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Poor haemorrhagic stroke outcomes during the COVID-19 pandemic are driven by socioeconomic disparities: analysis of nationally representative data

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ABSTRACT

Background Nationally representative studies evaluating the impact of the COVID-19 pandemic on haemorrhagic stroke outcomes are lacking.

Methods In this pooled cross-sectional analysis, we identified adults (≥18 years) with primary intracerebral haemorrhage (ICH) or subarachnoid haemorrhage (SAH) from the National Inpatient Sample (2016–2020). We evaluated differences in rates of in-hospital outcomes between the prepandemic (January 2016–February 2020) and pandemic (March–December 2020) periods using segmented logistic regression models. We used multivariable logistic regression to evaluate differences in mortality between patients admitted from April to December 2020, with and without COVID-19, and those admitted from April to December 2019. Stratified analyses were conducted among patients residing in low-income and high-income zip codes, as well as among patients with extreme loss of function (E-LoF) and those with minor to major loss of function (MM-LoF).

Results Overall, 309 965 patients with ICH (47% female, 56% low income) and 112 210 patients with SAH (62% female, 55% low income) were analysed. Prepandemic, ICH mortality decreased by ~1% per month (adjusted OR, 95% CI: 0.99 (0.99 to 1.00); p<0.001). However, during the pandemic, the overall ICH mortality rate increased, relative to prepandemic, by ~2% per month (1.02 (1.00 to 1.04), p<0.05) and ~4% per month (1.04 (1.01 to 1.07), p<0.001) among low-income patients. There was no significant change in trend among high-income patients with ICH (1.00 (0.97 to 1.03)). Patients with comorbid COVID-19 in 2020 had higher odds of mortality (versus 2019 cohort) only among patients with MM-LoF (ICH, 2.15 (1.12 to 4.16), and SAH, 5.77 (1.57 to 21.17)), but not among patients with E-LoF.

Conclusion Sustained efforts are needed to address socioeconomic disparities in healthcare access, quality and outcomes during public health emergencies.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Nationwide data on the potential impact of the COVID-19 pandemic on the trends in haemorrhagic stroke outcomes in the USA are lacking.

WHAT THIS STUDY ADDS

⇒ The rate of in-hospital mortality among patients with intracerebral haemorrhage increased significantly during the COVID-19 pandemic period, particularly among low-income patients.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study highlights the need for sustained and tailored efforts to address socioeconomic disparities in healthcare access, quality and outcomes during public health emergencies.

INTRODUCTION

The global outbreak of COVID-19, caused by the novel coronavirus, SARS-CoV-2, resulted in a pandemic that disrupted healthcare, especially among vulnerable populations.[1 2] COVID-19 infection may worsen vascular diseases by disrupting the coagulation cascade and exacerbating inflammatory responses.[3 4] Although prior studies have shown that COVID-19 increases the risk of poor outcomes among patients with ischaemic stroke,[5 6] there is a paucity of studies based on nationally representative data evaluating the potential impact of the COVID-19 pandemic on the trends in haemorrhagic stroke (intracerebral haemorrhage (ICH) and subarachnoid haemorrhage (SAH)) outcomes. Therefore, we used the largest publicly available all-payer inpatient healthcare database in the USA, the National Inpatient Sample (NIS), to evaluate the differences in the trends of haemorrhagic stroke outcomes before and during the COVID-19 pandemic and the sociodemographic and clinical factors potentially contributing to differences in haemorrhagic stroke outcomes between the prepandemic and pandemic periods.

METHODS

Ethics statement

Because this research used publicly available and deidentified data, it is considered exempt from review by the Houston Methodist Institutional Review Board. We followed the STrengthening the Reporting of OBservational studies in Epidemiology guidelines.[7]

Data availability

After completing a data use agreement training, qualified researchers can obtain NIS data through the Healthcare Cost and Utilization Project's central distributor (https://www.distributor.hcup-us.ahrq.gov/).

Study design, data source and case identification

NIS represents over 90% of all US hospitalisations.[8] In this pooled cross-sectional study, we used validated International Classification of Disease Tenth Revision (ICD-10) codes to identify adults (≥18 years) discharged with a principal diagnosis of ICH (ICD-10 codes: I61.0–I61.6 and I61.8–I61.9) or SAH (I60) from 2016 to 2020. We excluded patients with concurrent diagnoses of head trauma and/or arteriovenous malformation, as well as patients with missing age information. Also, we excluded patients transferred to an acute care hospital to avoid double counting the same patient, as the unit of observation in the NIS database is a hospitalisation encounter and not an individual patient. Among the ICH cohort, we additionally excluded patients with co-occurring diagnoses of intracranial aneurysms and brain malignancy.

