

Stroke Incidence and Outcome in a Population With COVID-19

The Neurohospitalist
2022, Vol. 12(2) 213–217
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DOI: 10.1177/19418744211043323
journals.sagepub.com/home/NHO



Moayd M. Alkhalifah, MD¹ , Ramzi Banda, MD¹, Shukri Alqudihy, MD²,
Shireen Qureshi, MD¹, and Jaffar A. Al-Tawfiq, MD^{3,4,5}

Abstract

Background and Purpose: COVID-19 is associated with systemic thromboembolism including stroke. The study evaluated the 30-days stroke incidence in SARS-CoV-2 PCR positive patients and described the outcome of such patients. **Methods:** This is a retrospective study of consecutive patients with a positive SARS-CoV-2 PCR test between March 1st, 2020 and August 30th, 2020. The study included COVID-19 patients who were hospitalized and had a stroke within 30 days from the positive PCR test. **Results:** During the study period, there were 4301 patients with a positive SARS-CoV-2 PCR test. Of those, 1786 patients (41.5%) were hospitalized and 4 patients developed a stroke within 30 days. The 30-days stroke incidence was 0.09% and 0.2% of all and hospitalized patients, respectively. The mean age of stroke patients was 78 years and 2 died during the same hospitalization. The 4 patients had comorbidities, one had pre-existing atrial fibrillation and all had ischemic stroke. **Conclusion:** This study showed a low 30-day incidence of stroke among COVID-19 patients.

Keywords

stroke, cerebrovascular disorders, infectious disease medicine, clinical specialty, epidemiology, techniques, outcomes

Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and its associated disease Coronavirus Disease 2019 (COVID-19) was first recognized in December 2019. The World Health Organization (WHO) declared a pandemic on March 11, 2020.¹ A year later, more than 118 Million cases have been identified and more than 2.6 Million people died because of this disease.

COVID-19 typically presents with fever, dry cough, shortness of breath, myalgia and headache.² Other less common presenting symptoms include anosmia, nausea and diarrhea. The clinical course of COVID-19 illness ranges from asymptomatic, to mild self-limiting symptoms, severe pneumonia, multiorgan failure and death.^{2,3} Systemic thromboembolism can be the presenting symptom or may develop as one of the disease complications.

Platelet-rich thrombi in the microvasculature of the pulmonary, cardiac, renal and hepatic circulation was found in autopsies of several confirmed COVID-19 patients.⁴ Generally, patients with history of stroke had more severe course of COVID-19 disease, were more likely to develop ARDS, and require mechanical ventilation and were less likely to recover.⁵ In a cohort of stroke associated with COVID-19 compared to historical strokes without COVID-19, stroke were more likely to be cryptogenic with a higher mortality

and younger patients with stroke due to emergent large vessel occlusion.⁶ The incidence of acute ischemic stroke among hospitalized COVID-19 patients or those presenting to the emergency department was 1.6% compared to 0.2% in patients hospitalized with influenza historically.⁷ The median duration from COVID-19 symptom onset to the diagnosis of acute ischemic stroke was 16 days.⁷

The mechanism of COVID-19 associated thromboembolism in general and stroke specifically is not fully understood.⁸ Globally, the overall incidence of stroke among all individuals with COVID-19 is unknown. Previous studies focused on determining the incidence rate of stroke among admitted

¹ Neurology Unit, Neurosciences Institute, Johns Hopkins Aramco Healthcare, Dhahran, Saudi Arabia

² Hospital Medicine Department, Johns Hopkins Aramco Healthcare, Dhahran, Saudi Arabia

³ Specialty Internal Medicine and Quality Department, Johns Hopkins Aramco Healthcare, Dhahran, Saudi Arabia

⁴ Infectious Disease Division, Indiana University School of Medicine, IN, USA

⁵ Infectious Disease Division, Johns Hopkins University School of Medicine, Baltimore, MD, USA

Corresponding Author:

Moayd M. Alkhalifah, Neurology Unit, Neurosciences Institute, Johns Hopkins Aramco Healthcare, Dhahran, Saudi Arabia.

Emails: alkhalifah.moayd@gmail.com; moaydm2@hotmail.com

COVID-19 patients. Yet, the incidence rate of stroke among all COVID-19 patients is not well investigated. In this study, we sought to calculate the incidence of ischemic stroke, intracerebral hemorrhage (ICH) and cerebral venous sinus thrombosis (CVST) in people with a positive SARS-CoV-2 nasopharyngeal swab and among admitted patients and identify significant risk factors for developing stroke.

