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Stroke: A neurological complication in COVID-19.

Abhigna M
JSS Medical College,Mysore,India, drvikrampatil@yahoo.com

Vikram Patil
JSS Medical College, JSS ACADEMY OF HIGHER EDUCATION AND RESEARCH,
drvikrampatil@rediffmail.com

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Stroke: A neurological complication in COVID-19.

Stroke: A unforeseen neurological effect in COVID-19.

Background:

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged as a new pathogenic virus in late 2019 and began infecting millions of people with severe lung infections. It spread worldwide in a short time and became a pandemic, after which the World Health Organisation (WHO) declared it a public health emergency. The SARS-CoV-2 infection that triggered this pandemic has been named Corona virus disease 2019 by the WHO (COVID -19). Stroke is now being recognized as a COVID-19 pandemic consequence, while the exact incidence is unknown. Stroke is the second leading cause of death worldwide, and absolute numbers of incident strokes, survivors, stroke-related deaths, and disability-adjusted life-years are increasing globally. Tremendous efforts in improving prevention, acute treatment, and neurorehabilitation have led to a substantial decrease in the burden of stroke over the past 30 years [1]. The COVID-19 clinical course is far more severe in older patients, men, and individuals with coexisting conditions such as hypertension, diabetes, heart disease, and obesity—all of which are risk factors for stroke [2]. Anosmia, hypogeusia, seizures, and strokes are among the neurological symptoms frequently seen with COVID-19 [3]. Although the exact reason is unknown, sepsis induced coagulopathy is linked to COVID-19 and may play a role in endothelial dysfunction, microthrombosis, and stroke. The RAS balance may be swayed in favour of the ACE-1-angiotensin II-AT1 axis by binding to and depleting ACE2, which can lead to endothelial dysfunction, organ damage, and stroke. It is important to note that not all people with COVID-19 will develop a stroke, and not all strokes in people with COVID-19 are directly caused by the virus. The increased risk of ischemic stroke is probably multifactorial, with activation of coagulation and inflammatory pathways as reflected in increased fibrin D-dimer levels, erythrocyte sedimentation rate, lactic acid dehydrogenase, and lymphopenia [4]. In this study we assessed imaging features of COVID-19 patients developing acute cerebrovascular disease and the stroke subtype and its implications in the COVID-19 pandemic.

Methods:

Study design and data collection

This was a retrospective-prospective cross-sectional study of 148 patients. The duration of the study was from December 1, 2020, to May 31, 2022 (18-month period), at the Department of Radiology, JSS Hospital, Mysuru. Retrospective data of all cases who met the inclusion criteria were gathered from May 2020 to November 2020 from the PACS and the hospital database. Patients with positive reverse transcription-polymerase chain reaction (PCR) for SARS-CoV-2 and COVID -19 probable case, defined according to the criteria of the WHO definition, who underwent cross-sectional imaging, were included. Patients who had recovered from COVID-19 were also included (All the cases were assessed within the time frame of 3 months after their COVID-19 infection). Excluded were subjects with head injury or pre-existing/incidental neoplastic lesions.

Statistical analysis

Data was analyzed using SPSS 22 and presented as frequencies/proportions for categorical data and mean/standard deviation for continuous data. Chi-square/Fischer's exact test and independent t-test were used for significance tests. Microsoft Excel and Word were used to create graphs. Results with a P-value <0.05 were considered significant.

Imaging protocol and imaging interpretation: The brain imaging findings were analysed with the help of 128 slice MDCT scanner and 3-Tesla MRI (Philips Intellispace portal 11.1.3.11608 software). MRI protocols used to evaluate the brain included T2-FSE- Axial, T1-FSE -Sagittal, Diffusion-weighted imaging, SWI, 3D- FLAIR and 3D TOF MRA.

