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Computed Tomography Findings in Patients Showing CNS Manifestations With COVID-19 Infection

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Abstract

Background: Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes coronavirus disease 2019 (COVID-19), which predominantly affects the respiratory system. However, other organ systems, including the central nervous system (CNS), may also be involved, resulting in manifestations such as acute cerebrovascular disease, viral encephalitis, and infectious toxic encephalopathy.

Objectives: This study aimed to describe the spectrum of computed tomography (CT) imaging findings in patients with COVID-19 presenting with CNS manifestations. The secondary objective was to explore the distribution of imaging patterns in relation to clinical characteristics and disease severity.

Methods: A total of 70 patients presenting with various CNS manifestations were included over one year, from January 1, 2021, to December 31, 2021. CT images were evaluated for different findings in patients diagnosed with COVID-19. Clinical characteristics, including body mass index (BMI), comorbidities, smoking history, oxygen saturation, D-dimer levels, and interleukin-6 (IL-6) levels, were also documented. Clinical outcomes were assessed during hospitalization until discharge or in-hospital death among patients with abnormal CT findings. Patients with normal CT findings were not included in the clinical outcome analysis.

Results: Of the 70 patients evaluated, 44 (62.9%) were male, and 26 (37.1%) were female. Overall, 25 (35.7%) patients had no significant imaging abnormality, whereas 45 (64.3%) demonstrated abnormal CT findings. Among these 45 patients, infarction was the predominant abnormality (27, 60.0%), followed by intracranial hemorrhage (12, 26.7%). Among patients with infarction, large-vessel involvement was observed in 15 (55.6%), compared with small-vessel/lacunar involvement in 12 (44.4%). The middle cerebral artery (MCA) territory was the most frequently involved isolated vascular territory (5/15, 33.3%). Loss of gray-white matter differentiation was the most consistent CT feature of large-vessel infarction (15/15, 100%), followed by sulcal effacement (9/15, 60.0%) and the insular ribbon sign (6/15, 40.0%). Among patients with hemorrhage, hyperdensity was observed in all 12 (100%), while perilesional edema and midline shift were present in 7 (58.3%) and 5 (41.7%), respectively. Severe COVID-19 (SpO_2 <90%) was observed in 18 (66.7%) patients with infarction and 9 (75.0%) with hemorrhage. Elevated D-dimer and IL-6 levels were observed in 25 (92.6%) and 26 (96.3%) patients with infarction, respectively, while all 12 (100%) patients with hemorrhage had elevated IL-6. Among the 45 patients with abnormal CT findings, 28 (62.2%) had a Glasgow Coma Scale (GCS) score of 13-15. Regarding clinical outcomes, 17 (37.8%) patients were discharged within 15 days, 19 (42.2%) required prolonged hospitalization, and 9 (20.0%) died.

Conclusion: CT is a valuable first-line imaging modality for evaluating neurological manifestations in patients with COVID-19, facilitating the rapid identification and characterization of clinically significant intracranial abnormalities. Cerebral infarction was the predominant imaging abnormality, followed by intracranial hemorrhage, with large-vessel and MCA territory involvement being frequent patterns.

Categories: Radiology, Internal Medicine, Infectious Disease
Keywords: covid 19, cvst, haemorrhage, infarct, neuroimaging, stroke

Introduction

Infection with Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) results in coronavirus disease 2019 (COVID-19), which originated as an epidemic in Wuhan, China, in December 2019 and was declared a pandemic by the World Health Organization (WHO) on March 11, 2020 [1,2].

COVID-19 predominantly affects the respiratory system; however, it has become apparent that many other organ systems, including the central nervous system (CNS), can also be involved, resulting in manifestations such as acute cerebrovascular disease, viral encephalitis, and infectious toxic encephalopathy. Neurological

manifestations most commonly seen include altered mental status and stroke [1].

Various mechanisms of targeting the CNS have been hypothesized. These include direct spread from the cribriform plate to the brain and hematogenous spread by injury to the vascular endothelial and epithelial cells, resulting in disruption of the blood-brain barrier. Neuronal pathways involve the vagus nerve from the lung and the enteric nerve from the intestine. Immune-mediated injury occurs through cytokine storm syndrome (CSS) and hypoxic injury owing to respiratory failure and prolonged ventilation. SARS-CoV-2-induced coagulopathy also contributes to the development of CNS manifestations [1-3].

Imaging plays an essential role in the diagnosis of all manifestations of the disease and related complications. Patients with COVID-19 who present with CNS symptoms should undergo non-contrast computed tomography (NCCT) of the head to identify vascular complications like stroke, hemorrhage, and venous sinus thrombosis. Contrast-enhanced CT can be used for imaging patients with suspected viral encephalitis and for assessing leptomeningeal enhancement in meningitis [1,3,4].

Although studies have extensively described the thoracic imaging manifestations of COVID-19, relatively fewer studies have specifically focused on the spectrum of CNS abnormalities detected on CT imaging [5]. During the pandemic, CT remained an important first-line neuroimaging modality in many clinical settings because of its rapid acquisition, widespread availability, relatively lower logistical requirements, and ability to identify acute, potentially life-threatening abnormalities such as intracranial hemorrhage, large-vessel infarction, and cerebral edema. Furthermore, MRI is not feasible in all patients, particularly those who were critically ill, hemodynamically unstable, required intensive care support, or posed challenges related to patient transportation and infection-control protocols [6].

