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Original Research Paper

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# NEUROLOGICAL MANIFESTATIONS OF COVID-19 IN A TERTIARY CARE CENTRE

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**ABSTRACT** SARS-CoV-2, is predominantly a respiratory viral infection, has affected more than 10 million individuals worldwide. Common symptoms include fever, dry cough, fatigue and shortness of breath. Some patients show neurological manifestations such as headache, smell and taste impairment, cerebrovascular disease, seizure, giddiness, myalgia.SARS-CoV-2 affects all aspects of the nervous system including the central nervous system (CNS), peripheral nervous system (PNS) and the muscular system.Clinicians should have a high-index of suspicion for COVID-19 in patients presenting with new-onset neurological symptoms.This will lead to early diagnosis and specific management.

**AIM OF THE STUDY:** To study neurological presentation in patients infected with covid-19. To analyze the age / sex distribution, presenting history, clinical findings and investigations on admission in the study group.

**MATERIALS AND METHODS:** The study was done in the KAPV Government Medical college, between june2020 to October 2020. This was a prospective study designed to analyze neurological manifestation in patients with covid-19.

**RESULTS:** Demographic distribution,male are more effected than female. Commonly effected age group in this study was 31-40yrs.Headache, Guillain-Barré syndrome, cerebrovascular disease , seizure, Anosmia, Ageusia, giddiness were seen in our study. Release of proinflammatory cytokines was pathophysiological mechanism for neurological manifestation in covid -19.

**KEYWORDS :** SARS-CoV-2, Neurological manifestations, Headache. cerebrovascular disease

## INTRODUCTION

Corona virus disease 2019 (COVID-19) is caused bysevere acute respiratory syndrome corona virus 2 (SARS-CoV-2). This virus originated in Wuhan, China, in December 2019. It is currently pandemic, and as of June 2020, there have been more than 10 million cases worldwide. The common symptoms in COVID-19 include fever, dry cough, fatigue and shortness of breath. Respiratory distress/ failure is seen in severe/critically ill COVID-19 patients. The SARS-CoV-2 primarily affects the respiratory system ,nervous system in a significant group of patients. Coronaviruses and the nervous system Previous studies suggest that four of the human coronaviruses— HCoV-229E, HCoV-OC43, severe acute respiratory syndrome coronavirus 1 (SARS- CoV-1) and Middle East respiratory syndrome coronavirus (MERS-CoV)—may involve the nervous system. For instance, in a postmortem study of the brains of patients with multiple sclerosis (MS), HCoV- 229E and HCoV-OC43 were detectedin some, suggesting neuroinvasion by these viruses 1. In cell-based studies, astrocytes, oligodendrocytes, neurons and microglia were susceptible to infection by HCoV-OC43. 2 Polyneuropathy, myopathy, rhabdomyolysis and large artery ischemic stroke have reported in a few patients with SARS-CoV-1. 3 The SARS-CoV-1 was detected in the cerebrospinal fluid (CSF) of some patients, and an autopsy study found SARS-CoV- 1 in the brain 4

## REVIEW OF LITERATURE:

Neurological manifestations by SARSCoV- 2.In a study done in Wuhan, China, Mao et al 6 noted neurological manifestations .In a study conducted in France, Helms et al 7 found 84% had neurological signs. Other studies found the neurological manifestations in COVID-19.[6,8,9,10]

### CNS manifestations

The main CNS manifestations observed are discussed below.

### Headache and dizziness

Headache and dizziness are the most common neurological manifestations recorded in several studies [6,8] caused by a direct effect of the infectionon the nervous system or due to other factors such as stress, fear or anxiety. Cerebrovascular disease. The CVD in COVID-19 may be due to high levels of inflammation and/or a hypercoagulable state. [10,11] Encephalopathy and delirium Encephalopathy and delirium may be due to direct invasion of the CNS by SARS-CoV-2, inflammation secondary to a cytokine storm or as a result of septic encephalopathy. [7,12]

### Other CNS manifestations

Reports of encephalitis and meningitis in COVID-19[5,13]Transverse myelitis[14,15],ADEM[17] Seizures [16] are coincidental or due to SARS-CoV-2 viral effects or the drugs used in treatment.

