association was no longer significant after adjusting for age, sex, and race.

Fever, (OR1=1.26), shortness of breath (OR1=2.03), headache (OR1=1.75), cough (OR1=1.96), chest pain (OR1=1.42), and fatigue (OR1=1.22) were significant predictors of mortality in univariate analysis (OR1). However, after adjusting for age, sex, and race, only shortness of breath (OR2=1.73) and cough (OR2=1.21) were significantly associated to death. After adjusting for demographics (OR2) and comorbidities (OR3), only shortness of breath was a significant predictor of death, with OR3 (95% CI) of 1.91 (1.61-2.28). Several laboratory markers were associated with increased risk of death, including lymphocytopenia (OR2=1.55, 1.30-1.86), lymphocytosis (OR2=1.21, 1.07-1.54), elevated CRP (OR=5.15, 3.38-7.84), CPK (OR2=1.54,1.20-1.98), troponin (OR2=3.00, 2.54-3.53), ferritin (OR2=2.18, 1.41-3.40), LDH (OR2=2.69, 1.94-3.53), D-dimer (OR2=2.26, 1.68-3.03), and elevated AST (OR2=2.63, 2.13-3.24) in univariate analysis (OR1) and after adjusting for the demographics (OR2) (Table 5). However, after adjusting for demographics and comorbidities, only CRP (OR3=4.59) and D-dimer (OR3=2.76) remained significant.

Treatment for hospitalized COVID-19 patients: Hydroxychloroquine (69.3%) followed by supplemental oxygen (50.5%), and glucocorticoids (44.1%) were the most used treatments (Supplemental Figure 2). Patients taking hydroxychloroquine (n=4079, 69.3%, p=0.001), Tocilizumab (n=21, 0.9%, p=<0.001), and steroids (n=2021, 44.1%, p=0.001) displayed significant high in-hospital mortality. Glucocorticoid use was associated with an OR2 of 1.66 (1.40-1.97) for mortality after adjusting for age/gender/race/center. In patients receiving mechanical ventilation, the OR2 for death was 9.78 (8.19-11.68) (Table 5).

Table 4: Clinical manifestations, laboratory parameters, and disease severity of COVID-19 patients among different race/ethnicities.

	African American (n %)	Caucasian (n %)	Latin American (n %)	Asian (n %)
Clinical Manifestations				
Fever (N=8737)				
Yes (3721)	2211(42.1)	648 (31.5)	601(69)	261(47.1)
No (5016)	3041 (57.9)	1412 (68.5)	270 (31)	293 (52.9)
Shortness of Breath (N=7501)				
Yes (3422)	2129 (46.7)	783 (40)	262 (56.5)	248 (47.7)
No (4079)	2431 (53.3)	1174 (60)	202 (43.5)	272 (52.3)
Cough (N = 9126)				
Yes (3921)	2422(43)	673(32.2)	580(68.8)	246 (42.9)
No (5205)	3217(57)	1417(67.8)	243(29.5)	328 (57.1)
Headache (N=7268)				
Yes (704)	497(11)	76 (4)	104(27.7)	27(5.4)
No (6564)	4007 (89)	1816 (96)	271 (72.3)	470 (94.6)
Chest Pain (N=6870)				
Yes (600)	311(8)	132(6.7)	130(22.5)	27(5.9)
No (6270)	3562 (92)	1827 (93.3)	447 (77.5)	434 (94.1)
Rhinorrhea (N=5594)				
Yes (394)	281(8.7)	38(2.2)	68(28.7)	7(1.7)
No (5200)	2956 (91.3)	1676 (97.8)	169 (71.3)	399 (98.3)
Fatigue (N=6821)				
Yes (1165)	707 (17.1)	282 (15)	90(28.1)	86(18.1)
No (5656)	3438(82.9)	1598(85)	230(71.9)	390(81.9)