Methods

This is a retrospective study to determine the incidence of ischemic and hemorrhagic stroke in people older than 18 years with a positive SARS-CoV-2 PCR test between March 1st, 2020 and August 30th, 2020. This is a retrospective chart review. Utilizing the hospital's electronic health record's COVID-19 report and stroke registry, patients with a positive SARS-CoV-2 PCR test were reviewed for admission to the hospital with an acute stroke within 30 days. Stroke is defined as a clinical presentation with an acute focal neurological dysfunction due to an acute cerebral ischemia or hemorrhage. Patients' demographic data, clinical presentation, laboratory and radiological findings and 30-days mortality were collected. Johns Hopkins ARAMCO Healthcare institutional review board approved the study (IRB # 20-38).

Electronic Health Records

Epic was used to review patients' charts and identify patients admitted to the 2 locations within our network. Epic COVID-19 report was generated and included all the patients with a positive SARS-CoV-2 PCR test during the study period. This report was matched with the hospital's Stroke registry to identify patients with an acute ischemic stroke, ICH or CVST within 30 days from the positive PCR test. The stroke registry includes all patients who were admitted or presented to the emergency department with a confirmed or suspected stroke as defined above.

Study Population

JHAH provides free medical care to Saudi Aramco employees and their dependents. Patients with a positive SARS-CoV-2 PCR test were enrolled in COVID-19 home monitoring program where they were monitored for COVID-19 symptoms and/or complications. Patients were discharged from the COVID-19 home monitoring program after recovery according to the Saudi Ministry of Health guidelines and continued to follow up with their primary health care provider within our network. Patients who developed severe symptoms or other medical illness requiring an admission were referred to the hospital for admission and inpatient management.

Statistical Analysis

Descriptive statistics were used to report the study population demographic data, admission rate and incidence of stroke.

Furthermore, descriptive statistics were used to describe the features of the patients with an acute stroke including demographic data and premorbid vascular risk factors and anticoagulation use in addition to the stroke presentation and outcome details.

Results

During the study period, there were 4301 patients with a positive SARS-CoV-2 RT-PCR. The median age was 45 years and 69.6% were men. Of those patients, 1786 patients (41.5%) were admitted to the hospital. Four patients developed a stroke within 30 days from the positive SARS-CoV-2 PCR test, 0.09% and 0.2% of the all and hospitalized patients, respectively.

The mean age of the stroke patients was 78 years and all of them were white (middle eastern) and they were previously diagnosed with hypertension and dyslipidemia (Table 1). In addition, 3 patients (75%) had an underlying diabetes mellitus and atrial fibrillation. One patient had atrial fibrillation and an ischemic stroke in the past but was not on an anticoagulant medication due to a history of major hemorrhage. All strokes were ischemic and none of them was eligible for IV thrombolysis or endovascular thrombectomy due to delayed presentation. The patients' delayed presentation was due to late arrival to the hospital and not directly related to COVID-19 precautions. All of the stroke patients were evaluated with a brain Computed Tomography (CT) and/or Magnetic Resonance Imaging (MRI). Cervical Carotid and Vertebral artery imaging was available for 3 patients and didn't reveal symptomatic stenosis. Magnetic Resonance Angiography (MRA) of the head was available for 2 patients and showed symptomatic stenosis related to the acute stroke in one patient (Table 2). Transthoracic Echocardiogram was available for 2 patients, one of them had low ejection fraction and a severely dilated left atrium. PT and aPTT was available and normal in 3 patients, D-dimer was high (>35 mg/L) in one patient only and all patients had a normal platelet count. All of the stroke patients were admitted to a stepdown unit except one who was admitted to the intensive care unit. Two patients with stroke were discharged home and the other two died in the hospital during the same admission.

Discussion

Among 4031 patients with a positive SARS-CoV-2 PCR test, 4 (0.2%) out of 1786 admitted patients had a stroke within 30 days. However, considering all COVID-19 positive cases, the incidence rate was 0.099%. In a large study of 8163 COVID-19 patients, 103 (1.3%) patients developed acute ischemic stroke.⁹ Other studies reported 0.5-5% of the patients with COVID-19 having a diagnosis of stroke.^{10,11} A study of 214 COVID-19 patients reported stroke in 2.8% of the patients and another study of 221 hospitalized COVID-19 patients showed 13 (5.8%) stroke cases.^{12,13} The mean time to the onset of ischemic stroke was 12 days in the course of

Table 1. A Summary of the COVID-19 Positive Cases With Stroke.

