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Original research article

Analysis of Neuroimaging in COVID-19 Patients - A Correlation Between Lung Severity and Brain Findings

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Abstract

Background: Corona virus emerged in China in December 2019 and quickly spread over the world, causing a pandemic. The probable link between the occurrence of neurological abnormalities and the CT severity score (CTSS) in COVID-19 participants is less understood. The purpose of this study was to look at the neurological symptoms of COVID-19 on CT head and determine whether there was a link between thorax and brain imaging abnormalities in COVID-19 patients.

Methods: Total 135 Hospitalized COVID positive patients with acute neurological symptoms underwent both CT head and CT thorax during their hospital stay were included in the study. All the patients with neuroimaging were divided into 2 groups: first being patients with acute neuroimaging findings and the second being the patients with chronic/normal neuroimaging findings.

Results: The most common CT head imaging findings in these individuals were acute ischemic infarcts in 54 (40%) and acute intracranial haemorrhage in 8 (6%). When compared to individuals with normal/chronic neurological results, a greater mean chest CTSS was found in patients with acute abnormalities on CT head (14.1 [SD-3.2] versus 6.5 [SD-3.3]). However, no statistical correlation could be shown between a greater CTSS and the occurrence of acute neurological disorders.

Conclusions: There was no link between a greater CTSS and the occurrence of neurological disorders on CT scans. As a result, increased lung involvement severity may not be a good predictor of brain involvement in COVID patients.
Keywords: COVID-19, neurological abnormalities, infarcts, haemorrhage.

Introduction

Corona virus first appeared in China in December 2019 and soon spread around the world, resulting in a pandemic **[1].** The imaging properties of the brain and thorax associated with Corona virus disease 2019 (COVID-19) have been studied previously **[2-13].** The characteristics of COVID-19 infection on thorax imaging, including as bilateral and peripheral ground-glass opacities (GGO) and consolidation, are now well established **[2-5].** Ischemic infarcts, haemorrhages, and diverse types of leukoencephalopathy are all well-known COVID-19-related brain imaging abnormalities **[6-13]**. Neurologic symptoms are more common in people with more severe pulmonary distress **[10,13].** There is growing evidence that persons with acute lung illness are at risk for brain damage as a result of hypoxia and inflammatory mediators that link the brain and lungs **[14-17].** However, less is known about the possible connection between the incidence of neurological findings and the CT severity score in COVID-19 individuals. The goal of this study was to analyse the neurological manifestations of COVID-19 on CT head and to see if there was a correlation between COVID-19 patients' thorax and brain imaging abnormalities.

METHODS

Population and Methodology

A retrospective study of 170 cases was undertaken in Varun Arjun Medical College, located in the Northern part of India. Out of total cases, 135 cases fit in our inclusion criteria **(Fig-1)**. Institutional Ethics committee clearance was taken for the research purpose. Our inclusion criteria include hospitalized COVID positive patients with acute neurological symptoms underwent both CT head and CT thorax during their hospital stay. We extracted clinical, laboratory, and demographic data from computerised medical records. The only criterion for exclusion was a lack of HRCT thorax and/or CT head, which might be owing to reluctant patients or situations such as pregnancy, children under the age of 6, or other factors.

Imaging protocol

A dedicated 64 slices Seimens 'Somatom go.UP' CT scanner with SAFIRE technology was used. Standard protocols were followed for all non-contrast head and thorax CT scans.

All the patients with neuroimaging were divided into 2 groups: first being patients with acute neuroimaging findings and the second being the patients with chronic/normal findings. The group of chronic/normal neuroimaging findings included patients with chronic white matter ischemic illness, chronic lacunar infarcts, or chronic demyelinating disease but no acute neuroimaging abnormalities. Acute findings include acute/subacute infarcts and haemorrhages and infections.