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Altered Mental Status (N=1804)				
Yes (280)	183(16.7)	77(13.8)	-	20(13.6)
No (1524)	910(83.3)	480(86.2)	-	127(86.4)
Myalgia (N=6807)				
Yes (921)	580(13.8)	147(7.9)	129(44)	65(14.9)
No (5886)	3631(86.2)	1720(92.1)	164(56)	371(85.1)
Loss of Smell/ Anosmia (N=6807)				
Yes (141)	42(1.3)	17(0.9)	76(21.1)	6(1.4)
No (5800)	3289(98.7)	1789(99.1)	284(78.9)	438(98.6)
Loss of taste/ Ageusia (N=3197)				
Yes (113)	69(3.5)	17(2.6)	16(4.9)	11(5.1)
No (3084)	1929(96.5)	638(97.4)	312(95.1)	205(94.9)
Any GI symptoms (N=7421)				
Yes (1632)	688 (14.5)	120 (6)	182 (52.6)	21 (5)
No (5789)	4380 (85.5)	1540 (94)	227 (47.4)	344 (95)
Abdominal Pain (N=6643)				
Yes (342)	220 (5.3)	33 (2.2)	61(10)	28(7.2)
No (6301)	3931(94.7)	1458(97.8)	552(90)	360(92.8)
Nausea (N=7652)				
Yes (856)	545(11.7)	154(7.8)	102(19)	55(11.2)
No (6796)	4106(88.3)	1818(92.2)	436(81)	436(88.8)
Vomiting (N=7321)				
Yes (628)	428(9.2)	92(5)	68(16.3)	40(9.4)
No (6693)	4200(90.8)	1756(95)	350(83.7)	387(90.6)
Diarrhea (N=7421)				
Yes (998)	570 (13.2)	173 (9.2)	190(25.7)	65(13.5)
No (6423)	3741(86.8)	1715(90.8)	549(74.3)	418(86.5)
GI Bleeding (N=4966)				
Yes (16)	12 (0.4)	4 (0.3)	-	-
No (4950)	3216(99.6)	1326(99.7)	103(100)	305(100)
Laboratory Parameters				
WBC (N=2556)				
Elevated (288)	154(10.6)	37(10.6)	63(10.6)	34(21.5)
Low (646)	315(21.7)	90(25.7)	175(29.5)	66(41.8)
Lymphocyte Count (N=5802)				
Elevated (602)	328(8.8)	78(6.3)	173(30.6)	23(8.3)
Low (2922)	1854(49.8)	753(61)	176(31.2)	139(50.4)
Platelets (N=1204)				
Elevated (41)	23(3.4)	2(1)	15(6.4)	1(1.1)
Low (355)	251(37.3)	44(21.9)	41(17.4)	19(20.2)
CRP (N=4864)				
Elevated (4411)	2754(89.7)	952(93.9)	422(89.2)	283(91.9)
Troponin (N= 5199)				
Elevated (1477)	953 (30.2)	351 (31)	87 (14.7)	86 (26.5)
Pro BNP (N=780)				
Elevated (344)	226 (41.1)	50(46.3)	41(67.2)	27(45)
Procalcitonin (N=3410)				

