FEATURE ARTICLE

Association of Patient Characteristics, Diabetes, BMI, and Obesity With Severe COVID-19 in Metropolitan Detroit, MI

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Identification of specific risk factors for severe coronavirus disease 2019 (COVID-19) is crucial for prevention of poor outcomes and mortality. This retrospective cohort study of patients hospitalized with COVID-19 demonstrated that older age, male sex, Black race, diabetes, elevated BMI, and elevated inflammatory markers were correlated with critical illness in COVID-19. Older age, male sex, diabetes, and inflammatory markers, but not elevated BMI, were associated with mortality. Despite having greater odds of critical illness, Black patients had lower odds of death than White patients. Older age, male sex, diabetes, and elevated inflammatory markers were significantly associated with venous thromboembolism. These findings suggest a need to aggressively identify and manage modifiable risk factors (i.e., diabetes and elevated BMI) and encourage vaccination of at-risk individuals to prevent poor outcomes from COVID-19.

The coronavirus disease 2019 (COVID-19) pandemic has tragically claimed millions of lives, profoundly affected well-being, and resulted in dramatic social and economic disruption. The state of Michigan has been deeply affected by COVID-19, having led the nation in the number of new infections and being the only state categorized as at a "severe" risk level in April 2021 (1). The estimated total cost from COVID-19 is >$16 trillion, with approximately half of that cost resulting from lost income from the COVID-19–induced recession and the rest from loss of health (2).

Although >94% of individuals survive infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (3), severe disease and death can occur, especially in individuals who are older, male, and have comorbid conditions (4). Furthermore, persistent "long-haul" symptoms have been reported among COVID-19 survivors, even in those who experienced an initial mild acute illness (5). The high likelihood of SARS-CoV-2 becoming endemic, lack of a cure, and possibility of severe disease, death, and long-term morbidity from illness reinforce the need to identify risk factors for poor outcomes from COVID-19.

The Henry Ford Health System (HFHS), a comprehensive, integrated, nonprofit health care organization that includes five hospitals in metropolitan Detroit, MI, provides a unique patient population to study risk factors for severe COVID-19. A significant portion of patients seen at HFHS comes from Detroit, which is the location of the 877-bed flagship hospital.

The aims of our study were to determine the incidence of severe outcomes (i.e., need for mechanical ventilation [MV], intensive care unit [ICU] admission, death, and venous thromboembolism [VTE]) in patients admitted for COVID-19 within a single health system, describe the clinical characteristics of these patients, and evaluate the correlation of poor outcomes with demographics, diabetes, BMI, obesity, and levels of inflammatory markers. Additionally, to identify potential risk factors that are unique to our patient population, we compared patient characteristics and the presence of multiple comorbidities in Black and White patients with COVID-19. Determination of risk factors associated with severe COVID-19, especially in a unique population with a large percentage of Black patients, can guide risk mitigation efforts and help to identify racial gaps in health care.

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Research Design and Methods

Study Design and Participants

This was a retrospective study of electronic medical records (EMRs) of adult patients (≥18 years of age) who were admitted to any of the five hospitals in the HFHS (Henry Ford Hospital in Detroit, Henry Ford West Bloomfield Hospital, Henry Ford Macomb Hospital, Henry Ford Wyandotte Hospital, and Henry Ford Allegiance Health in Jackson, MI) and were diagnosed with COVID-19 by real-time PCR between 1 March and 25 July 2020. Polymerase chain reaction testing was validated and performed on four platforms (NeumoDx 288, Cepheid GeneXpert and Infinity, Hologic Panther, and Diasorin Liaison MDX).

This study was approved by the HFHS's institutional review board. The need for informed consent was waived because this was a retrospective chart review with minimal risk and no intervention.

Data Collection

Demographic, clinical, laboratory, and outcome data were extracted from EMRs. These included age, sex, race (described as Black or White in the EMRs), BMI, A1C, and the presence of comorbidities, including diabetes, hypertension, chronic kidney disease (CKD), sleep apnea, chronic obstructive pulmonary disease (COPD), coronary artery disease (CAD), stroke, heart failure (HF), cirrhosis, HIV infection, and active malignancy. Additionally, the inflammatory markers D-dimer, ferritin, C-reactive protein (CRP), interleukin 6 (IL-6), and procalcitonin were collected. Primary outcomes evaluated were the need for MV, need for ICU admission, death, and development of VTE.

