



NEUROLOGICAL MANIFESTATIONS OF COVID IN A TERTIARY CARE CENTER IN TAMILNADU

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ABSTRACT Corona virus disease 2019 (COVID19) is a pandemic disease which started in December 2019 in Wuhan, China. Now it has spread all over the world with over 7 crore cases and still counting. The typical symptoms of COVID19 can range from mild to severe respiratory illness. Although the respiratory system complications COVID19 have been the most frequent and life threatening, there are increasing reports of central and peripheral nervous system (PNS) involvement. Various studies done in many countries showed that many COVID19 patients presented with neurological manifestations. There are many review studies available throughout the world describing them. There are not many studies in India, especially in southern states done in COVID19 patients. Hence this observational study is done in Thanjavur medical college hospital , a tertiary care center in Tamilnadu, India, to study the various neurological manifestations found in COVID19 patients.

KEYWORDS : COVID19,neurology, India, stroke, headache, death

INTRODUCTION

Infections due to COVID-19 virus were first detected in December 2019 in Wuhan, China and have rapidly spread to the rest of world. COVID-19 is a novel corona virus that probably emerged from an animal source, which is spreading rapidly from person to person. The infection may be asymptomatic as in most of the patients or symptomatic, when symptomatic it may range from mild to severe respiratory illness. Patients with co morbidities like diabetes (DM), hypertension (HTN), coronary heart disease (CAD), chronic obstructive pulmonary disease and elderly population are more likely to develop serious illness.

So far COVID-19 cases in India till December 2020 is around one crore and number of deaths is 1.4 lakhs. Worldwide, the total number of cases are 7.2 crores with 16 lakhs death. Although the respiratory system complications COVID-19 have been the most frequent and life threatening, there are increasing reports of central and peripheral nervous system (PNS) involvement. Large scale observational studies conducted worldwide concluded that many neurological manifestations have been observed in COVID-19 patients such as stroke, encephalopathy, Guillian-Barre Syndrome (GBS), headache, anosmia etc. This study was done in Thanjavur medical college hospital , a tertiary COVID-19 care centre in Tamil Nadu, India, to study the neurological manifestations in COVID-19 patients admitted in our hospital.

MATERIALS AND METHODS

Patients who were COVID-19 positive with RT PCR were included. Patients with neurological symptoms were identified and their details were collected in COVID-19 outpatient department and wards. Patients who developed neurological symptoms after admission were also included. Among them 600 patients were selected randomly. They were treated according to their symptoms and standard COVID-19 treatment protocol. Routine investigations were done for all patients. Computerised Tomography (CT)/ Magnetic Resonance Imaging (MRI) brain was done for patients who required evaluation. Their outcomes were monitored till their hospital stay.

RESULTS

Among the 600 patients studied, majority were between the age of 40 to 60 years of age i.e. 293(49%) patients, 127 (21%) patients were less than 40 years of age and 180(30%) patients were more than 60 years of age.

Males were 397(66.2%) and females were 203(33.8%) in number. Among the 600 patients, 251 patients had Diabetes Mellitus (DM)(41.8%), 121 (20.1%)had Systemic Hypertension (HTN), 35 (5.8%)had Coronary Artery disease (CAD), and 20 (3.3%)had Chronic Obstructive Pulmonary Disease (COPD)

