Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Clinical Neurology and Neurosurgery 199 (2020) 106227

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Clinical characteristics and admission patterns of stroke patients during the COVID 19 pandemic: A single center retrospective, observational study from the Abu Dhabi, United Arab Emirates

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ARTICLE INFO

Keywords:
COVID-19
Stroke
Ischemic
Hemorrhagic
Clinical characteristics
Admissions

ABSTRACT

Objective: To compare ischemic and hemorrhagic stroke patients with COVID-19 to non-COVID-19 controls, and to describe changes in stroke admission patterns during the pandemic.
Methods: This is a single center, retrospective, observational study. All consecutive patients admitted with primary diagnosis of ischemic/ hemorrhagic stroke between March1st -May10th 2020 were included and compared with the same time period in 2019.
Results: There was a 41.9% increase in stroke admissions in 2020 (148 vs 210,P = .001). When comparing all ischemic strokes, higher rate of large vessel occlusion (LVO) (18.3% vs 33.8%,P = .008) and significant delay in initiation of mechanical thrombectomy after hospital arrival (67.75 vs 104.30 minutes,P = .001) was observed in 2020. When comparing all hemorrhagic strokes, there were no differences between the two years. Among 591 COVID-19 admissions, 31 (5.24%) patients with stroke including 19 with ischemic (3.21%) and 12 with hemorrhagic stroke (2.03%) were identified. Patients with COVID-19 and ischemic stroke were significantly younger (58.74 vs 48.11 years,P = .002), predominantly male (68.18% vs 94.74%,P = .016), had lesser vascular risk factors, had more severe clinical presentation (NIHSS 7.01 vs 17.05,P < .001), and higher rate of LVO (23.6% vs. 63.1%,P = .006). There was no difference in the rate of endovascular thrombectomy, but time to groin puncture was significantly longer in COVID-19 patients (83.41 vs 129.50 minutes,P = .003). For hemorrhagic stroke, COVID-19 patients did not differ from non-COVID-19 patients.
Conclusions: Stroke continues to occur during this pandemic and stroke pathways have been affected by the pandemic. Stroke occurs in approximately 5% of patients with COVID-19. COVID-19 associated ischemic stroke occurs in predominantly male patients who are younger, with fewer vascular risk factors, can be more severe, and have higher rates of LVO. Despite an increase in LVO during the pandemic, treatment with mechanical thrombectomy has not increased. COVID-19 associated hemorrhagic stroke does not differ from non-COVID-19 hemorrhagic stroke patients.

1. Introduction

Coronavirus Disease 2019 (COVID-19) is an ongoing pandemic caused by infection with the severe acute respiratory syndrome corona virus-2 (SARS CoV-2)[1,2]. While the infection primarily causes respiratory symptoms, there are now multiple reports of COVID-19 affecting the central nervous system (CNS) ranging from meningitis/encephalitis to stroke[3–5]. In a single center study of 214 hospitalized patients with

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https://doi.org/10.1016/j.clineuro.2020.106227
Received 5 July 2020; Received in revised form 29 August 2020; Accepted 8 September 2020
Available online 11 September 2020

COVID -19 from Wuhan, China where the infection first occurred, up to 36.4% of patients had neurological manifestation including acute cerebrovascular disease with severe and non-severe infection in 5.7% and 0.8% of these patients respectively[3]. While the reasons for ischemic stroke in COVID-19 are unclear, hypotheses of an inflammatory cytokine storm triggered hypercoagulable state or endothelial damage have been postulated[6,7]. However, as it stands, the mechanisms, phenotype and optimal management of ischemic stroke associated with COVID-19 still remain uncertain. The association of COVID-19 on hemorrhagic cerebrovascular disease is also unclear.

The World Health Organization declared COVID-19 as a s a pandemic on 11th March 2020. As of June 1st, at the time of manuscript writing, a total of 6,164,784 patients have been diagnosed globally, with 371,995 deaths[8]. The first case of COVID-19 in the United Arab Emirates (UAE) was diagnosed on January 29th 2020. As of June 1 st, there are a total of 34,557 diagnosed patients, with 264 deaths in the UAE[8]. Multiple published and anecdotal reports suggest that during the pandemic, there has been a drastic fall in the number of stroke patients being evaluated in the emergency room or being admitted to the hospital across continents[9,10].

There is an urgent need to understand stroke patterns during this pandemic since stroke remains an emergency, and untreated stroke will likely result in poorer clinical outcomes with concurrent significant resource burden on patients, hospitals, health care systems and populations. Furthermore, we need to identify associations, predictors of severity, morbidly and mortality in patients with stroke and COVID-19 to better guide future management of these patients.

