Original Research Paper

Volume - 13 | Issue - 04 | April - 2023 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

General Medicine

ASSESSMENT OF RELATIONSHIP BETWEEN NEUROLOGICAL MANIFESTATIONS AND INFLAMMATORY MARKERS IN COVID-19 PATIENTS IN TERTIARY CARE HOSPITAL.

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ABSTRACT acute respiratory syndrome coronavirus 2, has resulted in more than 5.9 billion confirmed cases worldwide and more than 6.4 million deaths. Although the most common and important presentation is with respiratory disease, reports of neurological features are increasing. Characteristic cytokine storm incites severe metabolic changes and multiple organ failure. Profound coagulopathies may manifest with ischemic or hemorrhagic stroke. A prospective observational study was conducted in tertiary care government hospital in Kakinada for a period of 2months (April 1st, 2021 – May 31st, 2021). A total of 50 patients were participated in this study. Thorough clinical examination and relevant Lab, Radiological investigations were performed. Descriptive analysis of collected data was done. Mean age of the patients (SD) was 62.57(3.48). Majority of the patients were above 60years of age. 24(48%) were males and 26(52%) were females. Most common symptom was headache (60%), followed by focal neurological deficit (38%). 33(66%) of patients have Co-morbidities. 3(6%) patients were Vaccinated for Covid. There was a significant difference observed between inflammatory markers and Covid patients with respect to neurological manifestations. Out of 50 patients 11(22%) were succumbed while 39(78%) were survived.

KEYWORDS : Covid-19, Neurological manifestations, inflammatory markers

INTRODUCTION

COVID-19 pandemic, caused by the novel coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has resulted in more than 5.9 billion confirmed cases worldwide and more than 6.4 million deaths. Although the most common and important presentation is with respiratory disease, reports of neurological features are increasing. They can occur in patients with mild to severe COVID-19, but critically ill patients have a higher likelihood of neurologic complications.

The SARS-CoV-2 virus enters the brain either via a hematogenous route or olfactory system. Angiotensin-converting enzyme two receptors, present on endothelial cells of cerebral vessels, are a possible viral entry point. The most severe neurological manifestations, altered sensorium (agitation, delirium, and coma), are because of hypoxic and metabolic abnormalities. Characteristic cytokine storm incites severe metabolic changes and multiple organ failure. Profound coagulopathies may manifest with ischemic or hemorrhagic stroke.

This study is aimed to identify neurological manifestations in COVID-19 and its association with elevated inflammatory markers in active Covid-19 patients i.e., from onset of symptoms to first 14 days of infection.

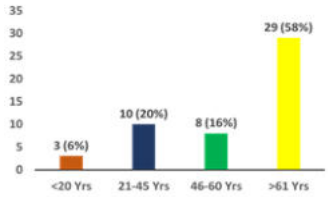
METHODOLOGY:

A prospective observational study was conducted in tertiary care government hospital in Kakinada for a period of 2months (April 1st, 2021 – May 31st, 2021). By using Universal sampling technique all active Covid-19 patients (confirmed by RT PCR or Rapid antigen or CORADS > 4) who developed neurological manifestations were included. Excluding those who are not willing to participate. A total of 50 patients were participated in this study. After obtaining ethical clearance and written consent, a detailed history including demographic data, personal history was taken. Thorough clinical examination and relevant Lab, Radiological investigations were performed. Descriptive analysis of collected data was done.

RESULTS:

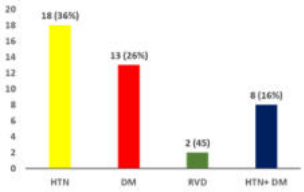
Mean age of the patients (SD) was 62.57(3.48). Majority of the patients were above 60years of age (fig 1). 24(48%) were males and 26(52%) were females. Most common symptom was headache (60%), followed by focal neurological deficit (38%), next was altered sensorium, vomiting and anosmia almost in equal ranges.

Fig 1: Age distribution



33(66%) of patients have Co-morbidities. Their details description was given in figure 2. 2(4%) patients had pulmonary TB history in past and used full course of ATT and 2(4%) patients were tested positive for HIV and are using on ART. 3(6%) patients were Vaccinated for Covid

Fig 2: Co-morbidities



In our study 34(68%) cases are RTPCR positive, 14(28%) cases are suspects with HRCT chest CORADS – 5 and 2(4%) cases are Rapid antigen test positive. Upon CT BRAIN analysis 18(36%) cases had normal study, 13(26%) cases had infarcts, 5(10%) cases had intra-parenchymal bleed and 14(28%) cases had cerebral atrophy changes. CVA and HIE cases are in equal frequency that is 19(38%) cases each, 8(16%) cases of Meningoencephalitis, 3(6%) cases of ICU dementia and 1(2%) case in Status Epilepticus.