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Elevated (1485)	983 (46.6)	278(35.6)	126(39.1)	98(49.2)
CPK (N=2174)				
Elevated (1034)	701 (56.8)	252 (35.1)	24 (32)	52 (35.4)
Glucose (N=2970)				
Elevated (1041)	676 (35.7)	268 (31.1)	16 (64)	81 (43.1)
Low (9)	9(0.5)	-	-	-
LDH (N=2615)				
Elevated (1866)	1219 (72.1)	224 (67.5)	297 (68.9)	126 (78.3)
D-Dimer (N=4209)				
Elevated (3401)	2068(81)	771(81.5)	341(81.8)	221(75.2)
Ferritin (N=4516)				
Elevated (3022)	1994(68.6)	601(60.4)	218(70.6)	209(68.1)
BUN (N=3288)				
Elevated (1590)	991(47.3)	461(52.2)	68(65.5)	79(38.9)
Creatinine (N=6232)				
Elevated (1979)	1329(34)	404(31.2)	164(23.7)	82(24.6)
Albumin (N=1942)				
Elevated (368)	227(23)	32(6.8)	66(22.9)	43(21.8)
Low (361)	160(16.2)	131(28)	47(16.3)	23(11.7)
AST (N=5680)				
Elevated (2814)	1737(50.9)	688(47.5)	174(44.7)	215(49.9)
ALT (N=4652)				
Elevated (737)	343(13.1)	197(14.6)	108(37.1)	90(21.8)
ALP (N=896)				
Elevated (100)	41(8.5)	7(7)	46(20)	6(7.4)
Total Bilirubin (N=4250)				
Elevated (552)	273 (11.9)	214 (17.6)	25(6.4)	40 (11.8)
Hemoglobin (N=3352)				
High (53)	32(1.5)	8(0.8)	12(11.3)	1(0.5)
Low (1875)	1182(56.7)	544(56.1)	43(40.6)	106(55.2)
Disease Severity				
ICU Admission (N=3544)				
Yes (1129)	877(39.8)	76(22.9)	121(15.1)	55(26.2)
No (2415)	1324(60.2)	256(77.1)	680(84.9)	155 (73.8)
Intubated in ER (N=7549)				
Yes (1024)	751(15.2)	116(7.1)	106(19.1)	51(12.5)
No (6525)	4197 (84.8)	1523 (92.9)	449 (80.9)	356 (87.5)
Mechanical Ventilation (N=6210)				
Yes (925)	683(17.1)	146 (10.5)	45 (9.5)	51 (14.4)
No (5285)	3318 (82.9)	1238 (89.5)	427 (90.5)	302 (85.6)
Outcome (N=8721)				
Alive (7134)	4524 (80.9)	1425 (82.4)	757 (83.8)	428 (85.9)
Death (1587)	1067 (19.1)	304(17.6)	146(16.2)	70(14.1)

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Table 5: Significant Predictors of mortality in hospitalized COVID-19 patients.