2. Methods

This is a retrospective, observational study of the effect of the COVID-19 pandemic on all admitted patients with primary diagnosis of acute ischemic or hemorrhagic stroke, all acute stroke alerts from the emergency room or for admitted inpatients, and all neurological consults for management of acute stroke. Data was collected and analyzed on all consecutive patients admitted with stroke in the time period spanning March 1 st to May 10th 2020 (10-weeks) and compared with the same time period in 2019.

Cleveland Clinic Abu Dhabi (CCAD) is a Joint Commission International certified stroke center for the city of Abu Dhabi and contiguous western regions in the UAE and provides comprehensive stroke services, including 24/7 access to emergency department, vascular neurologists, radiologists, neurointerventionalists, neurosurgeons, neurointensivists, and a dedicated neurological intensive care unit. The emirate of Abu Dhabi has an estimated population of 2.5 million and CCAD receives a large proportion of the patients in Abu Dhabi who are potential candidates for intravenous thrombolysis and/or endovascular mechanical thrombectomy for acute ischemic stroke, and for surgical/endovascular interventions for hemorrhagic stroke. During the COVID-19 pandemic, CCAD has continued to operate a fully functional cerebrovascular service, with the exception of elective surgeries, despite major reorganization in other clinical services and hospital operations as a designated center for the care of COVID-19 patients.

SARS CoV-2 PCR testing via a nasopharyngeal and oropharyngeal swab for all hospitalized patients at admission and every 72 -hs thereafter during the hospitalized period was started on 15th April 2020. In addition, intubated patients being tested for COVID-19 also had concurrent sputum samples obtained for SARS CoV-2 PCR testing. Prior to 15th April 2020, SARS CoV-2 PCR testing in hospitalized patients was performed only as clinically indicated.

Retrospective data collection points included details regarding demographics, stroke risk factors, clinical presentation, stroke scales, imaging results and laboratory investigations, acute treatments including intravenous thrombolysis and endovascular thrombectomy, time metrics, surgical interventions, stroke classification and etiology, ischemic stroke subtype classification based on the Trial of ORG 10172 in Acute Stroke Treatment[11], clinical outcomes and discharge disposition.

Information regarding SARS CoV-2 PCR test results from all available samples was documented. On positive patients, additional information was collected including non-neurological COVID -19 symptoms, transmission mode, inflammatory markers, chest imaging, pulmonary and critical care parameters, and treatment details specific for COVID-19. The total number of COVID-19 patients (all specialties) admitted to the hospital during this time period was also obtained.

Institutional Review Board approval was obtained prior to pursuing this study.

3. Statistical Methods

For baseline data, mean and standard deviations were calculated for continuous variables, while categorical variables were expressed as counts and percentages. P-values associated with group comparisons on continuous variables, categorical variables, and count variables were calculated using independent-sampled t-tests, Fisher's Exact test, and $\chi 2$ test respectively. All statistical analyses were performed using Microsoft R Open 3.5.1 software. The significance threshold was set at a 2-sided *P* value less than .05.

4. Results

From March 1st-May 10th 2020, there were 210 patients evaluated for acute stroke compared to 148 patients during the same 10-week period in 2019 [41.9% increase (P = .001)]. Fig. 1 demonstrates the total admissions and break down per stroke subtype. The difference in 2020 was driven by significant increases in ischemic stroke, intracerebral hemorrhage (ICH) and stroke mimics.

Characteristics of all ischemic stroke patients from 2019 compared to 2020 are detailed in Table 1. This included patients with ischemic stroke and TIA, while all mimics were excluded from the analysis. Compared to 2019, there was a significant increase in the number of ischemic strokes in 2020 (76 vs 103, P = .044) while TIA remained unchanged (33 vs 27, P = .439). More patients presented to the hospital via emergency medical services (EMS) in 2020 (6.6% vs 24.2%, P = .001). There were no differences in the age or gender between the two years. Mean age in both years was approximately 58 (33.4% of patients overall $\leq$ 50 years). Cardiovascular risk factors were balanced except for higher rates of hyperlipidemia and smoking in 2019. Severity of stroke presentation was higher in 2020 as recorded by the National Institute of Health Stroke Scale (NIHSS) (6.5 vs 8.9, P = .045). The rate of treatment with intravenous thrombolysis was similar in both years. The rate of large vessel occlusion (LVO) was significantly higher in 2020 [20 (18.3%) vs 44 (33.8%), P = .008], but endovascular thrombectomy rate was similar in both years. With regards to time metrics, presentation to the hospital from last known well (LKW) time and door to needle times for intravenous thrombolysis was similar. However, door to groin puncture times for endovascular thrombectomy was significantly longer in 2020 (67.75 vs 104.30 minutes, P = .001). There was no difference in stroke subtype classification per TOAST criteria. Sixteen-patients (12.3%) were still admitted in 2020 at last review of hospital charts. There was no difference in in-hospital mortality, discharge disposition or discharge/30-day modified Rankin Score (MRS).

