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Study and Analysis of Clinical Profile and Impact of Neurological Involvement in Disease Progression and Outcome in Patients with Neurological Symptoms in Covid-19 Positive Patients

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ABSTRACT

SARS-CoV-2 is an enveloped, single-stranded ribonucleic acid beta-coronavirus. This highly contagious pathogen is transmitted by respiratory droplets and aerosols, direct contact of mucous membranes and probably the fecal-oral route. The disease manifestations in the infected patients range from mild pneumonia to moderate pneumonia hypoxia requiring hospitalization and critical illness. The virus is believed to enter the CNS via the systemic circulation in the case of severe infection. Acute ischemic stroke is recognized as a neurologic complication of COVID-19 particularly in elderly, hypertensive and atrial fibrillation patients. The study was performed in the Department of Medicine of a tertiary care teaching hospital from October-September 2020-2021. 50 RT-PCR positive COVID-19 patients presenting with neurological manifestations admitted in the Wards and Intensive Care Unit of dedicated COVID 19 Care Hospital were included in the study. Findings on general and systemic examination along with investigations related to inflammatory markers of interest were collected and data was recorded in a specially designed proforma. Majority of patients presented with right sided (32%) hemiparetic (48%) weakness (62%) as common neurological symptom and were diagnosed with ischemic stroke (38%) with mortality rate of 34%. Majority of patients were diagnosed with midline shift (14%) on brain CT scan with parietal area (10%) and superior sagittal sinus (12%) as commonly affected areas. Non survivors and patients with moderate and severe COVID 19 infection diagnosed with Ischemic stroke tended to have NIHSS scores $\geq$4 and higher ICH Score. During the epidemic period of COVID-19, when examining patients with these neurologic manifestations, clinicians should consider SARS-CoV-2 infection as a differential diagnosis to avoid delayed diagnosis or misdiagnosis and prevention of transmission.

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Key Words
Covid-19, neurological, symptoms, SaRS-CoV-2, CNS

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INTRODUCTION

COVID-19 CS is defined as a state of hyper inflammation characterized by excessive cytokine release in a subset of patients with COVID-19[1]. CS can occur during the course of autoimmune diseases, malignancies and various infectious diseases such as severe acute respiratory syndrome coronavirus (SARS) Middle East Respiratory Syndrome (MERS) and H5N1 influenza[2,3]. Excessive increases in levels of cytokines such as interleukin-1β, interleukin-6 (IL-6) IP-10, IL-2R tumor necrosis factor-α and interferon-γ have been shown in CS. Recently, IL-6 a cytokine secreted by immune and stromal cells, has become the focus of interest in COVID-19 CS. It is a pro-inflammatory cytokine and plays a key role in CS by amplifying the immune response[4]. The level of IL-6 elevation correlates with the need for mechanical ventilation and increased mortality[5]. Although COVID-19 primarily involves the respiratory system, it often tends to spread in various organ systems. COVID-19 also causes serious disorders related to both the central and peripheral nervous systems[6]. Recently, neurological system involvement has been partially attributed to cytokine storm (CS)[2-7]. The virus is believed to enter the CNS via the systemic circulation in the case of severe infection. Another possible route of entry could be from the cribriform plate through the retrograde neuronal pathway, which is a possible explanation for hyposmia[8]. Besides, some viruses belong to the Coronaviridae family have been demonstrated to spread via a synapse-connected route to the medullary cardiorespiratory center from both the mechanoreceptors and chemoreceptors in the lungs as well as lower respiratory airways[9].

