Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Elevated Liver Enzymes, Ferritin, C-reactive Protein, D-dimer, and Age Are Predictive Markers of Outcomes Among African American and Hispanic Patients With Coronavirus Disease 2019

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Severe acute respiratory syndrome coronavirus 2 caused a worldwide outbreak. Its associated disease, coronaviruses disease 2019 (COVID-19), causes respiratory, gastrointestinal (GI), inflammatory, and neurologic symptoms.[1] In the United States, minorities such as African Americans (AA) and Hispanics (HSP) have shown a higher incidence of the disease.[2,3]. However, no detailed characterization of the disease's features in these populations has been performed.[4]

Although the initial focus was on saving lives and developing and delivering vaccines and therapeutics, the focus is shifting toward an assessment of specific features of the disease in different patient groups, variables that affect outcome, and, more importantly, factors that correlate with persistent and recurring symptoms.[5] In this study we describe the demographics, clinical features, and GI symptoms of hospitalized minority patients with confirmed severe acute respiratory syndrome coronavirus 2 infection at a tertiary hospital located in Washington, DC. We also sought to determine how these features relate to outcomes and which can be considered for prognosis assessment.

Methods

Patient Selection

A list of 447 hospitalized adult (March to September 2020 at Howard University Hospital) COVID-19 patients was obtained. This study was approved by the Institutional Review Board. Demographics, clinical values, comorbidities, laboratory test results, and treatment data were collected from patient charts.

Statistical Analysis

Patient demographics, symptoms, comorbidities, treatment, and clinical values in relation to outcome was assessed in the overall cohort and in a subgroup analysis of AA, whites (CAU), and HSP. Correlation coefficients were calculated together with a multivariate binary logistic regression analysis to establish associations with death as an outcome. SPSS version 26 (SPSS Inc, Chicago, IL) was used for these analyses.

Results

Overall Features of the Cohort

Our cohort consisted of 447 patients, with 309 AA (69.1%), 27 CAU (6%), and 111 HSP (24.8%) with 71 deaths overall (15.5%). AA and CAU had similar death rates, 18.1% and 18.5%, respectively, whereas HSP had 7.3% deaths. The overall age was 56.1 years, with 53.9 years for survivors vs 68.6 years for those who died. HSP were the youngest, at 44.9 years, whereas CAU were the oldest, at 61.1 years. There were more men (51.1%) than women (48.9%). Our cohort had an average body mass index of 30.6 kg/m^2, with HSP having lowest BMI (27.4 kg/m^2) vs AA with the highest (31.6 kg/m^2) (Table 1).

Overall, diarrhea was the most common GI symptom (19.4%) followed by abdominal pain (15.8%). GI bleeding was reported in 4.4%, pancreatitis in 0.9%, and cholecystitis in 1.6%. Diarrhea frequency was highest in AA (22.4%), whereas abdominal pain was highest in HSP (17.3%). Of note, 24% of the overall cohort presented these GI manifestations after admission.

The most common comorbidities in our study were hypertension (55.2%) followed by diabetes (38.4%) and cardiac disease (20.2%). With respect to GI comorbidities, the most common was history of liver disease (4.3%) and history of gastroesophageal reflux disease (10%). HSP had the lowest level of pre-existing liver disease, whereas CAU had the highest rate of gastroesophageal reflux disease/peptic ulcer disease history (15.3%), and only 1.3% of AA had a previous diagnosis of inflammatory bowel disease (Table 1).

Overall, 41% of our cohort had abnormal levels in their liver function test panel. CAU had the highest proportion of such patients (52.1%). Elevated alanine aminotransferase was reported in 77.1% of tested patients; this rate was the lowest in

Abbreviations used in this paper: AA, African Americans; CAU, whites; COVID-19, coronavirus disease 2019; GI, gastrointestinal; HSP, Hispanics.

