ORIGINAL RESEARCH PAPER
Volume - 10 | Issue - 01 | January - 2021 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

NEUROIMAGING OF PATIENTS WITH COVID – 19 : FINDINGS AT AN ACADEMIC INSTITUTION DURING THE HEIGHT OF OUTBREAK.

Radiodiagnosis

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ABSTRACT

Context: Much of the focus regarding the global pandemic of coronavirus disease of 2019(COVID - 19) has been on the cardiovascular, pulmonary and hematologic complications. However, a large spectrum of neurologic complications have been reported which arisen as an increasingly recognized area of morbidity and mortality.

Aims:

- To report on the frequency and prevalence of neurological findings seen in COVID-19 hospitalized and imaged at our institution.
- To evaluate the clinical and lab correlation between prevalent neurological manifestations and elevated D-Dimer in SARS-COV when controlling for conventional vascular risk factors.

Methods and Material: This is retrospective observational case series involving 456 patients with laboratory confirmed (Reverse Transcriptase Polymerase Chain reaction Positive) COVID-19 presenting in our institute Gujarat Adani Institute of Medical Sciences, Bhuj between 1st April to 26th August,2020 , of whom 102 underwent either CT or MR imaging of brain. Clinical and imaging data were extracted. The frequency and type of neurogical findings was correlated with clinical history and pathological reports such as D-Dimer and C-reactive protein..

Results: Among imaged patients, 61 (59.8 %) patients had normal brain imaging, out of 41 (40%) abnormal scans, the most common including cerebral infarctions(24.3%) followed by intracranial hemorrhage (19.5 %) and microhemorrhages (7 %) followed by cerebral venous thrombosis (12.1 %) then vasculitis (3%) followed by encephalitis (3%), Posterior reversible encephalopathy syndrome (9.7%) and olfactory bulb abnormalities (2.4%).

Conclusions: Neuroimaging plays a crucial role in investigating the cause of neurological manifestations in COVID-19 and thus suggests the need for further studies to optimize management for these patients.

KEYWORDS

CT,MRI, Brain, COVID 19, neuroimaging.

INTRODUCTION:

- First appearing in China, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for the coronavirus disease of 2019 (COVID-19), which the World Health Organization (WHO) declared a pandemic in March 2020. Despite the majority of the focus being placed on pulmonary and cardiovascular complications, emergency medicine clinicians must remain cognizant of the neurologic complaints such as altered mental status, syncope and focal neurologic deficit and unilateral/bilateral body weakness which can present subtly and add substantially to the morbidity and mortality. The underlying pathophysiologic mechanisms remain unclear. The purpose of this current study is to report on the frequency and type of neurological findings seen in SARS- COV positive patients hospitalized and imaged at our institution.

MATERIALS AND METHODS:

Retrospective study was conducted in Department of Radio-diagnosis in Gujarat Adani institute of medical Sciences,Bhuj from 1st April to 26th August,2020. Oxygen saturation <90 % or other signs of severe respiratory distress or any other severe systemic illness such as sepsis were used as guiding criteria for COVID-19 admission during the crisis.

After controlling all conventional vascular risk factors, which were obtained from the medical record, included hypertension, coronary artery disease, diabetes mellitus type 2, atrial fibrillation, congestive heart failure, dyslipidemia, current or former smoking status, evidence of prior stroke, and obesity : >25 kg/m2. A total of 102 patients from COVID positive wards were referred for CT/MRI brain scan to our department.

Noncontrast/contrast enhanced helical CT scan from base of skull to vertex was performed using 16 slice siemens somatoson system. Noncontrast/contrast MRI brain with/without angiography/ venography was performed and T1W, T2W, FLAIR, DWI, ADC, SWI images were obtained on a 1.5 tesla siemens scanner.

INCLUSION CRITERIA:

1) Diagnosis of COVID-19 based on detection of SARS CoV-2 via reverse transcriptase polymerase chain reaction assays on the nasopharyngeal, throat, or lower respiratory tract swabs.
2) Abnormal brain CT/MRI with acute or subacute abnormalities.

EXCLUSION CRITERIA:

1) Patients with missing or noncontributory data (lack of sequences, numerous artifacts) regarding brain MRI/CT.
2) Brain CT/MRI showing normal scan, traumatic intracranial hemorrhage ,ischemic infarcts, cerebral venous thrombosis, or chronic lesions unrelated to the current event.
3) Patients referred from out of Hospital.
4) Patients whose history and/or neurological examinations were not available.

After applying the above criteria, a total of 102 scans were included in the study.