Predictors of Mortality	Dead (N%)	OR 1 (95% CI)	OR 2 (95% CI)	OR 3 (95% CI)
Age (n = 9145)				
< 35 (n = 875)	27 (3.1)	-	-	-
35 to 44 (n = 931)	58 (6.2)	2.09 (1.61 - 2.82)	1.38 (1.04 - 3.22)	0.89 (0.56 - 1.67)
45 to 54 (n = 1428)	117 (8.2)	2.81 (1,21 - 3.36)	1.64 (1.68 - 2.36)	1.09 (0.78 - 1.88)
55 to 64 (n = 2001)	266 (13.3)	4.83 (2.94 - 5.02)	2.84 (1.94 - 3.79)	1.64 (1.12 - 2.08)
65 to 74 (n = 1867)	438 (23.5)	9.67 (6.35 - 12.90)	5.03 (3.15 - 8.03)	2.13 (1.94 - 4.09)
>= 75 (n = 2039)	745 (36.5)	18.16 (11.78 - 24.64)	9.24 (6.40 - 15.0)	5.16 (4.68 - 10.16)
Sex (n = 9151)				
Female (n = 4640)	709 (42.9)	-	-	-
Male (n = 4511)	942 (57.1)	1.46 (1.31 - 1.62)	1.51 (1.34 - 1.70)	1.54 (1.27 - 1.86)
Admitting Center (n = 9159)				
New York (n =2495)	774 (43.9)	3.61 (3.15 - 4.12)	3.51 (3.00 - 4.09)	3.54 (3.03 - 4.14)
Indiana (n = 140)	22 (1.2)	1.49 (0.93 - 2.38)	1.48 (0.91 - 2.43)	1.40 (0.85 - 2.28)
Rhode Island (n = 105)	0 (0)	0.00 (0.00 - 0.00)	0.00 (0.00 - 0.00)	0.00 (0.00 - 0.00)
Maryland (n = 146)	11 (8.3)	0.65 (0.35 - 1.22)	0.74 (0.39 - 1.42)	0.79 (0.41 - 1.54)
New Jersey (n = 564)	98 (5.7)	1.68 (1.32 - 2.14)	1.60 (1.26 - 2.12)	1.59 (1.19 - 2.11)
DC (n = 460)	71 (4)	1.53 (1.15 - 2.04)	1.72 (1.28 - 2.12)	-
Georgia (n = 712)	116 (6.6)	1.56 (1.24 - 1.95)	1.55 (1.22 - 1.98)	-
Kentucky (n = 700)	108 (6.1)	1.62 (1.21 - 2.01)	1.58 (1.24 - 2.08)	-
Louisiana (n= 775)	140 (7.9)	1.77 (1.43 - 2.18)	2.99 (1.56 - 3.65)	-
Texas (n= 88)	15 (0.8)	0.82 (0.56 - 1.91)	1.77 (1.41 - 2.22)	-
Michigan (n=3674)	407(23.1)	-	-	-
Ethnicity (n = 8721)				
African American (n = 5591)	1067 (67.2)	-	-	-
Caucasians (n = 1729)	304 (19.2)	1.12 (0.95 - 1.33)	1.10 (0.94 - 1.64)	1.21 (0.95 - 1.31)
Hispanics (n = 903)	146 (9.2)	0.45 (0.29 - 0.71)	0.75 (0.60 - 0.94)	0.73 (0.58 - 0.92)
Asian (n = 498)	70 (4.4)	0.12 (0.3 - 0.51)	0.86 (0.65 - 1.15)	0.89 (0.66 - 1.18)
BMI (n = 7016)				
Normal (n = 1746)	210 (16.1)	-	-	-
Overweight (n = 2008)	310 (29.9)	1.40 (0.74 - 2.01)	1.04 (0.87 - 1.23)	1.03 (0.86 – 1.23)
Obese (n = 3262)	675 (51.7)	2.65 (1.21 - 3.75)	1.14 (0.96 - 1.34)	1.11 (0.93 – 1.32)
Asthma	329 (26.3)	1.86 (1.61 - 2.13)	1.42 (1.19 - 1.69)	
COPD	208 (29.1)	2.09 (1.87 - 2.56)	1.45 (1.19 - 1.76)	
Cardiac Disease	338 (27.8)	2.29 (1.99 - 2.65)	1.32 (1.12 - 1.55)	
Hypertension	1060 (2.8)	2.31 (2.03 - 2.63)	1.58 (1.39 - 1.43)	
Diabetes Mellitus	701 (23)	2.04 (1.81 - 2.28)	1.20 (1.03 - 1.39)	
Malignancy	158 (26.5)	2.15 (1.77 - 2.61)	1.50 (0.92 - 1.79)	
Immunocompromised	88 (30.6)	1.40 (1.08 - 1.82)	1.46 (1.10 - 1.93)	
Fever	625 (17.9)	1.26 (1.12 -1.42)	0.95 (0.82 - 1.10)	
Headache	603 (19.3)	1.75 (1.44 - 2.11)	0.96 (0.75 - 1.23)	
Cough	159 (24.9)	1.96 (1.71 - 2.23)	1.21 (0.87 - 1.16)	