Statistical Analysis

Descriptive statistics were used to describe patient demographics, clinical characteristics, and multiple outcomes. Obese, overweight, and at least overweight were defined as BMI ≥30.0, 25.0–29.99, and ≥25.0 kg/m^2, respectively. We compared the incidence of comorbid conditions in Black and White patients who had confirmed COVID-19. The average value was used for cases in which patients had multiple BMI or A1C values during their admission. Two-group comparisons using χ^2 tests and Fisher's exact test (when counts were <5) assessed correlation of race with comorbidities and outcomes.

Multivariate logistic regression models were used to determine whether demographics, A1C >5.7%, diabetes, elevated BMI categories, or inflammatory markers (D-dimer, ferritin, CRP, IL-6, and procalcitonin) were significantly associated with the four outcomes. Each analysis controlled for the confounders of age, sex, race, diabetes, BMI, and eight additional comorbidities (hypertension, CKD, CAD, stroke, HF, COPD, sleep apnea, and active malignancy). The analyses for A1C >5.7% were controlled for all previously mentioned confounding variables except diabetes. For the BMI categories, multivariate logistic regression models were used to measure the effects of BMI ≥30.0, ≥25.0, and ≥30.0 vs. 25.0–29.99 kg/m^2 on each outcome. In cases with multiple values for the same inflammatory marker during the hospital stay, the earliest value was used. If the inflammatory marker was measured multiple times on the earliest day, then the average value on the earliest day was used. Statistical significance was determined if $P < 0.05$. All analyses were performed using SAS 9.4 software (SAS Institute, Cary, NC).

Results

Overall Characteristics and Main Outcomes

A total of 8,751 adults hospitalized with COVID-19 between 1 March and 25 July 2020 were included in this cohort study, of whom 682 (7.8%) required MV, 867 (9.9%) were admitted to the ICU, 753 (8.6%) died, and 430 (4.9%) were diagnosed with VTE. Of these patients, 4,447 (50.8%) were Black, 4,951 (56.6%) were women, and 5,152 (58.9%) were >50 years of age. Of the patients who had BMI recorded, 2,560 (50.3%) had a BMI ≥30.0 kg/m^2, 1,397 (27.5%) had a BMI of 25.0–29.99 kg/m^2, and 3,957 (77.8%) had a BMI ≥25.0 kg/m^2. Of the patients who had A1C checked, 1,138 (74.3%) had an A1C >5.7%. Diabetes and hypertension were the most frequent comorbidities (2,068 [23.6%] had diabetes and 1,164 [13.3%] had hypertension). Fewer than 10% had the following comorbidities: CKD in 400 (4.6%), sleep apnea in 125 (1.4%), COPD in 155 (1.8%), CAD in 321 (3.7%), stroke in 100 (1.1%), HF in 310 (3.5%), and malignancy in 300 (3.4%) patients. Fewer than 1% of patients had cirrhosis (n = 35 [0.4%]) or HIV diagnosis (n = 11 [0.1%]). All descriptive data are listed in Table 1.

Association of Demographics and Comorbidities With Race

Our data suggested a significant association between race (categorized as Black or White) and having multiple comorbid conditions (diabetes, hypertension, CKD, sleep apnea, COPD, CAD, and cirrhosis), an A1C

TABLE 1 Patient Characteristics and Main Outcomes of Patients With COVID-19 (N = 8,751)

Demographics	
Race	
Black	4,447 (50.82)
White	3,048 (34.83)
Other	1,256 (14.35)
Sex	
Male	3,800 (43.42)
Female	4,951 (56.58)
Age, years	
18–29	968 (11.06)
30–39	1,227 (14.02)
40–49	1,404 (16.04)
50–59	1,745 (19.94)
60–69	1,541 (17.61)
≥70	1,866 (21.32)
Clinical variables	
Diabetes	2,068 (23.63)
Hypertension	1,164 (13.30)
CKD	400 (4.57)
Sleep apnea	125 (1.43)
COPD	155 (1.77)
CAD	321 (3.67)
Stroke	100 (1.14)
HF	310 (3.54)
Cirrhosis	35 (0.40)
HIV	11 (0.13)
Active malignancy	300 (3.43)
Weight status (n = 5,088)	
Obesity (BMI ≥30.0 kg/m^2)	2,560 (50.31)
Overweight (BMI 25.0–29.99 kg/m^2)	1,397 (27.46)
At least overweight (BMI ≥25.0 kg/m^2)	3,957 (77.77)
A1C >5.7% (n = 1,532)	1,138 (74.28)
Outcomes	
MV	682 (7.8)
ICU admission	867 (9.9)
VTE	430 (4.9)
Death	753 (8.6)

Data are n (%).

