Ischaemic stroke associated with COVID-19 and racial outcome disparity in North America

A retrospective study from the COVID-19 outbreak in Wuhan, China demonstrated an incidence of acute ischaemic stroke of approximately 5% in hospitalised patients with severe disease.[1] However, there has been limited evidence on the influence of racial background in stroke outcomes in this pandemic. We report 69 cases of acute stroke in patients positive for SARS-CoV-2, including 27 of African–American background and 42 of other racial backgrounds, including Caucasian, Hispanic and Asian. All patients presented to 14 major hospitals in the USA and Canada, from 14 March 2020 to 14 April 2020. The study was maintained under IRB #s20-00765.

All patients had nasopharyngeal swab samples that were positive for SARS-CoV-2 on qualitative reverse-transcriptase-PCR assays. In the following, we present a dichotomised analysis of ischaemic stroke outcomes between patients of African–American background as reported on hospital intake questionnaire versus patients of all other backgrounds. All variables stratified to race (African–American vs others). For continuous variables, when the data are normal, t-test was used and data were presented in the form of mean (SD). If they were not normally distributed, the Wilcoxon rank-sum test was used and the data were presented in the form of median (IQR). For categorical variables, the Pearson χ^2 or the Fisher's exact test were used as appropriate.

Comparison between Caucasian, Hispanic and Asian backgrounds did not show disparities in stroke outcomes and are not shown in detail for brevity. We found no significant difference in age (64.4 vs 62.9 years) or the proportion of females (51.9% vs 38.1%, table 1). Diabetes mellitus was present significantly more in African–American cases versus others (63.0% vs 28.6%). No significant difference between groups was found regarding other comorbidities including smoking, atrial fibrillation, prior anticoagulation, coronary artery disease, congestive heart failure, hypertension, hyperlipidaemia, cerebrovascular accident, peripheral vascular disease or chronic kidney disease. With respect to presenting SARS-CoV-2 symptoms, we found no difference in exposure history, asymptomatic cases, fever, cough, dyspnoea, nausea or vomiting, chills, malaise or lethargy.

The African–American cohort had a similar mean National Institutes of Health Stroke Scale (NIHSS) score of 16.3 compared with 14.9 in other races (p=0.63). The door-to-CT time was also similar (23 vs 19 min). The proportion of patients presenting with a large vessel occlusion was not significantly different (40.7% vs 47 %). We noted 14.8% of African–American cases received intravenous tissue plasminogen activator (tPA) compared with 31% in other races, but this was not significantly different in this sample. The proportion of thrombectomy cases mirrored this (14.8% vs 31%). Laboratory findings were not significantly different between African–Americans and all others except for low-density lipoprotein which was higher in African–Americans (mean (SD): 103 (32.9) vs 74.8 (38.9)).

Regarding stroke functional outcomes, there was no difference between African–Americans and other races in terms of discharge modified Rankin Scale (mRS, p=0.30). For mRS 0–2, there was no significant difference noted (18.5% vs 19.0%). Symptomatic intracranial haemorrhage (sICH) was significantly higher for African–Americans (11.1% vs 3%, p<0.001). Mortality was significantly higher in African–Americans compared with other races (55.6% vs 28.6%, p=0.05).

The finding in this study that mortality rate of patients with stroke who were COVID-19 positive is greater than that previously reported in either COVID-19 respiratory infection alone, or acute ischaemic stroke alone, suggests an interaction that warrants further study.[2 3] COVID-19-related thromboembolism may follow multiple separate pathogenetic pathways. A peri-infectious/inflammatory link is likely at play, which via ACE-2 targetting has been shown to be multisystem in nature. This synergy may act by any or all of cardioembolic, paradoxical and in situ thrombotic pathways including at the microvascular level.

Furthermore, the reasons for increased mortality in African–Americans with COVID-19-associated stroke are unknown.[2] Racial disparities in case counts and outcomes during the COVID-19 pandemic have been highlighted, particularly regarding African–American communities.[4] Underlying biological, genetic or epigenetic characteristics may predispose to health differences and outcomes. Social determinants of health, access and geographical differences pertaining both to population density and other location-based factors may also be important. Differential rates of tPA and mechanical thrombectomy may have approached significance due to issues surrounding access to care, and similarly higher rates of mortality may relate to greater prevalence of subclinical or undiagnosed comorbidities. Caution should be exercised in interpretation pending larger-scale study.

