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Original Research Article

Stroke in COVID-19 Patients: An Observational Clinical Study

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Abstract

Background: The novel coronavirus is not exclusively a respiratory disease but have a neurological manifestation that is associated with high rates of mortality and morbidity. The aim of study was to examine stroke in COVID-19 patient in a tertiary care hospital.

Method: This was a single center retrospective, observational study of total 960 confirmed COVID-19 patients admitted in Ayush Hospital between July 1, 2020, and March 30, 2021. The medical history, demographic characteristics, laboratory and chest CT scan findings were extracted from electronic medical records. All neurological symptoms of stroke patients were reviewed and confirmed. The data were collected, segregated and analyzed.

Results: The study shows that 0.7% COVID-19 patients had stroke during hospitalization. Further, the older patients, co morbidity (hypertensive) and severity of infection were found to be associated risk factors.

Conclusion: The present study concludes that patients with older age group, co morbidity especially hypertensive and severe COVID-19 infection had possible risk factor for cerebrovascular disease like stroke.

Keywords: COVID-19; Stroke; Tertiary Care Hospital.

Introduction

COVID-19 is a virus that may damage many organs, including the brain, in addition to the lungs. According to a recent international investigation, SARS–CoV-2 infection is linked to both ischemic and hemorrhagic strokes. One of most severe neurological consequences of SARS–CoV-2 infection seems to be cerebrovascular accident (CVA). With the increase of COVID -19 cases in recent pandemic times, we are seeing a rising number of COVID -19 associated CVA patients, particularly in the state of Karnataka. Patients may be at risk for stroke owing to a variety of variables, including an overactive inflammatory response, hypercytokinemia, a prothrombotic condition, and endothelial dysfunction caused by angiotensin-converting enzyme 2 depletion, according to emerging hypotheses (ACE2) [1, 2].

India is a home of 1.37 million people where stroke is evolving a major limitation towards healthcare due to economic burdens, lack of awareness, fear of hospitalization and poor access to healthcare. This burden might have

created challenges for treating SARS CoV 2 associated with stroke.

The clinical profile, neuroimaging results, and consequences of COVID-19-related strokes are currently being researched, and it is unclear if COVID-19 may be observed a risk factor for CVA. The characteristics of COVID-19-related strokes from a referral hospital in the tiny city of Vijayapura, Karnataka, India, are reported here.

The goal of the study was to use neuroimaging data to explore contact of stroke in COVID-19 patients and to link these findings with clinical features. Also, to look at the risk variables linked with hospitalised COVID 19 stroke patients, such as age, gender, co-morbidity, and severity.

Methods:

Study Protocol

Single-center observational research was conducted. Between July 1, 2020, and March 30, 2021, 960 COVID-19 confirmed patients were acknowledge to AYUSH facility in Vijayapura. AYUSH Hospital was one of the first non-government self-financing hospitals in the region to be recognised as a COVID-19 Care Hospital by the government through early stages of the SARS-CoV-2 epidemic & is responsible for SARS-CoV-2 infection treatment.

Diagnosis

This investigation, all COVID-19 patients with respiratory symptoms, SARS-CoV-2-RT-PCR positive in a throat swab and viral-like pneumonia on chest HRCT were diagnosed according to WHO interim guidelines [3, 4].

Electronic medical records were used to extract demographic information, medical history, symptoms, clinical signs, laboratory and chest CT scan results. A brain CT scan and clinical symptoms confirmed diagnosis of acute ischemic or hemorrhagic stroke. Physicians and neurologists examined and confirmed all neurological complaints.

The day the symptoms were first recognised was the date of illness beginning. SARS-CoV-2 infection was verified utilising a SARS-CoV-2 nucleic acid detection kit and a real-time RT-PCR test. Trial of org 10172 in acute stroke treatment (TOAST) categorization was used to categorise the different kinds of ischemic stroke. The outcomes of 960 COVID verified stroke patients were evaluated in this study.