Acute ischemic stroke is recognized as a neurologic complication of COVID-19 particularly in elderly, hypertensive and atrial fibrillation patients although it could occur even in young patients with no risk factors[10]. Increasing evidence suggests that SARS-CoV-2 stimulates a prothrombotic environment which induces endothelial cell activation, tissue factor expression, thrombin production and hypercoagulability. Large-vessel occlusion has been found to occur with elevated D-dimer levels ($\geq$1000 μg L^{-1})[11]. Furthermore the presence of antiphospholipid antibodies could increase the risk of cerebral infarcts[12]. In a retrospective study from a local hospital in Wuhan, different neurologic manifestations suggestive of the central nervous system (CNS) peripheral nervous system (PNS) and musculoskeletal involvement were reported. CNS symptoms (24%) presented as dizziness, headache, impaired consciousness, cerebrovascular disease, ataxia and epilepsy. In a small number of patients (2–10%) hypogeusia, hyposmia and neuralgia were detected[13]. Epithelial cells of the nasal and oral cavity are enriched with ACE 2 receptors. It is postulated that SARS-CoV-2 could enter the CNS via the olfactory bulb and impair the function of sensory neurons. Post-infectious hypogeusia and hyposmia associated with COVID-19 are more frequently observed in younger patients and in females[14]. In the study, Mao *et al.* investigated the neurological manifestations of the COVID-19 skeletal muscle injury was detected in 19% of the patients with severe infection. Lactate dehydrogenase (LDH) and creatine phosphokinase (CPK) elevations consistent with muscular injury could be implicative of the possible invasion of the virus into the peripheral nerves and muscles[13]. Interestingly in a few reports, rhabdomyolysis associated with SARS-CoV-2 infection has been described[15,16]. In a few reports, acute disseminated encephalomyelitis (ADEM) linked to COVID-19 has been described. These cases presented with neurologic symptoms including dysphagia, dysarthria, aphasia and coma weeks after the initial infection. Consistent with ADEM, magnetic resonance imaging (MRI) demonstrated hyperintensities in the white matter and oligoclonal bands were present in cerebrospinal fluid (CSF) analysis[17]. ADEM appears to be caused by an autoimmune inflammatory reaction triggered by SARS-CoV-2 in genetically predisposed patients. Several studies have proposed that NLR can be a reliable predictor of COVID-19 progression and found that elevated NLR was associated with high mortality in COVID-19. NLR is cost-effective, readily available and easy to calculate laboratory marker[18].

Though India had sec largest burden of COVID-19 cases and mortality, neurological symptoms have not been evaluated adequately. Thus the above study was conducted for analysis of clinical profile and impact of neurological involvement in disease progression and outcome in patients with neurological symptoms in Covid-19 positive patients.

MATERIALS AND METHODS

Study place: The study was performed in the Department of Medicine of a tertiary care teaching hospital situated in western part India from October-September 2020-2021.

Study design: Retrospective, observational study.

Inclusion criteria: Patients aged 18 or more years, RT-PCR positive COVID-19 patients, Patients with COVID-19-associated neurological manifestations and those who were ready to give written informed consent.

Exclusion criteria: Patients aged less than 18 years, with known neurological disorders, non-COVID-19-associated neurological disorders and those unwilling to give written informed consent.

Sample size: Fifty patients were included in the study.

Data analysis: Data was collected and graphics were designed by Microsoft Office Excel 2019. The data was analysed with SPSS (IBM, Armonk, NY, USA) version 23.0 for Windows.

Ethical considerations: The Institutional Ethics Committee permission was taken before starting enrollement of the patients. The study involved review of case records and electronic Health Management Information System. After selection of patients, data was collected from these records. For each patient, complete history, signs, risk factors, biochemical and radiological markers, course of illness and events till discharge or death were reviewed. Chest CT was performed to assess the presence of COVID-19 related pulmonary fibrosis. CT severity score (CTSS) was determined at the time admission. On the basis of the involvement of each five lung zones, CT severity score (CTSS) was calculated. Following biochemical investigations were done on the day of admission which included complete blood count (NLR) liver function tests, renal function tests and electrolytes (serum sodium, potassium, calcium, magnesium) and inflammatory markers (IL-6, ESR, D-dimer and CRP). CSF analysis was done in indicated patients. Findings on general and systemic examination along with investigations related to inflammatory markers of interest were collected and data was recorded in a specially designed proforma.

RESULTS

Majority of the patients were in the age group of 51-60 years (36%) and 41-50 years (24%). While, least number of patients were in the age group of 18-30 years (6%). The age of the patients ranged from 26-78 years with a mean of 50.4±11.98 years Table 1 and 2.

