Association of Black Race with Outcomes in COVID-19 Disease: A Retrospective Cohort Study

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To the Editor:

Coronavirus disease-2019 (COVID-19) is an emergent threat to public health resulting from the novel coronavirus - Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). The World Health Organization officially declared COVID-19 as a pandemic on 3/12/2020[1].

Average global COVID-19 mortality is estimated at 4.0% but has varied significantly across countries[2]. Inpatient mortality, as high as 28% in early reports from China and Italy, has driven worldwide efforts to identify poor prognostic factors[3,4]. Initial studies suggest older age and male sex are associated with COVID-19 infection and hospital mortality[4-8]. Similarly, comorbidities, including hypertension, diabetes, and chronic lung disease, have been associated with poor outcome[3,7,9-11].

The US Centers for Disease Control and Prevention provided the first study examining race, which suggested that Black patients were disproportionately over-represented in hospitalized COVID-19 cases. However, data for COVID-19 mortality and cases not requiring hospitalization were lacking[12]. As over-representation of Blacks and other racial/ethnic minorities persists among infected, hospitalized, and deceased COVID-19 patients,[13-18] we performed a retrospective cohort analysis to examine the association of race with SARS-CoV-2 infection and outcomes.

Methods

Study design, setting, and data sources. All patients who underwent nasopharyngeal swab and SARS-CoV-2 PCR assays after clinical screening (1/1/2020-4/15/2020) at the University of Chicago were included in this retrospective analysis. As no privacy-sensitive data was utilized,

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patient consent was not required (IRB waiver#IRB20-0520). Survival status was imputed from the most recent electronic medical records. All de-identified data were obtained from SEE Cohorts from the Center for Research Informatics. Demographic information included age, self-identified sex, ethnicity, race, and partial home zip code. Individuals older than 90years were assigned a maximum age of 90 for analysis (n=41); one patient was excluded due to missing sex.

Statistical analysis. Data processing and analysis were performed using R statistical computing software (R-Foundation, v.3.6.3, Austria) and Stata (StataCorp 2019.R.16, TX, USA). Variable comparisons were determined by two-sided T-tests, Mann–Whitney U tests, or chi-square tests as appropriate. Logistic regression models were fitted for outcomes assessment in univariate analyses, and results were assessed for robustness to analytical technique by reanalyzing the main outcomes with multivariable logistic regression (using age, sex, ethnicity, and zip code as covariates). Additional sensitivity analyses were performed using Poisson generalized linear models with maximum likelihood estimation.

We performed additional analyses to improve the generalizability of our findings beyond age-specific adjustments in multivariable models. Recognizing that our cohort was skewed towards older patients, we utilized age proportions from the 2000 US Census to derive an age-adjusted dataset[19]. Combining SARS-CoV-2 positivity rates with reference population proportions allowed us to examine observed and expected differences among patients stratified by age group and race. We evaluated the population-derived age-adjusted SARS-CoV-2 infection rates, which enabled the prediction of the largest affected age-group in the US population.

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Results

Cohort demographics. Of 4413 individuals in our cohort, 17.8% tested positive, 57.6% were Black, and 24.3% were White (Table.1). SARS-CoV-2 positive individuals were more likely to be male (20.1% vs. 16.5%, *P*=0.003), older (52.0yrs vs. 44.5yrs, *P*<0.0001), and Black (24.3% vs. 8.9%, *P*<0.0001); however, SARS-CoV-2-positive Black patients were disproportionately female (62.5% vs 51.2%, *P*=0.01) all consistent with published data[6,9,18]. Overall mortality differed between Black and non-Black subjects (1.9% vs 0.8%, *P*=0.002).

Clinical association of COVID-19 disease with outcomes. SARS-CoV-2 positive subjects had a higher fatality rate when compared to SARS-CoV-2 negative subjects overall (2.5% vs. 1.2%; *P*=0.005), and amongst those hospitalized (6.0% vs. 1.2%; *P*<0.0001). There were no observed sex or racial differences in mortality among all SARS-CoV-2-positive patients in the entire cohort (*P*=0.48 and *P*=0.34, respectively). Analyses using univariate logistic regression models demonstrated that Black race was associated with SARS-CoV-2 infection (OR=3.30, 95%CI 2.75–3.97) and hospitalization (OR=3.77, 95%CI 2.38–5.99) but not mortality. These results remained consistent in multivariable logistic regression models (OR=2.16, 95%CI 1.73–2.70, and OR=1.51, 95%CI 1.03–1.05, respectively; Table.2), and in sensitivity analyses with Poisson generalized linear models using maximum likelihood estimation (data not shown).