### Peripheral nervous system manifestations

covid19 patients had peripheral nervous system manifestations[6].

### GBS and other variants

COVID-19-related GBS is mainly seen in the elderly while typical GBS can occur in all age groups[18 ,19]

### Loss of the sense of taste and smell

These symptoms may appear early in the course of the disease or in otherwise asymptomatic individuals.[6,20]

### Skeletal muscle injury

Skeletal muscle injury was recorded in COVID-19 patients[9] .

### Possible pathogenic mechanisms

Neurological involvement in COVID-19 may be due to direct SARS-CoV-2 viral damage to the nervous system or through indirect means. ACE2 receptors are highly concentrated in the substantia nigra and ventricles of the brain. It is also found in

many neurons, astrocytes, oligodendrocytes, middle temporal gyrus and posterior cingulate cortex.[21]A mouse cellculture study found ACE2 receptor expression on astrocytes. ACE2 receptors are also expressed on endothelial and arterial smooth muscle cells of blood vessels in the brain. Virus-like particles were observed budding out of endothelial cells in the blood vessels of the frontal lobe, thus pointing to a hematogenous pathway of spread through the blood–brain barrier.

In a study by Ding et al.,4 SARS-CoV-1 virus was detected exclusively in the neurons of the brain. The SARS-CoV-1 virus has also been found in the CSF. A transgenic-mouse study found SARS-CoV-1 entry into the brain via the olfactory bulb,[22]. The entry of SARS-CoV-2 to the olfactory bulb through the cribriform plate might explain smell impairment in COVID-19. Li et al.[23]suggest the SARS-CoV-2 virus may spread to the medullary cardiorespiratory center in the brainstem via chemo and mechanoreceptors in the lung, as has been observed with some other respiratory viruses. While ACE-2 receptors are found in the alveolar epithelium of the lung, the mechanism of viral movement from the lungs to the nervous system remains unclear. In addition to inflammatory effects in the brain, neurological manifestations may also be caused by hypoxia-related injuries, as alveolar and interstitial lung inflammation may lead to CNS hypoxia.

This in turn may cause cerebral vasodilatation and cerebral edema. The possibility that medications used to treat COVID-19 may cause neurological manifestations.

Headache is a common side effect of the monoclonal antibody Tocilizumab and Chloroquine. Tocilizumab-associated multifocal cerebral thrombotic microangiopathy and Tocilizumab related demyelinating disorders.

Chloroquine and hydroxychloroquine are also known to have side effects such as seizure, balance disorder, peripheral neuropathy, parasthesia and hypaesthesia. Individuals with MS and neuromuscular disorders may be prescribed medications which suppress the immune system and thus are at a higher risk of developing severe COVID-19

## AIM OF THE STUDY

To study neurological manifestations in patients infected with covid-19. To analyze the age / sex distribution, presenting history, clinical findings and investigations at admission in the study group.

## MATERIALS AND METHODS

The study was done in the setting of the tertiary care centre The study was observational in nature designed to analyze neurological manifestation in patients with covid-19.

## INCLUSION CRITERIA

- Patients who presented with neurological complaint.
- In patients who are covid-19 positive (RTPCR/CT positive [GGO/CORAD4/5]

## EXCLUSION CRITERIA

- History of trauma (past/present)
- History of electrolyte abnormalities
- History of old neurological disorders.

Clinical data was collected from patients and witnesses in a systematic manner and added to a database, which included a checklist of neurological symptoms. Detail history for provocation factors and features suggesting organicity were attempted. Significant past medical history if any were noted. A thorough clinical examination was performed at the time of admission and relevant findings recorded. A routine metabolic screening, which included blood sugar, urea, serum creatinine, electrolytes and liver function tests (if indicated), were done at the time of admission. Lumbar puncture and CSF analysis was done if infective etiologies were suspected. CT brain plain study in all patients and and contrast studies when necessary were done in the study group. MRI brain was done when indicated. EEG could not be done in a some cases owing to critical condition of patients.