Indication of scan, patient's relevant neurological complaints, manifestations, examination, levels of D-dimer ,C-reactive protein and CT/MRI findings were recorded. Positive cases were separated and analysed.

RESULTS:

In our study, Between 1st April to 26th August,2020 , Out of 102 patients , 41 (prevalence - 40%) had abnormal CT (19) and/or MRI (29 [13 with contrast]) neuroimaging findings with mean age of 58 years and male to female ratio of 1.4 :1 (24- male and 17-female). Cerebral infarction was found in 10 of the patients (24.3 %) including 1 hemorrhagic venous infarction secondary to dural venous sinus thrombosis, intracranial hemorrhage in 8 of the patients (19.5 %), isolated microhemorrhages in form of white matter abnormalities in 7 (17%) of patients, cerebral venous thrombosis in 5 (12 %) patients, followed by vasculitis in 3 (7.3 %) patients , encephalitis in 3 (7.3 %) patients, followed by PRES (posterior reversible encephalopathy syndrome) in 4 (9.7%) patients and olfactory bulb abnormalities (Foci of hyperintensity in olfactory bulb) in one (2.4 %) patient.

Two patients (25%) had subarachnoid hemorrhage , and rest of 6 (75%) had intraparenchymal hematomas. In acute infarction, with the most frequent territory of involvement being the MCA territory (5/8 patients [-75%]). A smaller subset of patients had infarcts in other territories, including posterior cerebral artery (2/8 patients [12.5%]), posterior inferior cerebellar artery (1/8 patients [12.5%]).

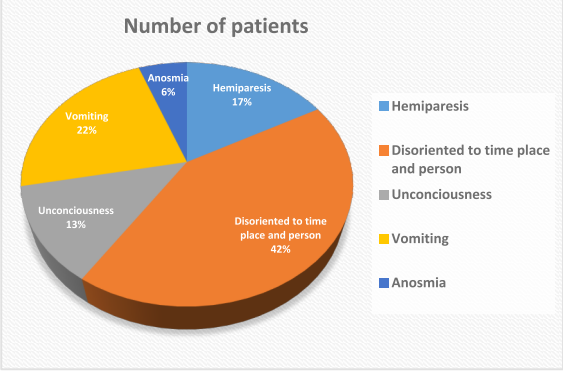
Table : 1 Demonstrates Total Frequency Of Neurological Findings In Sars-cov Positive Patients Admitted In Our Institution.

NEUROIMAGING FINDINGS	FREQUENCY OF PATIENTS	PERCENTAGE DISTRIBUTION (IN %)
Cerebral infarction	10	24. 3%
Intracranial hemorrhage	8	19.5%
Microhemorrhages	7	17 %
Cerebral venous thrombosis	5	12.1 %
Vasculitis	3	7.3 %
Encephalitis	3	7.3%
Posterior reversible encephalopathy syndrome	4	9.7%
Foci of hyperintensity in olfactory bulb	1	2.4%

TABLE: 2 demonstrated that out of total 41 cases, 24 had severly elevated D-Dimer. Here, Chi square value is 20.003 suggests that there is significant association between severly elevated D-Dimer and development of cerebral venous thrombosis , intracranial hemorrhage and cerebral infarction as evidenced by below data.

NEUROLOGICAL FINDINGS	>2000 D-DIMER	<2000 D-DIMER	TOTAL
Cerebral infarction	7	3	10
Intracranial hemorrhage	6	2	8
Microhemorrhages	6	1	7
Cerebral venous thrombosis	5	0	5
Vasculitis	0	3	3
Encephalitis	0	3	3
Posterior reversible encephalopathy syndrome	0	4	4
Foci of hyperintensity in olfactory bulb	0	1	1
Total	24	17	41

CHART :1



This above pie chart demonstrated that state of disorientation to time place and person (30/41)was the most common neurological manifestations seen during study followed by vomiting (16/41), hemiparesis(12/41) , unconsciousness (9/41) and anosmia (4/41).