		Patient 1	Patient 2	Patient 3	Patient 4
Demographic data	Age (years)	93	71	72	77
	Sex	Male	Female	Female	Male
	Race	White (middle eastern)	White (middle eastern)	White (middle eastern)	White (middle eastern)
Vascular Risk Factors	Hypertension	Y	Y	Y	Y
	Diabetes mellitus	N	Y	Y	Y
	Dyslipidemia	Y	Y	Y	Y
	Atrial Fibrillation	Y	Y	N	Y
	Coronary Artery Disease	N	N	Y	Y
	Chronic Kidney Disease	N	N	Y	N
	History of Stroke	Y	N	N	N
	Anticoagulation therapy	N	Y	N	Y
SARS-CoV-2 PCR tests indication	Screening	N	N	N	N
	Symptomatic	Y	Y	Y	Y
Admission before Stroke onset	Step down	Y	Y	Y	N
	Intensive care unit (ICU)	N	N	N	Y
Labs	WBC (x1000/cumm)	3	3.4	8.3	14.2
	Platelet (x1000/cumm)	130	303	455	196
	D Dimer (mg/L)	1.03	1.77	2.09	>35
	INR		1.1	0.9	1.1
	aPTT (Seconds)		40	26	25
	BUN (mg/dL)	17	13	22	43
Stroke	Creatinine (mg/dL)	0.9	0.6	1.5	0.9
	Ischemic Stroke	Y	Y	Y	Y
	Hemorrhagic Stroke	N	N	N	N
	Intravenous tPA therapy	N	N	N	N
	Mechanical thrombectomy	N	N	N	N
	30 days morality	Y	N	N	Y

Table 2. A Summary of the Stroke Workup Findings.

	Patient 1	Patient 2	Patient 3	Patient 4
Head CT	Right cerebellar hypodensity	-	-	-
Brain MRI		Left frontal cortical DWI restriction	Right Occipital and medial temporal (posterior cerebral artery territory) DWI restriction	Multiple bilateral anterior and posterior circulation DWI restrictions
Head MRA	-	-	Right posterior cerebral artery atherosclerotic stenosis and occlusion, right middle cerebral artery mild atherosclerotic stenosis	Mild right posterior cerebral artery atherosclerotic stenosis
Neck MRA	-	-	Mild asymptomatic right internal carotid artery stenosis	Normal
Carotid Duplex Ultrasound	-	Normal	-	-
Transthoracic ECHO	-	Ejection fraction 30-35%, severely dilated left atrium	-	Normal

COVID-19.¹⁴ In a large study of 3744 COVID-19 patients, only 6% had a stroke.¹⁵ However, a meta-analysis showed that the prevalence of cerebrovascular diseases was 9.9% with a range of 6.8% to 13.4%.¹⁶

The findings of this study suggested a lower incidence of stroke among all COVID-19 population. There were 2

possible explanations for this finding. First, this study included asymptomatic and outpatient individuals while other studies measured the incidence in patients admitted to the hospital or the emergency department, all of whom were symptomatic and had more severe diseases. Second, the overall COVID-19 case fatality, hence, severity in this part of the

world might be lower than that reported in other parts of the World such as New York (1.2% Vs 7.1%) where most of the stroke incidence reports were published. Disproportionate rates of COVID-19 hospitalizations and complications development was noted in specific populations with common socioeconomic status and race like Black and Hispanics.¹⁷⁻²⁰ The fatality rate was reported to be high in stroke with COVID-19 with rates of 34.4% (95% CI, 27.2%-42.2%).²¹ Similarly, 50% of patients in this case series had died. It is interesting to note that the majority (69.6%) of the included patients in this study were male. This finding may reflect the demographics of the study population and may not be generalizable to other population. An initial study from the same institute showed that about 60% of included patients in quarantine program were male.²²

The present study has several limitations. First, this was a small and a single-center retrospective study which may limit the study generalizability to other populations. Second, the number of patients with stroke was low, hence, it is difficult to identify clear variables associated with a greater risk of stroke or mortality or gender disparity. Third, despite the close follow up using the COVID-19 home monitoring program patients may have presented with an acute stroke to another healthcare facility. Fourth, a large proportion of the individuals with a positive SARS-CoV-2 PCR test were asymptomatic and were required to be admitted to the hospital based on the initial local guidelines from the Saudi Ministry of Health.^{2,22,23} This may have underestimated the true stroke incidence in patients COVID-19 disease. Nevertheless, this study shed light on the variability in stroke incidence among individuals with a positive SARS-CoV-2 PCR test. Larger scale, multi-center epidemiological studies may identify the risk factors for developing a stroke in the setting of COVID-19 disease and eventually identify the most appropriate preventive measures.


Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

ORCID iD

Moayd M. Alkhalifah  <https://orcid.org/0000-0002-1801-1686>

Supplemental Material

Supplemental material for this article is available online.

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