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Racial Disparities in Ischemic Stroke Among Patients with COVID-19 in the United States

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Background: Cerebrovascular prevalence is high in patients with coronavirus disease 2019 (COVID-19). However, whether racial disparities exist among this population have not been systematically explored. Methods: We performed a retrospective study to assess the prevalence of stroke stratified by race among patients aged 18 years or older with COVID-19 who visited emergency department (ED) up to August 13, 2020 in the United States (US). We used multivariable logistic regression to compare the odds of stroke in Black patients with COVID-19 compared to their non-Black counterparts while adjusting for the major potential confounders. Results: Among 8815 patients with ED visits with COVID-19, 77 (0.87%), 95% confidence interval CI: 0.69% to 1.10%) had ischemic stroke. The mean age of patients with stroke was 64 years (SD: 2 years); 28 (43%) were men, 55 (71%) had hypertension, and 29 (50%) were Black. The prevalence of ischemic stroke in Blacks, non-Hispanic Whites and Hispanics was 1.26% (95% CI: 0.86% to 1.83%), 0.84% (95% CI: 0.51% to 1.37%) and 0.49% (95% CI: 0.26% to 0.88%) respectively. After adjustment for age, sex, hypertension, diabetes, obesity, drinking and smoking, the likelihood of stroke was higher in Black than non-Black patients (adjusted odds ratio, 2.76; 95% CI, 1.13 to 7.15, p=0.03). Conclusions: Racial disparities in the prevalence of stroke among patients with COVID-19 exist, higher in Black population.

Key Words: COVID-19—Ischemic stroke—Racial disparity

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Background

Since coronavirus disease 2019 (COVID-19) first appeared as a respiratory illness in Wuhan, China in December 2019, there has been increasing acknowledgement of a COVID-19-associated coagulopathy (CAC) that predisposes patients to arterial thrombotic events such as ischemic strokes.1,2 For example, in a retrospective cohort of 1916 COVID-19 patients visiting the ED in two academic hospitals in New York City, New York, 1.6% had an acute ischemic stroke vs. only 3 of 1486 (0.2%) patients with influenza.3 In patients with COVID-19, strokes can occur as the presenting symptom of COVID-19 or later in the course of hospitalization, with averages of presentation ranging from 11.5 days to 21 days after symptom onset.4,5

Historically, stroke rates have been consistently higher among Blacks than in White counterparts. For example, the black-to-white stroke incidence ratio ranged from about 3.0 at age 45 to 54 to about 1.5 at age 65-74. In the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study, a population-based national cohort study of 30239 community-dwelling individuals aged ≥45 years at enrollment in 2003–2007, traditional stroke risk factors and socio-economic status (SES) adjustment accounted for nearly 50% of the disparity.6 Potential reasons for the excess risk not captured by the risk factors and SES include a more significant impact of the risk factors, particularly stroke in Blacks, residual confounders, or novel risk factors such as inflammation and hypercoagulability.

Given that inflammation and hypercoagulability are critical components of COVID-19 infection, there is a legitimate concern that the ongoing COVID-19 pandemic will exacerbate racial/ethnic disparities in stroke rates. For example, a recent study surveying 11 hospitals across New York has identified that Black or multiracial patients make up 58% of COVID-19 positive patients with strokes, but only 36% of COVID-19 negative patients with strokes.7 Further, data from 3 hospitals in Philadelphia showed that 80% of strokes in COVID-19 patients occurred in Black patients. It is unclear whether this occurred because of differences in COVID-19 positivity amongst Black and White...
patients, inequities in risk factors, SES, or other confounders. Furthermore, disruption of healthcare systems, including but not limited to the management of stroke risk factors may exacerbate the disparity in the occurrence of strokes. The broader impact of the pandemic’s economic downfall on minorities is an additional potential contributor to a purported disproportionate impact of COVID-19 in Blacks compared to Whites. There is uncertainty about the end of the COVID-19 pandemic and its long-term effects on chronic conditions such as stroke, including racial/ethnic disparity in stroke occurrence. This uncertainty further brings to focus the need to reduce disparity between races/ethnicities. We tested the hypothesis that among COVID-19 patients visiting the ED in the US, racial disparities in the prevalence of ischemic stroke persisted.

