RESEARCH ARTICLE

Outcomes of Covid 19 patients—Are Hispanics at greater risk?

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Abstract

Disparities in outcomes exist in outcomes of coronavirus disease-19 (COVID-19). Little is known about other ethnic minorities in United States. We included all COVID-19 positive adult patients (≥18 years) hospitalized between March 1, 2020 and February 5th 2021. We compared in hospital mortality, use of intensive care unit services and inflammatory markers between non-Hispanic whites with non-White/Black Hispanic. Multivariable Cox proportional Hazard models were used to adjust for differences between the two groups. There were 4059 hospital admissions with COVID-19 in the study period. Of the 3288 White, 789 (24%) required intensive care unit (ICU) admission in comparison to 187 (24.3%) of the 770 Hispanics. Unadjusted mortality was higher in Whites than Hispanics (17.1% vs. 10.7%; $p < 0.001$). After adjusting for confounding variables, in-hospital mortality was not statistically different for Whites in comparison to Hispanics (hazard ratio [HR]: 0.96, 95% confidence interval [CI]: 0.76–1.21, $p = 0.73$). The adjusted rates of ICU transfers were significantly higher in Hispanics (HR: 1.34, 95% CI: 1.11–1.61, $p = 0.002$). Hispanics had significantly higher C-reactive protein, lactate dehydrogenase, and fibrinogen when compared to Whites. Hispanics as compared to Whites with COVID-19 require higher rates of ICU admission but have a similar mortality. Hispanics as compared to Whites with COVID-19 require higher rates of ICU admission but have a similar mortality.

KEYWORDS
COVID-19, disparities, Hispanic

1 | BACKGROUND

Rapid global spread of the severe acute respiratory syndrome coronavirus 2 epidemic has highlighted racial and ethnic disparities in outcomes from this disease.[1] Whether these disparities are driven by geographical location, differential risk of exposure to the virus, genetic variations, burden of comorbid conditions, differences in

socioeconomic determinants of health or a combination of these factors is currently unclear.[2-7]

Recent data from the United States (US) and United Kingdom suggest that Black, Asian, and minority ethnic groups have disproportionately higher hospitalization rates and risk of death from coronavirus disease-19 (COVID-19).[8-11] While there is a preponderance of clinical and outcome data comparing black cohorts to

their white counterparts, little is known about other ethnic minorities in the United States.[12-14]

One plausible biological explanation for these differences is variation of the inflammatory host response by ethnicity.[15,16] As an example, investigators have reported that the 3p21.31 gene cluster may predispose COVID-19 patients to the development of acute respiratory failure.[17] A surrogate window to the assessment of inflammation is the use of markers such as ferritin, C-reactive protein (CRP) and D-dimers which are both routinely measured at the bedside and have prognostic significance in COVID-19.[18]

The Northeast Georgia Health System serves a large population of non-White Hispanics. We, therefore, sought to compare ethnic differences in clinical characteristics and outcomes amongst non-Hispanic Whites and non-White/Black Hispanics hospitalized with COVID-19. We reasoned that the differences would likely be most apparent in the sicker subset of COVID-19 patients and, therefore, also analyzed persons requiring intensive care unit (ICU) admission as a separate cohort. We hypothesized that there would be significant variation in markers of inflammation by ethnicity.

2 | METHODS

2.1 | Study design and data source

We performed a retrospective analysis of prospectively collected data of all adult COVID-19 patients (age ≥18 years) admitted to a large community hospital in a rural setting in Northeast Georgia between March 1st, 2020 and February 5th, 2021. COVID-19 patients were identified using positive PCR COVID testing. We obtained clinical and demographical details of patients from Epic® Caboodle data warehouse and Cerner APACHE® Outcomes. Systems integration was provided by IPC Global and we leveraged their in-Process Data Factory innovation running on an AWS® VPC. The study was reviewed and found exempt by the Northeast Georgia Health System IRB.

2.2 | Inclusion and exclusion criteria

We included all hospitalized COVID-19 positive adult patients (age 18 years and above) who were either non-Hispanic Whites or non-White/Black Hispanics. We only considered the initial hospitalization for COVID-19, readmissions were excluded from our analysis.

2.3 | Outcomes

Our primary outcome of interest was in hospital mortality. We also compared levels of inflammatory markers (ferritin, CRP, lactate dehydrogenase [LDH], fibrinogen and D-dimer) among the two ethnicities. Additionally, for persons who required ICU admission, we compared rates of mechanical ventilation, vasopressor use and renal replacement therapy which reflect intensity of ICU care.