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Table 1. Demography, Clinical Manifestations, and Comorbidities of COVID-19 Patients

	AA	*P*	CAU	*P*	HSP	*P*	Overall	*P*
Total no. of cases	309 (69.1)		27 (6)		111 (24.8)		447 (100)	
Deceased	56 (18.1)		5 (18.5)		8 (7.3)		71 (15.5)	.023[a]
Average age, y	59.7	<.001	61.1	.021	44.9	.009	56.1	<.001
Survivors	57.6		57.7		43.8		53.9	
Deceased	69.2		76.2		60.1		68.6	
Sex		.53		.825		.479		.41
Men	157 (50.8)		15 (55.6)		54 (49.5)		227 (51)	
Survivors	122 (77.7)		12 (80)		50 (90.9)		184 (81.1)	
Deceased	35 (22.3)		3 (20)		5 (9.1)		43 (18.9)	
Women	152 (49.2)		12 (44.4)		55 (50.5)		218 (49)	
Survivors	131 (86.2)		10 (83.3)		51 (94.4)		192 (88.1)	
Deceased	21 (13.8)		2 (16.7)		3 (5.6)		26 (11.9)	
Mean body mass index, kg/m^2	31.6	.155	30.5	.216	27.4	.288	30.6	.223
Normal							127 (31.2)	
Survivors	65 (76.5)		6 (75)		31 (91.2)		102 (80.3)	
Deceased	20 (23.5)		2 (25)		3 (8.8)		25 (19.7)	
Overweight	0.450		0.640		0.658		126 (31.4)	.552
Survivors	68 (81.9)		6 (75)		33 (94.3)		107 (84.9)	
Deceased	15 (18.1)		2 (25)		2 (5.7)		19 (15.1)	
Obese							154 (37.8)	
Survivors	100 (83.3)		9 (90)		21 (87.5)		130 (84.4)	
Deceased	20 (16.7)		1 (10)		3 (12.5)		24 (15.6)	
Fever	171 (56.4)		16 (59.2)		55 (52.9)		242 (55.8)	
Survivors	139 (81.3)	.773	14 (87.5)	.332	49 (89.1)	.192	202 (83.5)	.580
Deceased	32 (18.7)		2 (12.5)		6 (10.9)		40 (16.5)	
Cough	196 (65.7)		18 (66.6)		57 (57)		271 (63.8)	
Survivors	162 (82.7)	.631	15 (83.3)	.726	52 (91.2)	.743	229 (84.5)	.841
Deceased	34 (17.3)		3 (16.7)		5 (8.8)		42 (15.5)	
Shortness of breath	198 (65.7)		16 (61.5)		57 (55.3)		271 (63)	
Survivors	155 (78.3)	.032	13 (81.3)	.937	49 (86)	.008	217 (80.1)	.002
Deceased	43 (21.7)		3 (18.8)		8 (14)		54 (19.9)	
Abdominal pain	43 (15.4)		3 (13)		17 (17.3)		63 (15.8)	
Survivors	40 (93)	.75	3 (100)	.328	16 (94.1)	.824	59 (93.7)	.050
Deceased	3 (7)		0 (0)		1 (5.9)		4 (6.3)	
Diarrhea	67 (22.4)		6 (23)		10 (9.7)		83 (19.4)	
Survivors	56 (83.6)	.681	5 (83.3)	.856	9 (90)	.781	70 (84.3)	.994
Deceased	11 (16.4)		1 (16.7)		1 (10)		13 (15.7)	
Nausea	41 (14.2)		2 (8.3)		12 (12)		55 (13.3)	
Survivors	35 (85.4)	.661	2 (100)	.449	12 (100)	.311	49 (89.1)	.382
Deceased	6 (14.6)		0 (0)		0 (0)		6 (10.9)	
Vomiting	38 (12.9)		3 (11.5)		11 (10.6)		52 (12.3)	
Survivors	33 (86.8)	.465	3 (100)	.369	11 (100)	.311	47 (90.4)	.239
Deceased	5 (13.2)		0 (0)		0 (0)		5 (9.6)	
Fatigue	94 (47.4)		11 (50)		25 (35.2)		130 (44.7)	
Survivors	81 (86.2)	.782	9 (81.8)	.534	22 (88)	.428	112 (86.2)	.391
Deceased	13 (13.8)		2 (18.2)		3 (12)		18 (13.8)	
Loss of appetite	86 (33.8)		1 (4.7)		19 (20.9)		106 (29)	
Survivors	143 (85.1)	.445	1 (100)	.567	18 (94.7)	.793	89 (84)	.522
Deceased	25 (14.9)		0 (0)		1 (5.3)		17 (16)	
Loss of taste	19 (8)		2 (9)		7 (8.1)		28 (8.1)	
Survivors	17 (89.5)	.463	2 (100)	.421	7 (100)	.450	26 (92.9)	.247
Deceased	2 (10.5)		0 (0)		0 (0)		2 (7.1)	