Table 1: inflammatory markers in relation to patient outcome

Inflammatory Markers	Total (n= 50)	Recovered (n=39)	Deceased (n=11)	F- Value, Sig
CRP (mg/dL)	9.45 + 8.45	6.6 + 5.6	19.4 + 9.4	2.331, 0.029*
D-Dimer (mg/L)	4.03 + 2.37	3.69 + 2.13	5.2 + 2.9	2.468, 0.018*
Ferritin (ug/L)	798.1 + 268.3	733.7 + 244.9	1026.4 + 266.3	2.627, 0.015*

There was a significant difference observed between inflammatory markers and Covid patients with respect to neurological manifestations (table 1). Out of 50 patients 11(22%) were succumbed while 39(78%) were survived.

DISCUSSION

During the severe acute respiratory syndrome (SARS) pandemic of 2002–2003, neurological complications were reported in a subset of patients.[2],[14],[15],[16] SARS-CoV-2 virus shares close sequence homology to SARS-CoV-1. Both viruses use spike proteins on the viral surface to bind to the angiotensin-converting enzyme 2 (ACE2) receptor on mammalian host cells and then use serine protease transmembrane protease serine 2 (TMPRSS2) to prime the spike.[3],[17],[18] The presence of the ACE2 receptor in tissues determines viral cellular tropism in humans.

SARS-CoV-2 produces a plethora of neurological symptoms which affect the central and peripheral nervous systems and also the skeletal muscles. Neurological involvement occurs either through the hematogenous route or through olfactory neurons by retrograde transmission. Some of the effects are either due to cytokine-mediated hyperinflammatory response, host immune response to the viral replication, dysregulation of metabolic function, or caused due to disorders of anticoagulation.[1],[19]

In our study, the most common neurological involvement was acute stroke that affected 19 of the 50 cases. We noticed most of the strokes were due to anterior circulation involvement. As suggested by another study in the region, the reason for this could be that patients with anterior and middle cerebral artery strokes would approach hospitals for immediate management, whereas those with other minor anterior and posterior circulation strokes would not have presented to the hospital due to the lockdown procedures and fear of arriving to the hospitals.[4],[21],[22],[23]

We observed large vessel involvement in many of the patients, with thrombus occluding the vessels in majority of the patients. The reason for such involvement of the cerebral vasculature could be due to the competitive blockage of the virus against the ACE2, leading to elevated blood pressure. Another postulated reason is the SARS-CoV-2 infection is linked to a prothrombotic state causing venous and arterial thromboembolism, as demonstrated by our study in patients with COVID-19. Majority of our patients had elevated levels of D-dimer, LDH, ferritin, and CRP. Circulation of free thrombin, uncontrolled by natural anticoagulants, can activate platelets and lead to thrombosis.[5] Also, cytokine storm, which occurs with the release of proinflammatory cytokines such as interleukin (IL)-6, may contribute to such vascular events.[6] Eight patients developed encephalitis; the reason for encephalitis could be due to glycoprotein receptor or dysregulation of ACE2 receptor.[6]

Most of these patients with stroke were treated with antiplatelets and heparin, either unfractionated or low-molecular weight heparin. Thrombolysis was not initiated in any of the patients, as they were out of the window period. Delays could be due to delays in transport, lockdown measures, delay in arrival to the hospital in view of fear and anxiety, and isolation procedures. Stroke workup was also disturbed due to isolation procedures. COVID strokes were associated with higher mortality than non-COVID strokes (50%) in our study, as compared to other studies which reported 21%–31.3% mortality.[4],[9],[10],[20] There have been reports of both hemorrhagic and ischemic strokes among the critically ill, patients with COVID-19 had a higher risk of severe disability and death in a study based on the Global COVID-19 Stroke Registry.[9],[11] In a meta-analysis, prevalence of seizures was 0.3% (0.1%–0.9%), ischemic stroke was 1.2% (1%–1.4%), and hemorrhagic stroke was 0.5% (0.4%–0.6%) at a 95% confidence interval.[7]

CONCLUSIONS

Till date, SARS-CoV-2 has infected millions and affected billions of lives. Acute stroke was the most common type of neurological complication in our study sample and was associated with higher mortality 11 (22%). This necessitates the role of screening for COVID-19 in all stroke patients and careful monitoring if a positive diagnosis of COVID-19 is made. The understanding of neurological disease in patients with COVID-19 is evolving, and clinicians should continue to monitor patients closely for neurological disease. Early detection of neurological deficits may lead to improved clinical outcomes and better treatment algorithms. Further laboratory and clinical data, including tests of cerebrospinal fluid (CSF) and brain imaging, will be essential in elucidating the pathophysiology and potential for central nervous system (CNS) injury.

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