Age-adjusted SARS-CoV-2 infection rates in black and non-black patients. SARS-CoV-2 infection rate was 10-fold higher among subjects aged 30-50yrs than for those aged 0-18yrs (0.05 vs. 0.005; Figure 1). Age-adjusted SARS-CoV-2 positive rate (0.14) remained higher in Blacks compared to non-Blacks (0.19 vs. 0.07).

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Discussion

Our study examines the association of race with SARS-CoV-2 infection, hospitalization, and mortality among all subjects tested for SARS-CoV-2. These data suggest that Blacks are more likely to test positive and be hospitalized with SARS-CoV-2; however, we found no difference in mortality for Blacks vs non-Blacks. Possible hypotheses for these disproportionally high rates among Blacks include disparities in predisposing medical conditions, health insurance status, and access to medical care. Although we adjusted for residential zip code, we were unable to adjust for preexisting inequities of socioeconomic status and other critical social determinants of health, which could account for these findings[17,20]. Crowded home settings, care facilities for the elderly, over-representation in lower-wage public service occupations, and underlying comorbidities could conceivably increase the susceptibility of Black subjects to SARS-CoV-2 infection, raising the pre-test probability of death from severe COVID-19. Despite this higher risk, the absence of actual racial differences in mortality may imply that our conceptual categories of race reflect health care disparities and environmental risk factors more closely than any perceived biological differences[21].

Our study was limited by unavailable datapoints such as socioeconomic status, health insurance, comorbidities, and medication history, which could have enabled us to test the independent association of these outcomes with Black race, and fully assess potential confounders. While these factors may at least partially account for the observed disparities in infection and hospitalization rates, they are also highly co-linear, posing substantial challenges to any risk determination of race as an independent factor in outcomes. Also, as race and ethnicity are complex socially-defined constructs that are inherently imprecise, individually self-

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identified race may evolve or have different connotations that could impact the reliability of assignment to racial/ethnic categories in the larger population[22,23]. Additionally, our reliance on the electronic medical record for vital status verification may have underestimated mortality for patients treated outside of our health system. However, this systemic bias would not be expected to affect our final results.

Further, as individuals tend to associate more frequently with others of the same race, socioeconomic status, geographical location, and age, screening close contacts of persons with COVID-19 for SARS-CoV-2 positivity would likely violate statistical assumptions of independence for any associations of race with outcomes. Also, while most subjects in our cohort were from the greater Chicago area, the proportion of Blacks in our cohort (57.6%) substantially exceeds that of Chicago (30.1%) and the US (13.4%)[24]. However, as access to care is generally lower for Blacks, these subjects are likely to be sicker and undergo testing at a higher threshold than Whites. Importantly, our results, which project a total SARS-CoV-2 infection rate of 140 per 1000 patients, and mostly affects Blacks, could guide decision-making in COVID19 testing and health policy.

In conclusion, Black race was associated with SARS-CoV-2 infection and hospitalization. These findings may support the prevalence of racial disparities of health that disproportionately affect Blacks in the United States.

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Table 1. Demographic summary of patient cohort.

	SARS-CoV-2 Positive (n=785)	**SARS-CoV-2 Negative (n=3628)**	**Total (n=4413)**
Male, n (%)	313 (20.1)	1242 (79.9)	1555
Female, n (%)	472 (16.5)	2386 (83.5)	2858
Age, mean±SD, years	52.0±17.7	44.5±18.5	45.8± 8.6
Race (%)			
Black	619 (24.3)	1924 (75.7)	2543
White	75 (7.0)	996 (93.0)	1071
Asian/Mideast Indian	16 (8.7)	168 (91.3)	184
Native Hawaiian/Other Pacific Islander	0 (0)	6 (100)	6
American Indian or Alaska Native	0 (0)	5 (100)	5
More than once Race	26 (21.7)	94 (78.3)	120
Declined	4 (7.3)	51 (92.7)	55
Unknown	32 (13.0)	215 (87.0)	247
Not available	13 (7.1)	169 (92.9)	182
Ethnicity (%)			
Hispanic or Latino	25 (9.8)	229 (90.2)	254
Not Hispanic or Latino	705 (19.3)	2955 (80.7)	3660
Declined	4 (7.7)	48 (92.3)	52
Not available	18 (9.1)	179 (90.9)	197
Unknown	33 (13.2)	217 (86.8)	250

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Table 2. Univariate and Multivariable logistic regression analyses of SARS-CoV-2 infection and all-cause mortality