CT severity score (CTSS) was calculated on the basis of the lobar involvement of the lung parenchyma, as under:

(1)< 5%, (2) 5 - 25 %, (3) 26 - 50%, (4) 50 - 75 %, (5) > 75%. The CTSS score is the number of the individual scores of lobes and will range from 0 to 25. Zero score indicates normal scan while score of 25 denotes maximum involvement when all the five lobes have more than 75% involvement.

Statistical analysis

Continuous variables were displayed by mean [SD] or median. Percentages were used to display categorical variables. The correlation between acute neuroimaging abnormalities and the CTSS was explored applying the linear regression model. A P-value of 0.05 was used as the significant level.

RESULTS

A review of total 170 consecutive admitted COVID positive patients with acute neurological symptoms was done. Out of these, a total of 135 COVID positive patients came in the criteria of inclusion (Fig-1). The mean age was 68 [SD, 15.2] years (range - 15 to 90 years) with males contributing to 59.2% (n = 80) of the total study population. Epidemiological and neuro-clinical features has been shown in the **Table-1**.

Neuroimaging Characteristics

The main CT head imaging findings in these patients was acute ischemic infarcts in 54 (40%) and acute intracranial hemorrhage in 8 (6%) patients. Anterior circulation was involved in 45 out of 54 (83%) patients with MCA territory (42 out of 45 patients) being the most frequent. Out of 42 patients suffered from MCA territory infarcts, 20 were large to medium sized infarcts (ASPECTS Score less than 7) and 22 were small (ASPECTS Score more than 7) **(Fig-2 and Fig-3)**. Posterior circulation was affected in only 9 out of 54 (17%) patients. In posterior circulation infarcts, PICA was most commonly involved (7 out of 9 patients). Out of total 54 acute infarcts, 9 (17%) showed hemorrhagic transformation.

Acute hemorrhage was found in 8 (6%) of the total 135 patients with basal ganglia (4 out of 8), cerebellum (2 out of 8) and occipital lobe (2 out of 8) being the affected sites **(Fig-4)**.

Out of the total 135 patients, 73 patients had chronic/normal neuroimaging findings including chronic white matter ischemic changes, chronic lacunar infarcts, or chronic demyelinating changes, but absence of acute features on CT head imaging. It took an average of 8 days from admission to CT head imaging.

CT Chest Characteristics

The main CT thorax patterns were peripheral GGOs and/or consolidation **Table-1** . CTSS of these patients were divided into mild (CTSS of less than 8), moderate (CTSS of 8-15) and severe (CTSS of 16 to 25). Majority of the these patients, 75 out of 135 (55%), were in severe category. The mean CTSS was 11 [SD - 2.9] (range 5–24).

HRCT chest of our study population showed variety of opacity characteristics. Out of total patients, 96 patients (71%) had isolated Ground glass opacities (GGO) while another 30 patients (22%) had both GGO and consolidation and only 9 patients (7%) had isolated consolidation. CT chest imaging also showed some specific findings which includes pleural effusion in 7/135 patients (5.1%), pulmonary nodules in 30/135 patients (22.2%), mediastinal lymphadenopathy in 13/135 patients (9.6%) and cavitatory lesions in 2/135 patients (1.5%). Pneumomediastinum was seen in 2/135 patients **Table-1**.

Left lower lobe was the most involved lobe in 95 (70%) patients, followed by the right lower lobe in 82 (61%). Ninety five patients (70%) had predominant peripheral distribution, and 64 (47%) had involvement of lower zones. The distribution of other typical and atypical features of COVID-19 has been shown in **Table-1**

Correlation between Neuroimaging and CT thorax findings

A review of total 135 CT head and 135 CT thorax scans was done. Out of total patients, 62 (46%) had acute abnormalities on neuroimaging involving acute infarcts (54 patients) and hemorrhages (8 patients). The patients with acute findings on CT head had a quite higher average CTSS as compared to the patients having normal/chronic neurological findings (14.1 [SD-3.2] versus 6.5 [SD-3.3]). Most of the patients with acute neurological abnormalities [40 out of 62, (64.5%)] were having severe chest involvement (CTSS of 16 to 25) while 18 out of 62 (29%) were having moderate chest involvement (CTSS of 9 to 15). Only 4 patients (6.4%) with acute neurological abnormality on CT brain came under mild category of chest involvement (CTSS less than 8).