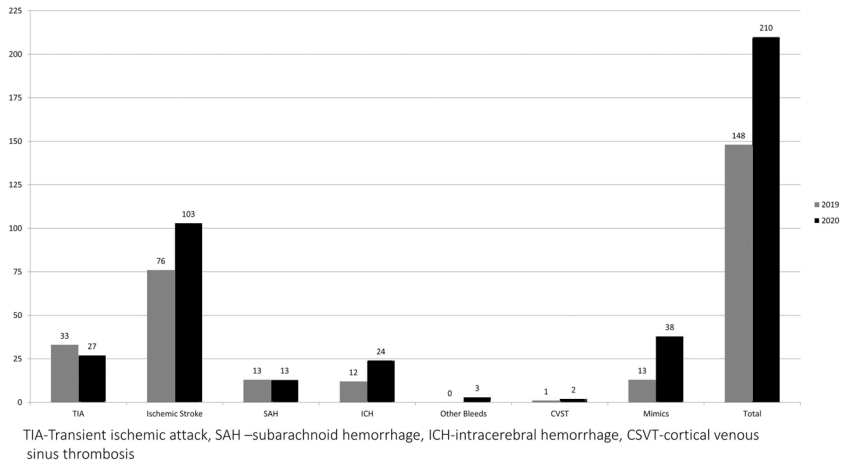

Fig. 1. Total admissions and stroke type by year.

Characteristics of all hemorrhagic stroke patients from 2019 compared to 2020 are detailed in Table 2. Compared to 2019, there was a significant increase in patients with ICH in 2020 (24 vs 12, P = .045). SAH and other intracranial bleeds remained unchanged. There were no differences in the age or gender. Mean age in both years was approximately 49 (55.8% of patients overall were ≤ 50 years of age). Cardiovascular risk factors were balanced. ICH score, Hunt-Hess score, modified Fischer Grade, and etiology of bleeds were similar. Surgical treatment including placement of an external ventricular drain, endovascular embolization and microsurgical clipping/resection or hematoma evacuation occurred at similar rates. There was no difference in in-hospital mortality or discharge/30-day MRS. Eight patients (19%) remained admitted in 2020 at last review of hospital charts. Discharge disposition was significantly different between the two years, but this was driven mainly by more patients in 2019 being repatriated to their home country which was limited in 2020 by air travel restriction.

Our hospital admitted its first COVID-19 patient on 11th February 2020. Subsequently, the hospital admitted 2, 59, 392 and 239 COVID-19 patients in the months of February, March, April and May respectively. In the 10-week study period, 591 patients with COVID-19 were admitted to the hospital. Of these, 31 (5.24%) patients with stroke including 19 with ischemic (3.21%) and 12 with hemorrhagic stroke (2.03%) were identified. Characteristics of all stroke patients with COVID-19 are detailed in Table 3. Patients were overwhelmingly male (90.32%) with mean age of 48.1 years. Majority (90.32%) contracted the virus via community transmission since they tested positive on tests performed at admission. Three-patients may have contracted the virus while in hospital. History of travel outside the country was documented in a single patient (3.23%). Up to 45% had hypertension, 29% had diabetes mellitus (DM), and 9.68% had coronary artery disease (CAD). None of the patients had prior respiratory or immunocompromised state comorbidities. Fever and respiratory symptoms were reported in a third of patients, while headache was present in up to half. Pneumonia on chest X ray (CXR) or chest computed tomography (CT) was seen in 16 (51.61%) patients. Treatment specific for COVID-19 was administered in 15 (48.39%) patients with hydroxychloroquine being used the most.

Table 4 compares characteristics of ischemic stroke patients with COVID-19 with all other ischemic stroke patients without COVID-19 from both years. Patients with COVID-19 and ischemic stroke were significantly younger (58.74 vs 48.11 years, P = .002) and more males (68.18 vs 94.74%, P = .016). Hypertension, hyperlipidemia and prior stroke were significantly lesser in COVID-19 ischemic stroke patients. Stroke severity was significantly higher in COVID-19 patients (NIHSS 7.01 vs 17.05, P < .001). There was significantly higher rate of LVO in COVID-19 patients [52 (23.6%) vs 12 (63.1%), P = .006] but there was no difference in the rate of endovascular thrombectomy. Time to groin puncture for endovascular thrombectomy was significantly longer in COVID-19 patients (83.41 vs 129.50 minutes, P = .003). While there were more strokes of undetermined cause in COVID-19 patients, this was not significant (31.82 vs. 42.11%, P = .183). In-hospital mortality was similar. Among the discharged patients, discharge disposition and discharge location were similar.