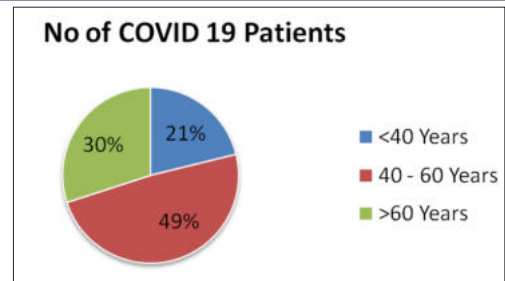


Figure 1: Incidence according to age

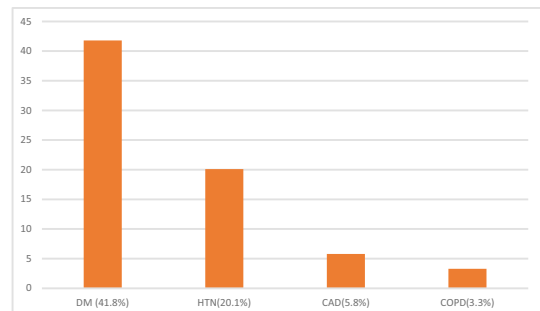


Figure 2: Prevalence of co morbidities

The neurological symptoms observed in those patients were headache 245 (40.8%), anosmia 172 (28.7%), myalgia 72 (12%), encephalopathy 60 (10%), focal neurological deficits other than cranial nerve palsies 39 (6.5%) seizure 36 (6%) cranial nerve palsy 13(2.2%), giddiness 46 (7.7%).

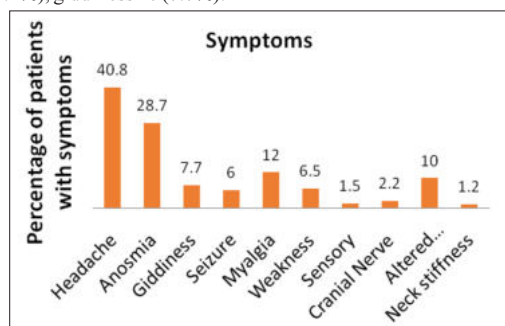


Figure 3: Percentage of patients with symptoms

After evaluation, neurological diagnosis was made in patients as follows; stroke 43 (7.1%), encephalopathy 60 (10%), GBS 4 (0.7%), meningitis 4 (0.7%), transverse myelitis 2 (0.3%). Among 43 stroke patients, 32 (74.4%) had Middle Cerebral Artery (MCA) infarct, 6 (14%) had cerebellar infarct, 3 (7%) pontine infarct, 2 (4.7 %) had hemorrhagic stroke.

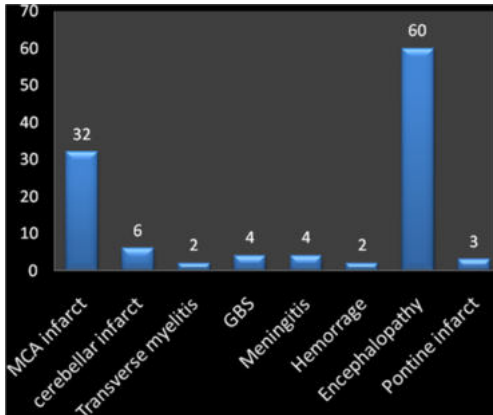


Figure 4: Percentage of neurological disorders

24 patients in this study died . 12 (50%) of them did not have any co morbidities. 6 (25%) of them had Diabetes Mellitus (DM), 4(17%) had both Diabetes Mellitus (DM) and Systemic Hypertension (HTN), 1(4%) had Coronary Artery Disease (CAD) and 1 (4%)had systemic Hypertension (HTN)

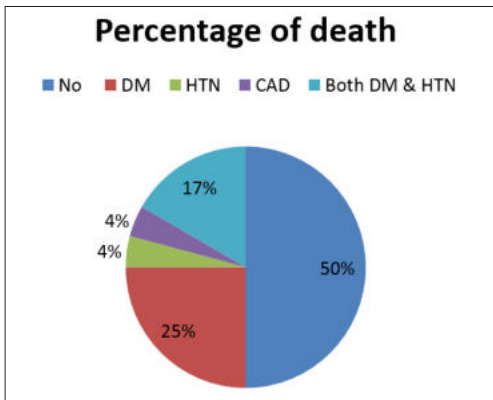


Figure 5: Percentage of death

DISCUSSION

Out of the 600 patients studied, majority were between 40 -60 years (21% < 40 yrs, 49% 40-60 years, 30% >60 yrs). All three groups almost had same symptoms except stroke (0.3% <40 yrs, 2.5 %in >40 years) and encephalopathy (1.2 %< 40 yrs, 3.6% 40-60 yrs, 5.2% >60 yrs) were seen more in elderly population. Majority had co morbidities, diabetes being most common 41.9% diabetes, 20.2% hypertension, 6% had CAD, 3.4% had COPD. Symptoms in diabetics were same as general population except that encephalopathy and respiratory symptoms were severe in them.