Methods

Design

The data that support the findings of this study are available from the corresponding author upon reasonable request. We performed a retrospective of all patients with COVID-19 registered in Covid-19 Research Database from December 30th, 2019 to August 13th 2020. The COVID-19 research database is pro-bono, cross-industry collaborative, composed of institutions donating technology services, healthcare expertise, and de-identified data. The database is a public-private consortium and enables public health and policy researchers to use real-world data to better understand and combat the COVID-19 pandemic. We used the Healthjump data set. Healthjump is a data management platform and interoperability solution for digital health vendors needing access to EMR data. They have EMR data on 40 million unique patients, updated daily. It is primarily outpatient data, but also includes inpatient data. More details about the data dictionary and other related information please see: https://covid19researchdatabase.org/wp-content/uploads/2020/06/Healthjump-Data-Dictionary.pdf and https://covid19researchdatabase.org/wp-content/uploads/2020/10/Healthjump-FAQ-2020-10-27.pdf

The query used to extract COVID-19 diagnosis is:

```
SELECT Count(DISTINCT client_id, patient_id) FROM (
    SELECT *
    FROM healthjump.PUBLIC.diagnoses WHERE (Upper (code) LIKE '%U07%1%')
    OR Upper(code) LIKE 'U07%2%') AND source_table = 'Diagnosis'
```

Details of the database access can be found: https://covid19researchdatabase.org/database-access/. The study population comprised patients aged 18 years or older with laboratory-confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and had an ED visit through August 13, 2020 and were captured in Covid-19 Research Database. The primary outcome was ischemic stroke in patients with COVID-19. Exposure of interest was race (classified as Black and non-Black). Patients with COVID-19 and stroke were identified by International Classification of Diseases, 10th Revision, (ICD-10) diagnosis for cerebrovascular disease (I60-I69) and SARS-CoV-2 (U07) during their ED visit.

Statistical analyses

We used descriptive statistics to describe the characteristics of the study population and to calculate proportions of patients with stroke in patients with COVID-19. Comparisons were made using the $\chi^2$ test or student t-test for unadjusted comparisons. For the primary analysis comparing the odds of ischemic stroke between the Black and non-Black patients, multivariable logistic regression model was adjusted for age, sex, hypertension, smoking, alcohol and obesity. Non-Black patients include non-Hispanic Whites and Hispanics. We reported adjusted odds ratios (OR) and corresponding 95% confidence intervals (95% CI). Level of statistical significance was set at $p<0.05$ (2-sided). All analyses were performed with freely available software (R-studio, version 3.4.3).

Results

Baseline characteristics

A total of 8815 patients who visited the ED were tested positive for COVID-19 and constitute our study sample. 35 states were represented (Supplemental Fig 1). Of these patients, 2296 (34%) were Black, 2026 (30%) were non-Hispanic White, and 2459 (36%) were Hispanic. Seventy-seven patients (0.87%) had a diagnosis of acute ischemic stroke. Ischemic stroke patients were older (64 ± 2 years vs. 51 ± 18 years). Of the 77 cases of ischemic stroke, 29 (50%) were Black, 17 (29%) were non-Hispanic White, and 12 (21%) were Hispanic. Detailed clinical characteristics are described in Table 1.

Prevalence and risk factors of ischemic stroke

The overall prevalence of ischemic stroke in the study population was 0.87% (95% CI: 0.69% to 1.10%). The prevalence in Blacks, non-Hispanic Whites and Hispanics was 1.26% (95% CI: 0.86% to 1.83%), 0.84% (95% CI: 0.51% to 1.37%) and 0.49% (95% CI: 0.26% to 0.88%) respectively. Table 2 shows details specific to the risk factors of ischemic stroke stratified by race. With exception of hypertension and diabetes, the remaining risk factors had similar distribution across race categories. Stroke rates were higher in the Southern states compared to Midwest and North-East states (Supplemental Fig 1).

Association of race and stroke in patients with COVID-19

In a multivariable logistic regression, adjustment for age, sex, hypertension, diabetes, obesity, drinking and
smoking, Black patients with COVID-19 were more likely to have ischemic stroke than non-black counterparts (adjusted odds ratio [OR], 2.76; 95% CI, 1.13-7.15, p=0.03, Table 3). The interaction between age and race was not significant.

**Discussion**

In this cohort of 8815 patients with COVID-19 in the US, we found that Blacks have approximately 3-fold higher odds of ischemic stroke than non-Blacks. The association was independent of age, sex, hypertension, diabetes, obesity, drinking and smoking.

The COVID-19 pandemic has uncovered healthcare racial/ethnic inequities in the US, with a disproportionate impact on minorities, including African Americans, Hispanics, and Native Americans. While non-Hispanic Whites, Hispanics, and Blacks represent respectively 61%, 18%, and 13% of the US population, in this analysis, among the unselected population of patients with COVID-19 and stroke, Black patients were more likely to have ischemic stroke than non-black counterparts.