Race/ethnicity was coded as non-Hispanic white (NHW), non-Hispanic black (NHB), Asian American and Pacific Islanders, Hispanic and others (including Native Americans and others). Income status was defined according to the income quartile of the patient's zip code, with quartiles 1 and 2 considered as low-income and quartiles 3 and 4 considered as high-income zip codes. The National Institutes of Health Stroke Scale score was only available for less than one-third (20.7%) of our analysis sample; therefore, we used the administratively derived All Patient Refined Diagnosis Related Group (APR-DRG) severity of illness scores to assess disease severity. We further grouped patients, based on their APR-DRG severity of illness score, into those with extreme loss of function (E-LoF) and those with minor to major loss of function (MM-LoF).[9] COVID-19 status was identified using ICD-10 code U07.1. This ICD code was released in late March of 2020 and is reserved for laboratory-confirmed cases of SARS-CoV-2.

The primary outcome is in-hospital mortality, and the secondary outcomes include home discharge, receiving craniotomy (for ICH cohort) and undergoing coiling or clipping (for SAH cohort).

Statistical analyses

Descriptive statistics were reported using medians and IQR . We used a series of univariable logistic regression models to evaluate the differences in the clinical and sociodemographic characteristics of patients admitted before the official declaration of national emergency response to the COVID-19 pandemic (January 2016–February 2020) (prepandemic period) and patients admitted during and after the emergency declaration (March 2020–December 2020) (pandemic period). Furthermore, we fit a series of unadjusted and adjusted segmented logistic regression models[10] (details in online supplemental methods) to evaluate the differences in the rates (slope) of in-hospital outcomes between the prepandemic and pandemic periods, as crude/adjusted odds ratios (OR/aOR) and 95% CI. The multivariable models included adjustments for sociodemographic factors (age, sex, race/ethnicity and insurance type), clinical factors (hypertension, diabetes, congestive heart failure, obesity, renal failure, Charlson Comorbidity Index and APR-DRG severity of illness score) and hospital-related factors (urban/rural location of hospital, teaching status of hospital and hospital bed size). To evaluate whether income modifies the association of the pandemic with ICH and SAH outcomes, we performed stratified analyses among patients residing in low-income and high-income zip codes.

Furthermore, we performed a series of secondary analyses to further understand the potential impact of COVID-19 infection on haemorrhagic stroke outcomes. First, to understand the characteristics of patients with comorbid COVID-19 and haemorrhagic stroke, we used a series of multivariable logistic regression models to evaluate the sociodemographic and clinical factors independently associated with having comorbid COVID-19 infection and ICH or SAH among a cohort of patients admitted from April to December 2020. We then used multivariable logistic regression models to assess the differences in mortality, between patients with ICH and SAH admitted from April to December 2020, with and without COVID-19, and patients admitted during a similar period in 2019. We performed stratified multivariable analyses among patients with MM-LoF and those with E-LoF to assess whether disease severity modifies the relationship between COVID-19 infection and haemorrhagic stroke outcomes. The confounding variables in all adjusted models were selected based on prior evidence demonstrating their association with haemorrhagic stroke outcomes. All analyses were conducted with 0.05 level of significance, using Stata 17.[11]

RESULTS

Overall, 309 965 patients with ICH (median age (IQR): 70 (58–80), 47% female, 56% residing in low-income zip codes) and 112 210 patients with SAH (median age (IQR): 60 (50–72), 62% female, 55% residing in low-income zip codes) were included (online supplemental table S1). Among the ICH cohort, 259 535 patients (median age (IQR): 70 (58–80), 47% female, 55% residing in low-income zip codes) were admitted during the prepandemic period, and 50 430 patients (median