Neurological manifestations observed in them were headache, anosmia and ageusia, myalgia, stroke, GBS, transverse myelitis, meningitis, encephalopathy and seizure with the first three being the most common.

Headache

Among the 600 patients 40.8% had headache; 21% of them had pre-existing headache that worsened during COVID-19 infection, 18.8% developed new onset headache which was holocranial, more in frontal and bitemporal, dull aching, moderate intensity, continuous, without any associated photo or phonophobia and lasted for about one week . 15% of patients had headache as the only symptom, 1% of patients had headache associated with stroke, meningitis and accelerated hypertension, remaining had other flu like symptoms. Proposed mechanisms by various studies says headache may be due to CGRP increase, possibly induced by both angiotensin II and IL-6 levels, as CGRP is clearly associated with trigemino vascular activation resulting in headache, increased gastrointestinal (GI) motility leading

to diarrhea, further triggering inflammation and vascular edema.⁽¹⁾

Anosmia and Ageusia

Anosmia and ageusia was the second most common neurological manifestation seen in our patients 28.7% it was the initial presenting symptom in 20% of the patients. Most of them experienced it within 5 days of exposure.

18% had only anosmia and ageusia as their only COVID-19 symptom. Among them 10% were < 40 yrs. In a retrospective observational study, Klopfenstein *et al* reported that 54 patients (47%) with confirmed SARS-CoV-2 infection developed and Anosmia was associated with dysgeusia in 85% of cases.⁽²⁾ In most patients, anosmia went away on its own within 3 weeks. Some authors reported three mechanisms for anosmia in COVID-19 patients. First it could be a local infection of support cells and vascular pericytes in the nose and olfactory bulb that may affect the function of bipolar neurons or mitral cells. Damage to support cells in the sensory epithelium that may indirectly influence the signalling pathway from sensory neurons to the brain and damage to sustentacular cells and Bowman's gland cells that could lead to diffuse morphological damage to the olfactory sensory epithelium and altering of smell perception.⁽³⁾

Stroke

Stroke manifested in 43 patients (7.1%). A retrospective study of data from the Covid-19 outbreak in Wuhan, China, showed that the incidence of stroke among hospitalized patients with Covid-19 was approximately 5% ⁽⁴⁾. Among them 6.8% had ischemic stroke, 0.3% had hemorrhagic stroke. 16 patients had no co morbidities. 14 patients were admitted in COVID-19 wards with other symptoms and developed stroke in hospital. 29 patients developed stroke and incidentally were found to have COVID-19 RT PCR positive . Among them 5 patients had previous history of stroke. COVID-19 infection in particular is associated with a vigorous inflammatory response accompanied by coagulopathy, with elevated D-dimer levels and the frequent presence of antiphospholipid antibodies, which may explain the high prevalence of thromboses seen in these patients. Patients with COVID-19 infection are at heightened risk for medical complications, such as atrial arrhythmias, myocardial infarction, heart failure, myocarditis, and venous thromboses, all of which likely contribute to the risk of ischemic stroke⁽⁵⁾.

GBS

Among 600 patients, 4 patients had GBS. Among them 3 patients presented with quadriplegia, 1 patient had paraplegia. All were areflexic with no sensory symptoms. 2 patients had bilateral LMN facial palsy. 1 patient developed GBS after 1 week of RT PCR positivity. 1 patient died of aspiration and respiratory failure. 3 patients recovered without Intravenous immunoglobulin. Molecular mimicry in which the pathogen likely share epitopes similar to the components of the peripheral nerves and the antibodies produced by the host immune system to fight the virus, cross-react and bind to the peripheral nerves causing neuronal dysfunction to cause GBS is the proposed mechanism⁽⁶⁾

Transverse myelitis

2 patients had transverse myelitis. They presented with paraplegia, a particular sensory level, urinary retention and an antecedent respiratory infection. They were diagnosed as transverse myelitis and later on routine testing showed COVID-19 positivity. Post-infectious etiology in terms of secondary immunogenic overreaction was proposed as the underlying mechanism for myelitis after COVID-19⁽⁷⁾.