A linear regression model was applied to find out if there was a correlation between lung CTSS and incidence of acute neurological abnormalities on CT head, which showed no significant correlation **(Fig-5)**. No statistically significant difference was seen in any of the other neurologic symptoms or patients' variables, such as age or medical history.

Table 1 - Demographic, neurological and HRCT chest characteristics of patients.

	COVID-19 patients with acute neurological symptoms		
	Total (N = 135)	**Acute CT Neuroimaging 62 (46%)**	**Normal/chronic CT neuroimaging 73 (54%)**
Gender			
Men	80/135 (59.2%)	30/62 (48.3%)	50/73 (68.4%)
women	55/135 (40.7%)	25/62 (40.3%)	30/73 (41%)
Age (y), mean ± SD	68.2 ± 15	65.4 ± 15.9	69.8 ± 14.5
<45	20/135 (15%)	11/62 (18%)	9/73 (12%)
>45	115/135 (85%)	51/62 (82%)	64/73 (88%)
Past medical history			
None	10/135 (7.4%)	5/62 (8%)	5/73 (6.8%)
Hypertension	70/135 (52%)	30/62 (48.3%)	45/73 (61.6%)
Diabetes	35/135 (26%)	11/62 (17.7%)	24/73 (32.8%)
Coronary Artery disease	35/135 (26%)	15/62 (24.2%)	20/73 (27.3%)
Cerebrovascular disease	17/135 (12.6%)	8/62 (13%)	9/73 (12.3%)
Malignancy	5/135 (3.7%%)	3/62 (4.8%)	2/73 (2.7%)
Neurologic signs			
Altered mental status	82/135 (60.7%)	32/62 (51.6%)	50/73 (68.4%)
Headache	20/135 (14.8%)	10/62 (16.1%)	10/73 (13.6%)
Myalgias	15/135 (11.1%)	5/62 (8%)	10/73 (13.6%)
Epilepsy	11/135 (8.1%)	5/62 (8%)	6/73 (8.2%)
Dizziness	9/135 (6.6%)	4/62 (6.4%)	5/73 (6.8%)
Neuralgia	6/135 (17%)	2/62 (3.2%)	4/73 (5.5%)
Ataxia	4/135 (3%)	1/62 (1.6%)	3/73 (4.1%)
Hyposmia	4/135 (3%)	1/62 (1.6%)	3/73 (4.1%)
CT characteristics			
Only GGO	96/135 (71%)	46/62 (74.2%)	50/73 (68.4%)
GGO + Consolidation	30/135 (22%)	10/62 (16%)	20/73 (27.4%)
Only consolidation	9/135 (7%)	6/62 (9.6%)	3/73 (4.1%)
Pleural effusion	7/135 (5.2%)	5/62 (8%)	2/73 (2.73)
Pulmonary nodules	30/135 (85.7%)	18/62 (29%)	12/73 (16.4%)
Mediastinal lymphadenopathy	13/135 (37.4%)	10/62 (16.1%)	3/73 (4.1%)

Cavitory lesions	2/135 (1.5%)	2/62 (3.2%)	0/73
Pneumothorax	2/135 (1.5%)	2/62 (3.2%)	0/73
CT chest severity			
Mild	29/135(22%)	4/62 (6.4%)	25/73 (34.2%)
Moderate	43/135 (32%)	18/62 (29%)	25/73 (34.2%)
Severe	63/135 (46%)	40/62 (64.5%)	23/73 (31.5%)
CT lung severity score			
Mean	11	9.9 ± 5.2	6.8 ± 4.3
Range	0-25	1-24	0-25