**Table 1. Demographic characteristics of patients with and without stroke in individuals with COVID-19 diagnosis.**

| Race* | Total COVID-19 patients | Ischemic Stroke=Yes | Ischemic Stroke=No |
|-------|-------------------------|---------------------|-------------------|
| Black | 2296 (34)               | 29 (50)             | 2267 (33)         |
| non-Hispanic White | 2026 (30)               | 17 (29)             | 2009 (30)         |
| Hispanic | 2459 (36)               | 12 (21)             | 2447 (36)         |
| Other  | 67 (1)                  | 0 (0)               | 67 (1)            |

**Table 2. Risk factors of stroke by race.**

| Risk factors            | Black n (2296) | Non-Hispanic White n (2026) | Hispanic n (2459) | Other n (67) |
|-------------------------|----------------|-----------------------------|-------------------|--------------|
| Age ≥ 55y old, n (%)    | 982 (43)       | 980 (48)                    | 843 (34)          | 25 (37)      |
| Male, n (%)             | 817 (36)       | 956 (47)                    | 1174 (48)         | 30 (45)      |
| Hypertension, n (%)     | 881 (38)       | 574 (28)                    | 493 (20)          | 15 (22)      |
| Diabetes, n (%)         | 482 (21)       | 272 (13)                    | 340 (14)          | 8 (11)       |
| Obesity, n (%)          | 312 (51)       | 263 (49)                    | 376 (52)          | 3 (25)       |
| Currently drinking, n (%) | 137 (6)     | 121 (6)                     | 87 (4)            | 2 (3)        |
| Current smokers, n (%)  | 74 (3)         | 50 (2)                      | 77 (3)            | 1 (1)        |
COVID-19 who visited ED 30%, 36%, and 34% were non-Hispanic Whites, Hispanics, and Blacks respectively; findings that mirror those of previous reports, and likely share the same proposed underlying reasons. Minorities are disproportionately impacted by structural racism, they are more likely to be uninsured and have higher rates of pre-existing and underlying health conditions, all of which may increase their vulnerability in situations of crisis like pandemics. The current analysis focused on disparities among patients with COVID-19 visiting ED across the US and carrying a clinical diagnosis of stroke, therefore providing insights into stroke prevalence disparity in the era of COVID-19 pandemic. Thus, this study expands well established evidence for an increased occurrence of stroke in minorities. This analysis confirms these observations and further suggests that Blacks unlike non-Hispanic Whites and Hispanics with COVID-19 have a higher rate of stroke. More Blacks than Hispanics or Non-Hispanic Whites have hypertension and diabetes mellitus, which together explain most of the excess risk of stroke in the general population. The differential in traditional stroke risk factors likely contributes the excess rate of stroke in COVID-19 patients. However, after adjusting for these traditional risk factors, Blacks diagnosed with COVID-19 had nearly 3-fold increased odds of stroke compared to their non-Black counterparts, suggesting that the difference in stroke rates is also explained by some factors not captured in this study. Hypercoagulability is a proposed stroke mechanism in COVID-19 patients and is more likely in patients with the severe form of the disease, such as in Blacks. Our findings are of great importance since stroke is a known risk factor of mortality in patients with COVID-19.

This study has limitations, mostly related to its retrospective nature. Although we found an association between race and stroke rate in COVID-19 patients we could not establish causality. Unmeasured confounders could mask the true link between stroke and race/ethnicity in COVID-19 patients. The database did not provide granular data such as the stroke type, mechanisms of stroke, etiologies of stroke, disease severity variables and blood coagulation parameters. Nevertheless, the sample size was large and covered 35 states including mostly rural states and those at the epicenter of the pandemic at the time the data were collected. Furthermore, it is possible that the observed association seen in this COVID-19 population is simply the same observation of disproportionate excess stroke risk in Blacks as shown in prior studies and is therefore not specific to COVID-19. In the current study we did not compare the rates between COVID-19 and non-COVID-19 populations. Furthermore, some of the differences may also be due to the racial mixture of the population analyzed and are likely very dependent on the higher proportion of Blacks in the COVID-19 population.

### Conclusions

Among COVID-19 patients who were seen in the ED, there were racial disparities in the prevalence of ischemic stroke, higher in the Black population. This difference is not completely explained by a higher prevalence of hypertension and diabetes mellitus.

### Declaration of Competing Interest

Authors have no conflicts of interest to declare.

### Acknowledgments

None.

### Sources of funding

We received no funding for the current study.

### Disclosures

None.

### Ethical publication statement

We confirm that have read the Journal’s position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

### Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.jstrokecerebrovasdis.2021.105877.

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