The most common symptom was weakness (62%) followed by headache (48%) and altered sensorium (40%). While, least common symptoms were postural giddiness, band like sensation above waist and bilateral lateral gaze palsy with bulbar weakness (each 2%).

The most common neurological diagnosis was ischemic stroke (38%) followed by CVST (22%) and intracerebral bleed (16%). While, least common neurological diagnosis was transverse myelitis (4%) Table 3 and 4. All the patients had raised levels of inflammatory markers. The mean values of NLR, IL-6, CRP, ESR and D-dimer were 4.09±1.22, 140.06±110.13 pg mL, 7.54±6.91 mg dL, 49.9±12.38 mm hr and 3.26±2.81 ng L, respectively. Most commonly affected areas were parietal (10%) occipital (6%) and cerebellar (4%). While, least commonly affected areas included frontal, temporal and brainstem (each 2%) Table 5 and 6. Majority of the patients had moderate COVID-19 (44%) followed by severe COVID-19 (32%).While, least number of patients had mild COVID-19 (24%) Fig 1 .

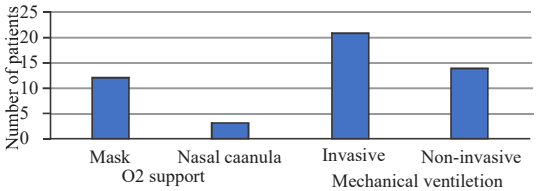

Fig. 1: Distribution of patients according to O2 support and mechanical ventilation

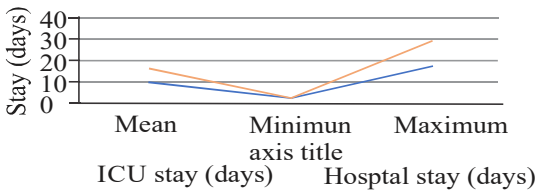

Fig. 2: Length of stay

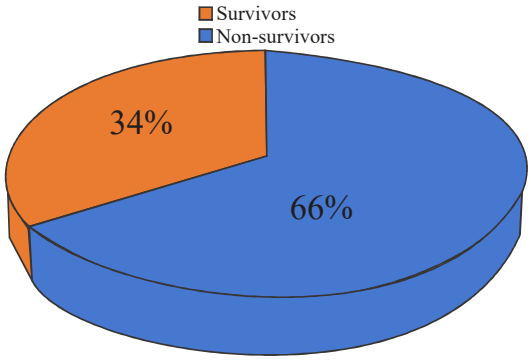

Fig. 3: Distribution of patients according to outcome

Distribution of patients according to O_2 support and mechanical ventilation: Majority of the patients required mechanical ventilation (70%) while 30% required O_2 support. Most of the patients required O_2 support through mask (24%) and invasive mechanical ventilation (42%) Fig 2.

Length of stay: The mean length of ICU and hospital stays were 9.84±4.26 and 16.10±8.59 days, respectively.

Distribution of patients according to outcome: Of 50 patients, 17 (34%) died, while remaining survived (66%). Thus the mortality rate was 34%. On analysis by independent sample t-test the non-survivors had significantly higher mean levels of NLR (5.56±0.92 vs 3.34±0.36 p<0.0001) IL-6 (262.79±84.55 pg mL^{-1} vs 76.83±53.58 pg mL^{-1} p<0.0001) CRP (16.27±4.65 mg dL^{-1} vs 3.05±0.98 mg dL^{-1} p<0.0001) ESR (64.12±8.49

Table 1: Distribution of patients according to age

Age (years)	N = 50	Percentage
18-30	3	6
31-40	7	14
41-50	12	24
51-60	18	36
>60	10	20

Table 2. Distribution of patients according to neurological symptoms

Neurological symptoms	N = 50	Percentage
Weakness	31	62
Headache	24	48
Altered sensorium	20	40
Convulsion	13	26
Slurring of speech	12	24
Deviation of angle of mouth	12	24
Aphasia	5	10
Bowel and bladder involvement	2	4
Postural giddiness	1	2
Band like sensation above waist	1	2
Bilateral lateral gaze palsy, bulbar weakness	1	2