Table 1. Continued

	AA	*P*	CAU	*P*	HSP	*P*	Overall	*P*
GI bleed	17 (5.6)		1 (3.7)		1 (1)		19 (4.4)	
Survivors	11 (64.7)	.057	1 (100)	.627	0 (0)	.001	12 (63.2)	.009
Deceased	6 (35.3)		0 (0)		1 (100)		7 (36.8)	
Pancreatitis	3 (1)		0 (0)		1 (1)		4 (0.9)	
Survivors	2 (66.7)	.477	0 (0)	N/A	1 (100)	.769	3 (75)	.594
Deceased	1 (33.3)		0 (0)		0 (0)		1 (25)	
Cholecystitis	6 (1.9)		0 (0)		1 (1)		7 (1.6)	
Survivors	5 (83.3)	.918	0 (0)	N/A	1 (100)	.769	6 (85.7)	.911
Deceased	1 (16.7)		0 (0)		0 (0)		1 (14.3)	
Cardiac disease	71 (24)		9 (34.6)		5 (5.1)		85 (20.2)	
Survivors	55 (77.5)	.334	6 (66.7)	.184	5 (100)	.496	66 (77.6)	.084
Deceased	16 (22.5)		3 (33.3)		0 (0)		19 (22.4)	
Diabetes mellitus	128 (43.1)		9 (34.6)		25 (25.3)		162 (38.4)	
Survivors	102 (79.7)	.576	5 (55.6)	.018	20 (80)	.11	127 (78.4)	.021
Deceased	26 (20.3)		4 (44.4)		5 (20)		35 (21.6)	
Hypertension	188 (63.3)		16 (61.5)		29 (29.3)		233 (55.2)	
Survivors	154 (81.9)	.656	11 (68.8)	.049	24 (82.8)	.031	189 (81.1)	.118
Deceased	34 (18.1)		5 (31.2)		5 (17.2)		44 (18.9)	
History of liver disease	14 (4.7)		1 (3.8)		3 (3)		18 (4.3)	
Survivors	9 (64.3)	.095	1 (100)	.619	3 (100)	.606	13 (72.2)	.171
Deceased	5 (35.7)		0 (0)		0 (0)		5 (27.8)	
History of inflammatory bowel disease	4 (1.3)		0 (0)		1 (1)		5 (1.2)	
Survivors	3 (75)	.742	0 (0)	N/A	1 (100)	.768	4 (80)	.812
Deceased	1 (25)		0 (0)		0 (0)		1 (20)	
History of gastroesophageal reflux disease/ peptic ulcer disease	33 (11.1)		4 (15.3)		5 (5)		42 (10)	
Survivors	28 (84.8)	.585	3 (75)	.750	5 (100)	.501	36 (85.7)	.734
Deceased	5 (15.2)		1 (25)		0 (0)		6 (14.3)	
Immunocompromised	22 (7.2)		2 (8)		4 (3.8)		28 (6.5)	
Survivors	15 (68.2)	.096	2 (100)	.461	3 (75)	.182	20 (71.4)	.060
Deceased	7 (31.8)		0 (0)		1 (25)		8 (28.6)	
Alcohol use	45 (19.9)		6 (27.2)		12 (15.4)		63 (19.3)	
Survivors	42 (93.3)	.079	5 (83.3)	.910	11 (91.7)	.933	58 (92.1)	.133
Deceased	3 (6.7)		1 (16.7)		1 (14.3)		5 (7.9)	
Elevated ferritin	166 (61.2)		14 (66.6)		47 (62.7)		227 (61.9)	
Survivors	125 (75.3)	.004	10 (71.4)	.469	41 (87.2)	.445	176 (77.5)	.02
Deceased	41 (24.7)		4 (28.6)		6 (12.8)		51 (22.5)	
Elevated D-dimer	244 (90)		18 (85.7)		62 (86.1)		324 (89)	
Survivors	193 (79.1)	.031	13 (72.2)	.296	55 (88.7)	.263	261 (80.6)	.008
Deceased	51 (20.9)		5 (27.8)		7 (11.3)		63 (19.4)	
Elevated C-reactive protein	148 (58.4)		14 (70)		47 (62.7)		210 (60)	
Survivors	109 (73.2)	<.001	10 (71.4)	.573	40 (85.11)	.124	159 (75.7)	<.001
Deceased	40 (26.8)		4 (28.6)		7 (14.9)		51 (24.3)	
Elevated procalcitonin	98 (38.5)		7 (31.8)		20 (29.4)		125 (36.3)	
Survivors	56 (57.1)	<.001	3 (42.9)	.009	14 (70)	.003	73 (58.4)	<.001
Deceased	42 (52.9)		4 (57.1)		6 (30)		52 (41.6)	
Mean elevated creatinine	55.5		34.6		23.4		48.7	
Survivors	0.46	<.001	0.19	0.002	0.18	<.001	0.37	<.001
Deceased	0.96		1.00		0.87		0.95	

