

COVID-19 and Acute Ischemic Stroke; An Indian Experience

Sir,

Since Dec 2019, the entire world is experiencing pandemic of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The disease typically manifests with respiratory system involvement. Neurological complications including acute ischemic stroke (AIS) have been increasingly described.^[1-4] We report our experience of AIS in COVID-19 patients.

We conducted retrospective study in 2 hospitals in Pune, India. Deenanath Mangeshkar Hospital has treated >3,500 COVID-19 patients while Noble hospital has treated >1,200 COVID-19 till 20 Jul 2020. Patients

with COVID-19 who suffered AIS were included in this study. Their demographic details, history, neurological manifestations, systemic manifestations, laboratory results, imaging findings, treatment and progress were reviewed.

COVID-19 was diagnosed if clinical syndrome was consistent with disease and patient had positive real-time reverse transcriptase polymerase chain reaction (RT-PCR) or rapid antigen test on throat swab sample for SARS-CoV-2. AIS is diagnosed as sudden onset neurological deficit consistent with stroke and appropriate computerised tomography (CT) and/or magnetic resonance imaging (MRI) findings.

Table 1: Baseline characteristic of AIS patients

Demographic characteristics		Number	%	
Sex	Male	13	100	
	Female	0	0	
Age	<40 years	3	23.1	
	>60 years	10	76.9	
Medical illnesses	Diabetes mellitus	7	53.8	
	Hypertension	3	23.1	
	Ischemic heart disease	2	15.4	
	Previous stroke	2	15.4	
	Atrial fibrillation	1	7.7	
	Brachial artery thrombosis	1	7.7	
	Carcinoma colon	1	7.7	
	Chronic obstructive pulmonary disease	1	7.7	
	Chronic kidney disease	1	7.7	
	Dementia	1	7.7	
	None	2	15.4	
	COVID symptoms	Fever	8	61.5
		Cough	6	46.2
Dyspnoea		7	53.8	
Gastro-intestinal		2	15.4	
Poor appetite		1	7.7	
Myalgia		1	7.7	
COVID diagnosis	RTPCR	12	92.3	
	Rapid antigen	1	7.7	
Laboratory investigations	High d dimer (>500 ng/ml)	11	84.6	
	High CRP (> 6 mg/L)	13	100	
Drugs	Aspirin	5	38.4	
	Heparin	5	38.4	
	Aspirin + heparin	4	30.8	
	Oral anticoagulation	1	7.7	

(COVID-coronavirus related disease, RTPCR- reverse transcriptase polymerase chain reaction, CRP- C reactive protein)

RESULTS

We identified 13 patients suffering from AIS and COVID-19 infection amongst 4,796 admitted patients with COVID-19. The incidence of AIS is 0.27%. Their demographic and baseline characteristic are described in Table 1.

Three patients were younger than 40 years; 10 were >60 years. Eleven patients had associated medical diseases. Diabetes mellitus (53.8%) was commonest comorbidity. Common COVID-19 symptoms were fever (61.5%), dyspnoea 53.8%) and cough (46.2%). D dimer levels were elevated in 84.6%. CRP was raised in all.

Patients were prescribed various antiplatelet agents and anticoagulant as part of COVID-19 treatment before stroke had occurred. Five patients were taking aspirin, 1 rivaroxaban, 5 heparin and 4 were taking both aspirin and heparin.

Three (23.7%) patients presented with stroke and developed clinical manifestations of COVID-19 2, 3 and 7 days later.

Table 2: Stroke characteristic of AIS patients

Stroke characteristic		Number	%
Days from onset of symptoms	Before COVID symptoms	3	23.1
	<7 days	2	15.4
	7 to 14 days	5	38.4
	>14 days	3	23.1
Stroke symptoms	Hemiparesis	11	84.6
	Aphasia	2	15.4
	Neglect	2	15.4
	Hemianopia	1	7.7
	Ataxia	1	7.7
	Seizure	1	7.7
NIHSS	Mild (<8)	5	38.4
	Moderate (9-15)	2	15.4
	Severe (>16)	6	56.2
Imaging classification	Total anterior circulation	4	30.8
	Partial anterior circulation	3	23.1
	Lacunar	1	7.7
	Posterior circulation	2	15.4
	>1 territory	2	15.4
	Not able to classify	1	7.7
Angiography	Normal	4	30.8
	Extracranial disease	1	7.7
	Intracranial disease	3	23.1
	Not done	5	38.4
Treatment	Aspirin	13	100
	Clopidogrel	7	53.8
	Heparin	9	69.2
	Thrombolysis	1	7.7
Outcome	Improved	3	23.1
	Same	5	23.1
	Worsened	1	7.7
	Died	4	23.1