age (IQR): 69 (57–79), 46% female, 57% residing in low-income zip codes) were admitted during the pandemic period. Among the SAH cohort, 93 855 patients (median age (IQR): 60 (50–72), 62% female, 56% residing in low-income zip codes) were admitted during the prepandemic period, and 18 355 patients (median age (IQR): 60 (50–71), 60% female, 57% residing in low-income zip codes) were admitted during the pandemic period. In univariate analyses, patients with ICH admitted during the pandemic period were significantly more likely to be insured via Medicaid (OR, 95% CI: 1.23 (1.14 to 1.33)) or private (1.08 (1.01 to 1.15)) insurance (versus Medicare) and have heart failure (1.13 (1.06 to 1.20)), obesity (1.30 (1.21 to 1.39)), renal failure (1.07 (1.01 to 1.13)) and higher Charlson Comorbidity Index (1.03 (1.02 to 1.04)) (online supplemental table S1).

In the prepandemic period, the mortality rate among patients with ICH was decreasing by approximately 1% per month (aOR, 95% CI: 0.99 (0.99 to 1.00); p<0.001). However, the overall mortality rate during the pandemic period increased by about 2% per month relative to the monthly rate in the prepandemic period (1.02 (1.00 to 1.02), p<0.05) (see figure 1A and table 1). Among patients residing in low-income zip codes, the mortality rate during the pandemic period increased by 4% per month relative to the prepandemic period (1.04 (1.01 to 1.07)). However, there was no significant change in mortality trend during the pandemic period among patients with ICH residing in high-income zip codes (1.00 (0.97 to 1.03)) (table 1 and figure 1B,C). Also, there was no significant change in the trend for other ICH outcomes or any SAH outcomes during the pandemic period (versus prepandemic).

Among patients admitted between April and December 2020 (ICH, 44 405 without COVID-19 and 935 with COVID-19; SAH, 16 205 without COVID-19 and 395 with COVID-19), males (aOR, 95% CI: 1.42 (1.03 to 1.97))