Table 5 compares characteristics of hemorrhagic stroke patients with COVID-19 with all other hemorrhagic stroke patients without COVID-19from both years. In contrast to ischemic stroke, age and sex were balanced in hemorrhagic stroke patients with and without COVID-19. There was no difference in the rate of risk factors. ICH score, Hunt-Hess score, modified Fischer Grade, and etiology of bleeds were similar. Surgical treatment occurred at similar rates. There was no difference in in-hospital mortality. Among the discharged patients, there was no difference in the discharge mars or discharge disposition.

5. Discussion

This is the largest retrospective study from the Middle East that highlights the impact of the COVID-19 pandemic on patients hospitalized at our center with both ischemic stroke and hemorrhagic stroke. CCAD has played a unique role during this pandemic in that not only did it serve as a COVID-19 center, but it continued to serve as the center of excellence for stroke care within the emirate of Abu Dhabi and therefore has continued to receive a large proportion of stroke patients. During the study period there was an increase in stroke alerts and admissions for both ischemic and hemorrhagic stroke when compared to 2019. This could be explained by other centers no longer taking care of such patients during the current pandemic and by a possible alteration in referral patterns. There was also a dramatic increase in presentation of ischemic strokes by EMS which may be due to a variety of factors including severity of disease, a shift in EMS referral patterns but also the effects of curfew hours and prohibition of self-travel. These results are in contrast to other comprehensive stroke centers which have reported a decrease in stroke alerts and overall stroke admissions [10,12–14]. Siegler et al. reported a mean 38% decrease rate of new stroke diagnoses in a comprehensive stroke center in comparison to the months preceding the COVID-19 pandemic, which coincided with an overall 59% drop in transfers from other hospitals. The effects on clinical pathways were more extensive as the authors observed decreased number of stroke telemedicine consultations (25% less), walk in patients (55% less) and direct ambulance transfers (29% less)[10]. According to the most recent European Stroke Organization press release there was an 80% drop in stroke service provision in 426 stroke services surveyed, as well as a

Table 1
: Comparison of all patients with ischemic stroke in 2019 and 2020

Variable	2019	2020	P-value
Total(n)	109	130	.174
Ischemic stroke(n)	76	103	.044
Transient ischemic attack(n)	33	27	.439
Mode of Arrival(n,%)			
Self	44 41.5%)	39(30.5%)	
Emergency medical services	7(6.6%)	31(24.2%)	.001
Transfer from other hospital	53(50%)	57(44.5%)	
Inpatient	2(1.9%)	1(0.8%)	
Age(years, mean, SD)	58.4 +/- 14.6	57.5 +/- 14.3	.651
Male(n,%)	74(67.9%)	94(72.31%)	.479
Past Medical History(n,%)			
Hypertension	67(61.5%)	89(68.9%)	.273
Hyperlipidemia	53(48.6%)	44(34.1%)	.025
Diabetes Mellitus	54(49.5%)	55(42.6%)	.299
Smoking	19(17.4%)	8(6.2%)	.007
Atrial fibrillation	17(15.6%)	13(10.1%)	.241
Prior stroke	31(28.4%)	23(17.8%)	.062
Wake up(n,%)	23(21.3%)	15(12.2%)	.076
NIHSS(mean, SD)	6.5 +/- 7.6	8.9 +/- 10.2	.045
Treatment with intravenous alteplase(n,%)	13(11.9%)	17(13.1%)	.846
Large vessel occlusion(n,%)	20(18.3%)	44(33.8%)	.008
Internal carotid artery(n,%)	8(40%)	10(22.7%)	
Middle cerebral artery M1-segment	6(30%)	22(50%)	
Middle cerebral artery M2-segment	2(10%)	7(15.9%)	.289
Basilar artery	4(20%)	5(11.4%)	
Endovascular thrombectomy(n, %)	12 (11%)	21 (16.1%)	.266
Time metrics(minutes, mean, SD)			
Last known well-Door	620.6 +/- 743.7	516.6 +/- 556.86	.293
Door-Needle(intravenous thrombolysis)	35.5 +/- 12.7	42.7 +/- 14.8	.171
Door-Groin(endovascular thrombectomy)	67.7 +/- 20.4	104.3 +/- 32.8	.001
TOAST classification(n,%)			
Small vessel disease	13(11.9%)	25(19.2%)	
Large vessel disease	28(25.7%)	31(23.8%)	.527
Cardioembolic	25(22.9%)	32(24.6%)	
Other determined cause	3(2.7%)	4(3.1%)	
Undetermined cause	40(36.7%)	38(29.2%)	
In-hospital mortality(n,%)	1(0.9%)	4(3.1%)	.379
Discharge location(n,%)			
Home	87(80.6%)	95(86.4%)	
Acute rehabilitation facility	5(4.6%)	7(6.4%)	.246
Long term acute care	1(0.9%)	1(0.9%)	
Other hospital/Repatriation	15(13.9%)	7(6.4%)	
Discharge/30 day modified Rankin Scale(n,%)			
0-2	60(55%)	69(53.1%)	
3-5	48(44%)	57(43.8%)	.621
6	1(0.9%)	4(3.1%)	