Patient Characteristic	**SARS-CoV-2 Infection**			**Mortality among SARS-CoV-2-positive**		
SARS-CoV-2 infection and mortality[a]	Odds Ratio (95% CI)	Adj Odds Ratio (95% CI)	*P*-value	Odds Ratio (95% CI)	Adj Odds Ratio (95% CI)	*P*-value
Black Race	3.30 (2.75-3.97)	2.16 (1.73-2.70)	<0.001	2.46 (0.56-10.69)	1.01 (0.20-5.04)	0.99
Age (continuous)	1.02 (1.01-1.03)	1.01 (1.00-1.01)	0.01	1.07 (1.03-1.10)	1.05 (1.02-1.09)	0.001
Sex (male)	1.27 (1.09-1.49)	1.01 (0.83 - 1.22)	0.96	1.52 (0.63-3.71)	1.22 (0.48-3.11)	0.68
Ethnicity (Hispanic)	0.49 (0.32-0.74)	1.00 (0.61-1.63)	0.99	---	---	0.48
Zip Code (606)[b]	1.98 (1.63-2.41)	1.20 (0.96-1.52)	0.11	2.02 (0.46-8.79)	1.05 (0.22-5.10)	0.95
Hospitalization	---	---	0.94	8.29 (2.74-25.05)	4.67 (1.46-14.91)	0.01
	Hospitalization in SARS-CoV-2-positive			**Mortality in Hospitalized SARS-CoV-2-positive**		
SARS-CoV-2 hospitalizations and hospital mortality[a]	Odds Ratio (95% CI)	Adj Odds Ratio (95% CI)	*P*-value	Odds Ratio (95% CI)	Adj Odds Ratio (95% CI)	*P*-value
Black Race	3.77 (2.38-5.99)	1.51 (1.03-1.05)	<0.001	0.68 (0.14-3.18)	0.68 (0.12-3.72)	0.66
Age (decile)	1.04 (1.03-1.05)	1.04 (1.03-1.05)	<0.001	1.04 (1.01-1.08)	1.04 (1.01-1.08)	0.001
Sex (male)	1.95 (1.44-2.63)	2.25 (1.62-3.13)	<0.001	1.28 (0.46-3.53)	1.34 (0.47-3.84)	0.58
Ethnicity (Hispanic)	0.48 (0.18-1.3)	1.44 (0.46-4.51)	0.53	---	---	0.99
Zip Code (606) [b]	2.38 (1.53-3.7)	1.51 (0.93-2.46)	0.10	0.82 (0.18-3.79)	0.72 (0.14-3.81)	0.70

Abbreviations: Adj=adjusted/multivariable model with adjustments for covariates.

[a]Adjusted/multivariable models include race, age, sex, ethnicity, partial zip code of residence, hospitalization status, and SARS-CoV-2 positive status.

[b]Denotes geographic boundary roughly equivalent to the City of Chicago.

All p-values depicted were for adjusted odds ratios and were two-sided; a level of 0.05 was considered statistically significant.

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Figure Legend:

Figure 1. Comparison of SARS-CoV-2 infection rates. Dot plots of observed and age-adjusted SARS-CoV-2 infection based on race. Observed (circles) and age-adjusted (squares) infection rates in Black (filled black circles/squares) and non-Black cohort patients (white open circles/squares).

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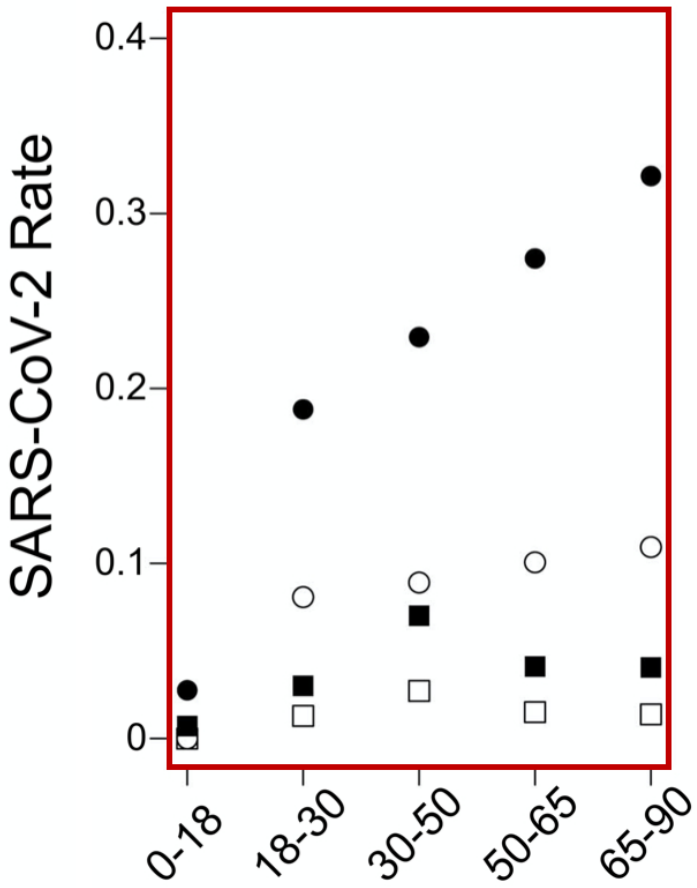

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