In this context, documenting the spectrum of CNS manifestations of COVID-19 based on CT findings, in conjunction with available clinical and laboratory evidence, is important. We aimed to study the spectrum of imaging findings on computed tomography (CT) in COVID-19 patients with CNS manifestations. The secondary objective was the evaluation of the relationship of imaging patterns with clinical characteristics and disease severity. By focusing on CT findings rather than relying exclusively on multimodality imaging, this study provides clinically relevant information on the neuroimaging patterns encountered in routine and resource-constrained clinical practice. Such documentation may contribute to a better understanding of the neurological involvement associated with COVID-19 and serve as a reference for the recognition and interpretation of CNS abnormalities in similar clinical settings.

Materials And Methods

An observational cohort study was conducted in the Department of Radiodiagnosis, Maulana Azad Medical College, and associated Lok Nayak Hospital, New Delhi, for a period of one year (1 January 2021 to 31 December 2021) with a sample size of 70 patients. The data of the patients were enrolled after institutional ethical clearance (F.1/IEC/MAMC/82/10/2020/No.194, dated 28.12.2020).

Adults aged 18 years or older who presented with CNS manifestations such as altered mental status, headache, delirium, seizure, dizziness, neuralgia, ataxia, focal neurological deficit, anxiety, or depression (from a previous diagnosis/DASS-21 scoring and clinical symptoms) and presented within six hours to two weeks of RT-PCR-confirmed COVID-19 were included in the study. Exclusion criteria comprised pregnant patients, patients with a previous history of stroke, and those presenting with head trauma or with a known history of brain tumor, intracranial vascular malformations, cerebral aneurysm, or any previous neurological disorder.

Patients were consecutively enrolled from those who met the above eligibility criteria and presented to the outpatient department or the emergency department of Maulana Azad Medical College and Lok Nayak Hospital during the study period.

The procedure was explained to the patient, and informed consent in the vernacular language was obtained in every case. Clinical details, including age, sex, relevant medical history, and clinical examination findings, were recorded. Relevant laboratory investigations, including reverse transcription polymerase chain reaction (RT-PCR), D-dimer, and interleukin-6 (IL-6), were documented. D-dimer levels were classified as normal when ⩽500 ng/mL and elevated when >500 ng/mL. Interleukin-6 (IL-6) levels were considered normal when ⩽13 pg/mL and elevated when >13 pg/mL, based on the laboratory reference thresholds used in the study. Kidney function tests (KFTs) were documented when contrast administration was planned.

Imaging

All patients underwent non-contrast CT of the head, and intravenous non-ionic iodinated contrast media was administered wherever indicated. The scans were acquired using a Siemens SOMATOM Emotion CT scanner (Siemens Healthineers, Erlangen, Germany) dedicated to imaging patients with COVID-19 at Lok Nayak Hospital.

NCCT of the brain was performed with patients in the supine position. The CT images were systematically evaluated for the spectrum of intracranial abnormalities associated with neurological manifestations of COVID-19. The assessment included acute and subacute infarctions, hemorrhagic lesions, cerebral venous thrombosis (CVT), intracranial arterial thrombus, white matter abnormalities, hypoxic-ischemic encephalopathy (HIE), posterior reversible encephalopathy syndrome (PRES), meningitis, and encephalitis.

Cerebral infarctions were evaluated for their location, distribution, and extent and were classified as acute or subacute based on the interval between symptom onset and CT examination. Infarctions imaged within 6-48 hours of symptom onset were classified as acute, whereas those detected after 48 hours and up to two weeks were classified as subacute. Infarctions were classified according to their distribution into large-territory infarctions involving the ACA (anterior cerebral artery), MCA (middle cerebral artery), or PCA (posterior cerebral artery) territories, and small-vessel (lacunar) infarctions.

Particular attention was given to watershed-zone and lacunar infarctions. Hemorrhagic abnormalities were classified as extra-axial or intra-axial. Extra-axial hemorrhages included subarachnoid, subdural, epidural, and intraventricular hemorrhages, whereas intra-axial hemorrhages included lobar or parenchymal, striatothalamic, brainstem, and cerebellar hemorrhages. Small hemorrhagic foci were documented wherever identifiable on CT; however, the detection of cerebral microbleeds was limited by the absence of MRI susceptibility-weighted imaging.

CVT and intracranial arterial thrombosis were suspected based on abnormal hyperdensity within the cerebral venous sinuses or intracranial arteries on NCCT, with confirmation by CT venography (CTV) or CT angiography (CTA), wherever available. In patients with suspected CVT, the involved venous sinuses, the presence of the empty delta sign or dense vessel/cord sign, and associated parenchymal abnormalities, including venous edema, hemorrhage, and infarction, were evaluated. White matter abnormalities were assessed for focal or diffuse hypodensities, including features suggestive of leukoencephalopathy. HIE was considered in the presence of diffuse cerebral edema, loss of gray-white matter differentiation, and hypodensities involving the deep gray nuclei. PRES was suspected when bilateral, predominantly posterior parieto-occipital hypodensities suggestive of vasogenic edema were identified, particularly when the abnormalities did not conform to a specific vascular territory.

Meningitis was suspected based on abnormal leptomeningeal or pachymeningeal enhancement on contrast-enhanced CT, wherever available, and hyperdensity of cerebrospinal fluid (CSF) within the basal cisterns or sulci on NCCT. Cerebritis was suspected in the presence of focal or diffuse parenchymal hypodensities and oedematous changes, particularly involving the temporal lobes or other characteristic anatomical regions. These findings were interpreted in conjunction with the clinical presentation and available CSF examination results.

The imaging findings were primarily assessed on the basis of CT appearances and correlated with the available clinical and laboratory information. Additional investigations, including MRI, CTA, CTV, and CSF analysis, were performed wherever feasible. However, owing to the constraints imposed by the COVID-19 pandemic, these investigations could not be performed in all patients. Therefore, the final classification was based on the available clinical, imaging, and laboratory evidence, and certain diagnoses were considered radiologically suspected rather than definitively confirmed.