2.4 | Statistics

We performed all statistical analysis using STATA MP 16.0 (Stata-Corp.). We describe categorical data using frequency count and percentages. We report means and SD or medians and interquartile ranges for continuous variables as appropriate for their distribution. We used Chi square tests and Wilcoxon Rank tests to compare categorical and continuous variables, respectively. For all analyses we deemed statistical significance a p value <0.05.

For the primary outcome of mortality, we performed time to event analysis and used the log rank test for equity of survivor function. Time to event was calculated from date of hospital admission and right censored on February 5th, 2021. We then constructed multivariable cox regression model to determine the independent association of race with in-hospital mortality. Missing values of inflammatory markers were present in less than 25% of cases and we imputed median values for these in regression models. First, we tested univariate association of putative risk factors with mortality. Variables that were associated with mortality at a p value of <0.1 were candidates for inclusion in our final model. We then used the backward elimination method and kept variables that were significant at a p value of <0.05. Variables previously known to be associated with mortality were kept in the model regardless of their significance. The model was then boot-strapped using 2000 bootstrap replicates and case resampling with replacement from the original dataset.

Similarly, we developed multivariable logistic regression models to determine the association of race with likelihood of ICU admission, receipt of mechanical ventilation, vasopressor requirement and acute kidney injury (AKI) requiring hemodialysis. We performed competing risk analysis to reduce effect of patients who died before requiring these outcomes. We also performed linear regression to determine the association of race with inflammatory markers; for these models we log transformed (natural logs) the markers as they were not normally distributed. For D-dimer we used deciles as we were unable to normalize its distribution.

3 | RESULTS

There were 4059 hospital admissions with COVID-19 in the study period. Of the 3288 White, 789 (24%) required ICU admission in comparison to 187 (24.3%) of the 770 Hispanics.

3.1 | Overall characteristics and outcomes

Whites were significantly older (mean age 70 vs. 51; $p < 0.001$) than Hispanics. The proportion of males were similar in both groups. Whites had numerically higher rates of obesity, hypertension, congestive heart failure, chronic obstructive pulmonary disease, cirrhosis, venous thromboembolism, and cancer while Hispanics had higher rates of ESRD (Table 1). During hospitalization Hispanics more often

TABLE 1 Demographical and clinical characteristics of COVID-19 patients

	White	Hispanic	p
Total	**3289**	**770**	
*Age in years, median (IQR)	70 (58–79)	51 (37–63)	<0.001
Male (%)	52.7	51.7	0.63
*BMI, median (IQR)	29.7 (25.4–35.4)	30.5 (27.3–36)	0.0003
Co-morbidities (%)			
Hypertension	77.5	46.9	<0.001
Congestive heart failure	33.4	12.0	<0.001
Diabetes Mellitus	44.1	40.6	0.08
HbA1c >10	19.4	17.5	0.23
COPD	40.2	19.0	<0.001
ESRD	2.8	5.8	<0.001
Cirrhosis	12.9	9.7	0.015
Cancer	14.7	6.9	<0.001
Venous thromboembolism	6.8	2.1	<0.001
Medications at home (%)			
On anticoagulation	14.1	2.9	<0.001
On Aspirin	17.6	15.5	0.16
On Plavix	6.1	2.5	<0.001
On ACEI or ARB	31.1	20.4	<0.001
On beta blockers	32.8	13.9	<0.001
On statin	32.9	19.1	<0.001
COVID-19 medications (%)			
Vitamin C	81.5	78.6	0.06
Vitamin D	26.0	16.5	<0.001
Thiamine	7.7	3.9	<0.001
Ivermectin	4.6	3.3	0.10
Zinc	80.8	78.3	0.11
Hydroxychloroquine	3.4	12.7	<0.001
Tocilizumab	4.8	10.6	<0.001
Steroids	70.2	55.7	<0.001
Convalescent plasma	25.9	24.6	0.41
Remedesivir	56.7	47.7	<0.001
Anticoagulation	75.0	74.5	0.84
SOFA score at admission	1 (0–2)	0 (0–1)	<0.001

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; ESRD, end stage renal disease; IQR, interquartile range.

*Median (interquartile range), number of samples.

received hydroxychloroquine and tocilizumab while whites received remedesivir and steroids more often.

SOFA score on admission were higher in whites, however, markers of inflammation were significantly higher in Hispanics. This included ferritin, CRP, LDH and fibrinogen (Appendix: Tables S1 and S2). D-dimer was higher in whites. The highest level of inflammatory markers during the hospital stay were also significantly higher in Hispanics except for the D-dimer. This difference persisted when different age groups were compared (Appendix: Table S4).