>5.7%, a BMI ≥25.0 kg/m^2, and a BMI ≥30.0 kg/m^2 in patients with COVID-19. Comparison of Black and White patients revealed that significantly greater percentages of Black patients had a BMI ≥25.0 kg/m^2 (81.9 vs. 71.2%, P <0.001), a BMI ≥30.0 kg/m^2 (57.7 vs. 41.5%, P <0.001), an A1C >5.7% (75.7 vs. 69.7%, P = 0.022), diabetes (27.7 vs. 19.9%, P <0.001), hypertension (17.7 vs. 9.5%, P <0.001), CKD (6.2 vs. 3.4%, P <0.001), and sleep apnea (2.1 vs. 0.7%, P <0.001). The data also suggested that a smaller proportion of Black patients in this population had COPD, CAD, and cirrhosis compared with White patients. Associations of demographics and comorbidities with race are shown in Table 2.

Multivariate Regression Analysis of Patient Characteristics and Serious Outcomes

Multivariate logistic regression models were used to determine whether demographic and clinical factors were associated with the four outcomes (MV, ICU admission, death, and VTE). Each analysis was controlled for confounding variables, including age, sex, race, diabetes, BMI, and the eight additional comorbidities listed in STATISTICAL ANALYSIS. Results of multivariate regression analysis are shown in Table 3.

Age and male sex were significantly associated with all four outcomes. For age, odds ratios (ORs) indicated that for every 1-year increase in age, the odds of needing MV rose by a factor of 1.03 (95% CI 1.03–1.04, P <0.0001), being admitted to the ICU rose by a factor of 1.02 (95% CI 1.02–1.03, P <0.0001), dying rose by a factor of 1.08 (95% CI 1.07–1.09, P <0.0001), and developing VTE rose by a factor of 1.02 (95% CI 1.01–1.03; P <0.0001). Men were more likely to require MV (OR 2.02, 95% CI 1.70–2.41, P <0.0001), be admitted to the ICU (OR 1.82, 95% CI 1.56–2.13, P <0.0001), die (OR 1.82, 95% CI 1.52–2.19, P <0.0001), and develop VTE (OR 1.29, 95% CI 1.04–1.60, P = 0.0193).

Black patients had significantly greater odds of MV (OR 1.44, 95% CI 1.13–1.83, P = 0.0009) and ICU admission (OR 1.43, 95% CI 1.15–1.77, P = 0.0002), but not VTE, than White patients. Black patients had significantly lower odds of death than White patients (OR 0.77, 95% CI 0.60–0.97, P = 0.0200).

Diabetes was significantly associated with all four outcomes. The presence of diabetes was associated with

TABLE 2 Associations of Demographics and Comorbidities With Race in Patients With COVID-19 (N = 7,495)

	Black (n = 4,447)	White (n = 3,048)	P*
Age >50 years	2,556 (57.5)	1,846 (60.6)	0.008
Male sex	1,824 (41.0)	1,369 (44.9)	<0.001
Diabetes	1,233 (27.7)	606 (19.9)	<0.001
Hypertension	786 (17.7)	291 (9.5)	<0.001
CKD	275 (6.2)	103 (3.4)	<0.001
Sleep apnea	95 (2.1)	21 (0.7)	<0.001
COPD	75 (1.7)	75 (2.5)	0.019
CAD	146 (3.3)	152 (5.0)	<0.001
Stroke	58 (1.3)	36 (1.2)	0.638
HF	179 (4.0)	118 (3.9)	0.737
Cirrhosis	10 (0.2)	20 (0.7)	0.004
HIV	9 (0.2)	2 (0.1)	0.218
Active malignancy	167 (3.8)	121 (4.0)	0.635
	(n = 2,690)	(n = 1,779)	
At least overweight (BMI ≥25.0 kg/m^2)	2,202 (81.9)	1,267 (71.2)	<0.001
Obese (BMI ≥30.0 kg/m^2)	1,553 (57.7)	739 (41.5)	<0.001
	(n = 950)	(n = 399)	
A1C >5.7%	719 (75.7)	278 (69.7)	0.022

Data by racial group are n (%). *Two-group comparisons were performed with χ^2 test (or Fisher's exact test when expected cell counts were <5) to determine associations between race/ethnicity (categorized in EMRs as Black or White) and each variable. Statistical significance is determined if P <0.05.