Contrast-enhanced CT (CECT) was performed in the indications of suspected meningeal or parenchymal inflammation, intracranial infection, and evaluation of abnormal intracranial lesions. The presence of abnormal leptomeningeal or parenchymal enhancement was assessed. A dedicated CTA or CTV was considered separately when intracranial arterial thrombosis or CVT was suspected. However, owing to the constraints imposed by the COVID-19 pandemic, vascular imaging investigations could not be performed in all patients.

CT findings were recorded independently by two radiologists, and if any discrepancy was found, a consensus diagnosis was obtained, or the senior radiologist's diagnosis was considered final.

The level of consciousness was assessed using the Glasgow Coma Scale (GCS), which evaluates eye-opening, verbal, and motor responses, with a total score ranging from 3 to 15. GCS scores were categorized as mild impairment (13-15), moderate impairment (9-12), and severe impairment (3-8) [7]. GCS analysis was performed among patients with abnormal CT findings.

The primary outcome measures included the spectrum and distribution of CT-detected CNS abnormalities in patients with COVID-19 presenting with neurological manifestations. Clinical outcomes were assessed during hospitalization until discharge or in-hospital death among patients with abnormal CT findings. Hospital stay was categorized as discharge within 15 days or prolonged hospitalization exceeding 15 days, with in-hospital mortality recorded separately. Patients with normal CT findings were excluded from the clinical outcome analysis.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 25 (Released 2017; IBM Corp., Armonk, New York). Descriptive statistics were used to summarize the demographic characteristics, clinical manifestations, laboratory parameters, disease severity, CT imaging findings, and clinical outcomes. Categorical variables were expressed as frequencies and percentages. Percentages were calculated using the total study population or the relevant imaging subgroup as the denominator, as appropriate. No inferential statistical tests were performed, as the study was primarily descriptive in nature.

Results

Demographic characteristics

The study included 70 COVID-19-positive patients presenting with CNS manifestations, with ages ranging from 18 to 91 years and a mean age of 57 years. The most common age group was 51-60 years, comprising 17 (24.3%) patients, followed by 61-70 years, with 14 (20.0%) patients. Males predominated, accounting for 44 (62.9%) patients, while females constituted 26 (37.1%), as shown in Table *1*.

Characteristic	Category	n (%)
Age group (years)	18–25	3 (4.3)
	26–40	10 (14.3)
	41–50	10 (14.3)
	51–60	17 (24.3)
	61–70	14 (20.0)
	71–80	11 (15.7)
	>80	5 (7.1)
Sex	Male	44 (62.9)
	Female	26 (37.1)
Total		70 (100.0)

TABLE 1: Demographic Characteristics of the Study Population (N = 70)

Values are expressed as frequency (percentage). Percentages are calculated using the total study population (N = 70) as the denominator.

Presenting CNS symptoms and signs

Patients presented with a range of neurological and neuropsychiatric manifestations, with some patients experiencing more than one symptom. Altered sensorium was the most frequent presentation, observed in 34 (48.6%) patients, followed by headache in 30 (42.9%). Anxiety and depression were reported in 18 (25.7%) patients, while hemiparesis was observed in 13 (18.6%). Delirium occurred in 10 (14.3%) patients, and dizziness was reported in 6 (8.6%). Seizures were documented in 5 (7.1%) patients, while dysarthria was present in 4 (5.7%). Ataxia and neuralgia were less common, occurring in 2 (2.9%) and 1 (1.4%) patients, respectively. Table *2* shows the CNS signs and symptoms among the patients.

Clinical manifestation	n (%)
Altered sensorium	34 (48.6)
Headache	30 (42.9)
Anxiety and depression	18 (25.7)
Hemiparesis	13 (18.6)
Delirium	10 (14.3)
Dizziness	6 (8.6)
Seizures	5 (7.1)
Dysarthria	4 (5.7)
Ataxia	2 (2.9)
Neuralgia	1 (1.4)

TABLE 2: Distribution of Presenting Neurological and Neuropsychiatric Manifestations (N = 70)

Values are expressed as frequency (percentage). Percentages are calculated using the total study population (N = 70) as the denominator. Patients could present with more than one manifestation.

CT findings

All 70 patients underwent non-contrast CT (NCCT) of the head, while contrast-enhanced CT (CECT) was performed in selected patients where clinically indicated. Of the 70 patients evaluated, 25 (35.7%) had no significant imaging abnormality, whereas 45 (64.3%) demonstrated abnormal CT findings. Among the latter, infarction was the most common abnormality, observed in 27 (60.0%) patients, followed by hemorrhage in 12 (26.7%), CVT in 2 (4.4%), meningitis in 2 (4.4%), cerebritis in 1 (2.2%), and PRES in 1 (2.2%). Table *3* shows the CT imaging findings among the study cohort of 70 patients.

CT imaging findings	Number of patients (n)	Percentage (%)
No significant imaging abnormality	25	35.7
Abnormal CT findings	45	64.3
Type of abnormality (n = 45)		
Infarction	27	60.0
Hemorrhage	12	26.7
Cerebral venous thrombosis (CVT)	2	4.4
Meningitis	2	4.4
Cerebritis	1	2.2
Posterior reversible encephalopathy syndrome (PRES)	1	2.2

TABLE 3: CT Imaging Findings Among the Study Patients (N = 70)

Percentages for individual abnormalities are calculated using the 45 patients with abnormal CT findings as the denominator. Percentages for overall imaging findings are calculated using all 70 patients. The abnormality categories sum to 45 patients (100%).