Table 3. Distribution of patients according to neurological diagnosis

Neurological diagnosis	N = 50	Percentage
Ischemic stroke	19	38
CVST	11	22
Intracerebral bleed	8	16
GBS	5	20
Meningitis	5	20
Transverse myelitis	2	4

Table 4. Inflammatory markers

Parameters	Mean±SD	Minimum	Maximum
NLR	4.09±1.22	2.9	7.1
IL-6 (pg mL)	140.06±110.13	21.9	431.14
CRP (mg dL)	7.54±6.91	1.5	25.3
ESR (mm hr)	49.9±12.38	32	77
D-dimer (ng L)	3.26±2.81	0.55	9.8

Table 5. Distribution of patients according to areas of brain affected

Areas affected	N = 50	Percentage
Parietal	5	10
Occipital	3	6
Cerebellar	2	4
Frontal	1	2

Table 6. Distribution of patients according to COVID-19 clinical severity

COVID-19 clinical severity	N = 50	Percentage
Mild	12	24
Moderate	22	44
Severe	16	32

Table 7. Association of inflammatory markers with outcome

Parameters	Survivors (n = 33)	Non-survivors (n = 17)	p-value
NLR	3.34±0.36	5.56±0.92	< 0.0001
IL-6 (pg mL)	76.83±53.58	262.79±84.55	< 0.0001
CRP (mg dL)	3.05±0.98	16.27±4.65	< 0.0001
ESR (mm hr)	42.58±5.96	64.12±8.49	< 0.0001
D-dimer (ng L)	1.41±0.64	6.85±1.62	< 0.0001

mm hr vs 42.58±5.96 mm hr p<0.0001) and D-dimer (1.41±0.64 ng L^{-1} vs 6.85±1.62 ng L^{-1} p<0.0001) than survivors Fig 3.

DISCUSSIONS

Out of 50 cases the age group interval of 51-60 years had maximum cases (36%). This was followed by cases pertaining to age group interval of 41-50 years (24%) and 31-40 years (14%). Least number of cases were contained in age group interval of 18-30 years (6%). The mean age of the patients recruited in our study population was 50.4±11.98 years ranging from 26-78 years. Zhao *et al.*[19] (reported median age of 64 years ranging from 47-70 years with maximum patients in age interval of more than 60 years (50.2%). Similar findings were noted by Hashem *et al.*[20] who found maximum cases more than 55 years (64.1%) in their study who underwent ICU admission.

The neurological signs and symptoms observed in the COVID-19 cases could be a manifestation of complicated process with interactive mechanism involved. The interaction between the coronavirus and microvascular endothelial cells conduces to the access of CNS symptoms[21]. SARS-CoV-2 could also cause damage to the central nervous system indirectly. Viruses do not have to enter the brain to cause damage they can activate an immune response that triggers subsequent damage within neuronal tissue. SARS-CoV-2 has been reported to cause a massive release of cytokines a syndrome known as “cytokine storm” downstream effects of this immune response include endothelial damage, disseminated intravascular coagulation and disrupted cerebral auto-regulation. Immune-mediated hyperplasia leads to extensive glial cell proliferation, inflammatory cell infiltration and neuronal necrosis[22]. Study, our patients presented with various neurological symptoms. Majority of them presented with focal weakness (62%) followed by headache (48%) and altered sensorium (40%). Of all the patients having focal weakness, majority had hemiparesis (48%) followed by paraparesis (10%) and quadriparesis (4%). Moreover, hemiparesis was more on right side (32%) than the left side (16%). Of all the patients with altered sensorium, majority of the patients had normal GCS score of 13-15 (60%) followed by a score of 5-12 (34%) followed by a score of 3-4 (6%). Other estimated neurological symptoms were convulsions (26%) slurred speech and deviated angle of mouth (each 26%) aphasia (10%) and bowel bladder involvement (4%). While, least common neurological symptoms were postural giddiness, band like sensation above waist and bilateral lateral gaze palsy with bulbar weakness (each 2%). Majority of patients had unconsciousness (5.6%) coma (5.4%) dysphoria (3.9%) somnolence (2.7%) and convulsion (0.2%). These symptoms appeared at median of 14 days corresponding to around five days after hospital admission and last for three 3 days. When the symptoms were separately considered, somnolence was the earliest one, presenting at 12 days and coma was the latest one presenting at 16 days after symptom onset[17]. A retrospective study from China reviewed 274 cases of COVID-19, of which 8.8% developed hypoxic encephalopathy[23]. Ischemic stroke is another clinical entity which can present in patients with COVID-19 infection. This presentation may arise secondary to a cytokine storm syndrome which can cause endothelial damage, disseminated intravascular