DISCUSSION:

In this study, Surprisingly, cerebral infarction (MCA territory commonly) was commonly reported in cases of both mild and severe COVID-19 infection, suggesting that ischemic stroke may be a result of a virally-induced hypercoagulable state and not merely a consequence of severe systemic disease. Hemorrhagic events were also a commonly reported finding, but in contrast to ischemic infarction, the prevalence of hemorrhage appears to be more specific for severe COVID-19 patients.[1]

Our findings slightly differed from those of P. Simon et al which showed that most common neuroradiological findings in severe COVID-19 infection (from 42 positive patients) was white matter abnormalities in 21 of patients (50%) followed by ischemic infarct in 13 of patients (33.3%) , cerebral hemorrhage in 13 (31.0%) , posterior reversible encephalopathy syndrome in 4 (9.5%) and venous thrombosis 1 patient. (2.4%).[2]

The high prevalence of ischemic infarction, white matter abnormalities in form of microhemorrhages and hemorrhage found on neuroimaging of COVID-19 patients support these disease mechanisms. Given the wide range of potential neurological symptoms reported in COVID-19 patients, it is likely that many or all of these mechanisms are involved to some degree across the patient population.[2]

Cerebral venous thrombosis and intracranial hemorrhages as complications are recognized as crucial aspects of disease progression. The correlation that we describe between prothrombotic state and neuroimaging findings may indeed reflect the involvement of thromboembolic events underpinning the diverse range of neuroimaging findings in these patients. These mechanisms are speculative and in need of additional study.[3]

On MR venography, thromboses were seen in the dural venous sinuses, deep cerebral veins, and cortical veins. Notably, the internal cerebral veins are thrombosed in four out of five cases . In one case, source of hemorrhagic venous infarct was thrombotic microangiopathy due to compromised flow in deep medullary veins.[3]

To assess the potential relationship between COVID-19 and PRES on the basis of a small case series is challenging. However, One study by Franceschi et al. proposed that there are several potential mechanisms for PRES in the setting of COVID-19, including breakdown of the BBB, either indirectly due to cytokine storm syndrome and/or directly via endothelial dysfunction from binding of the SARS-CoV2 to endothelial-expressed ACE2 receptors. Notably,out of four patients of PRES in our case series,three patients had labile blood pressure, a well-known risk factor for PRES.[3]

Many pathophysiological mechanisms of nervous system involvement in COVID-19 infection have been proposed. These include a hypercoagulable state leading to thromboembolic events, endothelial cell and neurovascular injury via ACE2-mediated tropism and subsequent hemorrhage, hypoxic ischemia secondary to acute respiratory failure, direct neurotropism and access to the brain via hematogenous spread or retrograde migration along the olfactory nerve, and inflammatory injury secondary to cytokine storms.[4]

Viral entry into the CNS may result from either hematogenous dissemination or retrograde peripheral nerve propagation within the brain, with the latter appealing for the explanation of anosmia in the COVID-19 population. Cases of encephalitis and foci of hyperintensity in olfactory bulb in our study was an evidence for above described mechanism. [4]

The included study consisted mostly of patients who had severe neurologic manifestations, were admitted to the ICU, or were under mechanical ventilation. Furthermore, the mean patients ages were over 52 years, indicating that the patients belonged to older age groups that are more vulnerable to severe disease. Therefore, such predispositions would make the patients included in this study more susceptible to developing abnormal neuroimaging findings.[5]

Kremer et al mentioned in their article about COVID in CSF analysis that Thirty-one patients underwent a lumbar puncture, and among them, 21 had increased markers of inflammation (high white blood cell count, high proteinorachia, elevated immunoglobulin G level, or a combination thereof). One patient demonstrated the presence of SARS-CoV-2 on a reverse transcriptase polymerase chain reaction assay in CSF. Whereas, in our study, lumbar puncture came negative for SARS-Cov-2 in all the positive patients of neuroimaging. [6]

Central nervous system symptoms were the main form of neurologic injury in patients with COVID-19 in this study. The pathologic mechanism may be from the CNS invasion of SARSCoV-2, similar to SARS and MERS viruses. As with other respiratory viruses, SARS-COV-2may enter the CNS through the hematogenous or retrograde neuronal route. The latter can be supported by the fact that some patients in this study had smell impairment.[7]

Overall, the neurologic events associated with coronavirus infection (especially SARS-CoV-2) suggest a possible causal or synergetic relationship between cerebral ischemic/hemorrhagic/inflammatory events and CoV infection. [8]

CONCLUSION:

In conclusion, in this institutional study, we reported 41 patients with SARS-CoV and abnormal brain CT/MRI scans (excluding ischemic infarcts) with simultaneous clinical and possible lab correlation. Eight main neuroradiologic patterns could be distinguished, and the presence of hemorrhage was associated with worse clinical status.The findings of this study may help increase awareness of the wide range of COVID-19-related neuroimaging findings among radiologists worldwide. Being aware of these patterns will ensure clinicians consider COVID-19 infection when encountering unexplained neurologic findings, particularly during the current COVID-19 pandemic.

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