MV (OR 2.0, 95% CI 1.68–2.38, P <0.0001), ICU admission (OR 2.01, 95% CI 1.72–2.36, P <0.0001), death (OR 1.50, 95% CI 1.25–1.80, P <0.0001), and VTE (OR 1.47, 95% CI 1.17–1.84, P = 0.0009). A1C >5.7% was also significantly associated with MV (OR 1.97, 95% CI 1.28–3.05, P = 0.0022) and ICU admission (OR 2.11, 95% CI 1.44–3.07, P = 0.0001) but not death or VTE.

Weight categories of being at least overweight (BMI ≥25.0 kg/m^2), obese (BMI ≥30.0 kg/m^2), and obese relative to overweight (BMI 25.0–29.99 kg/m^2) status were significantly associated with MV (OR 1.84, 95% CI 1.46–2.32, P <0.0001; OR 1.55, 95% CI 1.29–1.86, P <0.0001; and OR 1.31, 95% CI 1.07–1.61, P = 0.0096, respectively) and ICU admission (OR 1.34, 95% CI 1.10–1.63, P = 0.0036; OR 1.40, 95% CI 1.19–1.65, P <0.0001; and OR 1.36, 95% CI 1.12–1.64, P = 0.0017, respectively). However, none of the weight categories were associated with death or VTE.

Multivariate Regression Analysis of Inflammatory Markers and Serious Outcomes

Multivariate logistic regression models analyzed the presence of various inflammatory markers on the four outcomes in all patients, controlling for age, sex, race, diabetes, BMI, and the eight additional comorbidities listed in STATISTICAL ANALYSIS. Results of the multivariate logistic regression are in Table 4.

All inflammatory markers (D-dimer, ferritin, CRP, IL-6, and procalcitonin) were significantly correlated with

TABLE 3 Multivariate Regression Analysis of Characteristics of Patients With COVID-19 and Serious Outcomes

Variable	MV		ICU Admission		Death		VTE	
	OR (95% CI)	*P**	OR (95% CI)	*P**	OR (95% CI)	*P**	OR (95% CI)	*P**
Age, years	1.03 (1.03–1.04)	<0.0001	1.02 (1.02–1.03)	<0.0001	1.08 (1.07–1.09)	<0.0001	1.02 (1.01–1.03)	<0.0001
Male sex	2.02 (1.70–2.41)	<0.0001	1.82 (1.56–2.13)	<0.0001	1.82 (1.52–2.19)	<0.0001	1.29 (1.04–1.60)	0.0193
Black vs. White race	1.44 (1.13–1.83)	0.0009	1.43 (1.15–1.77)	0.0002	0.77 (0.60–0.97)	0.0200	0.95 (0.71–1.27)	>0.99
Diabetes	2.00 (1.68–2.38)	<0.0001	2.01 (1.72–2.36)	<0.0001	1.50 (1.25–1.80)	<0.0001	1.47 (1.17–1.84)	0.0009
At least overweight (BMI ≥25.0 kg/m^2)	1.84 (1.46–2.32)	<0.0001	1.34 (1.10–1.63)	0.0036	0.90 (0.74–1.11)	0.3205	0.91 (0.70–1.17)	0.4450
Obese (BMI ≥30.0 kg/m^2)	1.55 (1.29–1.86)	<0.0001	1.40 (1.19–1.65)	<0.0001	1.09 (0.90–1.32)	0.4010	1.13 (0.90–1.41)	0.3051
Obese (BMI ≥30.0 kg/m^2) vs. overweight (BMI 25.0–29.99 kg/m^2)†	1.31 (1.07–1.61)	0.0096	1.36 (1.12–1.64)	0.0017	1.17 (0.93–1.46)	0.1843	1.24 (0.94–1.62)	0.127

*Multivariate logistic regression controlled for age, sex, race, diabetes, BMI, hypertension, CKD, CAD, stroke, HF, COPD, sleep apnea, and active malignancy. Statistical significance was determined if P <0.05. †Results for obese versus overweight represent the odds of the outcome for those who are obese (BMI ≥30.0 kg/m^2) relative to the odds of the outcome for those who are overweight (BMI 25.0–29.99 kg/m^2).

risk of MV and death in all patients. All inflammatory markers except IL-6 were significantly correlated with ICU admission in all patients. D-dimer, CRP, and procalcitonin were associated with VTE in all patients, whereas IL-6 and ferritin were not.