Our preliminary data suggest that there may be a mortality difference among patients with stroke of African–American background afflicted with COVID-19. This association requires further investigation.

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Table 1 Characteristics of African–Americans versus other races in stroke with COVID-19

	African–American (n=27)	Other races (n=42)	Overall (n=69)	P value
Age, mean (SD)	64.4 (11.8)	62.9 (17.3)	63.5 (15.3)	0.7
Sex				
Female	14 (51.9%)	16 (38.1%)	30 (43.5%)	0.26
Male	13 (48.1%)	26 (61.9%)	39 (56.5%)	
Comorbidities				
Smoking[1]	4 (14.8%)	7 (16.7%)	11 (15.9%)	0.88
Atrial fibrillation	3 (11.1%)	7 (16.7%)	10 (14.5%)	0.73
Prior anticoagulation[2]	0 (0%)	6 (14.3%)	6 (8.7%)	0.08
Coronary artery disease[3]	4 (14.8%)	11 (26.2%)	15 (21.7%)	0.37
Congestive heart failure[4]	5 (18.5%)	4 (9.5%)	9 (13.0%)	0.28
Diabetes mellitus[5]	17 (63.0%)	12 (28.6%)	29 (42.0%)	0.01*
Hypertension	21 (77.8%)	32 (76.2%)	53 (76.8%)	0.72
Hyperlipidaemia[6]	10 (37.0%)	23 (54.8%)	33 (47.8%)	0.22
Cerebrovascular accident[7]	6 (22.2%)	8 (19.0%)	14 (20.3%)	0.7
Peripheral vascular disease[8]	2 (7.4%)	0 (0%)	2 (2.9%)	0.09
Chronic kidney disease[9]	3 (11.1%)	5 (11.9%)	8 (11.6%)	0.9
Others	11 (40.7%)	24 (57.1%)	35 (50.7%)	0.18
Presentation				
Fever[10]	8 (29.6%)	20 (47.6%)	28 (40.6%)	1
Cough[11]	11 (40.7%)	18 (42.9%)	29 (42.0%)	1
Dyspnoea[12]	12 (44.4%)	13 (31.0%)	25 (36.2%)	1
Nausea or vomiting[13]	2 (7.4%)	0 (0%)	2 (2.9%)	1
Chills[14]	3 (11.1%)	3 (7.1%)	6 (8.7%)	1
Malaise or lethargy[15]	1 (3.7%)	6 (14.3%)	7 (10.1%)	1
Asymptomatic[16]	4 (14.8%)	4 (9.5%)	8 (11.6%)	1
Exposure history[17]	5 (18.5%)	13 (31.0%)	18 (26.1%)	0.32
Awareness of COVID[18]	3 (11.1%)	17 (40.5%)	20 (29.0%)	0.17
NIHSS[19], mean (SD)	16.3 (12.3)	14.9 (8.72)	15.4 (10.1)	0.63
ASPECTS[20]				
ASPECTS 0–5	2 (7.4%)	4 (9.5%)	6 (8.7%)	1
ASPECTS 6–10	11 (40.7%)	27 (64.3%)	38 (55.1%)	
Door to CT[21], median (IQR)	23.0(27.0)	19.0(22.0)	22.5(22.3)	0.18
Large vessel occlusion[22]	11 (40.7%)	20 (47.6%)	31 (44.9%)	1
Labs				
NLR[25], median (IQR)	5.39(7.26)	5.41(5.03)	5.41(6.61)	0.67
D dimer[26], median (IQR)	1120(7070)	2160(4540)	1780(5560)	0.87
INR[27], median (IQR)	1.11(0.228)	1.20(0.200)	1.20(0.215)	0.09
aPTT[28], median (IQR)	30.5(3.78)	32.5(6.10)	31.0(5.70)	0.44
Fibrinogen[29], mean (SD)	515 (243)	509 (309)	511 (285)	0.96
ESR[30], mean (SD)	45.3 (33.5)	66.3 (35.5)	52.0 (34.9)	0.17
C-reactive protein[31], median (IQR)	22.0(152)	29.2(72.6)	26.4(138)	0.58
Ferritin[32], median (IQR)	510(723)	566(1010)	530(963)	0.59
White blood cells[33], median (IQR)	7.70(2.91)	7.90(4.30)	7.90(3.91)	0.7
Absolute neutrophil[34], median (IQR)	5.75(2.73)	6.30(4.25)	6.10(3.78)	0.81
Absolute lymphocyte[35], median (IQR)	1.11(0.600)	1.20(0.650)	1.16(0.600)	0.77
Platelets[36], mean (SD)	222 (98.8)	256 (109)	243 (106)	0.2
Creatinine[37], median (IQR)	1.36(1.80)	1.10(0.928)	1.20(1.23)	0.28
GFR[38], median (IQR)	60.0(19.0)	60.0(21.0)	60.0(20.3)	0.48
LDH[39], median (IQR)	768(770)	513(283)	640(560)	0.19
Triglycerides[40], median (IQR)	114(55.0)	153(82.0)	142(80.0)	0.31
Troponin[41], median (IQR)	0.0300(0.135)	0.0200(0.118)	0.0210(0.131)	0.46
CPK[42], median (IQR)	216(2520)	135(189)	153(294)	0.17
LDL[43], mean (SD)	103 (32.9)	74.8 (38.9)	83.1 (38.9)	0.05*
HgA1C[44], median (IQR)	7.20(3.80)	6.30(1.48)	6.65(2.63)	0.28
Aspirin[45]	15 (55.6%)	23 (54.8%)	38 (55.0%)	0.61