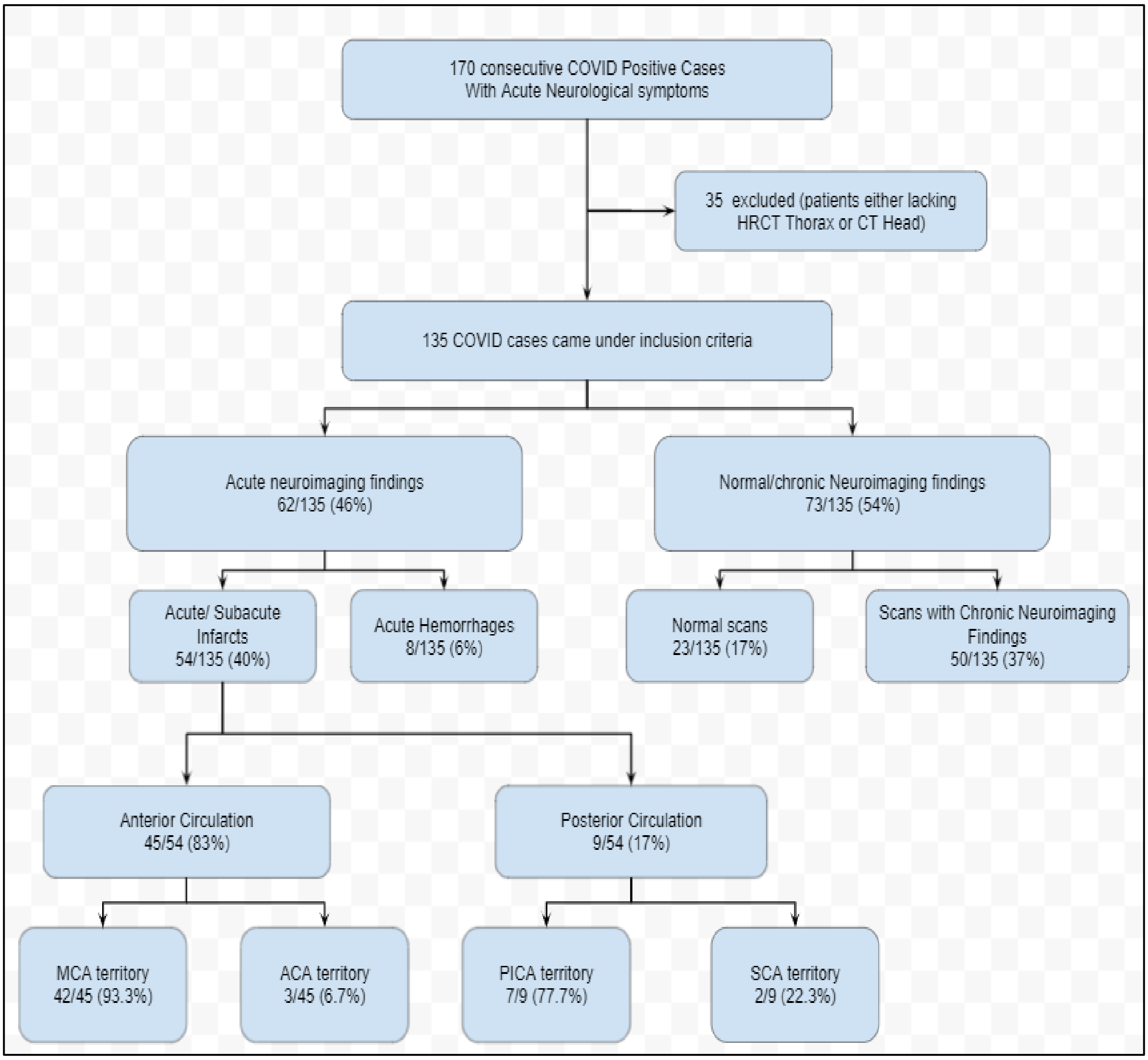

Fig-1

Flow chart showing distribution of the patients according to etiology.