Characteristics of patients with abnormal CT imaging

The distribution of CT imaging findings according to BMI, comorbidities, and smoking history among those who had abnormalities in CT is presented in Table *4*. Among patients with cerebral infarction (n = 27), 13 (48.1%) were overweight, and 9 (33.3%) were obese. Hypertension was present in 13 (48.1%) patients, while 6 (22.2%) had type 2 diabetes mellitus, 2 (7.4%) had coronary artery disease, and 14 (51.9%) had a history of

smoking. Among patients with hemorrhage (n = 12), 5 (41.7%) were overweight, 7 (58.3%) had hypertension, and 6 (50.0%) had a history of smoking.

Imaging findings	Underweight, n (%)	Normal BMI, n (%)	Overweight, n (%)	Obese, n (%)	HTN, n (%)	Type 2 DM, n (%)	CAD, n (%)	Smoker, n (%)
Infarct (n = 27)	2 (7.4)	3 (11.1)	13 (48.1)	9 (33.3)	13 (48.1)	6 (22.2)	2 (7.4)	14 (51.9)
Hemorrhage (n = 12)	2 (16.7)	3 (25.0)	5 (41.7)	2 (16.7)	7 (58.3)	2 (16.7)	1 (8.3)	6 (50.0)
CVT (n = 2)	0 (0)	0 (0)	2 (100)	0 (0)	2 (100)	1 (50.0)	0 (0)	1 (50.0)
Meningitis (n = 2)	1 (50.0)	1 (50.0)	0 (0)	0 (0)	0 (0)	1 (50.0)	0 (0)	1 (50.0)
PRES (n = 1)	0 (0)	1 (100)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)
Cerebritis (n = 1)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)

TABLE 4: Distribution of COVID-19-Positive Patients According to CT Imaging Findings, BMI, Comorbidities, and Smoking History

Note: Percentages are calculated within each imaging-finding category, using the number of patients with that finding as the denominator. BMI categories are underweight (less than 18.5 kg/m²), normal (18.5–24.9 kg/m²), overweight (25.0–29.9 kg/m²), and obese (30 kg/m² or higher).

Abbreviations: BMI, body mass index; HTN, hypertension; DM, diabetes mellitus; CAD, coronary artery disease; CVT, cerebral venous thrombosis; PRES, posterior reversible encephalopathy syndrome.

In patients with CVT (n = 2), overweight status and hypertension were observed in 2 (100%) patients, while type 2 diabetes mellitus and a history of smoking were each reported in 1 (50%) patient. Among patients with meningitis (n = 2), underweight status and normal BMI were each observed in 1 (50%) patient, while type 2 diabetes mellitus and a history of smoking were each reported in 1 (50%) patient. The single patient with PRES had a normal BMI and hypertension. The patient with cerebritis also had a normal BMI and coronary artery disease. No patient with PRES or cerebritis had a history of smoking.

Severity of COVID-19 and investigations among abnormal CT findings

In our hospital, patients were classified into mild, moderate, and severe COVID-19 infection according to MOHFW (Ministry of Health and Family Welfare) guidelines (version 4). Patients with mild COVID infection were those with blood oxygen saturation (SpO2) more than 94%. Patients with moderate infection had SpO2 between 90% and 94%, and those with severe infection had SpO2 less than 90%. The proportion of patients with different severities of mild, moderate, and severe COVID-19 who presented with various CT imaging findings is shown in Table *5*. Furthermore, D-dimer and IL-6 (interleukin-6) were assessed for each patient and classified as normal or elevated. The proportion of those with elevated IL-6 or D-dimer is shown in Table *5*.

Imaging findings	Mild, n (%)	Moderate, n (%)	Severe, n (%)	Normal D-dimer, n (%)	Elevated D-dimer, n (%)	Normal IL-6, n (%)	Elevated IL-6, n (%)
Infarct (n = 27)	3 (11.1)	6 (22.2)	18 (66.7)	2 (7.4)	25 (92.6)	1 (3.7)	26 (96.3)
Hemorrhage (n = 12)	1 (8.3)	2 (16.7)	9 (75.0)	7 (58.3)	5 (41.7)	0 (0)	12 (100)
CVT (n = 2)	0 (0)	0 (0)	2 (100)	0 (0)	2 (100)	0 (0)	2 (100)
Meningitis (n = 2)	0 (0)	0 (0)	2 (100)	2 (100)	0 (0)	0 (0)	2 (100)
Cerebritis (n = 1)	0 (0)	0 (0)	1 (100)	1 (100)	0 (0)	0 (0)	1 (100)
PRES (n = 1)	0 (0)	1 (100)	0 (0)	1 (100)	0 (0)	1 (100)	0 (0)

TABLE 5: Distribution of Severity of COVID-19, D-dimer, and IL-6 Levels According to Abnormal CT Imaging Findings

Note: Mild disease: SpO_2 >94%; moderate disease: SpO_2 90–94%; severe disease: SpO_2 <90%. D-dimer levels were classified as normal when ≤500 ng/mL and elevated when >500 ng/mL. Interleukin-6 (IL-6) levels were considered normal when ≤13 pg/mL and elevated when >13 pg/mL.

Abbreviations: CVT, cerebral venous thrombosis; PRES, posterior reversible encephalopathy syndrome; D-dimer, fibrin degradation product; IL-6, interleukin-6.

Among the 45 patients with abnormal CT findings, a GCS score of 13-15, indicating mild or no impairment of consciousness, was observed in 28 (62.2%) patients. Moderate impairment of consciousness (GCS score 9-12) was observed in 12 (26.7%) patients, while severe impairment (GCS score ≤8) was noted in 5 (11.1%) patients.