(COVID- coronavirus related disease, NIHSS- national institute of health stroke scale, GCS- Glasgow coma scale, CT- computerised tomography, MRI- magnetic resonance imaging)

Remaining 10 (76.3%) suffered stroke during course of the illness; mean 10.6 days after onset of COVID-19 symptoms. The stroke characteristics are described in Table 2.

Hemiparesis was commonest (84.6%) clinical manifestation of stroke. Aphasia, neglect, hemianopia, seizure and ataxia were less common manifestations. As per NIHSS criteria, stroke was mild (score <5) in 5, moderate (9-15) in 2, and severe (>16) in 6 patients. On imaging, 4 patients had large infarcts involving middle cerebral artery territory (MCA), 3 had partial infarcts in anterior circulation, 1 thalamic lacunar infarct, 2 posterior circulation infarcts (pontine and posterior cerebral artery (PCA) territory) and 2 had >1 arterial territorial infarct (1 bilateral MCA, 1 MCA and PCA). One patient of right hemiparesis with reduced level of consciousness showed few ischemic lesions on CT scan. His imaging features could not be classified. CT or MRI angiogram were performed in 8 patients; 4 of which were normal, 1 had extracranial internal carotid artery (ICA)

stenosis and 3 had intracranial occlusion (MCA in 2, PCA in 1).

All patients were treated with aspirin, 7 with additional clopidogrel, 9 with heparin while 1 patient was thrombolysed with tissue plasminogen activator (tPA). During the available short follow-up period of 2 weeks, 3 patients improved, 1 worsened, 5 did not improve while 4 died.

DISCUSSION

The incidence of AIS with COVID-19 varies between 0.9 and 2.7% with pooled incidence 1.2% in hospitalized patients.^[2] In our study, the incidence of stroke was 0.27% which is lower than reported incidence. In the earlier part of pandemic, both hospitals were admitting even mildly symptomatic patients. Such mildly affected patients very rarely develop complications. This led to higher denominator of our ratio of number of strokes to the total COVID admissions, resulting in lower incidence of AIS in our population.

Demographic features, stroke severity, imaging features, and mortality rates of our series match with previous reports.^[2-4]

Since the stroke mechanism in COVID-19 is not exactly known and is multifactorial,^[5] best preventive strategy is not known. Many patients in our series were either on antiplatelets (38.5%), or on anticoagulation (46.2%). We could thrombolysed 1 patient with tPA. Logistic issues, comorbidities and delayed recognition of in-hospital strokes were possible factors for less thrombolysis. In the treatment aspirin, either alone (100%), or with clopidogrel (53.8%) or with heparin (62.9%) were used. Heparin has been routinely used in the treatment protocols of COVID-19 in view of high incidence of pulmonary thrombo-embolism which can explain the high percentage of use of heparin in our series.

The important observations of the study are: (1) Incidence of AIS in COVID-19 patients was 0.27%. (2) AIS occurred in older persons with stroke risk factors in >75%. (3) AIS can be an uncommon presenting manifestation of COVID-19 and in >75% it occurred during the course of illness average 10 days after COVID symptoms. (4) More than 60% strokes were moderate to severe and about 70% were large artery strokes. (5) Elevated levels of d dimer and CRP was a common finding. (6) About a third patients developed strokes in spite of being on aspirin and/or heparin. (7) Mortality rate was 23.1%.

There are many unanswered questions about COVID-19 strokes. Do we need to screen all patients presenting with AIS for COVID-19 in the current pandemic? Whether these strokes are directly caused by COVID-19 and need different treatment approach? Which is the best preventive approach to avoid AIS? Large multicentric studies are needed to answer these questions.

To the best of our knowledge, this is first report of AIS with COVID 19 from India.

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Conflicts of interest

There are no conflicts of interest.

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