(MCA- Middle cerebral artery, ACA- Anterior cerebral artery, PICA- Posterior inferior cerebellar artery, SCA- Superior cerebellar artery)

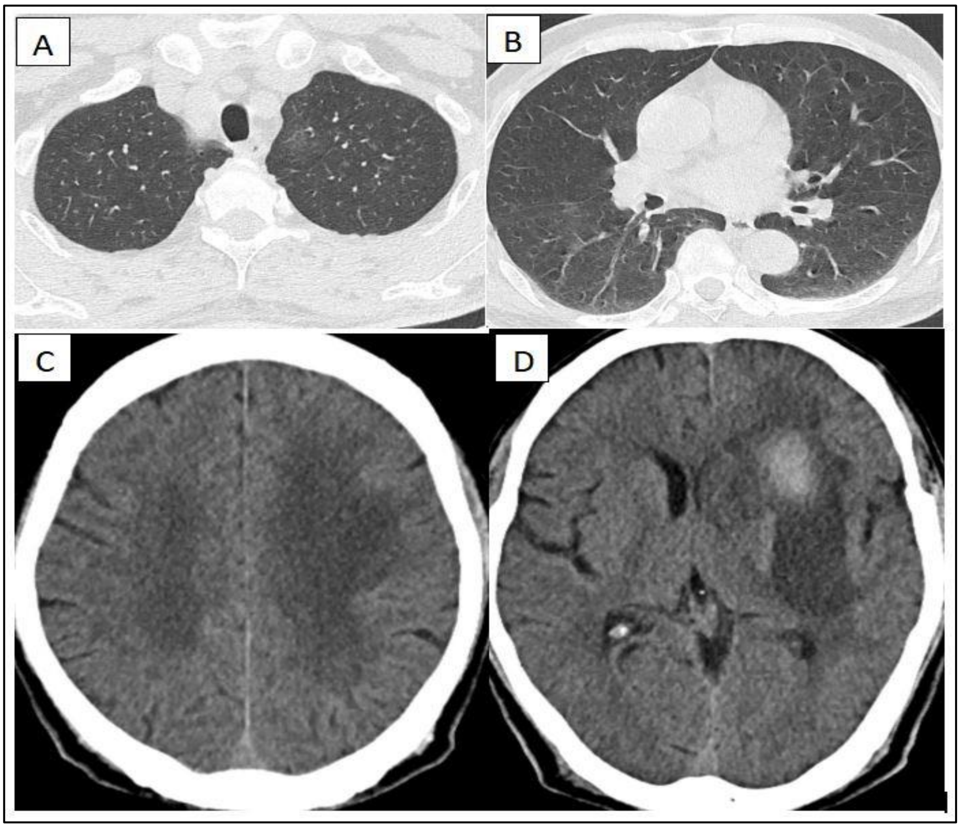

Fig-2
Axial HRCT thorax (A and B) of 46 years old male patient showing near normal lung fields. During his hospital stay he got sudden onset weakness in right upper and lower limbs. Axial CT head (C and D) revealed large acute to subacute infarct in left MCA territory with haemorrhagic component.