## RESULTS:

Neurological manifestation in 300 covid-19 patients were studied; of which 195 are males and 105 are females

**Table 1 sex distribution**

| Sex | Percentage | Number of patients |
|---|---|---|
| Male | 65% | 195 |
| Female | 35% | 105 |

**Table 2 :distribution of various age group**

| Age group | Percentage | Number of patients |
|---|---|---|
| 15-20 | 4% | 12 |
| 21-30 | 11% | 33 |
| 31-40 | 23% | 69 |
| 41-50 | 18% | 54 |
| 51-60 | 18% | 54 |
| 61-70 | 15% | 45 |
| >70 | 11% | 33 |

**Table 3 Neurological symptoms on admission**

| Neurological symptoms on admission | percentage | Number of patients |
|---|---|---|
| Headache | 33% | 99 |
| Altered sensorium | 12% | 36 |
| Anosmia | 11% | 33 |
| Cerebrovascular disease | 10% | 30 |
| Guillain-Barré syndrome | 10% | 30 |
| Cranial neuropathy ($7^{th}$ cranial nerve palsy) | 8% | 24 |
| Ageusia | 6% | 18 |
| New onset Seizure | 5% | 15 |
| Giddiness | 5% | 15 |

**Table 4 enumerates past medical history**

| Comorbidty | percentage | Number of patients |
|---|---|---|
| DIABETES | 34% | 102 |
| HYPERTENSION | 27% | 81 |
| CAD | 10% | 33 |
| HYPOTHYROID | 2% | 6 |
| PSYCHIATRY DISORDER | 1% | 3 |

**Table 5 pathophysiological effects resulting neurological manifestation**

| pathophysiological effects | Percentage | Number of patients |
|---|---|---|
| Hypoxia | 52% | 156 |
| Infarct | 23% | 69 |
| Demyelination | 10% | 30 |
| Encephalopathy | 5% | 15 |
| Hemorrhage | 2% | 6 |
| Meningitis | 1% | 3 |
| Encephalitis | 1% | 3 |
| CVT | 1% | 3 |

Total of 300 patients with neurologic manifestations that involved CNS, PNS with RT PCR positive were taken up for the study. Analysing demographic distribution (Table 1) Two third of patients were males, male to female ratio 1.8:1. 4% were effected between age group of 15-20yrs,23% were between 31-40yrs,18% were between 41-50yrs&51-60yrs,15% were between 61 -70yrs,>70yrs were 11% .In patients with neurological manifestations (Table 3), headache -33%, altered sensorium-12% , anosmia-11% cerebrovascular

disease -11%, Guillain-Barré syndrome-10%, cranial neuropathy(7th cranial nerve palsy)-8%,ageusia-6%,new onset seizure- 5% and giddiness-5%. Of these patients,(Table 4) 225 had co-morbidity : diabetes (34%), hypertension (27%), cardiac disease (10%), hypothyroid (2% ) and psychiatry disorder (1%)

## DISCUSSION:

In this study most neurologic manifestations occurred early in the illness. patients without typical symptoms (fever, cough, anorexia, and diarrhea) of COVID-19 came to the hospital with only neurological manifestation as their presenting symptoms. As with other respiratory viruses, SARS-COV-2may enter the CNS through the hematogenous or retrograde neuronal route. The pathologic mechanism may be from the CNS invasion of SARSCoV- 2, similar to SARS and MERS viruses. Therefore, for patients with COVID-19, we need to pay close attention to their neurologic manifestations, especially for those with severe infection. Patients with severe infection had higher D-dimer levels. This may be the reason why patients with severe infection are more likely to develop cerebrovascular disease. other reason was the infection mediated harmful immune response that caused the nervous system abnormalities. we donot have any comparative studies during early part of pandemic in like population

## CONCLUSIONS

Neurological manifestations have been reported in some COVID-19 patients. The nervous system may be affected via indirect mechanisms such as hypoxia, inflammation or an immune-mediated damage and vascular involvement which can be parainfectoius or postinfectious. Future studies using brain imaging, CSF analysis and histopathology would provide a clearer understanding of the effect of SARSCoV- 2 on the nervous system. This study may offer clinical information on COVID-19 that would help clinicians raise awareness of its neurological manifestations. When seeing patients with these neurologic manifestations such as headache, cerebrovascular disease, GBS, New onset of seizures, clinicians should consider SARSCoV- 2 infection as a differential diagnosis to avoid delayed diagnosis and prevention of transmission.

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