Patient Management

On admission all moderate to severe COVID 19 cases received standard pharmacological treatment as per ICMR guidelines [5]. Cases with moderate seviarity (RR> 24/min with dyspnea or sp02 <93% on room air) received oxygen therapy with rebreathing masks with or without awake proning. Corticosteroid therapy (with inj. methyl prednisolone or inj. dexamethasazone), anticoagulant therapy (with low molecular weight heparin/unfractionated heparin), with prophylactic antibiotic treatment, zinc and Vit C supplementation was given.

Severe cases (with RR> 30/min with dyspnea or Spo2<90% on room air) were admitted in ICU with NIV, HFNC support. Intubation was considered in patients with dropping saturation and who had increased work of breathing. Antiviral therapy (Favipiravir /inj. Remdesvir), antimonolconal immunomodulatory therapy (inj. Tocilizumab) was considered in specific situations based on limited evidence.

Statistical Analysis:

Between patients with and without new onset of stroke, constant variables were reported as means, SD, or median and range values. Counts and percentages were used to express categorical data.

Results:

Following COVID-19 infection, 7 patients (0.7%) experienced new onset of Stroke out of 960 patients with confirmed SARS-CoV-2 infection. **Table 1** showing clinical features of COVID-19 individuals who had a stroke or did not have a stroke.

Table 1: Clinical characteristics of patients with COVID-19

Clinical characteristics	COVID-19 WITH STROKE (N=7)		COVID-19 WITHOUT STROKE (N=953)	
	N	%	N	%
AGE (YEARS)	56 to 79 years		18 to 79 years	
<50 Years	0	0.0%	778	78.3%
>50 Years	7	100.0%	215	21.7%
Sex				
Male	4	57.1%	668	67.3%
Female	3	42.9%	325	32.7%
COVID 19 SEVERITY				
Severe	6	85.7%	134	13.5%
Moderate	1	14.3%	160	16.1%
Mild	0	0.0%	699	70.4%
COMORBIDITY HISTORY				
Diabetes Mellitus	4	57.1%	379	38.2%
Hypertension	6	85.7%	347	34.9%
IHD	2	28.6%	84	8.59%
COPD	0	0.0%	28	2.89%

Table 1 clearly shows that all the stroke patents were above 50 years old. Further Table 1 indicates 85.7% patient among stroke patient were n severe category as compared to only 13.5% of COVID-19 without stroke. The result also shows that 85.7% stroke patient has hypertensive as comorbidity.

Table 2 shows demographic and clinical characteristics of COVID-19 patients.

Table 2: Baseline Characteristics of Stroke Patients with COVID-19

	Type of Stroke	Age (yrs)	Sex	Blood pressure	Blood glucose	Smoking history	Alcoholism history	Severity of COVID 19	Time gap between infection and onset of stroke	Treatment of stroke	Outcome
P1	Intracerebral hemorrhage	64	F	150/90	170	_	_	Severe	6 days	Anti-edema measures and supportive therapy.	Improved & Discharged
P2	Acute ischemic stroke	75	M	130/70	232	+	+	Severe	20 days	Antiplatelets + Anticoagulants	Diseased
P3	Acute ischemic stroke	62	M	140/90	382	+	_	Severe	16 days	Antiplatelets + Anticoagulants	Diseased
P4	Acute ischemic stroke	56	M	180/100	133	+	_	Severe	11 days	Antiplatelets + Anticoagulants	Improved & Discharged
P5	Acute ischemic Stroke	59	F	170/100	242	_	_	Severe	10 days	Antiplatelets + Anticoagulants	Diseased
P6	Acute ischemic Stroke	79	F	170/100	122	_	_	Moderate	5 days	Antiplatelets + Anticoagulants	Improved & Discharged
P7	Acute ischemic stroke	73	M	100/60	64	_	_	Severe	15 days	Antiplatelets + Anticoagulants	Improved & Discharged

Table 2 shows 7 cerebrovascular confirmed COVID patients, of which 6 patients (85%) were diagnosed with ischemic stroke and 1 patient (15%), had intracerebral hemorrhage. The participants varied in age from 56 to 79 years old (median 67.5 years). Three patients (42%) had a history of smoking, and one (14%) had a history of alcohol consumption. At the time of stroke diagnosis, 6 patients (85.7%) had high BP (130/80 mm Hg) and 4 patients (57.1%) had high blood glucose levels (>6.1 mmol/L).