Meningitis

4 patients were found to have meningitis. Clinically patients had headache, neck stiffness and altered sensorium. CSF analysis was suggestive of aseptic meningitis. CT brain was normal. They were found to be COVID-19 positive after 3 days of admission. All patients were above 50 years. Mechanism proposed in other studies were Direct spread of SARS-CoV-2 to brain, Spread through neuronal and Haematogenous ,Immune mediated injury and Hypoxic related CNS injury⁽⁸⁾ .

Seizure

Seizure was found in 6% (36 patients). 8 patients were known case of seizure disorder. 28 patients had new onset seizures. 15 patients had alcohol withdrawal seizures. 7 patients had hyperglycemic seizures. 3 patients had hyponatremic seizures. 1 patient had seizure with hemorrhagic stroke, 1 patient had seizure with meningitis. CNS viral

infections and subsequent activation of neuro-inflammatory pathways are known to lower the threshold for seizures and potentially facilitate epileptogenesis in certain individuals.⁽⁹⁾

Myalgia

Myalgia was the third most common symptom found in these patients (72 patients, 12%) 9% had generalised myalgia, 3% had proximal lower limb pain. In 8% myalgia was the initial presenting symptom and 4% developed after one week of diagnosing COVID-19. It could be because of direct invasion of the muscle by the virus. Viruses have the ability to penetrate the cells that express ACE2 receptors. LDH increases when the virus damages muscles and other tissues. Due to both increased LDH and anaerobic glycolysis, lactate level may increase excessively. Cytosolic pH may decrease more. Muscle pain may increase further due to increased lactate levels, low pH, and low oxygen levels⁽¹⁰⁾.

Encephalopathy

60 patients (10%) were found to have encephalopathy. 38 patients had hypoxic encephalopathy, 10 patients had diabetic ketoacidosis with dyselektrolytemia. 4 patients had meningitis. 8 patients had hyponatremia. Among the 60 patients who had encephalopathy, 22 patients died. A retrospective study, from Wuhan, China, that included 214 patients, observed impaired consciousness in 16 (7.5%) patients and the causes were similar to our study.⁽¹¹⁾

Death

In this study 24 patients died. Among them 22 patients had encephalopathy and was mostly hypoxic encephalopathy. 1 GBS patient died of aspiration and respiratory failure. 1 patient had sudden respiratory arrest. 4 patients were < 40 yrs and 12 patients had no co morbidities. A study from Italy had analysed the outcome of patients in COVID-19 and found it to be similar to our study.⁽¹²⁾

CONCLUSION

Among the 600 patients majority were middle aged between 40 to 60 years and majority were males. Headache, anosmia, ageusia, myalgia were the commonest symptoms. 50% of them had co morbidities and they were found to have severe illness. Among patients with stroke, majority had ischemic stroke (Middle Cerebral Artery infarct is the most common). The findings in our study were similar to studies conducted world wide.^(12,13,14) Many patients did not have typical flu symptoms but pure neurological manifestations. Patients presenting with these neurological manifestations should be screened for COVID-19 in our present situation to provide appropriate treatment. COVID-19 virus is still evolving and the manifestations are varies in various countries. The mechanism involved in these manifestations is still not clear and further studies are required to come to a conclusion. This study gives a glimpse of neurological manifestations in this southern part of India.

LIMITATION

In a developing nation like India, with huge population and many people in poor economic conditions, it is difficult to conduct various investigations and follow them up. Magnetic Resonance Imaging of Brain and Cerebro-Spinal Fluid analysis could not be done in our study in majority of the patients due to logistic reasons.

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