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Shortness of Breath	737 (20.2)	2.03 (1.52 - 2.69)	1.73 (1.48 - 2.02)	1.63 (1.33 - 1.99)
Chest Pain	67 (12.8)	1.42 (1.10 - 2.13)	0.73 (0.53 - 0.99)	
Fatigue	162 (16.6)	1.22 (1.01 - 1.47)	0.59 (0.47 - 1.01)	
Lymphocyte Count				
High	190 (17.2)	1.41 (1.22 - 1.64)	1.21 (1.07 - 1.54)	
Low	575 (52.1)	2.50 (2.03 - 3.06)	1.55 (1.30 - 1.86)	
Elevated CPK	221 (54.8)	1.43 (1.15 - 1.77)	1.54 (1.20 - 1.98)	
Elevated CRP	999 (97.2)	4.19 (2.85 - 6.14)	5.15 (3.38 - 7.84)	4.59 (2.55 - 8.27)
Elevated Troponin	531 (47.1)	2.91 (2.5 - 3.34)	3.01 (2.58 - 3.53)	
Elevated Ferritin	665 (74.1)	1.88 (1.57 -2.25)	1.90 (1.56 - 2.32)	
Elevated LDH	451 (69.3)	2.10 (1.60 - 2.76)	2.69 (1.94 - 3.53)	
Elevated AST	658 (66.1)	2.18 (1.88 - 2.52)	2.24 (1.90 -2.63)	
Elevated D-Dimer	756 (92.3)	2.75 (1.97 - 3.61)	2.26 (1.68 - 3.03)	2.76 (1.91 - 3.99)
Glucocorticoid Treatment	513 (51.6)	1.49 (1.27 - 1.69)	1.66 (1.40 - 1.97)	
Mechanical Ventilation	524 (48.2)	10.67 (9.15 - 12.45)	9.78 (8.19 - 11.68)	

Discussion

Our study comprehensively analyzed demographics, clinical manifestations, and outcomes of COVID-19 patients hospitalized at 15 hospitals across the US. The SARS-CoV-2 positive rate was exceptionally high at the pandemic's start in New York State (NY), which emerged as a national epicenter for the disease in March 2020. New York had the highest odds to have in-hospital death than other states in the US. In contrast, hospital mortality was very low in Rhode Island, Michigan, and Maryland. Gastrointestinal symptoms were significantly more common among AA patients with diarrhea being the most prevalent symptom. Abdominal pain, anosmia, ageusia, and factors indicating hepatic dysfunction including the presence of chronic liver disease, elevated AST, bilirubin, and low albumin levels were significantly associated with death. Our findings are consistent with prior observations indicating older age and male sex were associated with the risk of death [12-15,8]. Gender differences in adaptive and innate immune systems as well as hormonal differences have been previously reported and may account for the female benefit in COVID-19. Females have a considerably higher number of CD4+ cells, more potent CD8+, increased B-cell immunoglobulin production, and more type 1 interferon (IFN), a potent anti-viral cytokine [14]. More importantly, these gender and age differences in mortality could be due to a higher level of expression of Transmembrane Protease Serine 2 (TMPRSS2), and Angiotensin-Converting Enzyme 2 (ACE2) receptors which facilitate viral entry in to the host cells [16,8]. Our cohort consisted of 64.1% AA, 19.8% Caucasian, 10.4% Hispanic, and 5.7% Asian patients, with an overall mortality of 18.1%. AA showed the highest mortality compared to other races/ethnicities. However, after adjustment for age, sex, geographic location and comorbidities, there was no significant race-based difference in mortality, similar to the findings from Yehia et al [17]. We noticed higher prevalence rates of comorbid conditions such as diabetes mellitus, hypertension, chronic kidney disease, and obesity among AA patients, similar to prior studies [18,19]. AAs had higher ICU admission rates and required mechanical ventilation significantly more than other races/ethnicities [20]. The conjunction of social, economic, and biologic factors, concurrently with a higher prevalence of comorbidities resulted in a greater COVID-19 burden and worse outcomes among minority populations. The excessive burden of COVID-19 among Hispanics and AAs also may be partially explained by their overrepresentation as an essential workers, resulting in higher exposures [21,22]. Pre-existing conditions of asthma, COPD, cardiac disease, hypertension, diabetes, and malignancy were significantly associated with death in our study. Supporting our findings, Choi et al. identified that COVID-19 mortality rates of patients with diabetes, COPD, immunosuppression, hypertension, CKD, and cardiovascular diseases were approximately 2.5-4 times higher than those without underlying conditions [23]. Obesity has been described as a negative factor for COVID-19 patient outcome, primarily because of obesity-associated pro-inflammation, excessive oxidative stress, impaired immunity, and a trigger/stimulus of metabolic syndrome [24]. Our cohort was 45.6% obese, 28.6% overweight, and 24.9% with normal BMI. Obese patients were significantly more prone to death. However, this trend was not significant after age/sex/race adjustments. Shortness of breath was significantly associated with death after adjusting for demographics and