3.2 | ICU characteristics and outcomes

There was no difference in the proportion of persons requiring ICU admission amongst White or Hispanics. However, Hispanics were significantly younger, and a larger proportion were men (Table 2). Although there was no difference in the proportion of persons receiving mechanical ventilation and time to mechanical ventilation, Hispanics had poorer PF ratio (53 vs. 64, p < 0.001) and a greater proportion of Hispanics required paralytic (52.6% vs. 27.7%, p < 0.001) and inhaled pulmonary vasodilator therapy (20.6% vs. 7.2%, p < 0.001). Similarly, the average length of mechanical ventilation was greater in Hispanics (13 vs. 6 days, p < 0.001).

Unadjusted mortality in the entire cohort was higher in Whites than Hispanics (17.1% vs. 10.7%; p < 0.001). Similarly, the proportion of persons who transitioned to comfort measures was greater in Whites (5.8% vs. 1.3%, p < 0.001). Of the survivors, a larger proportion of Hispanics were discharged home while the proportion requiring home health care or acute care facilities was larger in Whites (Table 3).

3.3 | Adjusted analysis

After adjusting for confounding variables, in-hospital mortality for the entire cohort as well as those admitted to the ICU was no different for Whites in comparison to Hispanics (hazard ratio [HR]: 0.96, 95% confidence interval [CI]: 0.76–1.21, p = 0.73) for entire cohort and (HR: 0.94, 95% CI: 0.71–1.25, p = 0.68) for ICU admissions) (Table 4). Variables associated with increased in-hospital mortality in COVID-19 patients included age, use of vasopressors and ferritin and LDH levels. Variables associated with lower mortality were use of remedesivir and tocilizumab.

The adjusted rates of ICU transfers were significantly higher in Hispanics (Appendix: Table S3). The adjusted likelihood for use of mechanical ventilation, vasopressor was also higher in Hispanics, though use of mechanical ventilation did not reach significance. Use of hemodialysis for newly diagnosed AKI was not different between the two groups. However, inflammatory markers like CRP, LDH and fibrinogen were significantly higher in Hispanics even after adjusting

TABLE 2 Demographical and clinical characteristics and outcomes of COVID-19 patients admitted in ICU

	White	Hispanic	p
Total number requiring ICU stay	**789 (24%)**	**187 (24.2%)**	
SOFA score at ICU admission[a]	1 (0–3)	1 (0–4)	0.24
Age in years, median (IQR)	70 (60–77)	56 (46–64)	<0.001*
Male (%)	58.2	68.5	0.01
BMI, median (IQR)	30.6 (26.2–36.5)	30.5 (27.3–36.6)	0.42
Days from Hospital admission to ICU transfer[a]	0.29 (0.09–1.82)	0.33 (0.14–1.78)	0.14
Use of mechanical ventilation, N (%)	361 (45.8%)	97 (51.9%)	0.19
Length of mechanical ventilation (in days)[a]	6 (2–14)	13 (6–26)	<0.001*
Lowest PF ratio	64 (50–101)	53 (44–66)	<0.001*
Paralytic (%)	27.7	52.6	<0.001*
Inhaled vasodilator (%)	7.2	20.6	<0.001*
Tracheostomy (%)	14.1	19.6	0.19
Use of vasopressors (%)			
Required norepinephrine	45.6	48.7	0.42
Required vasopressin	21.7	25.1	0.31
Required epinephrine	8.9	11.2	0.32
Required angiotensin2	1.3	3.2	0.06
Required dobutamine	4.3	7.0	0.13
Central lines	30.5	40.0	0.018
Died (%)	42	32.1	0.013
Hospice (%)	7.5	3.2	0.035
Disposition (%)			<0.001
Home	40.0	71.6	
Home with health	28.7	13.4	
Rehab/SNF/LTAC/ acute care	25	11.8	
Others	6.4	3.2	
Readmissions	13.3	10.2	0.35

Abbreviations: ICU, intensive care unit; IQR, interquartile range.
[a]Median (interquartile range).
*p < 0.05.

TABLE 3 Outcomes and complications in covid-19 patients—according to races

Outcomes	Whites	Hispanics	p
Total	3289	770	
Complications (%)			
Acute kidney injury	15.5	14.8	0.63
Acute kidney injury requiring hemodialysis	2.3	2.3	0.88
Atrial fibrillation	20.6	4.3	<0.001
Acute DVT	3.1	3.3	0.80
Acute PE	2.5	1.6	0.13
Acute stroke	2.7	2.7	0.10
Acute intra cranial hemorrhage	1.3	1.2	0.81
Chest tube for pneumothorax	2.2	2.9	0.29
Transfusion—PRBC	9.0	9.0	0.97
Died (%)	17.1	10.7	<0.001
Hospice (%)	5.8	1.3	<0.001
LOS in survivors, median days (IQR)	5 (3–9)	5 (3–8)	0.04
Time to death, median days (IQR)	10 (5–18)	15.5 (6–22)	0.007
Disposition (%)			<0.001
Home	59.6	87.9	
Home with health	21.6	6.3	
Rehab/SNF/LTAC/acute care	15.9	3.6	
Others	2.9	2.2	
Subsequent readmissions in survivors, n (%)	408 (15%)	54 (7.9%)	<0.001
Subsequent deaths during the readmissions, n (%)	101 (21.9%)	11 (19.3%)	0.65