NIHSS- National Institute of Health Stroke Scale, TOAST- Trial of ORG 10172 in Acute Stroke Treatment

Table 2
: Comparison of all patients with hemorrhagic stroke in 2019 and 2020

Variable	2019	2020	P-value
Total(n)	26	42	.102
Intracerebral hemorrhage(n)	12	24	.045
Subarachnoid hemorrhage(n)	13	13	.999
Others(n)	1	5	.102
Mode of Arrival(n,%)			
Self	3(11.5%)	1(2.4%)	
Emergency medical services	3(11.5%)	11(26.2%)	.138
Transfer from other hospital	20(76.9%)	30(71.4%)	
Age(years, mean, SD)	49.3 +/- 14.1	48.9 +/- 14.7	.913
Male(n,%)	21(80.8%)	28(66.7%)	.272
Past Medical History(n,%)			
Hypertension	12(46.5%)	25(59.5%)	.323
Hyperlipidemia	4(15.4%)	7(16.7%)	.999
Diabetes Mellitus	5(19.2%)	8(19%)	.999
Smoking	4(15.5%)	2(4.8%)	.193
Atrial fibrillation	1(3.8%)	2(4.8%)	.999
Prior stroke	0(0%)	3(7.1%)	.281
Anticoagulation	1(3.8%)	1(2.4%)	.999
Intracerebral hemorrhage score (mean, SD)	1 +/- 1	1.56 +/- 1.29	.211
Hunt-Hess Score(n,%)			
1-3	12(92.3%)	10(76.9%)	.593
4-5	1(7.7%)	3(23.1%)	
Modified Fischer Grade(n,%)			
0-2	8(61.5%)	5(38.5%)	.434
3-4	5(38.5%)	8(61.5%)	
Etiology(n,%)			
Hypertension	9(37.5%)	15(36.6%)	
Cerebral amyloid angiopathy	0(0%)	1(2.4%)	
Aneurysm	6(25%)	8(19.5%)	
Arteriovenous malformation	1(4.2%)	5(12.2%)	.942
Other vascular malformation	0(0%)	1(2.4%)	
Anticoagulation	1(4.2%)	2(4.9%)	
Other	7(29.2%)	9(21.9%)	
Surgical interventions(n,%)			
External ventricular drain	4(15.4%)	6(14.3%)	.999
Endovascular coiling/embolization	6(23.1%)	8(19%)	.762
Surgical evacuation/clipping/ resection	3(11.5%)	8(19%)	.512
In-hospital mortality(n,%)	1(3.8%)	4(9.5%)	.642
Discharge location(n,%)			
Home	13(52%)	18(60%)	
Acute rehabilitation facility	2(8%)	7(23.3%)	.007
Long term acute care	0(0%)	3(10%)	
Other hospital/ Repatriation	10(40%)	2(6.7%)	
Discharge/30 day modified Rankin Scale(n,%)			
0-2	12(46.1%)	18(43.9%)	
3-5	13(50%)	20(48.8%)	.858
6	1(3.8%)	3(7.3%)	

decrease in hospital attendance of stroke patients[15].While the increase in stroke patient volumes cannot be generalized to imply an increase in incidence of stroke during the pandemic, it does highlight the importance of having capacity and access for stroke patients in healthcare systems, as the data from this review suggests that strokes continued to occur in this part of the world during the pandemic.

With regards to our institutional stroke pathway workflow, there was

Table 3
: Baseline characteristics of all COVID-19 patients

Variable	
Total(n)	31
Age(years, mean, SD)	48.1 +/-11.6
Male(n, %)	28(90.3%)
Community transmission(n,%)	28(90.3%)
History of recent travel(n,%)	1(3.23%)
Past Medical History(n,%)	
Hypertension	14(45.2%)
Hyperlipidemia	2(6.4%)
Diabetes Mellitus	9(29%)
Smoking	1(3.2%)
Prior coronary artery disease	3(9.7%)
Prior stroke	1(3.2%)
Asthma/COPD/ILD	0(0%)
Previous transplant	0(0%)
Immunocompromise	0(0%)
Malignancy	0(0%)
Symptoms	
Fever	10(33.3%)
Cough/Shortness of breath	11(36.7%)
Headache	14(46.7%)
Arthralgia/Myalgia/Fatigue	4(13.3%)
Laboratory parameters(mean, SD)	
Hemoglobin(g/L)	141.7 +/- 18.4
White blood cell count(x10*9/L)	10.5 +/- 4.7
Platelet(x10*9/L)	288.4 +/- 115.4
Creatinine(umol/L)	82.8 +/- 33.7
C-reactive protein(mg/L)	72.7 +/- 84.7
Ferritin(mcg/L)	637.7 +/- 370.4
D-dimer(mcg/mL FEU)	2.02 +/- 1.09
Pneumonia on Chest X-ray or Chest CT(n,%)	16(51.6%)
Treatment for COVID-19(n,%)	15(48.4%)
Medications(n,%)	
Hydroxychloroquine	8(25.8%)
Lopinavir/ritonavir	6(19.3%)
Favipiravir	6(19.3%)
Remdesivi	0(0%)
Corticosteroids	0(0%)
Tocilizumab	7(22.6%)
Convalescent plasma	0(0%)
Intensive care unit admission for COVID(n,%)	8(25.8%)
Acute respiratory failure	8(25.8%)
Mechanical ventilation	7(22.6%)
Prone ventilation	2(6.4%)
Extracorporeal membrane oxygenation	1(3.2%)