Continued

Table 1 Continued

	African–American (n=27)	Other races (n=42)	Overall (n=69)	P value
Plavix[46]	4 (14.8%)	11 (26.2%)	15 (21.7%)	0.67
Heparin[46]	8 (29.6%)	9 (21.4%)	17 (24.6%)	0.58
Enoxaparin[46]	8 (29.6%)	10 (23.8%)	18 (26.1%)	0.26
IV tPA[23]	4 (14.8%)	13 (31.0%)	17 (24.6%)	0.16
Thrombectomy[24]	4 (14.8%)	13 (31.0%)	17 (24.6%)	0.16
mRS				
0	1 (3.7%)	2 (4.8%)	3 (4.3%)	0.3
1	2 (7.4%)	4 (9.5%)	6 (8.7%)	
2	2 (7.4%)	2 (4.8%)	4 (5.8%)	
3	2 (7.4%)	11 (26.2%)	13 (18.8%)	
4	4 (14.8%)	7 (16.7%)	11 (15.9%)	
5	1 (3.7%)	4 (9.5%)	5 (7.2%)	
6	15 (55.6%)	12 (28.6%)	27 (39.1%)	
mRS				
0–2	5 (18.5%)	8 (19.0%)	13 (18.8%)	1
3–6	22 (81.5%)	34 (81.0%)	56 (81.2%)	
sICH[47]	3 (11.1%)	1 (3.0%)	4 (4.8%)	<0.001
Mortality	15 (55.6%)	12 (28.6%)	27 (39.1%)	0.05*

[1–47]Data missing for some patients.
sICH, symptomatic intracranial haemorrhageaPTT, activated partial thromboplastin time; ASPECTS, The Alberta Stroke Programme Early CT Score; CPK, creatine phosphokinase; ESR, erythrocyte sedimentation rate; GFR, glomerular filtration rate; INR, international normalised ratio; LDH, lactate dehydrogenase; LDL, low-density lipoprotein; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; NLR, neutrophil–lymphocyte ratio; IV tPA, intravenous tissue plasminogen activator.

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Contributors AAD, AX and AT conceived and designed the research. AAD, KP, CS, FS, MKSH, AE, ALK, ASP, BKM, MD, SS1, AM, LYL, AMM, BV, SS2, AKW, HW, AX and AT collected and reviewed the data. AAD, KP, and MD analysed the data and performed the statistical analysis. AX and AT handled the funding and supervision of the research. AAD and AT drafted the manuscript. AAD, KP, CS, FS, MKSH, AE, ALK, ASP, BKM, MD, SS1, AM, LYL, AMM, BV, SS2, AKW, HW, AX and AT revised the manuscript and reviewed the final version.

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Correction: Ischaemic stroke associated with COVID-19 and racial outcome disparity in North America

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