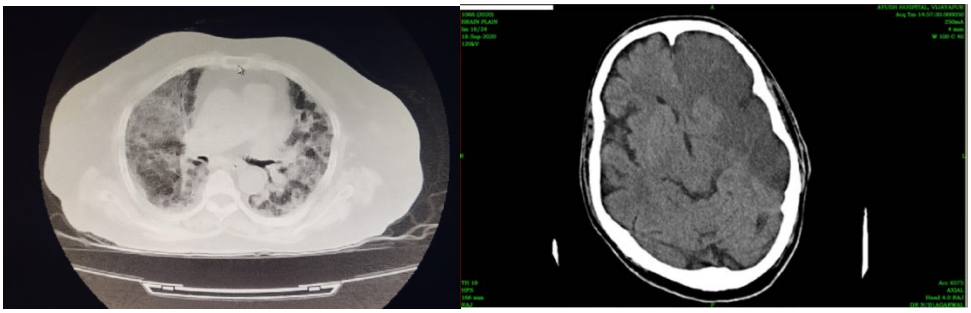
Three of six patients with ischemic stroke had National Institute of Health stroke scale ratings <8, whereas the other three had values of greater than or equal to 8.

Table 3: Laboratory findings of COVID-19 patients

	P1	P2	P 3	P4	P5	P6	P 7	Mean± SD	Median
WBC (in per cm)	7950	4020	20470	5920	8270	14510	13700	10691.4±5344.0	8270
Neutrophils (%)	86.2	75	88	73.2	85.7	92.1	87.1	83.9 ± 6.5	86.2
Lymphocytes (%)	11.2	15.4	5.5	19.2	10.9	5.1	8.9	10.9 ± 4.7	10.9
NLC RATIO	7.69	5	16	3.81	7.86	18.05	9.78	9.7 ± 5.0	7.86
Platelet Count (Lakhs/cm)	2.98	1.65	5.5	3.25	2.99	4.05	2.59	3.3 ± 1.1	2.99
Hb% (Gm%)	11.9	12.5	9.2	14.9	12.4	11.8	13	12.2 ± 1.6	12.4
CRP (Mg/dl)	16.6	111	92.4	36.9	43.9	92.5	93.9	69.6 ± 33.6	92.4
D –DIMER (Mg/dl)	940	1774	808	1076	1799	9403	4547	2906.7±2903.9	1774
ALT (IU/L)	10	33	27	30	27	12	34	24.7 ± 9.0	27
AST (IU/L)	19	61	12	29	34	56	54	37.9 ± 17.9	34
S. Creatinine (Mg/dl)	1	1	1.8	1.2	0.9	1.3	1.14	1.2 ± 0.3	1.14
IL6 (pg/ml)	10	260	>500	40	>500	124.1	268	300.3 ± 268.7	260
LDH (Mg/dl)	360	738	607	522	875	900	654	665.1 ± 177.9	654
HRCT THORAX SCORE (out of 25)	7	20	24	4	24	24	24	18.2 ± 8.1	24

The laboratory results of COVID-19 individuals are shown in **Table 3**. Patients with stroke exhibited a greater inflammatory response, with higher WBC, neutrophil counts, and C reactive protein (CRP) levels, but decreased lymphocyte counts (10.9%), indicating immunosuppression. D-Dimer levels were similarly increased in stroke patients. In addition, patients with stroke had elevated serum creatinine and also had severe disease with High score on HRCT thorax.