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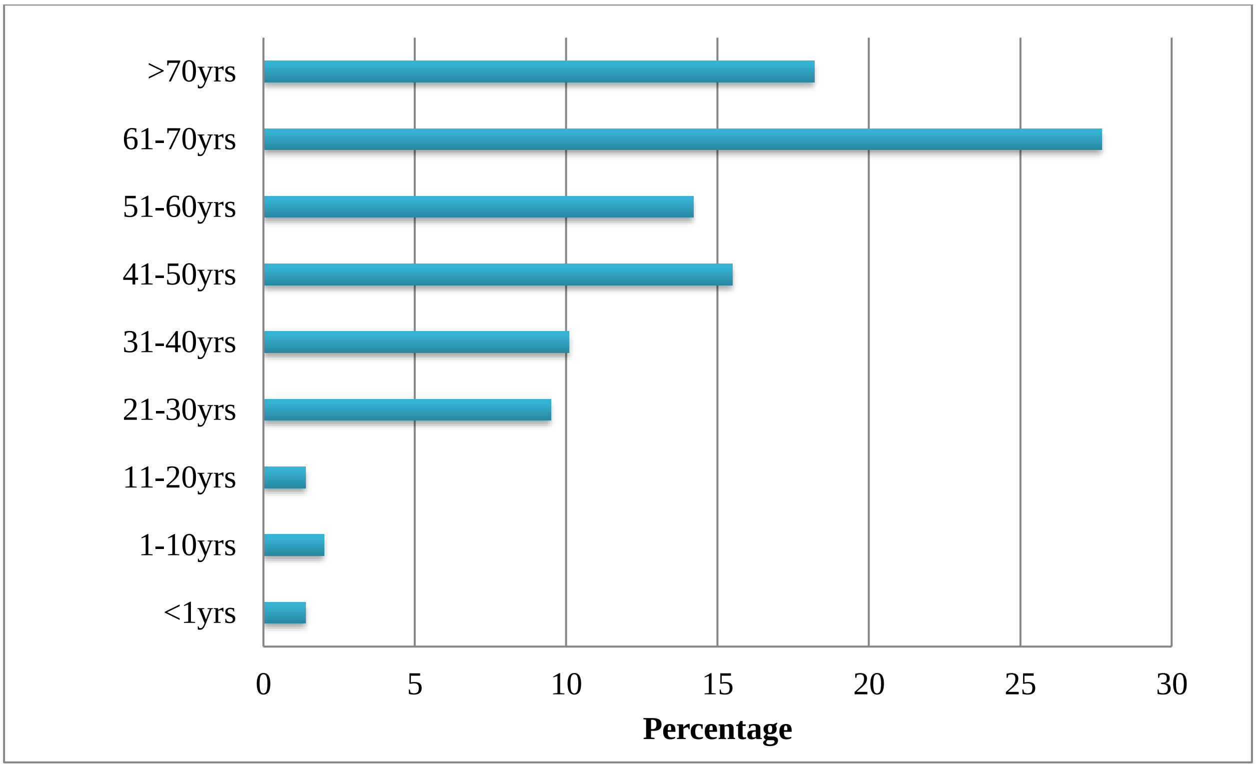
Results:

Figure I: Graph showing distribution of subjects according to age group



The age range of study participants was 8 days to over 70 years, with majority (27.7%) being between 61-70 years old. [Represented in table and Fig I]

Table I: Distribution of subjects according to gender

	Frequency (n)	Percentage
Female	**57**	**38.5**
Male	**91**	**61.5**

Total	**148**	**100.0**

Majority of the subjects were males (91 cases), among the total 148 cases.[Represented in table I]

Table II: Distribution of subjects according to COVID-19 status

	Frequency (n)	Percentage
COVID	98	66.2
COVID like illness.	10	6.8
POST COVID	40	27.0
Total	148	100.0

Of the 148 cases, 66.2% were positive for COVID-19 RT-PCR, 27% were post-COVID-19, and 6.8% had COVID-like illness– Represented in Table II

Table III: Distribution across time period

Time period	Cases
MAY 20-DEC 20	34
JAN 21-JUN 21	68
JUL 21-DEC 21	42
JAN 22-MARCH 22	4
TOTAL	148

Most of the cases were during the year 2021 in the first half as represented in the Table III.

Table IV: Distribution of subjects according to modality

Modality	Frequency(n)	Percentage %
CT	**111**	**75.0**
CT Cerebral angiography	**2**	**1.4**

MRI	**35**	**23.6**
Total	**148**	**100.0**

The study subjects underwent non contrast CT head (75%), followed by non contrast MRI and CT cerebral angiography as represented by table IV.