coagulation, and disrupted cerebral auto-regulation. Mao *et al.*[24], reported that 6 (2.8%) patients, out of the 214 reviewed COVID-19 cases, developed ischemic stroke. Of these 6 patients, 2 arrived at the emergency department owing to sudden onset of hemiplegia. In patients with CNS manifestations the most common reported symptoms were dizziness (16.8%) and headache (13.1%). In patients with peripheral nervous system symptoms the most common reported symptoms were taste impairment (5.6%) and smell impairment (5.1%)[13]. In an Iranian study by Moein *et al.*[23] majority of patients with olfactory dysfunction reported that the onset of the olfactory dysfunction (Loss of smell/taste sensation) occurred at the same time or immediately after the onset of their other COVID-19 symptoms. Hyposmia and anosmia the common symptoms, have been explained by the entry of SARS-CoV-2 into brain tissues via dissemination and spread from the cribriform plate, which is in close proximity to the olfactory bulb. Yue *et al.*, reported a 65-year-old female case, who was admitted to the hospital for a left facial droop preceded by a 2-day history of pain in the mastoid region and a positive throat swab RT-PCR for SARS-CoV-2 virusx[25]. Headache is, indeed, one of the most common neurological manifestations of SARS-CoV-2 infection, with a variability range of 8-39% of cases[26,27]. Headache can be a primary process in these patients or part of a broad spectrum of neurological syndromes such as meningitis, encephalitis, vasculitis, elevated intracranial pressure and other clinical conditions associated with COVID-19's neuroinflammatory mechanisms and other underlying systemic causes[28]. The mean values of NLR, IL-6, CRP, ESR and D-dimer were 4.09±1.22, 140.06±110.13 pg mL^{-1}, 7.54±6.91 mg dL^{-1}, 49.9±12.38 mm hr and 3.26±2.81 ng L^{-1}, respectively. For serum electrolytes, we analyzed serum Sodium, Potassium, iCalcium and Magnesium levels. The mean values of Sodium, Potassium, iCalcium and Magnesium were 135.44±5.68 mEq L^{-1}, 3.94±0.59 mEq L^{-1}, 4.49±0.79 mg dL^{-1} and 1.70±0.36 mg dL^{-1}, respectively. As observed above, our results were consistent with the study of Mao *et al.*, who noted that patients had more increased inflammatory response, including higher white blood cell counts, neutrophil counts, lower lymphocyte counts and increased C-reactive protein levels. Raised C-reactive protein and D-dimer levels were indicative of consumptive coagulopathy which was observed by Mao *et al.* and the results are concordant with our study[13]. In a multicentric study conducted in Wuhan China, median IL-6 level was 43pg mL^{-1} ranging from 17-91 pg mL^{-1}, median CRP was 55 mg L^{-1} ranging from 18-94 mg L^{-1}, median NLR was 5 ranging from 3.2-9.8 and mean D-dimer was 0.4 mcg mL^{-1} ranging from 0.2-0.7 mcg mL^{-1}[29]. These finding supported our study data. Mean values of NLR, CRP and D-dimer were 4.7±5.0, 3.79±4.95 mg dL^{-1} and 1.3±2.3 ng L^{-1}, respectively as per Hashem *et al.*[20] which were also supportive of our study data. In CT scan, out of 50 patients, 8 patients diagnosed with Intracranial hemorrhage out of which midline shift was found in 7 (14%) and intraventricular extension was observed in 5 (10%). The mean ICH score was 3.63±1.51 with a range of 1-5. Out of 19 patients of Ischemic stroke, NIHSS score was $\geq$4 in 13 (36%) patients and $\leq$4 in 5 (10%) patients. Most commonly affected brain areas were parietal (10%) occipital (6%) and cerebellar (4%) and frontal (2%).