Infarction-related CT findings

Among the 27 patients with infarction, 14 (51.9%) had acute and 13 (48.1%) had subacute infarction. Among patients with acute infarction, 10 (71.4%) had large-vessel and 4 (28.6%) had small-vessel/lacunar involvement. Among those with subacute infarction, 5 (38.5%) had large-vessel and 8 (61.5%) had small-vessel/lacunar involvement. Overall, large-vessel infarction was observed in 15 (55.6%) patients and small-vessel/lacunar infarction in 12 (44.4%) (Table *6*).

Infarction type	Large-vessel, n (%)	Small-vessel/lacunar, n (%)	Total, n (%)
Acute	10 (37.0)	4 (14.8)	14 (51.9)
Subacute	5 (18.5)	8 (29.6)	13 (48.1)
Total	15 (55.6)	12 (44.4)	27 (100.0)

TABLE 6: Distribution of Infarction According to Time of Infarction and Vessel Involvement (N = 27)

Percentages are calculated using the total number of patients with infarction (N = 27) as the denominator.

Multiple anatomical sites were involved in several patients; therefore, the percentages for individual locations are not mutually exclusive. Among the 27 patients with infarction, the frontal lobe was involved in 12 (44.4%), followed by the parietal lobe in 9 (33.3%), the temporal lobe in 7 (25.9%), and the occipital lobe in 3 (11.1%).

Among the 27 patients with infarction, as for the deep structures, the globus pallidus and internal capsule were each involved in 7 (25.9%) patients, while the thalamus was involved in 4 (14.8%) and the caudate nucleus in 6 (22.2%). The pons was involved in 2 (7.4%) patients, while no involvement of the midbrain or medulla was reported. The cerebellum was involved in 3 (11.1%) patients. In addition, the corona radiata and centrum semiovale were involved in 10 (37.0%) and 6 (22.2%) patients, respectively.

Among the 15 patients with large-vessel infarction, the MCA territory alone was the most frequently involved, observed in 5 (33.3%) patients. A representative CT image of a case of acute MCA infarct is shown in Figure 1.

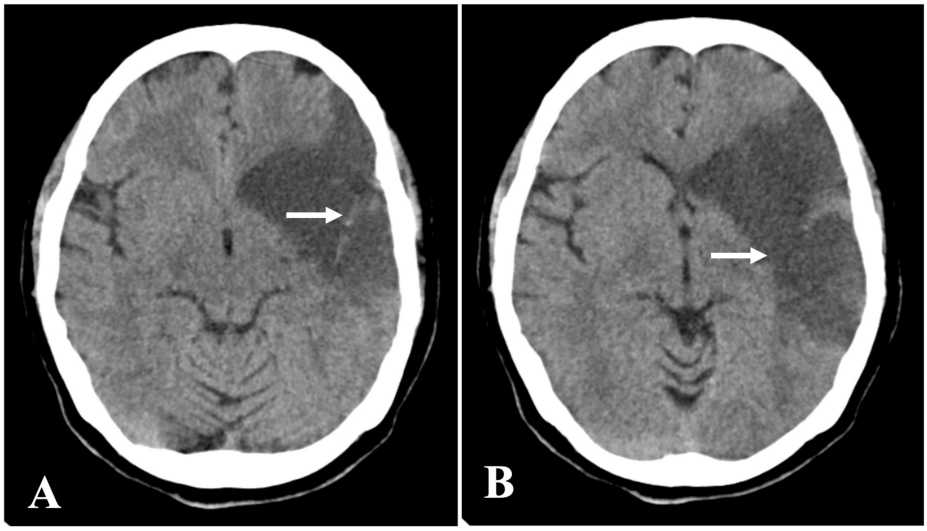


FIGURE 1: Non-contrast axial CT scan in a COVID-positive patient showing acute infarct of the left MCA territory. (A) shows a large hypodensity in the left cerebral hemisphere involving the left MCA territory with a hyperdense MCA (white arrow). An axial section at a higher level (B) reveals hypodensity in the basal ganglia involving the caudate nucleus, globus pallidus, and anterior limb of the internal capsule (white arrow).

Original CT image obtained from a patient enrolled in the present study. The image contains no personally identifiable patient information, and informed consent for investigations and subsequent publication of clinical images was obtained from the patient.

Abbreviations: CT: computed tomography; MCA: middle cerebral artery.

The ACA territory alone was involved in 2 (13.3%), while isolated PCA territory involvement was observed in 1 (6.7%) out of 15 cases of large-vessel infarction.

Among the 15 patients with large-vessel infarction, loss of gray-white matter differentiation was observed in 15 (100%), sulcal effacement in 9 (60.0%), midline shift in 2 (13.3%), insular ribbon sign in 6 (40.0%), hyperdense MCA sign in 1 (6.7%), and hemorrhagic transformation in 6 (40.0%) patients.

Hemorrhage-related CT features

The anatomical distribution of hemorrhage among COVID-19 patients with abnormal CT features is shown in Table 7.