Table V: Distribution of subjects according to imaging findings.

	Frequency (n)	Percentage %
Acute infarcts	24	16.2
Sub-acute infarcts	12	8.1
Intraparenchymal hematoma	3	2.0
CVT	2	1.4
OTHERS	16	10.8
Chronic infarcts	9	6.08
No significant abnormality	82	55.4
Total	148	100.0

Table VI: Shows mean age of different neurological manifestations.

	Age in years	
	Mean	**SD**
Acute infarcts	56.304	21.1648
Subacute infarcts	63.833	11.3204
CVT	37.000	15.5563
Intraparenchymal hematoma	58.333	17.6730
Chronic infracts	68.375	13.0706

Table VII: Shows mean age of different neurological manifestations.

Comorbidities	Yes	No	Total
With acute stroke	29	12	41
Without	62	45	107
Total	91	57	148

Table VIII: Distribution of subjects according to according to COVID status.

	COVID		COVID LIKE illness.		POST COVID	
	n	%	n	%	n	%
Acute infarcts	19	19.4%	2	20.0%	3	7.5%
Subacute infarcts	8	8.2%	2	20.0%	2	5.0%
Intraparenchymal hematoma	2	2.0%	0	.0%	1	2.5%
CVT	2	2.0%	0	.0%	0	.0%
Chronic infracts	6	6.1%	0	.0%	2	5.0%

Table IX: Distribution of subjects with acute/subacute infarcts according their pattern of involvement.

	Number (N)	Percentage (%)
Watershed territories	**8**	**22.2**
Embolic	**4**	**11.1**
Thrombotic	**10**	**27.7**
Combined	**2**	**0.05**
No specific pattern	**12**	**33.3**

Table X: Follow up of the cases.

	Yes	N (8)	No	N (140)
Follow up	Hemorrhagic transformation	1		
	New infarcts	3		
	Nil	4		

Out of the total 148 cases, 8 of them underwent follow up imaging, among which 1 of them had hemorrhagic transformation of the infarcts and 3 of them had new infarcts.

RESULTS:

Between May 2020 and May 2022, 148 patients who met the study criteria underwent neuroimaging studies. The age range of the study group was from 8 days to over 70 years, with a mean age of 51.65 +/- 23.36 years. [Fig- I] Although strokes were more prevalent in older adults (mean age 56 years) due to comorbidities, a significant number of strokes were also observed in younger subjects. Most subjects were referred from the emergency department or intensive care units and had comorbidities, among which 36 patients had ischemic infarcts, 3 had spontaneous intracranial hemorrhage, 2 cases had cerebral venous thrombosis with associated venous infarcts. Old infarcts were the only findings in a few cases that could not be attributed to ongoing or previous COVID-19 viral infection. Of the total 36 cases with ischemic infarcts, 10 had demonstrable thrombotic occlusion of the great vessels, 4 subjects had an embolic pattern, 8 had infarcts in external and internal watershed zones, and some (n: 12) were distributed without a specific pattern. A total of 5 subjects had acute infarcts in the post-COVID-19 period, in contrast to the majority of cases observed during active infection (31 cases). Out of the total 148 cases, 8 of them underwent follow-up imaging; among which 1 of them had hemorrhagic transformation of the infarcts and 3 of them had new infarcts [Table XII]. There was no statistically significant difference between subjects who had a stroke and those who did not in terms of study variables such as mean age, sex, COVID, or comorbidity status.