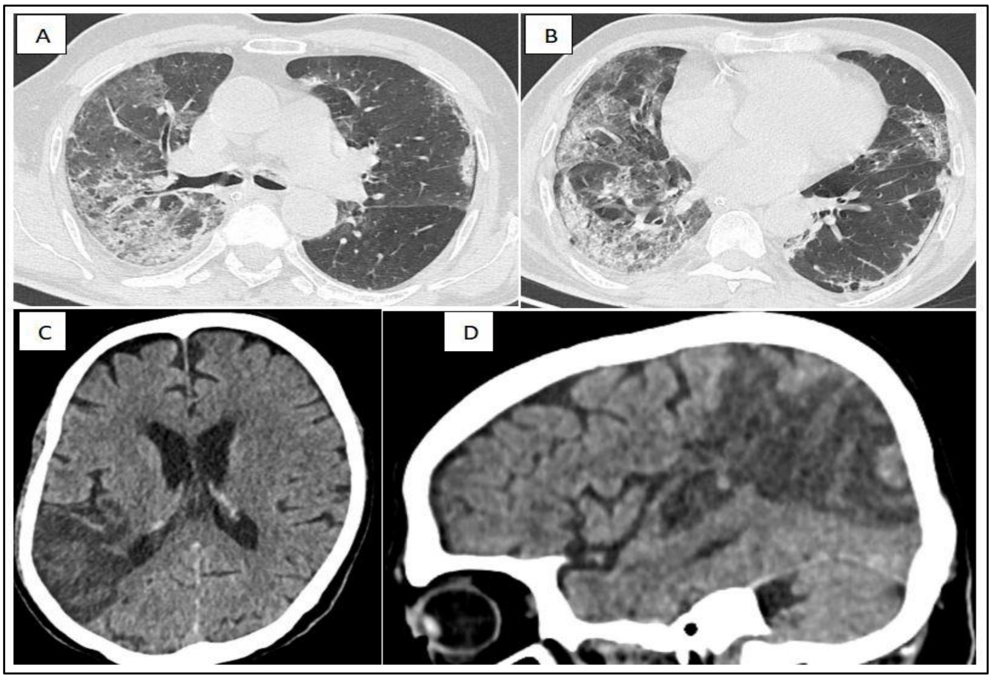

Fig-3
Axial HRCT thorax scan (A and B) of 54 years old male patient showing areas of ground glass opacities and consolidation with severe lung involvement (CTSS of 17/25). Patient complaint of acute neurological

symptoms like headache, loss of consciousness and left hemiparesis. CT head (C and D) revealed large acute to subacute infarct in posterior parietal lobe in MCA territory.