Abbreviations: ICU, intensive care unit; IQR, interquartile range.

for age, gender, co-morbidities and use of COVID-19 medications (Appendix: Table S3). The adjusted levels of ferritin and D-dimer were similar in both groups.

4 | DISCUSSION

In a rural population in Northeast Georgia, we observed that Hispanic admissions for COVID-19 comprised of significantly younger persons as compared to Whites. Despite being younger, proportions requiring mechanical ventilation were like Whites although the severity of respiratory failure was more severe and length of mechanical

TABLE 4 Comparison of in hospital mortality between Hispanics and Whites in Covid-19

		Hazard ratio	95% Confidence interval	p
Model 1	Hispanics vs. White	0.59	0.47–0.75	<0.001
Model 2	Hispanics + age	0.97	0.76–1.23	0.81
Model 3	Hispanics + gender	0.59	0.47–0.75	<0.001
Model 4	Hispanics + inflammatory markers	0.60	0.47–0.76	<0.001
Model 5	Hispanics + co-morbidities	0.72	0.56–0.92	0.009
Model 6	Hispanics + Covid-19 medications	0.68	0.53–0.86	0.002
Model 7	Hispanics + mechanical ventilation, vasopressors, renal failure with hemodialysis, DVT, stroke	0.55	0.43–0.70	<0.001
Model 8	Hispanics + all the above variables	0.96	0.74–1.23	0.75
Model 9	Model 8 Bootstrapped 2000 times	0.96	0.76–1.21	0.73
Model 10	Hispanics + 4 C score	0.94	0.74–1.19	0.61

Note: White is the comparison group.

ventilation longer in Hispanics. These observations were accompanied by findings of significantly greater elevations of inflammatory markers in Hispanics as compared to Whites despite lower SOFA scores. Although mortality rates were higher in Whites, the differences were no longer apparent once we accounted for the older age of White patients.

Similar proportions of the White and Hispanic cohorts receiving invasive mechanical ventilation is counterintuitive because one would expect that rates would be lower in the younger Hispanic population with significantly lesser comorbidities than Whites. Our findings also suggest that the severity of respiratory failure and subsequent intensity of ICU care is greater in Hispanics than Whites as evidenced by higher use of paralytic agents and longer durations of mechanical ventilation in Hispanics. Moreover, these findings once adjusted for age did not result in mortality differences between the two ethnic cohorts.[9,11] It is possible that, resiliency associated with younger age counteracts greater severity of illness, confers protection, aids recovery and improves outcomes. It is also plausible that reasons such as social and structural vulnerabilities such as access to healthcare and other socioeconomic determinants may lead to delays in presentation in the Hispanic population which in turn delay early therapy causing clinical deterioration.[19] Socioeconomic determinants and differential access to healthcare rather than biological susceptibilities are known to drive disparities in outcomes in other time sensitive diseases.

Though we report our experience with over 4000 covid-19 patients, our study has important limitations. First, ours is a single center study with population mix of rural Georgia. This limits its generalizability, and it is difficult to extrapolate our results to other geographical areas which may have different demographic profiles, socio economic status and support systems available in community. Second, the retrospective nature of the study prevents us from drawing any causative conclusions. Third residual confounding may

have prevented capture of important unknown factors that affect differences in outcomes between ethnicities. Fourth, there were about 25% missing values with respect to the inflammatory markers. These may have affected the precision of our estimates.

5 | CONCLUSION

Despite these limitations we show that in a single rural health system in Northeast Georgia Hispanics as compared to Whites with COVID-19 are younger, require higher rates of ICU admission but have a similar mortality.

AUTHOR CONTRIBUTIONS
Gagan Kumar: study design, data analysis, manuscript writing. **Mark Meersman:** data validation. **Drew Dalton:** data validation. **Dhaval Patel:** study design, manuscript writing. **Ankit Sakhuja:** Study design, data analysis, manuscript writing. **Achuta Kumar Guddati:** study design, data analysis, Manuscript writing. **Rahul Nanchal:** study design, data analysis, manuscript writing.

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SUPPORTING INFORMATION

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