Discussion

This retrospective cohort study of patients hospitalized with COVID-19 within a large health system in metropolitan Detroit showed that older age, male sex, Black race, diabetes, elevated BMI, and elevated inflammatory markers were correlated with critical illness in COVID-19. Older age, male sex, diabetes, and inflammatory markers, but not elevated BMI, were associated with mortality. Despite having greater odds of critical illness, Black patients had lower odds of death than White patients. Older age, male sex, diabetes, and elevated inflammatory markers were significantly associated with VTE.

Incidence of Poor Outcomes From COVID-19

Fewer than 10% of our study population was found to require MV or ICU admission, to be diagnosed with VTE, or to die. In contrast, the Centers for Disease Control and Prevention (CDC) estimated that 12% (age <50 years) to 21.6% (age >50 years) of patients with COVID-19 needed MV, 23.8% (age <50 years) to 35.7% (age >50 years) required ICU admission, and 2.4% (age <50 years) to 18.3% (age >50 years) died (3). Overall, VTE incidence is estimated to be 21% (6). The incidence of poor outcomes was lower that CDC estimates in our study, possibly because of earlier intervention with more effective therapies, the large proportion of patients <50 years of age, and effective transition of care from in-person to virtual. Our study included patients who were admitted a few months into the pandemic, when rapidly evolving treatment algorithms started to include regular use of corticosteroids, prone positioning in the ICU, anticoagulation therapy, and use of remdesivir. A large proportion (40%) of our study population was relatively young (<50 years of age), which may partially explain the lower incidence of severe outcomes. HFHS also has a well-established EMR system and had been offering virtual visits before the pandemic, resulting in a smooth and immediate transition to virtual outpatient visits and continued access to health care when the pandemic began, possibly contributing to improved management of comorbid conditions and lower incidence of poor outcomes.

TABLE 4 Multivariate Regression Analysis of Inflammatory Markers in Patients With COVID-19 and Serious Outcomes

Outcome	Inflammatory Marker	Unit Change	OR (95% CI)	*P*
MV				
	D-Dimer	1	1.06 (1.04–1.08)	<0.0001
	Ferritin	100	1.02 (1.01–1.02)	<0.0001
	CRP	1	1.07 (1.06–1.08)	<0.0001
	IL-6	10	1.02 (1.01–1.03)	0.0021
	Procalcitonin	1	1.03 (1.01–1.04)	<0.0001
ICU admission				
	D-Dimer	1	1.07 (1.05–1.08)	<0.0001
	Ferritin	100	1.01 (1.01–1.02)	<0.0001
	CRP	1	1.06 (1.05–1.07)	<0.0001
	IL-6	10	1.01 (1.00–1.02)	0.2506
	Procalcitonin	1	1.02 (1.01–1.03)	0.0003
Death				
	D-Dimer	1	1.06 (1.04–1.07)	<0.0001
	Ferritin	100	1.01 (1.01–1.02)	<0.0001
	CRP	1	1.05 (1.04–1.07)	<0.0001
	IL-6	10	1.01 (1.00–1.02)	0.0067
	Procalcitonin	1	1.04 (1.03–1.05)	<0.0001
VTE				
	D-Dimer	1	1.10 (1.08–1.12)	<0.0001
	Ferritin	100	1.00 (0.99–1.01)	0.3518
	CRP	1	1.02 (1.01–1.03)	0.0094
	IL-6	10	1.00 (1.00–1.00)	0.7546
	Procalcitonin	1	1.01 (1.00–1.03)	0.0201

Multivariate logistic regression models evaluated whether inflammatory markers (D-dimer, ferritin, CRP, IL-6, and procalcitonin) were associated with each outcome while controlling for age, sex, race, diabetes, BMI, hypertension, CKD, CAD, stroke, HF, COPD, sleep apnea, and active malignancy. In cases with multiple values for the same inflammatory marker during the hospital stay, the earliest value was used. If the inflammatory marker was measured multiple times on the earliest day, then the average value on the earliest day was used. Statistical significance was determined if $P < 0.05$.