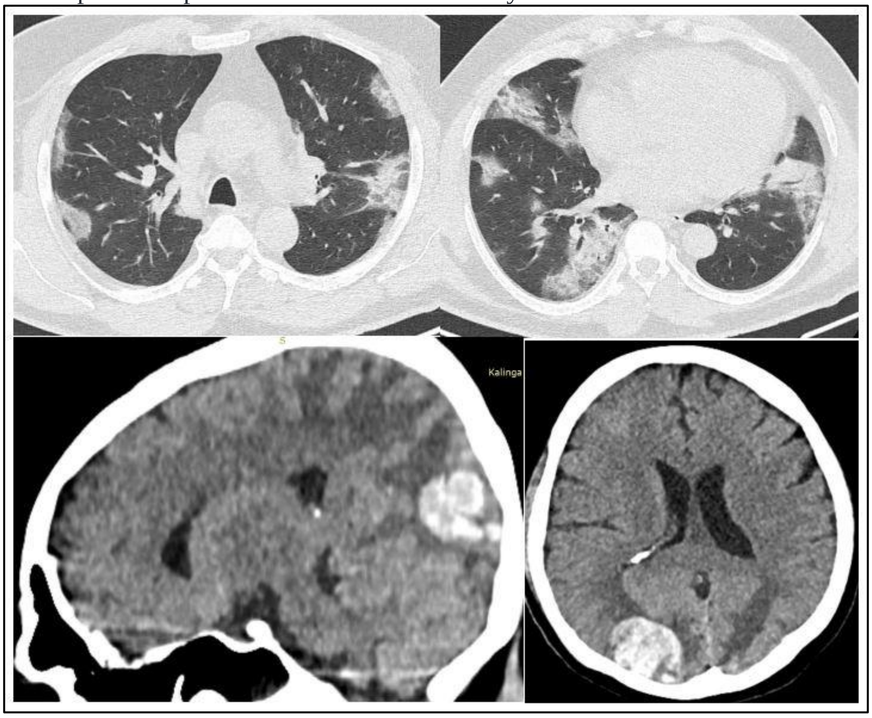

Fig-4

Axial HRCT scans (A and B) of 49 years old female showing moderate involvement of lung fields with a CTSS of 13/25. Patient developed sudden onset of headache and seizure followed by vomiting. CT head (A and B) revealed acute haemorrhage with perifocal edema in right occipital lobe.

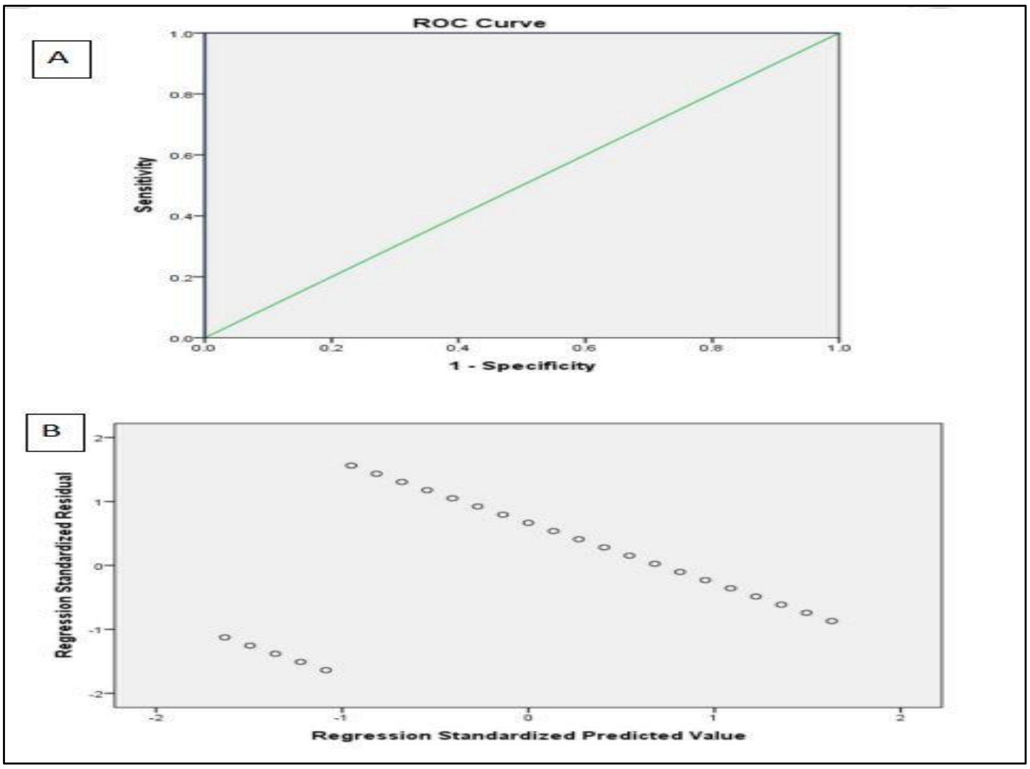

Fig-5

A) Linear regression curve showing area under the curve less than 0.5 indicating no significant correlation between higher lung CTSS and incidence of acute brain abnormalities. This finding was also confirmed on scatter plot (B) analysis.