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comorbidities similar to previous studies [25]. This finding suggests that shortness of breath, should be given special attention in managing hospitalized COVID-19 patients. The ACE2 receptor, the target of the SARS-CoV-2 virus SPIKE protein, and TMPRSS2 that is required for its cleavage and entry, are expressed in the gastrointestinal track, suggesting that GI symptoms could be the consequences of a direct virus effect. Diarrhea was the most common presenting symptom consistent with previous studies [26]. Evidence of liver dysfunction such as low albumin, elevated AST and elevated total bilirubin was significantly associated with death. Other studies have reported similar results [27-29]. Our study additionally showed that COVID-19 patients with splenomegaly were more prone to death. The increase in spleen size is correlated with COVID-19 disease severity score calculated on the chest CT data in a study conducted by Tahtabasi et al. [30]. This pathological change is due to microthrombus-related end organ (kidneys, heart, spleen and central nervous system) damage mainly caused by impairment of coagulation mechanisms and immune response by the SARS-CoV-2 virus infection [30]. Alternatively, pre-existing splenomegaly may indicate prior liver compromise and portal hypertension. In our study, only a limited number of patient data regarding splenomegaly was available. Further studies related to splenomegaly as a predictor of mortality for COVID-19 may be required. Our study attempted to assess the association of specific laboratory biomarkers (CRP, LDH, ferritin and D-dimer) with outcome from COVID-19. Consistent with prior studies, serum inflammatory markers such as elevated D-dimer, LDH, CRP, ferritin, troponin were significantly associated with death [31,32]. Thus, the continuous search for markers associated with the course of the disease can aid a better assessment of the severity and management of the disease. Such attempts may help clinical decision-making. Thousands of patients have received hydroxychloroquine outside of clinical trials without evidence of its beneficial effects. A collaborative meta-analysis of 28 published and unpublished RCTs, that included 10319 patients by Axfors et al., showed that treatment with hydroxychloroquine was associated with increased mortality in COVID-19 patients, and there was no benefit from treatment [33]. Similarly, treatment with hydroxychloroquine was associated with increased mortality in our COVID-19 cohort. Our study identified use of steroids for hospitalized COVID-19 patients was an independent predictor of death after adjusting for demographics and baseline comorbidities. However, in a prospective meta-analysis of clinical trials of critically ill patients with COVID-19, administration of systemic corticosteroids, compared with usual care or placebo, was associated with lower 28-day all-cause mortality [34]. In contrast, a metanalysis including 32 studies that included 14659 COVID-19 patients showed no significant decrease in all-cause mortality in critically ill COVID-19 patients treated with corticosteroids [35]. Our data reflects precautionary measures at the beginning of the pandemic when specific protocols including timing of glucocorticoids were not yet developed. Multivariate logistic regression models showed that patients on mechanical ventilation were nine times more prone to death. Mortality of patients with COVID-19 who required invasive mechanical ventilation was reported to be significantly high in many previous studies [36,37].