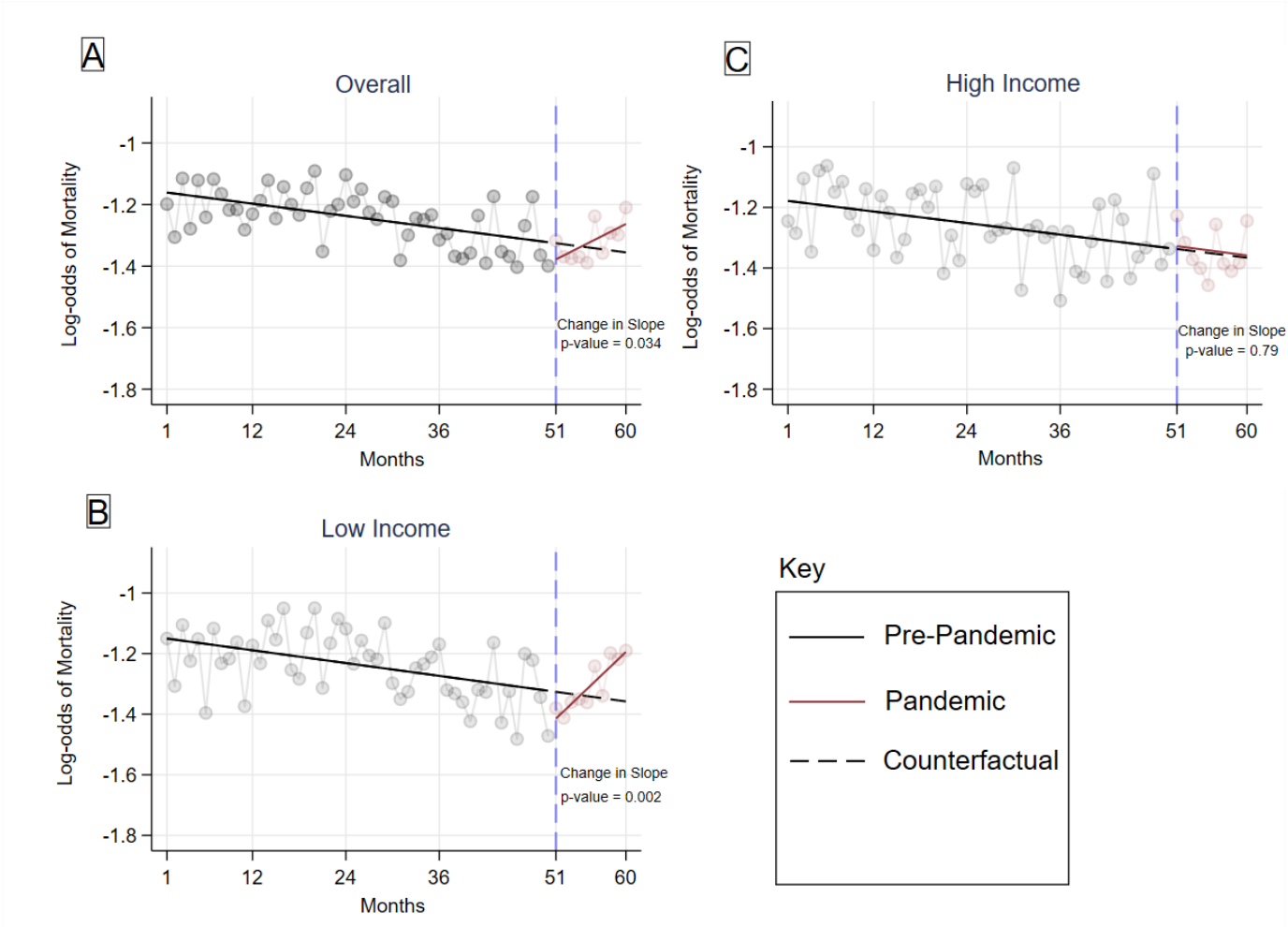

Figure 1 Segmented logistic regression of the effect of the COVID-19 pandemic on intracerebral haemorrhage (ICH) mortality, overall (A)and disaggregated by low-income (B)and high-income (C) residence status. Segmented logistic regression of the effect of the COVID-19 pandemic on ICH mortality—unadjusted. The solid lines run through preintervention and postintervention unexponentiated coefficients (logit), while the dotted lines represent what the postpandemic trend would have been had the pandemic not occurred (counterfactual). The coefficients used for this plot have not been adjusted for confounding variables; however, the reported p values for the difference in slope between prepandemic and postpandemic periods have been adjusted for confounding. P<0.05 indicates that there is a significant change in trend (slope) between the prepandemic and postpandemic mortality rates.

Table 1 Effect of the COVID-19 pandemic on ICH and SAH mortality

Adjusted models		
	ICH mortality	SAH mortality
Overall		
Precovid slope	0.99 (0.99 to 1.00)***	1.00 (0.99 to 1.00)*
Postcovid slope	1.02 (1.00 to 1.04)	0.99 (0.96 to 1.02)
Difference between precovid and postcovid slopes	1.02 (1.00 to 1.04)*	0.99 (0.96 to 1.03)
Low income		
Precovid slope	1.00 (0.99 to 1.00)***	1.00 (0.99 to 1.00)
Postcovid slope	1.04 (1.01 to 1.06)**	0.99 (0.95 to 1.03)
Difference between precovid and postcovid slopes	1.04 (1.01 to 1.07)**	0.99 (0.95 to 1.04)
High income		
Precovid slope	0.99 (0.99 to 1.00)***	1.00 (0.99 to 1.00)
Postcovid slope	0.99 (0.96 to 1.02)	0.98 (0.93 to 1.03)
Difference between precovid and postcovid slopes	1.00 (0.97 to 1.03)	0.99 (0.94 to 1.04)
Unadjusted models		
	ICH mortality	SAH mortality
Overall		
Precovid slope	1.00 (1.00 to 1.00)***	1.00 (0.99 to 1.00)*
Postcovid slope	1.01 (1.00 to 1.03)	1.00 (0.98 to 1.03)
Difference between precovid and postcovid slopes	1.02 (1.00 to 1.03)	1.01 (0.98 to 1.03)
Low income		
Precovid slope	1.00 (0.99 to 1.00)**	1.00 (0.99 to 1.00)
Postcovid slope	1.02 (1.00 to 1.05)*	1.00 (0.97 to 1.04)
Difference between precovid and postcovid slopes	1.03 (1.01 to 1.05)*	1.01 (0.97 to 1.04)
High income		
Precovid slope	1.00 (0.99 to 1.00)**	1.00 (0.99 to 1.00)
Postcovid slope	1.00 (0.97 to 1.02)	0.99 (0.95 to 1.04)
Difference between precovid and postcovid slopes	1.00 (0.98 to 1.02)	1.00 (0.96 to 1.04)

*p<0.05; **p<0.01; ***p<0.001.
ICH, intracerebral haemorrhage; SAH, subarachnoid haemorrhage.