In our study ischemic stroke was noted in 19 patients (38%) followed by CVST in 11 patients (22%) IC hemorrhage in 8 cases (16%) GBS and Meningitis in 5 cases each (10% each) and Transverse Myelitis (MRI proven) in 2 cases (4%). In cases of ischemic stroke out of 19 patients, 12 had dominant lobe involvement. Out of 19 patients, 11 patients had NIHSS $\geq$4 and 8 had $\leq$4. While amongst the 11 patients of cerebral venous sinus thrombosis the most commonly affected sinuses were superior sagittal (12%) transverse (6%) and sigmoid (6%).

The results of our study are consistent with the study by Hameed *et al.*[30] in which out of 24 patients of Cerebrovascular accidents (Ischemic Stroke and Intracranial hemorrhage) 16 patients had dominant lobe involvement. CVST was the presenting feature in 13 cases (65%) whereas 7 cases (35%) developed CVST while being treated for COVID-19 infection. In above study, distribution of patients according to COVID-19 clinical severity shows that out of 50 cases 22 patients had moderate COVID-19 (44%) followed by severe COVID-19 in 16 patients (32%) and mild COVID-19 in 12 patients (24%). In present study, distribution of patients according to COVID-19 CT severity appraised that 23 patients had moderate COVID-19 (46%) followed by severe COVID-19 (40%). While, least number of patients had mild COVID-19 (14%). Tony *et al.*[31] determined that patients with CNS manifestations had the most severe COVID (CO-RAD IV and CO-RAD V in 36.3% and 26.5%, respectively). However moderate and mild (CO-RAD II and CO-RAD I in 54.2% and 29% respectively) were predominant in patients with peripheral nervous system involvement. However findings in our cohort showed that patients with severe neurological manifestations (Ischemic strokes with NIHSS$\geq$4, Intracranial hemorrhage with ICH score $\geq$3) had moderate COVID Infection followed by severe COVID 19 infection.

In above study, patients needed either O_2 support or mechanical ventilation. We found that 35 patients (70%) of the patients required mechanical ventilation, out of which 21 (42%) patients required invasive

ventilation and 14 case (28%) required non-invasive ventilation. Out of 35 patients requiring Mechanical ventilation 19 patients had severe Covid 19, disease16 patients (45.7%) were having moderate clinical and CT severity of COVID 19 disease. While 15 patients 30% required O_2 support out of which 7 patients each were moderate and mild cases COVID-19 disease and 1 was severe COVID-19 disease. In a study by Abdel-Mannan *et al.*[32] 42% required invasive mechanical ventilation and 14.8% cases required non-invasive mechanical ventilation followed by 24% O_2 support through mask. Nlandu *et al.*, valued that 26.4% cases needed mechanical ventilation, while 64.8% cases needed high concentration oxygen support in COVID patients[33].

Also, in above study, we had survivors and non-survivors as outcomes. Of 50 patients, 17 (34%) were non-survivors, while remaining 33 patients, survived (66%). Thus the mortality rate was 34%. On analysis by independent sample t-test, there was statistical significant difference established between survivors and non-survivors with regards to all inflammatory markers (all p<0.0001). The non-survivors had significantly higher mean levels of NLR (5.56±0.92 vs 3.34±0.36) IL-6 (262.79±84.55 pg mL^{-1} vs 76.83±53.58 pg mL^{-1}) CRP (16.27±4.65 mg dL^{-1} vs 3.05±0.98 mg dL^{-1}) ESR (64.12±8.49 mm hr vs 42.58±5.96 mm hr) D-dimer (1.41±0.64 ng L^{-1} vs 6.85±1.62 ng L^{-1}) than survivors. Results of our study are consistent with study of Hashem *et al.*[34] in which Mean values of NLR, CRP, and D-dimer were 4.7±5.0, 3.79±4.95 mg dL^{-1} and 1.3±2.3 ng L^{-1}, respectively and Gursoy *et al.*[35] which had findings that IL-6, CRP, ferritin, NLR, neutrophil count, procalcitonin, D-dimer, troponin I, creatinine, AST, LDH and CK level were higher in the cytokine storm group than non-CYTOKINE STORM group (p:0.001, p:0.001, p:0.001, p:0.00, p:0.046, p:0.001, p:0.001, p:0.018, p:0.008, p:0.010, p:0.001 and p:0.003, respectively) while lymphocyte count was lower (p:0.003) presence of neurological comorbidity was more frequent in the CYTOKINE STORM group than in the non-CYTOKINE STORM group. Cytokine storm may be responsible for the severe involvement seen in both the neurological and other systems in COVID-19. This hypercytokinemic inflammation may be responsible for end-organ damage. Frontera *et al.* study showed Admission inflammatory biomarkers (interleukin-6, D-dimer) were increased in patients with neurologic disorders compared to those without (both p<0.01).