Representative CT brain image of patient 6 with new onset of acute ischemic stroke and HRCT chest with extensive bilateral ground glass opacities are shown in **Figure 1.**



(a) **(b)**

Figure 1: Chest (a) and brain images (b) of COVID-19 patient 6 with stroke. HRCT thorax showing bilateral ground glass opacities (a) and CT brain shows new onset of acute ischemic stroke (b).

Discussion:

This is follow-up study of 960 COVID-19 patients who had a new start of stroke. Following infection with COVID-19, seven individuals suffered a stroke. Stroke patients were older and had a higher likelihood of having cardiovascular and cerebrovascular risk factors. These results showed that older COVID-19 patients are more expected to have a stroke, and that older patients with cerebrovascular risk part should be given greater attention.

Importantly, 6 out of 7 stroke patients had severe SARS-CoV-2 infection, signifying that severe infection possibly linked to stroke, particularly acute ischemic stroke. Many studies have previously shown that very ill individuals are more prone to acquire neurological symptoms [6]. Endothelial apoptosis and neuronal damage are caused by SARS-CoV-2, which contains spike protein surface unit that binds strongly to the human ACE2 receptor [7, 2].

COVID-19 infection has been shown in studies to hasten the development of acute stroke [8, 9]. Previous research on COVID-19 in a broad sample of patients has convincingly demonstrated connection between stroke and COVID-19 and poor result[7]. In addition, an imaging screening of inpatients research on COVID-19 patients indicated that COVID 19 was linked to very high D-Dimer levels. Patients with a record of stroke were also shown to be 2.5 times more possible to have severe COVID-19 [10].

These observations were corroborated with our present study on stroke patients.

Inflammation has been identified as a major player in the pathophysiology of strokes [11], as well as in the acute intravascular events induced by a blood supply disruption. Several investigations have discovered a link between increased CRPs & D-Dimer levels in COVID-19 patients [12 -16].

Clinically, the higher D-Dimer and CRP values in this study suggest that COVID 19 may have caused inflammation, and that it may have developed a hypercoagulable state as a result of improved concentrations of proinflammatory cytokine [1, 3] and serum inflammatory factors (e.g., interleukin and CRP), which were accountable for early molecular events triggered by coagulation abnormalities among the stroks [17, 18].

Further, the present study reveals that patients with stroke had higher blood CRP & D-Dimer than patients with COVID 19 without stroke, which indicate D-Dimer as an important biomarker for understanding pathophysiology of stroke or any cardiovascular disorder.

The present study had median durations of 10 days (range 1-29). The days of onset of stroke after admission due to COVID 19 were widely variant with having a mean of 10 days. This study is in accordance with the previous studies [19-22].

According to the TOAST classification, two of the six patients with ischemic stroke had large-vessel atherosclerosis, three had small-vessel occlusion, one cardioembolism type. All of these individuals had an elevated inflammatory response as well as a hypercoagulable condition. The decision of antiplatelet/anticoagulant therapy for ischemic stroke was made at caution and judgement of treating team after a thorough evaluation of TOAST classification, clinical syndrome, and laboratory result. Antiplatelet therapy with aspirin or clopidogrel was given to all six ischemic stroke patients, as well as anticoagulant therapy with enoxaparin. The total mortality rate was 42 percent (3/7) till March 24, 2021. After 15 days, the intracerebral haemorrhage patient improved.

Thus, diagnosing COVID-19 based on clinical symptoms and laboratory testing early on and implementing steps, particularly for the older age group of patients with co-morbidities, may help to avoid COVID-19 development and minimise the risk of stroke.

Conclusion:

Stroke is not uncommon among COVID-19 individuals, according to the findings of this study. Patients with stroke were older, had many co-morbid conditions, including hypertension, and had a severe COVID infection, all of which are potential risk factors for cerebrovascular illness. The median period from infection with SARS-CoV-2 to start of a stroke was around ten days. As a result, physicians should pay greater awareness to older COVID-19 patients with comorbidities while treating them for cerebrovascular problems such as stroke.

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Ethical approval:

The study was approved by the Institutional Ethics Committee

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