Table 1. Continued

	AA	*P*	CAU	*P*	HSP	*P*	Overall	*P*
Elevated IL-6	93 (98.9)		8 (100)		28 (100)		129 (99.2)	
Survivors	71 (76.3)	.77	5 (62.5)	N/A	27 (96.4)	N/A	103 (79.8)	.800
Deceased	22 (23.7)		3 (37.5)		1 (3.6)		26 (20.2)	
Abnormal platelet count	35.3 (109)	.18	22.2 (6)	.571	31 (27.9)	.360	Low 146 (32.9)	.02
	23.6 (73)		25.9 (7)		22 (19.8)		Elevated 102 (23.1)	
Abnormal lymphocyte count	1 (3)	.582	1 (3.7)	.782	106 (95.5)	.814	Low 1.3 (6)	.628
	295 (95.1)		25 (92.6)		2 (1.8)		Elevated 95.3 (434)	
Elevated cholesterol	5 (6)		1 (9)		0 (0)		6 (5.2)	
Survivors	5 (100)	.166	1 (100)	.621	0 (0)	N/A	6 (100)	.174
Deceased	0 (0)		0 (0)		0 (0)		0 (0)	
Elevated low-density lipoprotein	4 (1.3)		1 (3.7)		0 (0)		5 (4.4)	
Survivors	4 (100)	.210	1 (100)	.621	0 (0)	N/A	5 (100)	.208
Deceased	0 (0)		0 (0)		0 (0)		0 (0)	
Elevated high-density lipoprotein	1 (1.2)		0 (0)		0 (0)		1 (0.9)	
Survivors	1 (100)	.542	0 (0)	N/A	0 (0)	N/A	1 (100)	.583
Deceased	0 (0)		0 (0)		0 (0)		0 (0)	
Elevated triglycerides	34 (38.6)		3 (27.2)		6 (30)		43 (36.1)	
Survivors	24 (70.6)	.721	2 (66.7)	.425	3 (50)	.004	29 (67.4)	.118
Deceased	10 (29.4)		1 (33.3)		3 (50)		14 (32.6)	
Elevated liver function test values on admission	107 (37)		12 (52.1)		44 (51.2)		163 (41)	
Survivors	72 (67.3)	<.001	8 (66.7)	.159	41 (93.2)	.417	121 (74.2)	<.001
Deceased	35 (32.7)		4 (33.3)		3(6.8)		42 (25.8)	
Mean elevated alanine aminotransferase peak	25 (78.1)		1 (33.3)		11 (84.6)		37 (77.1)	
Survivors	60.1	.258	65.6	.386	58.8	.326	60.1	.878
Deceased	113.3		51.2		703.3		180.1	
Mean elevated aspartate aminotransferase peak	15 (46.9)		2 (66.7)		7 (53.8)		24 (50)	
Survivors	75.5	.228	74.2	.386	56.3	.612	70.6	.121
Deceased	246.8		77.2		1518.5		388.1	
Pneumonia	255 (84.4)		23 (85.1)		71 (68.9)		349 (80.8)	
Survivors	202 (79.2)	.007	18 (78.3)	.302	63 (88.7)	.048	283 (81.1)	<.001
Deceased	53 (20.8)		5 (21.7)		8 (11.3)		66 (18.9)	

Values are n (%) unless otherwise defined. N/A, Chi square statistical test is not applicable.
[a]Comparing mortality rate between ethnicities.