In above study, we divided length of stay in hospitals and ICU. The mean length of ICU and hospital stays were 9.84±4.26 and 16.10±8.59 days, respectively. On analysis by independent sample t-test, there was statistical significant difference established between survivors and non-survivors in regards to ICU as well as hospital stay (all p<0.0001). The survivors had significantly longer mean length of ICU stay (12.55±2.08 day's vs 4.59±1.18 days) and hospital stay (21.91±3.13 days vs 4.82±1.47 days) than non-survivors. Also, length of hospital and ICU stay had statistical significant difference established between survivors and non-survivors in regards to all neurological diagnoses like ischemic stroke, CVST, IC bleed as well as other causes. (all p<0.0001) As per study by Abdel-Mannan *et al.*[32] the ICU stay was for a median 6.5 (range, 2-14) days. Regarding the average of hospital length of stay the results by Garbin *et al.*, show a mean of 10.5±11.8 days slightly close to our study data[36].

CONCLUSION

The mean age of the patients recruited in above study population was 50.4±11.98 years ranging from 26-78 years. Majority of them presented with focal weakness (62%) followed by headache (48%) and altered sensorium (40%). Of all the patients having focal weakness, majority had hemiparesis (48%) followed by paraparesis (10%) and quadriparesis (4%). Moreover, hemiparesis was more on right side (32%) than the left side (16%). Majority of patients presented with right sided (32%) hemiparetic (48%) weakness (62%) as common neurological symptom and were diagnosed with ischemic stroke (38%) with mortality rate of 34%. The mean values of inflammatory markers like NLR, IL-6, CRP, ESR and D-dimer were 4.09±1.22, 140.06±110.13 pg mL^{-1}, 7.54±6.91 mg dL^{-1}, 49.9±12.38 mm hr and 3.26±2.81 ng L^{-1}, respectively. Patients with severe COVID-19 infection had higher NLR, ESR, CRP, D-dimer levels than that of patients with non-severe infection. This may be the reason why patients with severe infection are more likely to develop cerebrovascular disease. There was statistical significant difference between survivors and non-survivors with regards to all inflammatory markers (all p<0.0001). Majority of patients were diagnosed with midline shift (14%) on brain CT scan with parietal area (10%) and superior sagittal sinus (12%) as commonly affected areas. There was predilection for large vessel thromboembolic disease with involvement of dominant hemisphere particularly frontal lobe affecting executive and language functions with right sided hemiparesis. Non survivors and patients with moderate and severe COVID 19 infection diagnosed with Ischemic stroke tended to have NIHSS scores $\geq$4 and higher ICH Score. Majority of patients were diagnosed with moderate COVID-19 clinical severity (44%) as well as moderate COVID-19 CT severity (46%) and were managed by mechanical ventilation (70%). Length of hospital stay had statistical significant difference between survivors and non-survivors in regards to all neurological diagnoses like ischemic

stroke, CVST, IC bleed as well as other causes (all p<0.0001). During the epidemic period of COVID-19, when examining patients with these neurologic manifestations, clinicians should consider SARS-CoV-2 infection as a differential diagnosis to avoid delayed diagnosis or misdiagnosis and prevention of transmission.

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