(versus females), NHB (1.94 (1.28 to 2.95)), Hispanics (3.59 (2.29 to 5.64)) and the "other" race/ethnicity category (3.66 (2.16 to 6.19)) (versus NHW) had significantly higher odds of having comorbid ICH and COVID-19, while Hispanics (versus NHW) have significantly higher odds of having comorbid SAH and COVID-19 (4.73 (2.88 to 7.79)) (figure 2).

In multivariable analyses, patients with ICH and SAH with comorbid COVID-19 had a significantly higher likelihood of mortality compared with patients admitted between April and December 2019, overall (aOR, 95% CI: 1.83 (1.33 to 2.51) for ICH and 2.76 (1.68 to 4.54) for SAH) and among patients with MM-LoF (2.15 (1.12 to 4.16) for ICH and 5.77 (1.57 to 21.17) for SAH). However, among patients with E-LoF, there was no significant difference in the likelihood of mortality between patients with ICH and SAH with comorbid COVID-19 admitted between April and December 2020 and patients admitted during a similar period in 2019. Furthermore, among patients with ICH and SAH without comorbid COVID-19, the likelihood of mortality was similar across April to December 2020 and 2019 cohorts.

Online supplemental tables S2 and S3 provide details of the univariate comparisons of the characteristics of patients with ICH and SAH with comorbid COVID-19 (admitted between April and December 2020) and patients admitted during a similar period in 2019 (model group 1). Online supplemental tables S2 and S3 also provide univariate comparisons of patients with ICH and SAH admitted between April and December 2020 with and without comorbid COVID-19 (model group 2).

DISCUSSION

We evaluated the association of the COVID-19 pandemic with ICH and SAH in-hospital outcomes in a nationally

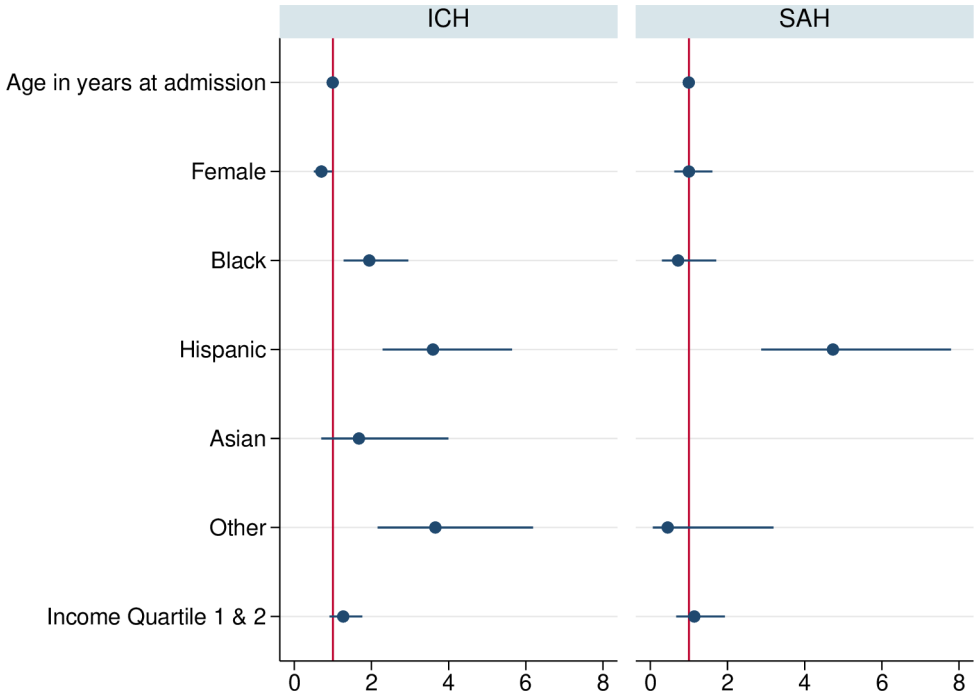

Figure 2 Sociodemographic factors associated with having comorbid COVID-19 and ICH/SAH. ICH, intracerebral haemorrhage; SAH, subarachnoid haemorrhage.

representative sample. Relative to the prepandemic period, we observed a significant increase in the monthly rate of in-hospital mortality among patients with ICH during the pandemic period. This increase was primarily driven by patients with ICH residing in low-income zip codes, whereas no change in mortality was observed among patients residing in high-income zip codes. We also demonstrate that comorbid COVID-19 was associated with higher likelihood of mortality among patients with ICH and SAH with MM-LoF, but not among patients with E-LoF.