CAU (33.3%). Elevated aspartate aminotransferase was reported in 50% and was highest in CAU (66.7%). Other abnormal test results were elevated D-dimer in 89%, abnormal IL-6 in 99.2%, and elevated ferritin in 61.9% (Table 1).

Variable Correlations With Death as an Outcome

Older age ($P < .001$), shortness of breath ($P < .001$), abdominal pain ($P = .050$), GI bleeding ($P = .009$), diabetes ($P = .021$), elevated ferritin ($P = .02$), D-dimer ($P = .008$), C-reactive protein ($P < .001$), elevated procalcitonin ($P < .001$), elevated creatinine ($P < .001$), altered platelet ($P = .002$), high liver function test values on admission ($P < .001$), pneumonia ($P < .001$), intensive care unit admission/transfer ($P \leq .001$), sepsis ($P \leq .001$), vasopressors ($P < .001$), and mechanical ventilation ($P < .001$) were statistically associated with death in the overall cohort

(Supplementary Table 1). For AA, shortness of breath ($P = .032$), elevated ferritin ($P = .004$), D-dimer ($P = .031$), C-reactive protein ($P < .001$), procalcitonin ($P < .001$), liver function test values on admission ($P < .001$), pneumonia ($P = .007$), intensive care unit admission ($P \leq .001$), intensive care unit transfer ($P < .001$), sepsis ($P < .001$), vasopressors ($P < .001$), and mechanical ventilation ($P = .020$) were significantly associated with death (Supplementary Table 1). For HSP, shortness of breath ($P = .008$), GI bleeding ($P = .001$), hypertension ($P = .031$), elevated procalcitonin ($P = .003$), elevated triglycerides ($P = .004$), pneumonia ($P = .048$), intensive care unit admission ($P = .004$), intensive care unit transfer ($P < .001$), sepsis ($P = .004$), extracorporeal membrane oxygenation ($P = .020$), vasopressors ($P < .001$), Remdesivir ($P = .043$), and mechanical ventilation ($P < .001$) were associated with death as an outcome (Supplementary Table 1). For CAU, only associated with death were diabetes ($P = .018$), hypertension ($P = .049$), elevated procalcitonin ($P = .009$), mechanical ventilation ($P = .023$), and vasopressors ($P = .033$; Supplementary Table 1).

Discussion

In the overall cohort analysis, age was a major effector of outcome. This was further confirmed in subgroup analyses. Indeed, HSP, the youngest group, had the lowest death rate, whereas CAU, the oldest group, had the highest death rate. Respiratory issues such as shortness of breath and pneumonia requiring intensive care unit care and mechanical ventilation were strongly associated with poor outcome in our patients, regardless of race. Elevated procalcitonin was also a common risk factor. Procalcitonin is primarily increased in response to bacterial-triggered inflammation, pointing to potential opportunistic pathogen activity in the course of COVID-19. Vasopressor use in critically ill patients was also associated with poor outcome, attesting to unstable hemodynamics independent of race.[6]

The association of diabetes with poor outcome was noted in CAU only, whereas hypertension was common with HSP. This finding reflects the weight of metabolic syndrome in CAU that were the oldest group in our cohort. The small number of CAU in our cohort is a limitation of the study. Within HSP, high triglyceride level was a risk factor reflecting the negative impact of blood fat in coronary artery disease and outcome. Although HSP had a lower body mass index compared with AA, the cumulative effects of high triglyceride levels and hypertension point to the impact of the metabolic syndrome in this group, even though it was the youngest. GI bleeding was reported as a risk factor in HSP as well. Whether this symptom is a cause or consequence risk of hemodynamic instability remains to be explored. Indeed, such cases were reported in patients with thromboembolism.[7] Elevated ferritin, D-dimer, and C-reactive protein were major and unique risk factors to AA in the subgroup analysis, highlighting the prevalence of systemic inflammation and coagulopathies in this group.

Of note, elevated liver function test values on admission were significantly associated with poor outcome in our study cohort. A study reported that patients with chronic liver disease were more likely to develop severe COVID-19.[8] However, liver function alterations were also reported as a result of COVID-19 or antiviral treatment during hospitalization. Diarrhea frequency and abdominal pain were highest in AA and HSP, respectively. They are likely to affect post-discharge patient condition because the virus persists longer in the GI tract after clearance from the respiratory system.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org and at 10.1053/j.gastro.2021.03.043.

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Conflicts of interest
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