COPD- Chronic obstructive pulmonary disease, ILD- Interstitial lung disease, CT- Computed tomography

no significant increase in door to needle times for intravenous thrombolysis for ischemic stroke during the pandemic. However, a significant delay in door to groin times for mechanical thrombectomy was observed. This can be explained by the institution of a protected code stroke in our institution based on recommendations by various panels and Societies[16–20]. Our protocol includes administration of general endotracheal anesthesia for all patients undergoing mechanical thrombectomy in a negative pressure room as well as donning of personal protective equipment for all involved to mitigate COVID-19 transmission. With delays in stroke treatments and especially mechanical thrombectomy, outcomes will likely deteriorate. However, this effect was not demonstratable in our cohort and additional studies will be required with larger samples to see if these delays in treatment are

Table 4
: Comparison of COVID-19 ischemic stroke versus non COVID-19 ischemic stroke

Variable	Non COVID-19 (N = 220)	COVID-19 (N = 19)	P-value
Age(years, mean, SD)	58.7 +/-14.5	48.1 +/- 10.8	.002
Male(n,%)	150(68.2%)	18(94.7%)	.016
Past Medical History(n,%)			
Hypertension	149(67.3%)	7(36.8%)	.011
Hyperlipidemia	96(43.6%)	1(5.3%)	.001
Diabetes Mellitus	103(46.8%)	6(31.6%)	.236
Smoking	27(12.3%)	0(0%)	.141
Atrial fibrillation	30(13.6%)	0(0%)	.142
Prior stroke	54(24.5%)	0(0%)	.009
NIHSS(mean,SD)	7.0 +/- 8.4	17.0 +/- 12.7	<.001
Treatment with intravenous alteplase(n,%)	28(12.7%)	2(10.5%)	.999
Large vessel occlusion(n,%)	52(23.6%)	12(63.1%)	.006
Internal carotid artery(n,%)	16(30.8%)	2(16.7%)	
Middle cerebral artery M1-segment	19(36.5%)	9(75%)	
Middle cerebral artery M2-segment	9(17.3%)	0(0%)	0.115
Basilar artery	8(15.4%)	1(8.3%)	
Endovascular thrombectomy(n,%)	28(12.7%)	5(26.3%)	.154
Time metrics(minutes, mean, SD)			
Last known well-Door	559.3 +/- 649.8	556.9 +/- 561.2	.988
Door-Needle(intravenous thrombolysis)	39.4 +/- 12.2	42.5 +/- 19.1	.769
Door-Groin(endovascular thrombectomy)	83.4 +/- 29.2	129.4 +/- 31.4	.003
Laboratory parameters(mean, SD)			
Hemoglobin(g/L)	130.4 +/- 27.1	142.4 +/- 14.6	.585
White blood cell count(x10*9/L)	9.6 +/- 8.0	10.6 +/- 3.8	.610
Platelet(x10*9/L)	263.2 +/- 87.4	331.6 +/- 112.4	.001
International normalized ratio	1.1 +/- 0.3	1.1 +/- 0.1	.923
Activated partial thromboplastin time(sec)	32.1 +/- 22.9	28.9 +/- 2.9	.545
Creatinine(umol/L)	95.8 +/- 95.4	76.3 +/- 18.5	.374
Hemoglobin A1c(%)	7.1 +/- 2.1	8.2 +/- 3.1	.032
Low density lipoprotein cholesterol (mmol/L)	2.8 +/- 1.1	2.6 +/- 0.8	.354
TOAST classification(n,%)			
Small vessel disease	38(17.3%)	0(0%)	
Large vessel disease	53(24.1%)	6(31.6%)	.183
Cardioembolic	53(14.1%)	4(21%)	
Other determined cause	6(2.7%)	1(5.3%)	
Undetermined cause	70(31.8%)	8(42.1%)	
In-hospital mortality(n,%)	4(1.8%)	1(5.3.1%)	.341
Discharge location(n,%)			
Home	176(83.4%)	6(85.7%)	
Acute rehabilitation facility	12(5.7%)	0(0%)	.723
Long term acute care	2(0.9%)	0(0%)	
Other hospital/ Repatriation	21(9.9%)	1(14.3%)	
Discharge/30 day modified Rankin Scale(n,%)			
0-2	122(55.4%)	7(36.8%)	
3-5	94(42.7%)	57(57.9%)	.149
6	4(1.8%)	1(5.3%)	