One of the main strengths of the study was our ability to collect comprehensive patient data from admission to the primary endpoints: discharge or death. Also, data were obtained by detailed medical records review. Our study included patients from the North and Midwest, East, and South of the US. However, despite valiant efforts, we were not successful in obtaining data from Western states. A review of COVID-19 literature from Western states showed similar results to ours. Male gender and older patients (>70 years) are more likely to die from COVID-19 [38-40].

Limitations of the study include its retrospective nature and the fact that it involves areas in the US that were hit by the pandemic asynchronously. This might have affected our findings as the New York area was hit first and very hard by the pandemic and as such displayed higher mortality than other regions that might have not matured in case saturation. There was not uniform data regarding some clinical manifestations and laboratory parameters from all the centers. However, our analyses are consistent with other published studies, and this consistency suggests that our data is robust and validated. In summary, analysis of hospitalized COVID-19 patients across 11 states in the US showed that older age, male sex, AA race, patients in the New York state have higher in-hospital mortality. Other predictors of mortality include the presence of comorbid conditions, shortness of breath, cough, elevated serum inflammatory markers, altered lymphocyte count, elevated AST, and low serum albumin. This study suggests that African Americans carried a disproportionate burden of COVID-19 death in the US in 2020.

Declarations

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Conflict-of-interest statement

The authors declare no conflicts of interest.

Financial Disclosure

No Financial disclosure applied for this research.

Author contributions

HA designed the study, HA, HB and LGC wrote the manuscript, John M. Carethers & Farin Kamangar, Zaki A. Sherif, Fatimah Jackson reviewed and edited the paper; Antonio Pizuorno, Folake Adeleye, Maryam Mehdipour Dalivand, Suryanarayana Reddy Challa, Boubini Jones-Wonni, Sheldon Rankine, Camelita Thrift, Chiamaka Ekwunazu, Abigail Banson, Rachel Kim, Chandler Gilliard, Elizabeth Ekpe, Nader Shayegh, Constance Nyaunu, Chidi Martins, Ashley Slack, Princess Okwesili, Malachi Abebe, Yashvardhan Batta, Do, Ly, Ogwo Valarie, Tori Smith, Kyra Watson, Oluwapelumi Kolawole , Sarine Tahmazian, Sofiat Atoba, Myra Khushbakth, Gregory Riley, Warren Gavin, Areeba Kara, Manuel Hache-Marliere, Leonidas Palaiodimos, Vishnu R Mani, Aleksandr Kalabin, Vijay Reddy Gayam, Pavani Reddy Garlapati, Joseph Miller, Vinod Rustgi, and Lakshmi Gayathri Chirumamilla collected and analyzed the clinical data. Gholamreza Oskrochi performed statistical analysis. All authors read and approved the final manuscript.

Data availability statement

Data are available on reasonable request. Please contact corresponding author, Dr. Hassan Ashktorab, email: hashktorab@howard.edu

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Ethical statement

The study was approved by Howard University Intuitional Review Board 355 (IRB-20-MED-26).

Abbreviation list

C-Reactive Protein (CRP); Lactose dehydrogenase (LDH); Creatine Phosphokinase (CPK); Intensive Care Unit (ICU); Aspartate Transaminase (AST); Odds Ratio (OD).