Age and Outcomes From COVID-19

CDC data show that the risk of hospitalization and death from COVID-19 increases with age, starting even at 18 years of age, and that a striking increase in risk starts in the 65- to 74-year age range, with the highest risk noted for those ≥85 years of age (up to 8,700-fold higher risk) (7). Our data revealed increased odds of MV and ICU admission, death, and VTE per age year, corroborating the CDC data analysis and findings from studies reporting older age to be associated with higher risk of hospital admission (8,9), higher mortality (10–15), and risk of MV (11,16).

Comparisons between studies is difficult because of the heterogeneity of age categories and outcomes studied. Many studies adjusted for some confounders in their analyses, but usually fewer than in our study, perhaps resulting in the lower ORs we observed (1.03–1.08) relative to other studies in similar health care settings with a similar patient population (1.73–5.3) (11,15,17). The only meta-analysis specifically evaluating the effect of age on outcomes included 12 studies, all from China, and emphasized the importance of adjusting for confounders. These authors found significant bias in results and a marked decrease in the influence of age on COVID-19 disease severity and mortality after adjustment for important age-related risk factors (18). We controlled for 13 risk factors and still found a significant association of increasing age with severe disease and mortality.

The etiology of an age-related effect on poor outcomes in patients with COVID-19 has been described to be related to increasing baseline inflammation, possibly resulting from increasing levels of senescent cells with age. Senescent cells can activate endothelial cells lining capillaries in the lungs and increase expression of natural killer cell receptor ligands that recruit natural killer-

like T cells, which cause collateral lung destruction (19).

Male Sex and Outcomes From COVID-19

Male sex has been associated with higher risks of hospital admission and critical illness from COVID-19 (1.3–2 times greater) (8,13,20–22), as well as higher case fatality rate (1.46–1.7 times greater) than for women (16,20–25). Our results similarly found that male sex, controlling for multiple confounders, was significantly associated with all four severe outcomes (ORs 1.29–2.02).

Male predominance of deaths was also observed in previous epidemics from SARS-CoV and Middle East respiratory syndrome (26–28). Postulated underlying etiologies include sex-biased expression of the virus entry receptor angiotensin-converting enzyme 2 (ACE2) and regulation of cellular transmembrane serine protease 2 (the enzyme that primes the spike protein of the virus), which could increase the susceptibility of men to SARS-CoV-2 compared with women (25). Furthermore, differences based on sex may exist in innate immunity, possibly related to the location of immune regulatory genes on the second X chromosome and higher CD4+ lymphocytes (and therefore better viral clearance), higher antibody production, higher protective levels of estrogen, and lower production of inflammatory IL-6 in women compared with men (29).

Black Race and Outcomes From COVID-19

The literature to date provides strong evidence that Black patients have higher incidences of SARS-CoV-2 infection and hospitalization for COVID-19 compared with White patients. Data on severe outcomes and mortality in Black compared with White patients are less clear; some studies and meta-analyses have found an association of Black race with more severe disease (MV) (14) and COVID-19–related death (13,30–32) compared with White race, whereas other studies have not found any differences (14,33–35).

Our study includes a large percentage of Black patients (50%), consistent with the large Black population in Detroit (78.3%) (36). Our results suggested a significant association of Black race with critical illness, but not increased mortality, relative to White patients, adding to the mixed findings in the literature on this topic. The lack of association of Black race with higher mortality is similar to findings from three studies that had similar geographic and racial demographics to our study (56–72% Black patients in the Detroit metropolitan area) (15,17,37). In fact, our data suggested that Black patients had significantly lower odds of death than White patients, similar to results of a smaller study conducted at HFHS by Miller et al. (37).

In contrast to other studies, our study also looked at specific differences in the presence of comorbid conditions in Black compared with White patients, finding that Black patients had a significantly higher prevalence of elevated BMI, A1C >5.7%, diabetes, hypertension, CKD, and sleep apnea than White patients. Because we controlled for a variety of comorbidities and other variables (age, sex, race, diabetes, and BMI), the association between Black race and greater odds of critical illness relative to White race may be explained by other variables such as lower socioeconomic status and decreased access to health care or health insurance. We did not evaluate for these factors, but based on 2019 U.S. Census Bureau data for Detroit, 35% of people in this majority Black city are in poverty, and 9.6% of the population do not have health insurance (36), suggesting that socioeconomic hardships are prevalent and likely to contribute to poor health and outcomes.