NIHSS- National Institute of Health Stroke Scale, TOAST- Trial of ORG 10172 in Acute Stroke Treatment

Table 5
: Comparison of COVID-19 hemorrhagic stroke versus non COVID-19 hemorrhagic stroke

Variable	Non COVID-19 (N = 56)	COVID-19 (N = 12)	P-value
Age(years, mean, SD)	49.3 +/- 14.6	48.1 +/- 13.3	.788
Male(n, %)	39(69.6%)	10(83.3%)	.487
Past Medical History(n,%)			
Hypertension	30(53.6%)	7(58.3%)	.999
Hyperlipidemia	10(17.9%)	1(8.3%)	.673
Diabetes Mellitus	10(17.9%)	3(25%)	.687
Smoking	5(8.9%)	1(8.3%)	.999
Anticoagulation	1(1.8%)	1(8.3%)	.324
Intracerebral hemorrhage score (mean, SD)	1.3 +/- 1.2	2 +/- 1.4	.185
Hunt-Hess Score(n,%)			
1-3	18(81.8%)	4(100%)	.999
4-5	4(18.2%)	0(0%)	
Modified Fischer Grade(n,%)			
0-2	12(54.5%)	1(25%)	.593
3-4	10(45.4%)	3(75%)	
Laboratory parameters(mean, SD))			
Platelet(x10*9/L)	265.5 +/- 70.3	220 +/- 85.7	.057
International normalized ratio	1.1 +/- 0.3	1.1 +/- 0.1	.982
Activated partial thromboplastin time (sec)	30.1 +/- 4.4	29.2 +/- 4.1	.530
Etiology(n,%)			
Hypertension	21(39.6%)	3(25%)	
Cerebral amyloid angiopathy	1(1.9%)	0(0%)	
Aneurysm	12(22.6%)	2(16.7%)	
Arteriovenous malformation	6(11.3%)	0(0%)	.204
Other vascular malformation	1(1.9%)	0(0%)	
Anticoagulation	1(1.9%)	2(16.7%)	
Other	11(20.7%)	5(41.7%)	
Surgical interventions(n,%)			
External ventricular drain	6(10.7%)	4(33.3%)	.067
Endovascular coiling/embolization	12(21.4%)	2(16.7%)	.999
Surgical evacuation/clipping/ resection	11(19.6%)	0(0%)	.191
In-hospital mortality(n,%)	3(5.4%)	2(16.7%)	.211
Discharge location(n,%)			
Home	26(54.2%)	5(71.4%)	
Acute rehabilitation facility	9(18.7%)	0(0%)	.750
Long term acute care	3(6.2%)	0(0%)	
Other hospital/ Repatriation	10(20.8%)	2(28.6%)	
Discharge/30-day modified Rankin Scale(n,%)			
0-2	24(42.9%)	6(50%)	
3-5	29(51.8%)	4(33.3%)	.238
6	3(5.4%)	2(16.7%)	

adversely impacting outcomes.

The increase in door to groin time reflects the impact of the pandemic as a real-world experience and has also been observed by other colleagues in France[13]. A center in Spain[12] has been able to prevent a delay in thrombectomy timings which is commendable, however it is not clear what proportion of patients that underwent mechanical thrombectomy were being intubated in this study. Balancing the need to protect caregivers while maintaining a system of care and stroke chain of survival for all stroke patients against the need for efficient and swift treatment is what hospitals and healthcare systems will likely struggle with during this ongoing pandemic.