Similar to a previous report,[12] our analyses demonstrate that ICH mortality was significantly declining during the prepandemic period. However, this trend was reversed during the pandemic period, particularly among patients residing in low-income zip codes. Relative to the prepandemic period, the overall ICH mortality rate increased by 2% per month in the pandemic period. This acceleration of mortality rate seems to be largely driven by patients residing in low-income zip codes, among whom the ICH mortality rate increased by 4% per month during the pandemic period, whereas no significant change in mortality was observed among patients residing in high-income zip codes during the pandemic period. These findings suggest that the COVID-19 pandemic may have slowed down the sustained improvement in ICH mortality observed during the prepandemic period, particularly among the low-income population. Though our analyses do not definitively outline the reasons for disparate COVID-19-associated ICH outcomes, higher comorbidity burden, lack of access, awareness and even disparities in care (including delayed care) may be postulated as potential drivers of such disparities. Most importantly, our analyses are yet another demonstration of the pandemic's disproportionate impact on vulnerable populations and highlight the need for continued focus on uncovering and addressing the reasons for the now widely reported socioeconomic disparities, particularly among patients with cerebrovascular disease.[13]

Similar to prior smaller studies, we also report that patients who have haemorrhagic stroke (ICH and SAH) with comorbid COVID-19 have significantly higher mortality compared with patients without COVID-19.[14 15] However, our data uniquely demonstrate, at the national level, that comorbid COVID-19 was only associated with a higher likelihood of in-hospital mortality among patients with ICH and SAH with MM-LoF, whereas among patients with E-LoF, COVID-19 status was not a significant driver of mortality. These findings have significant clinical relevance, and though we are limited from conducting a clinically detailed exploration of the biological mechanisms driving the differences in mortality between patients who have haemorrhagic stroke with and without comorbid COVID-19, it is reasonable to surmise, from previous studies, that a heightened systematic inflammatory response to the COVID-19 virus and its directed end organ damage may be potentiating these poor outcomes.[16] However, further studies are needed to elucidate the mechanisms driving poorer outcomes among patients who have haemorrhagic stroke with comorbid COVID-19. Also, given that minority races/ethnicities are at a higher likelihood of having comorbid COVID-19, the findings of this research highlight the need to further investigate the biological and environmental factors potentially driving socioeconomic disparities in the association between COVID-19 and haemorrhagic stroke outcomes.

Our study has some limitations. First, this study covers only the first wave of the COVID-19 pandemic. Hence, future studies are needed to explore the trends in the subsequent waves of the pandemic as data for ensuing years become available. Second, our analysis may have missed COVID-19 patients who did not require or receive in-hospital care for COVID-19 and potentially underestimated the prevalence of COVID-19 among patients with ICH and SAH. Third, we did not have detailed data on the timing of haemorrhagic stroke and COVID-19 diagnosis. Finally, we did not have access to more granular clinical data, including patients' imaging data (to ascertain haemorrhage location, volume or other haemorrhage characteristics) and information on the COVID-19 variants. Nevertheless, the insights provided by this study will be useful in guiding the readiness of public health authorities to implement strategies addressing sociodemographic disparities during public health emergencies.

CONCLUSIONS

The study found a significant acceleration of in-hospital mortality rate among patients with ICH during the post-pandemic period, particularly among those residing in low-income zip codes. Sustained efforts are needed to better understand the impact of the pandemic on stroke outcomes, particularly among vulnerable populations, as well as to address disparities in healthcare access, quality and outcomes during public health emergencies.

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Contributors AB and FSV conceived and designed the study. AB performed the data analysis. AB, TP, APP, TP, KAB and FSV contributed to the interpretation of the data. FSV and GWB contributed to data acquisition. AB drafted the manuscript. AB, TP, APP, TP, KB, GB and FSV critically revised the manuscript for important intellectual content. AB accepts full responsibility for the work and the conduct of the study, had access to the data, and controlled the decision to publish the study. All authors offered final approval of the submitted version.

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