Diabetes and Outcomes From COVID-19

High prevalence rates of diabetes (22–38.4%) have been found in patients hospitalized for COVID-19 in the United States and other countries (8,15,17,37–41), and meta-analyses have demonstrated that the prevalence of diabetes is higher in patients with more severe COVID-19 (42). Our study cohort had a similar diabetes prevalence (23.6%). Prevalence of A1C >5.7% in our study population was even higher (74.3%) among the 1,532 patients who had A1C measured. Reported rates of diabetes and prediabetes in the general U.S. population (10.5 and 34.5%, respectively) are lower than in studies of patients with COVID-19 (43), pointing to a likely relationship between diabetes and prediabetes and severe COVID-19.

The association of diabetes with critical illness and mortality in our study (ORs 1–2) is similar to reports in the literature of a 1.5- to 4.6-fold higher risk of mortality and a 2- to 2.7-fold higher risk of severe disease in patients with COVID-19 and diabetes than in COVID-19 patients without diabetes (10,40,44–52). Our results are consistent with those of previous smaller studies of shorter duration conducted in our health system (17,37). The results from a well-cited multicenter study of patients with diabetes who were hospitalized with COVID-19 in France did not find glycemic control to be

an independent predictor of mortality, which contrasts with our study and with published meta-analyses, but 20.3% required MV and 10.6% died as early as 7 days after admission, still suggesting an association of diabetes with poor outcomes (53).

Less has been published on prediabetes (A1C 5.7 to <6.5%) or A1C ≥5.7% and outcomes in COVID-19. Smaller studies with 184–453 patients found an association of prediabetes with MV, ICU admission, and mortality (54–56) and an association of A1C ≥5.7%, with higher markers of inflammation and coagulability and lower oxygen saturation (57). The presence of A1C >5.7% in our cohort was found to be associated with MV and ICU admission, but not death. A possible explanation for why elevated A1C was not found to be associated with mortality is that A1C cannot evaluate for glycemic variability and higher glucose levels seen during acute illness, both of which are known to contribute to poor outcomes. Elevated fasting plasma glucose levels have been found to be a better predictor of infection severity and mortality than A1C in COVID-19 patients (55). Comparing studies is difficult because of differences in A1C categories and cutoffs and measured outcomes. Our study differs from previous ones by its inclusion of a larger patient cohort (1,532 patients) who had A1C measured.

Postulated reasons for poor outcomes in COVID-19 in patients with elevated A1C and diabetes include the associations of diabetes with older age, other comorbidities, chronic inflammation, higher inflammatory markers, and a prothrombotic state (10,44,48). Higher levels of inflammation-related biomarkers (IL-6, erythrocyte sedimentation rate, CRP, serum ferritin, D-dimer, and fibrinogen) found in patients with COVID-19 and diabetes (58,59) may predispose to an inflammatory cytokine storm, impaired T-cell responses, lung injury, and possibly increased infectivity related to abnormal ACE2 expression and increased furin, all of which are potential underlying mechanisms of more severe COVID-19 in diabetes (60,61).

Our findings provide evidence to support greater diabetes screening and use of A1C to detect and allow earlier treatment of prediabetes and diabetes during the COVID-19 pandemic to prevent poor outcomes.

BMI and Outcomes From COVID-19

Studies of COVID-19 have described a prevalence of obesity in patients that ranges from 16.3% in Italy to 57.6% in Detroit (8,17,37–39,62–64). Higher obesity prevalence rates have been found in U.S. studies, especially in Detroit (17,37), as reported in our study, with 50.3% of patients in the obese range. Higher obesity prevalence in hospitalized COVID-19 patients than in the general U.S. and Michigan populations (42.4 and 36% in 2017–2018, respectively) (65) suggests an association of obesity with more severe disease. On the other hand, the prevalence of being merely overweight in hospitalized COVID-19 patients (21–37% in various studies; 27.5% in our study cohort) (8,53,66,67) has not been found to be much higher than the general population (31.1% in the United States in 2017–2018 [68] and 34.9% in Michigan in 2014 [69]).