Anatomical distribution	Number of patients, n (%)
Type of hemorrhage (N = 12)	
Intra-axial hemorrhage	7 (58.3)
Extra-axial hemorrhage	3 (25.0)
Intraventricular hemorrhage	2 (16.7)
Intra-axial location (n = 7)	
Frontal lobe	4 (57.1)
Parietal lobe	3 (42.9)
Occipital lobe	1 (14.3)
Temporal lobe	0 (0)
Thalamus	2 (28.6)
Globus pallidus	2 (28.6)
Internal capsule	2 (28.6)
Caudate nucleus	1 (14.3)
Pons	1 (14.3)
Cerebellum	1 (14.3)
Midbrain	0 (0)
Medulla	0 (0)
Intraventricular hemorrhage (n = 2)	
Isolated intraventricular hemorrhage	1 (50.0)
Secondary intraventricular hemorrhage	1 (50.0)
Extra-axial hemorrhage (n = 3)	
Unilateral subdural hemorrhage	1 (33.3)
Bilateral subdural hemorrhage	1 (33.3)
Subarachnoid hemorrhage	1 (33.3)
Extradural hemorrhage	0 (0)

TABLE 7: Anatomical Distribution of Hemorrhage Among Patients With CT-Detected Hemorrhage (N = 12)

Percentages for the overall hemorrhage types are calculated using 12 patients as the denominator. Percentages for intra-axial locations, intraventricular hemorrhage, and extra-axial hemorrhage are calculated using seven, two, and three patients, respectively. Multiple anatomical sites could be involved in the same patient; therefore, percentages for intra-axial locations may exceed 100% when summed.

A representative case of a CT image of intraparenchymal hemorrhage in the frontal lobe is shown in Figure *2*.

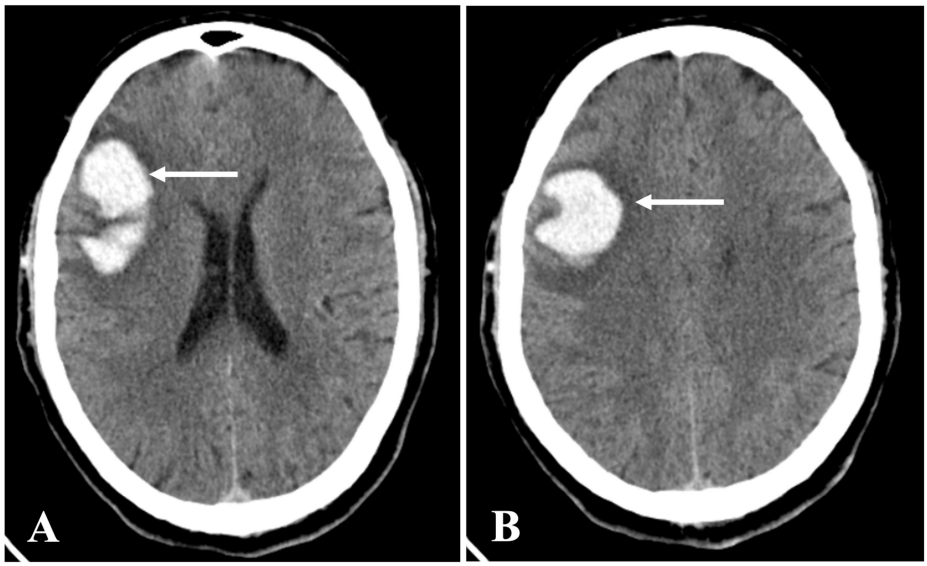


FIGURE 2: Non-contrast axial CT scans in a COVID-positive patient (A) and (B) reveal a hyperdensity in the right frontal lobe with peri-lesional edema and mass effect in the form of effacement of the right lateral ventricle and sulcal spaces of the right cerebral hemisphere - Intraparenchymal Hemorrhage in the Frontal Lobe.

Original CT image obtained from a patient enrolled in the present study. The image contains no personally identifiable patient information, and informed consent for investigations and subsequent publication of clinical images was obtained from the patient.

Additionally, hyperdensity was observed in all 12 (100%) patients with hemorrhage. Perilesional edema was present in 7 (58.3%) patients, midline shift was observed in 5 (41.7%) patients, and fluid-fluid levels were identified in 2 (16.7%) patients.

CVT-related CT features

Among patients with CVT (n = 2), superior sagittal sinus and transverse sinus involvement were each observed in 1 (50.0%) patient. No involvement of the straight sinus, sigmoid sinus, deep cerebral venous system, or cavernous sinus was reported. The empty delta sign was present in 2 (100%) patients, while the dense vessel/cord sign was absent in both. Venous edema and parenchymal hemorrhage were each observed in 1 (50.0%) patient, whereas venous infarction was not identified in either patient.

Meningitis-related CT features

Among the two patients with meningitis (n=2), hyperdense CSF was observed in the basal cisterns in 2 (100%) cases and in the Sylvian fissures in 1 (50%) case on NCCT. On CECT, pachymeningeal enhancement was observed in 2 (100%) cases, while leptomeningeal enhancement was seen in 1 (50%) case. Mild ventriculomegaly was also observed in 1 (50%) case. No blurred ventricular margins were reported.

Clinical outcomes

Clinical outcomes were reported for the 45 patients with abnormal CT findings, as shown in Table *8*, while those with normal CT findings were not followed. Among the 27 patients with infarction, 12 (44.4%) were discharged within 15 days, 11 (40.7%) required hospitalization for more than 15 days, and 4 (14.8%) died. Among the 12 patients with hemorrhage, 4 (33.3%) were discharged within 15 days, 5 (41.7%) had prolonged hospitalization, and 3 (25.0%) died. Of the two patients with CVT, one (50.0%) required prolonged hospitalization and 1 (50.0%) died. Similarly, among the two patients with meningitis, 1 (50.0%) required prolonged hospitalization and 1 (50.0%) died. The single patient with cerebritis was discharged within 15 days, while the patient with PRES required prolonged hospitalization. Overall, among the 45 patients with abnormal CT findings, 17 (37.8%) were discharged within 15 days, 19 (42.2%) had prolonged hospitalization, and 9 (20.0%) died.