Amongst all patients with COVID-19 admitted to the hospital, 5.24 % of them presented with a stroke either ischemic or hemorrhagic which is similar to data coming out of China during this pandemic[3]. COVID-19 patients with ischemic stroke are overall younger, predominantly male, and less likely to have underlying vascular risk factors of hypertension, hyperlipidemia, prior stroke and smoking. A younger age of onset along with less prevalence of traditional stroke risk factors among COVID-19 patients with stroke has also been reported by other centers. Oxley et al[21] published a case series of 5 young patients with COVID-19 and LVO of which 3 (60%) of them had vascular risk factors for stroke. In our cohort of ischemic stroke, 12 had LVO of which 9 were less than 50 years of age. Among these, only 3 (33.3%) had traditional risk factors of stroke which is in contrast to Oxley et al. Yagi et al [22] in their case series of 32 patients, 11 were age 50 or below, out of which 45 % had vascular risk factors. However, it is not clear how many of these patients had LVOs. Traditionally the UAE has had a younger age of onset for stroke with male predominance as a result of poorly controlled vascular risk factors amongst expatriate migrant male workers [23,24] However our comparison to historical controls confirms an even younger age of onset. COVID-19 has had more severe systemic involvement amongst males[3] which could manifest as more ischemic strokes related to endothelial injury and hypercoagulable state. In addition, our cohort of COVID-19 ischemic strokes suffered more severe strokes with higher NIHSS and had significantly higher rate of LVOs. This has been observed by other series across the globe which suggests an association between a COVID-19 mediated hypercoagulable state and thromboembolism[25–28]. In addition to a sepsis induced coagulopathy that can be seen with COVID 19 there is evidence that the SARS-CoV-2 virus binds to the Angiotensin converting enzyme 2 (ACE2) receptor present on brain and endothelial smooth cells that consequently can increase inflammation, clotting and vasoconstriction that could potentially lead to ischemic stroke[29]. One recent case series has also highlighted three COVID 19 cases of multiple cerebral and limb infarctions and elevated antiphospholipid antibodies which have an association with both arterial and venous thrombotic events[30]. Our current review did not include any data on these biomarkers. Further studies looking at inflammatory hypercoagulable markers along with the ACE2 pathway will need to be done to establish the pathophysiology of COVID-19 in ischemic stroke.

A striking and simultaneously concerning finding in our study is that though the LVO rate in our COVID-19 ischemic stroke cohort was substantially higher, the rate of endovascular thrombectomy did not increase. This could be explained by overall severity of systemic illness and advanced stages of ischemia at the time of presentation that may have prevented patients from being eligible for treatment with endovascular thrombectomy.

Our data has limited longitudinal follow up as we are still in the midst of the crisis. However preliminarily data suggests that COVID-19 patients with ischemic stroke tend to have poorer outcomes which can be as a consequence of the severity of the stroke but also the presence of severe multisystemic disease related to the infection itself.

Conversely in our hemorrhagic stroke cohort, while there was an increase in ICH patients being admitted to our center, all other associated parameters including age, gender, presence of vascular risk factors, severity and outcomes were similar both between the current study period and the historical controls. This was also the case when comparing hemorrhagic stroke between COVI-19 positive and COVID-19 negative patients. The novel observation of no major differences in hemorrhagic patients gives credence to proposed pathophysiological mechanisms centered around endothelial dysfunction, hypercoagulability and intravascular thromboses and consequent thromboembolism and that perhaps ICH (not related to cerebral venous sinus thrombosis) is not influenced by the infection. Al Saigheh[31] et al. have published two cases with primary SAH and hemorrhagic conversion of an ischemic stroke related to COVID-19. However, no other larger case series

showing a similar trend were observed in the literature at the time of this publication. The increase in ICH at our institution again could be explained by a change in referral patterns and perhaps access to vital primary care services, medications and control of vascular risk factors during the lockdown which needs to be studied further from a population health standpoint.

6. Limitations

Our study is limited by the fact that it is a retrospective observational study with a small sample at a single center leading to inherent selection bias. Both ischemic and hemorrhagic stroke patients admitted during the two time periods were well balanced as far as baseline demographics and risk factors are concerned, allowing for a valid comparison of patients. However, stroke patients with or without COVID-19 could have been admitted to other centers during the study period. As we are still in the midst of the pandemic, longitudinal outcome data is limited.

7. Conclusions

Our initial experience has highlighted some important trends. Firstly, stroke continues to occur during this pandemic and health systems need to have capacity to deal with stroke. Secondly COVID-19 associated ischemic stroke occurs in predominantly male patients who are younger, with fewer vascular risk factors, and can be more severe, with higher rates of LVO. Thirdly despite an increase in LVO during the pandemic treatment with mechanical thrombectomy has not increased which will likely translate to worse outcomes. Fourthly COVID-19 associated hemorrhagic stroke does not differ from non COVID-19 hemorrhagic stroke patients. Finally stroke pathway times have and will be impacted by the pandemic and it is vital that stroke centers continue to analyze their own data to reduce time to treatments while also balancing safety and personal protection of the caregivers involved. To assess the full impact of the pandemic on stroke care a post pandemic multicenter retrospective review will aid in drawing more meaningful conclusions.

Credit Author Statement

All authors have reviewed the manuscript thoroughly and consent to its submission to Clinical Neurology and Neurosurgery. There are no conflicts of interests for any of the authors. We also confirm that this manuscript is submitted solely to Clinical Neurology and Neurosurgery and is not under consideration with any other journal.

Grant support/Funding

None

Declaration of Competing Interest

None

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