DISCUSSION

In this study investigating the characteristics and outcomes of patients infected with SARS-CoV-2 and suffering a stroke, 27% of the individuals had acute CVA in COVID-19. Individuals with COVID-19 who experienced concomitant stroke were more likely to be older and have preexisting cardiovascular comorbidities. Most patients had been admitted with COVID-19 symptoms, with stroke occurring a few days later. Ischemic stroke was the commonest stroke subtype and was frequently characterized by multiple cerebral infarctions and cryptogenic etiology. In our study, the severity of the infective disease as assessed by the CT severity index had no significant association with stroke severity. Moreover, we found that people with COVID-19 developing a stroke were older, although a significant increase in the occurrence of stroke in the young was noted. This may be partly explained by the higher proportion of vascular risk factors in older age group. There have been several reports on young patients without vascular risk factors admitted for large-artery stroke during the pandemic[5-7]. Similarly, other studies highlighted a younger age of patients undergoing thrombectomy compared to the pre-pandemic period [8-10]. Another study found that acute infarction, which affects 31% of patients, is the primary neuroimaging signature, with just 3% of patients experiencing cardioembolic events and 6% experiencing intracranial haemorrhages (8). Acute cerebrovascular accidents in COVID-19 are likely complex in origin, with preexisting diseases such as hypertension, diabetes, and cardiovascular disease, as well as the severity of those diseases, being the major contributors. Although the precise function of SARS-CoV-2 is yet unknown, autopsy reports have shown that COVID-19 is linked to an increased frequency of thromboembolic events [11]. The etiology of acute cerebrovascular accidents in COVID-19 is probably multifactorial, with preexisting conditions, like hypertension, diabetes, cardiovascular disease, and their severity of disease playing the main part. The exact role of SARS-CoV-2 remains unclear, but it has been documented in autopsy reports that COVID-19 is associated with an increased incidence of thromboembolic events [12]. In a literature review [13] about intracranial hemorrhage in COVID-19 patients, intraparenchymal hemorrhage was the most common variety (62.6%), followed by subarachnoid hemorrhage (15.0%), subdural hemorrhage (11.6%), and intraventricular hemorrhage (1.4%). Although no direct association has been found between the manifestations and the demographics/comorbidities in the present study, the interplay between these factors and the effect on neurological manifestations is yet to be studied in depth.

Conclusions:

It is well known that COVID -19 infection can lead to a variety of symptoms in different organ systems. Understanding the neurologic and imaging findings associated with COVID - 19 is critical for proper patient evaluation and therapy. It is well recognised that the disease manifests differently in different age groups. The most common neuroradiological abnormality in COVID -19 patients and in sequelae after COVID -19 was cerebral vascular events. Although most of the stroke cases were in the older age group, significant proportion of cases was also seen in the young. It is critical to comprehend long COVID and how they manifest, as much neurological impairment often does not appear until after COVID -19 recovery. In addition, it is important to monitor and follow up patients who have had COVID-19 infection. There was no statistically significant difference between subjects who had stroke and those who did not in terms of study variables such as mean age, sex, COVID, or comorbidity status. There was no correlation between the severity of pulmonary COVID -19 infections, as assessed by the CT severity index, and neurologic manifestations, suggesting that stroke could occur even in the absence of severe pulmonary infection. Routine neuroimaging and follow-up is to be considered in patients with neurological symptoms or deficits, ensuing active COVID-19 infection. High index of suspicion of COVID-19 infection as one of the possible causes, for neurological deficits occurring in the post infective period should be taken into account.

Limitations: Most of the patients, who underwent NCCT head for initial evaluation, had no significant abnormality, even in the presence of neurological deficits and symptoms. NCCT was not so sensitive, to detect stroke in the window period and few other subtle neurological abnormalities. The assessment of such patients became a tedious task in the study. Follow-up MRI brain was carried out only in few of the instances. The limited study sample size and the lack of follow-up gave inconclusive results in some of the cases.

Declarations:

- Ethics approval and consent to participate: This study is approved by the Ethics committee of the JSS Academy of Higher Education and Research, Mysore, Karnataka, India. Only anonymous patient details were used for data collection and analysis. No interventions were done. The Institutional Ethics committee's reference number–JSS/MC/ PG/5156/2020-21 dated on 22 January 2021.

- Consent for publication: Not applicable.
- Availability of data and materials: The study is in the JSS University database. Please exclude this source while analysing plagiarism.
- Competing interests: The authors declare that they have no competing interests.

- Funding: Not applicable.

- Authors' contributions: Dr Abhigna S Moudgalya—study conception and design, analysis, and interpretation of data, draft manuscript preparation. Dr Vikram Patil—study conception and design,supervision of the project, analysis, and interpretation of data.

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