Imaging findings	Discharged within 15 days, n (%)	Hospitalization >15 days, n (%)	Death, n (%)	Total, n (%)
Infarction	12 (44.4)	11 (40.7)	4 (14.8)	27 (100)
Hemorrhage	4 (33.3)	5 (41.7)	3 (25.0)	12 (100)
CVT	0 (0)	1 (50.0)	1 (50.0)	2 (100)
Meningitis	0 (0)	1 (50.0)	1 (50.0)	2 (100)
Cerebritis	1 (100)	0 (0)	0 (0)	1 (100)
PRES	0 (0)	1 (100)	0 (0)	1 (100)
Overall	17 (37.8)	19 (42.2)	9 (20.0)	45 (100)

TABLE 8: Clinical Outcomes According to Abnormal CT Imaging Findings (N = 45)

Note: Percentages are calculated within each imaging-finding category, except for the overall row, where the denominator is 45 patients with abnormal CT findings. Patients with normal CT findings were not followed for clinical outcomes.

Abbreviations: CVT, cerebral venous thrombosis; PRES, posterior reversible encephalopathy syndrome.

Discussion

Patients with COVID-19 and ischemic stroke have commonly been reported in the age group of 52-70 years, with increasing age associated with higher mortality in previous studies [8]. In the pre-COVID era, ischemic and hemorrhagic strokes were more frequently reported among elderly individuals, particularly those aged >80 years [9]. Cardioembolism and atherosclerosis were the predominant stroke mechanisms, with conventional vascular comorbidities including advanced age, dyslipidemia, smoking, hypertension, diabetes, and obesity [10]. In the present study, the mean age of patients was 57 years, with a substantial proportion belonging to younger age groups. This observation suggests that neurological manifestations of COVID-19 are not restricted to the elderly population and may also be encountered in relatively younger individuals.

The pathogenesis of cerebrovascular complications in COVID-19 is multifactorial and involves systemic inflammation, endothelial dysfunction, platelet activation, and hypercoagulability. SARS-CoV-2 infection may trigger an exaggerated inflammatory response with increased cytokine production, including interleukin-6, along with elevated D-dimer levels and activation of the coagulation cascade [11]. Endothelial injury and inflammation may further contribute to vascular dysfunction and thrombosis [11,12]. In our study, elevated D-dimer and IL-6 levels were frequently observed among patients with abnormal CT findings, particularly those with infarction and hemorrhage. These findings provide a descriptive overview of the laboratory profile of the study population but do not establish a direct relationship between inflammatory or coagulation abnormalities and specific neuroimaging findings.

Neurological manifestations are well recognized in COVID-19 and may occasionally represent the initial presentation of infection [10]. In our study, neuroimaging abnormalities were predominantly represented by ischemic infarction and intracranial hemorrhage, consistent with previous reports [3,13,14]. Other reported neuroimaging manifestations of COVID-19 include CVT, PRES, encephalitis, meningitis, nontraumatic subarachnoid hemorrhage, and HIE [15]. Previous studies have also described the coexistence of COVID-19-associated coagulopathy and conventional vascular comorbidities, including hypertension, diabetes, and cardiovascular disease, among patients presenting with cerebrovascular complications [16].

Among patients with ischemic stroke, acute infarctions were slightly more frequent than subacute infarctions in our study. This distribution is consistent with previous observations in hospitalized patients with COVID-19 [3,17]. The relatively higher frequency of acute lesions represents the imaging pattern observed in our cohort; however, the temporal relationship between SARS-CoV-2 infection and the onset of cerebrovascular events cannot be established from the present study.

Our study demonstrated a greater frequency of large-vessel involvement compared with small-vessel (lacunar) involvement. This differs from some previous reports describing multiple cortical and subcortical lacunar infarcts and a higher frequency of small-vessel involvement in COVID-19 [18,19]. Such differences may reflect variations in patient selection, disease severity, imaging modality, and the distribution of conventional vascular comorbidities across study populations. In our cohort, the MCA territory was the most frequently involved isolated vascular territory. Loss of gray-white matter differentiation was the most consistent CT feature of large-vessel infarction, followed by sulcal effacement and the insular ribbon sign. These findings provide a description of the distribution and characteristic CT appearances of large-vessel infarction in the study population. However, the underlying mechanisms responsible for the observed

predominance of large-vessel involvement cannot be determined from the available data.

Intracranial hemorrhage has also been described in patients with severe COVID-19, with parenchymal hemorrhage being one of the commonly reported patterns [20]. Benger et al. reported a predominance of lobar intracerebral hemorrhage, particularly involving the frontal lobe, among patients with COVID-19 [21]. In contrast, intracerebral hemorrhage in the general population commonly involves the basal ganglia and thalamus, particularly among individuals with chronic hypertension, where small-vessel arteriopathy and microaneurysm formation are recognized mechanisms of vessel rupture [22]. In COVID-19, systemic inflammation, endothelial dysfunction, coagulation abnormalities, and disruption of the blood-brain barrier have also been discussed as possible mechanisms underlying intracerebral hemorrhage [21,23]. In our study, lobar hemorrhage was more frequently observed than deep gray matter hemorrhage. Hyperdensity was present in all patients with hemorrhage, while perilesional edema and midline shift were additional imaging features. These findings describe the anatomical distribution and CT characteristics of hemorrhage in our cohort without establishing a specific underlying mechanism.

CVT is another cerebrovascular manifestation described in association with COVID-19-related coagulopathy. The superior sagittal and transverse sinuses have been frequently reported as involved sites [23]. Imaging findings may include direct visualization of thrombus or filling defects, while indirect findings include venous edema, venous infarction, and parenchymal hemorrhage. In our study, CVT was identified in only two patients, with superior sagittal sinus and transverse sinus involvement observed in one patient each. The empty delta sign was present in both cases. Given the small number of patients, these findings are presented descriptively and do not permit further interpretation of the distribution of venous involvement.