Our results demonstrated that obesity and elevated BMI starting even at ≥25.0 kg/m^2 (overweight levels) were significantly associated with the need for MV and ICU admission, but not with death or VTE. Most published reports support the association of obesity with critical illness (MV, ICU admission, and acute respiratory distress syndrome) (8,39,40,53,67,70–74), but the association of being overweight with critical illness is less consistent, with only some studies finding a relationship of being overweight with MV (53,66), but not others (8,67,75). The relationship of higher BMI and death in COVID-19 patients is also not clear. Most studies, including a meta-analysis of 33 studies on obesity and COVID-19, the CORONADO (Coronavirus SARS-CoV-2 and Diabetes Outcomes) study of patients with diabetes and COVID-19, a recent Chinese study, and two large studies from New York, found an association of obesity with higher risk of death (8,53,66,67,70); however, several U.S. studies did not find obesity to be associated with mortality from COVID-19 (15,37,39,40). Being overweight was not found to be associated with higher risk of death in the few studies evaluating this weight category (8,66,67). Our results add to this variable literature, supporting the findings that obesity and elevated BMI starting even at the overweight category are associated with critical illness but not death. More research on the effects of weight and BMI on COVID-19 mortality needs to be done.

Molecular mechanisms linking obesity with poor prognosis from COVID-19 include *1*) alteration in adipose tissue resulting in a proinflammatory state with increased secretion of cytokines (monocyte chemoattractant protein-1, tumor necrosis factor-α, IL-1β, IL-6, and interferon-γ), contributing to risk of cytokine storm; *2*) upregulation of ACE2, the functional receptor for SARS-CoV-2, and dipeptidyl peptidase 4, another

potential SARS-CoV-2 receptor, facilitating virus entry and a severe inflammatory and immune response; and *3*) expression of furin, a priming protease for SARS-CoV-2 in vascular endothelial cells, which may contribute to inflammation, damage to vascular endothelium, and coagulopathy (76). Also, obesity negatively affects lung function through mechanical/restrictive means and excess inflammation (76).

Inflammatory Markers and Outcomes From COVID-19

Many studies, including several meta-analyses, have shown a relationship between higher levels of proinflammatory markers such as CRP, IL-6, erythrocyte sedimentation rate, procalcitonin, ferritin, and D-dimer and more severe disease and mortality from COVID-19 (8,39,44,77–83). However, not all studies have shown a strong correlation between inflammatory markers and clinical outcomes in COVID-19 (84,85). Our results added to the literature supporting the inflammatory state as a major mechanism of severe COVID-19.

Limitations

Our study has several limitations, including its retrospective design. The study population included only patients hospitalized for COVID-19 in one health care system. This cohort may have had additional risk factors for admission that were not measured in this study, such as socioeconomic status or work and home situations, all of which may contribute to severity of illness. Because patients admitted to the hospital tend to be sicker and to have comorbidities, the cohort may not be representative of the general population. Because data collected on patient clinical variables was based on *International Classification of Diseases*, 10th revision, diagnosis codes, some diagnoses may have been missed if the diagnosis or code was not entered for a patient. Data on BMI and A1C were not present for all patients, although we still had >5,000 patients with BMI recorded and >1,500 with A1C results. We used diagnosis of diabetes instead of elevated A1C, as this method captured more patients with diabetes. Analysis by A1C should be further investigated in large observational studies because of the potential for gathering incomplete data and potential skewing of results, since A1C tends to be measured only in those predicted to have high levels.

Conclusion

This large retrospective study identified older age, male sex, Black race, diabetes, elevated BMI, and elevated inflammatory markers as potential risk factors for severe COVID-19. Our findings emphasize the need to *1*) better identify patients with prediabetes and diabetes through screening with A1C, *2*) check for elevated BMI in all patients, and *3*) more aggressively address and treat these conditions to reduce risk. The urgency to identify and address diabetes and elevated BMI during and after the pandemic is evident from data indicating that 42% of adults gained almost 30 lb, and almost half delayed or canceled health care services during the pandemic (86). Recently published recommendations for the management of diabetes and obesity during COVID-19 can help providers mitigate risk (87,88). Furthermore, our results indicate a need to work to reduce disparities in health care for Black patients. Increasing the use of telemedicine may help to improve health care equity and reduce barriers. Vaccinations are also now widely available and should be encouraged for those at risk for severe COVID-19, given current lack of definitive treatment for this new infectious disease.

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DUALITY OF INTEREST

No potential conflicts of interest relevant to this article were reported.

AUTHOR CONTRIBUTIONS

J.H. researched the data, contributed to writing the manuscript, and reviewed the manuscript. E.T. contributed to the statistical analysis of the data and reviewed and edited the manuscript. S.W.L. researched the data, wrote the manuscript, and reviewed and edited the manuscript. S.W.L. is the guarantor of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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