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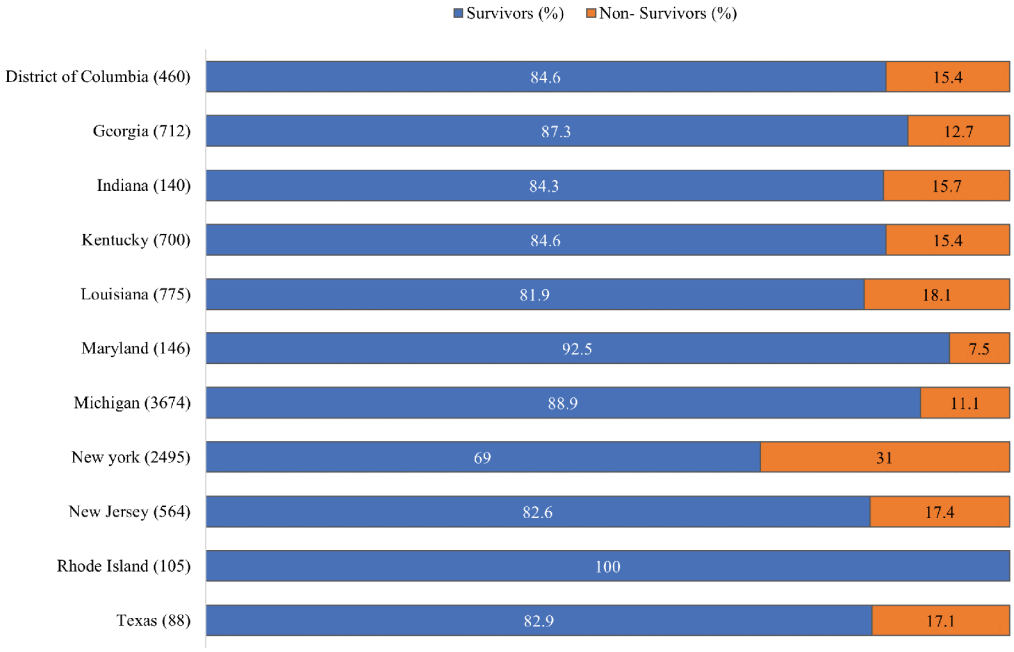
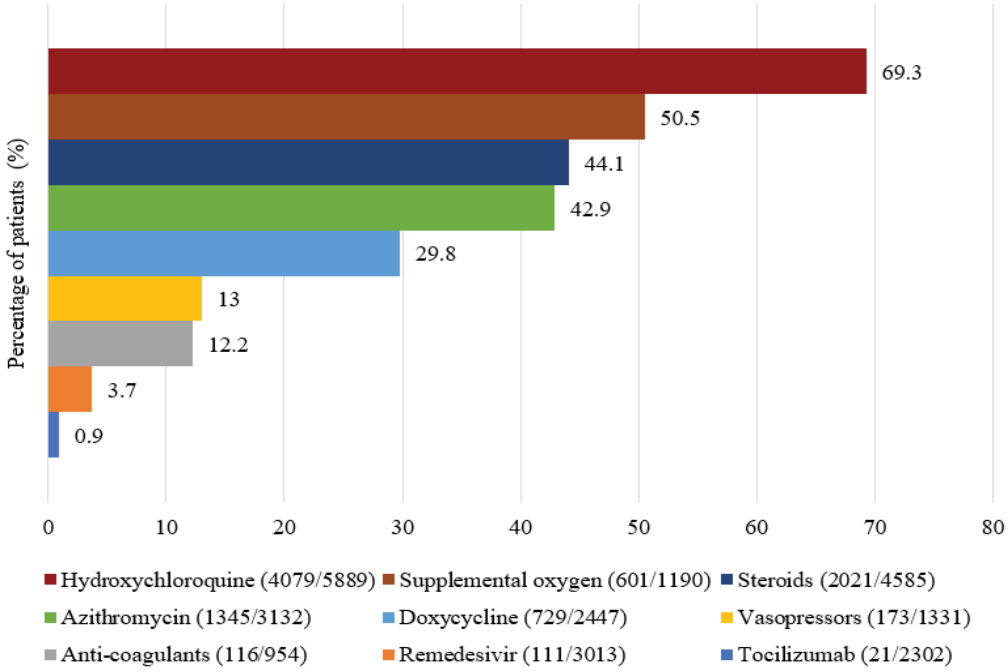
SUPPLEMENTARY FILES



Supplement Fig 1: COVID-19 Mortality in different states across the 11 states in the United States



Supplement Fig 2: Treatment for hospitalized COVID-19 patients

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