Meningitis and encephalitis were less frequent than thromboembolic manifestations, consistent with previous reports [13]. Their imaging manifestations may include leptomeningeal enhancement and other inflammatory changes. In our study, the two patients with meningitis demonstrated hyperdense CSF and pachymeningeal enhancement, while leptomeningeal enhancement was observed in one patient. PRES has also been described in critically ill patients with COVID-19 and may be related to blood pressure fluctuations, endothelial dysfunction, and systemic inflammatory responses [8]. In our study, PRES was identified in only one patient, limiting further characterization of this imaging manifestation.

Regarding clinical outcomes, among the 45 patients with abnormal CT findings, 17 (37.8%) were discharged within 15 days, 19 (42.2%) required hospitalization for more than 15 days, and 9 (20.0%) died. Mortality varied across the different imaging categories, with deaths also recorded among patients with infarction, hemorrhage, CVT, and meningitis. These observations provide a descriptive account of in-hospital outcomes among patients with abnormal CT findings. However, since patients with normal CT findings were not followed for clinical outcomes and outcome data were incomplete, a comparison of mortality according to imaging status or an assessment of the prognostic significance of individual imaging abnormalities was not possible.

Overall, our findings demonstrate a broad spectrum of CNS abnormalities in patients with COVID-19, with ischemic infarction and intracranial hemorrhage being the predominant neuroimaging manifestations. Large-vessel involvement, particularly within the MCA territory, was a frequent pattern among patients with infarction, while lobar involvement was commonly observed among patients with hemorrhage. CVT, meningitis, cerebritis, and PRES were less frequent findings. The study provides a descriptive overview of the CT manifestations and clinical profiles of patients with COVID-19 presenting with neurological manifestations. The findings should be interpreted in the context of the observational study design, limited sample size, absence of a control group, lack of inferential statistical analysis, and incomplete outcome follow-up. Larger prospective studies with appropriate statistical comparisons and comprehensive longitudinal follow-up are needed to further characterize the relationship between clinical features, neuroimaging patterns, disease severity, and clinical outcomes.

Limitations

This study has certain limitations. First, the relatively small sample size and single-center design may limit the generalizability of the findings to other populations. Additionally, the inclusion of hospitalized patients presenting with neurological or neuropsychiatric manifestations may have introduced selection bias, as the study population may not represent the entire spectrum of neurological involvement in patients with COVID-19. Second, the observational nature of the study precludes establishing a causal relationship between COVID-19 and the observed neurological abnormalities. Third, the absence of systematic longitudinal follow-up, particularly among patients with normal initial CT findings, limited our ability to identify neurological abnormalities that may have developed subsequently or were not apparent on initial imaging. Fourth, the presence of conventional cerebrovascular risk factors such as hypertension, diabetes, dyslipidemia, and cardiovascular disease may have contributed to the imaging findings, making it difficult to distinguish the independent effect of SARS-CoV-2 infection. Fifth, although elevated inflammatory and coagulation markers such as IL-6 and D-dimer were observed, their associations with individual neuroimaging patterns could not establish specific underlying pathogenic mechanisms. Furthermore, certain imaging diagnoses could not be independently confirmed in all cases using additional imaging modalities or other diagnostic investigations, which may have resulted in some degree of diagnostic uncertainty. Finally,

variations in the timing and modality of neuroimaging in relation to disease onset and clinical deterioration may have influenced the detection and classification of neurological abnormalities. In particular, reliance on non-contrast CT for the initial assessment may have resulted in under-detection of certain abnormalities, particularly small lacunar and posterior circulation infarcts, and may have affected the accuracy of infarct territory classification. Larger prospective multicenter studies with standardized imaging protocols, appropriate confirmatory investigations, and longitudinal follow-up are warranted to better define the spectrum, mechanisms, and prognostic significance of neurological complications in COVID-19.

Conclusions

CT is a valuable first-line imaging modality for evaluating neurological manifestations in patients with COVID-19, facilitating the rapid identification and characterization of clinically significant intracranial abnormalities. Cerebral infarction was the predominant imaging abnormality, followed by intracranial hemorrhage. Among patients with infarction, large-vessel territory involvement was slightly more frequent than small-vessel (lacunar) involvement, with the MCA territory being the most commonly affected. Loss of gray-white matter differentiation was the most consistent CT feature of large-vessel infarction, while hyperdensity, perilesional edema, and mass effect were important imaging features of intracranial hemorrhage. Less frequent manifestations included CVT, meningitis, cerebritis, and PRES. In-hospital mortality was observed in 20% of patients with abnormal CT findings, although outcomes varied across the different imaging categories. These findings provide an overview of the spectrum of CT-detectable CNS abnormalities in patients with COVID-19 presenting with neurological manifestations. The study highlights the importance of prompt neuroimaging and clinical correlation in this population. However, given the descriptive observational design, limited sample size, absence of a control group, and incomplete outcome follow-up, the findings do not establish causal relationships or independent associations between imaging abnormalities, disease severity, and mortality. Further studies involving larger cohorts, appropriate statistical analyses, and comprehensive longitudinal follow-up are warranted.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Akanksha Johare, Sandeep Garg

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Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. The Institutional Ethics Committee of Maulana Azad Medical College and Associated Hospital issued approval F.1/IEC/MAMC/82/10/2020/No.194. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. All procedures involving human participants were conducted in accordance with applicable ethical standards, with due consideration given to participants' privacy, confidentiality, and rights. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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