Discussion

Although mounting data shows that individuals having severe COVID-19 may suffer from a storm of cytokine, causing multi-organ inflammatory syndrome, the exact patho-physiology of COVID-19's brain and lungs relationship remains unknown **[9,18,19].** The abundance of Angiotensin Converting Enzyme- 2 (ACE-2) receptors in different sites, comprising the nervous and pulmonary systems, might explain the multisystemic signs of COVID-19 **[10,20]**. Currently, there is poor understanding of the mechanism of neurologic manifestations whether they are the result of severe illness, direct invasion of CNS by corona virus, or sequelae of COVID-19 treatment therapies **[9,21].** Furthermore, it was postulated that the direct invasion of virus or immune-mediated destruction across numerous organ arterial beds may induce endothelial damage, resulting in stroke, bleeding, and thrombotic events **[9,22].**

According to Mao et al. **[10],** more than 50% of the patients with neurological symptoms also had critical pulmonary illness, although, there was lack of description of head and thorax imaging abnormalities in that study. In our research, we found various patterns of abnormalities in brain which is in line with other researches in which neuroimaging features in severe COVID-19 were described **[7,8,13]**, however, all these studies lack the demonstration of an association of CT head findings with lung CTSS.

According to our study, patients of COVID-19 who had neurological symptoms and acute CT head findings had a substantially higher lung CTSS on average than those who were having chronic/normal CT head findings. However, statistically the correlation between higher CTSS and incidence of acute neurological abnormalities could not be established. So, we infer that although acute neurological findings in CT usually occured in patients with high CTSS, higher CTSS didn't predict the occurrence of neurological abnormalities even if acute neurological symptoms were there. This observation was against the line of findings of Mahammedi A et al. **[23]** who found that the threshold CTSS of more than 8 had a sensitivity of 74% and a specificity of 65% for neurological abnormalities.

The neuroimaging findings of these individuals were varied without a clear pattern, however acute infarction and cerebral haemorrhage were the most common. Anterior circulation (especially MCA territory) was commonly affected. Out of total 8 cases of haemorrhages, 5 were having history of hypertension indicating towards a possibility of higher chances of cerebral bleeds in patients with co-existing hypertension, but of course, a large sample size of COVID-19 patients with cerebral haemorrhage is needed to establish a statistically significant correlation with hypertension.

Our CT thorax findings correlated previous researches indicating ground glass opacities and consolidation with usually bilateral and peripheral distribution as the most common chest presentation of COVID-19 **[2-5].**

In one of the previous studies, they found that almost 20% of the patients with a brain injury were complicated by lung damage leading to a bad prognosis **[14]**. Patients with severe respiratory distress are at risk of brain damage as a result of hypoxia and inflammatory mediators that link the CNS and pulmonary system **[15,17]**. Sensory neuronal pathways in the respiratory system may detect the inflammation in lungs leading to a feedback mechanism to the brain, exhibiting CNS-pulmonary communication **[15].** Future analysis of the connection between lungs and brain should aid in the development of more effective medicines, notably for stroke prevention. Future research might look into our findings in order to create prophylactic and treatment measures for COVID-19 patients with better outcomes.

Our study has few significant limitations, including a retrospective design. Second, the patients' reduced conscious made clinico-radiologic correlations difficult. Third, contrast CT scans and MR imaging were not feasible due to excessive patient load in COVID crisis. Finally, compared to MR brain, CT brain has a lower sensitivity in cases of white matter diseases and hyperacute infarcts, which might lead to underestimation of findings in individuals who had only CT neuroimaging.

Conclusions

Acute infarcts were the common acute neurological abnormalities with anterior circulation being most commonly affected. COVID-19 patients who had neurological symptoms and acute CT head findings had a higher CTSS. However, there was no significant correlation between higher CTSS and incidence of neurological abnormalities on CT head. Therefore, higher severity of lung involvement may not be a solitary reliable predictor for brain involvement in COVID patients. Thus, Other variables such as clinical neurological exams in COVID patients should be given greater weight than lung severity in the triage of individuals for neuroimaging

Abbreviations

COVID-19 - Corona virus disease 2019
HRCT -High resolution computed tomography
CTSS - CT severity score
MCA - Middle cerebral artery
ASPECTS - Alberta stroke programme early CT score
GGOs - Ground glass opacities

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