

Abnormalities of brain imaging in COVID-19 patients with neurological symptoms

Received: 07 Mar. 2023
Accepted: 09 May 2023

Soroor Advani¹, Seyyed Mohammad Mahdi Hosseini^{2,3}, Rama Bozorgmehr⁴, Arash Khameneh-Bagheri⁵, Sevda Mohammadzadeh², Taha Hasanzadeh², Laya Jalilian², Mohammad Vahidi², Amir Hasan Nofeli², Zahra Hooshyari⁶

¹ Men's Health and Reproductive Health Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

² School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

³ Student Research Committee, Shahid Beheshti University of Medical Sciences, Tehran, Iran

⁴ Clinical Research Development Unit, Shohada-e Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

⁵ Department of Radiology, Shohada-e Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

⁶ Psychiatry and Psychology Research Center, Tehran University of Medical Sciences, Tehran, Iran

Keywords

COVID-19; Brain; Neuroimaging; Chest Computed Tomography Scan; Stroke

Abstract

Background: Coronavirus disease 2019 (COVID-19) is a multisystem disease, manifested by several symptoms of various degrees. Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) can affect the central nervous system (CNS) through several mechanisms and brain imaging plays an essential role in the diagnosis and evaluation of the neurological involvement of COVID-19. Moreover, brain imaging of patients with COVID-19 would result in a better understanding of SARS-CoV-2 neuro-pathophysiology. In this study, we evaluated the brain imaging findings of patients with COVID-19 in Shohada-e Tajrish Hospital, Tehran, Iran.

Methods: This was a single-center, retrospective, and observational study. The hospital records and chest

and brain computed tomography (CT) scans of patients with confirmed COVID-19 were reviewed.

Results: 161 patients were included in this study (39.1% women, mean age: 60.84). Thirteen patients (8%) had ischemic strokes identified by brain CT. Subdural hematoma, subdural effusion, and subarachnoid hemorrhage were confirmed in three patients. Furthermore, there were four cases of intracranial hemorrhage (ICH) and intraventricular hemorrhage (IVH). Patients with and without abnormal brain CTs had similar average ages. The rate of brain CT abnormalities in both genders did not differ significantly.

How to cite this article: Advani S, Hosseini SMM, Bozorgmehr R, Khameneh-Bagheri A, Mohammadzadeh S, Hasanzadeh T, et al. Abnormalities of brain imaging in COVID-19 patients with neurological symptoms. *Curr J Neurol* 2023; 22(3): 162-9.

Moreover, abnormal brain CT was not associated with increased death rate. There was no significant difference in lung involvement (according to lung CT scan) between the two groups.

Conclusion: Our experience revealed a wide range of imaging findings in patients with COVID-19 and these findings were not associated with a more severe lung involvement or increased rate of mortality.

Introduction

Since the first cases in December 2019, the novel severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has caused the third outbreak of the coronavirus family in the 21st century, following the severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) epidemics. The disease caused by SARS-CoV-2 was designated as coronavirus disease 2019 (COVID-19) by World Health Organization (WHO). COVID-19 has so far caused over 500 million cases and 6 million deaths worldwide, making it the largest outbreak since the 1918 influenza pandemic.¹ Thus, WHO declared the ongoing COVID-19 pandemic a public health emergency of international concern.²

COVID-19 is a multisystem disorder manifested by multiple symptoms of varying severity. Fever and respiratory-related symptoms, such as coughing and dyspnea, are the most common symptoms of COVID-19.³ However, alongside the increasing number of patients with COVID-19 worldwide, other less common symptoms also emerged, such as neurological symptoms.²

SARS-CoV-2 can affect both the central nervous system (CNS) and peripheral nervous system (PNS) through several mechanisms;⁴ some proposed mechanisms are as follows:

- 1) The virus can spread in a retrograde fashion, to the CNS through the olfactory bulb.
- 2) SARS-CoV-2 can invade the nervous system during viremia by binding to angiotensin-converting enzyme 2 (ACE2) receptors on the brain vascular endothelium.
- 3) Due to the immune response to SARS-CoV-2, hypercoagulation and systemic inflammation may develop, resulting in cerebrovascular events.
- 4) An injury to the lungs caused by COVID-19 can lead to hypoxia in the brain, resulting in neurological dysfunction.⁵

Mao *et al.* reported that a significant proportion of patients diagnosed with COVID-19 had neurological symptoms.⁴ The prevalence and severity of neurological manifestations correlate

directly with COVID-19 severity.^{4,6} COVID-19-associated neurological manifestations include headache, dizziness, taste or smell impairment, seizure, ataxia, altered consciousness, and cerebrovascular events.^{4,7} Neurological manifestations may be the first and only signs of COVID-19 and some of these manifestations such as impaired sense of smell and taste have been strongly associated with COVID-19. Therefore, COVID-19 should be included in the differential diagnosis of neurological symptoms during the COVID-19 pandemic. These complications can be life-threatening or cause lifelong disability; therefore, they require early diagnosis and treatment.

Brain imaging plays a crucial role in the diagnosis and evaluation of neurological diseases. In addition, brain imaging of patients with COVID-19 would provide insight into the neuropathophysiology of SARS-CoV-2.⁵ Along with the growing impact of the neurological manifestations of COVID-19, various studies have evaluated and documented brain imaging of patients with COVID-19.^{6,8-11} Likewise, in the present study, we report the findings of brain imaging in patients with COVID-19 hospitalized at Shohada-e Tajrish Hospital, one of the COVID-19 referral hospitals in Tehran, Iran.

Materials and Methods

We retrospectively reviewed the clinical records, and laboratory and radiologic findings of SARS-CoV-2-infected patients who were admitted to Shohada-e Tajrish Hospital, affiliated with Shahid Beheshti University of Medical Sciences, Tehran. This hospital was one of the main hospitals for admitting and treating patients with COVID-19 that required hospitalization. The medical records of all patients with COVID-19 that were hospitalized from March to June 2020 were reviewed. All the patients with definite COVID-19 infection that had available brain and chest computed tomography (CT) scans were enrolled in the study. The exclusion criteria were significant missing data and history of the cerebrovascular event in the recent 6 months or traumatic accident. The hospital records of each patient were reviewed by trained medical students.

CT imaging was performed on a 16-slice multidetector-row CT scanner, Siemens Somatom Emotion. For brain CT scan, the scans were performed with 5 mm section thickness. Coverage was from the foramen magnum to the vertex.

Neuroimaging was reviewed by a certified neuroradiologist and a neurologist. Chest CT scans were reviewed by a radiologist and a pulmonologist, working as a team.

To assess the involvement of the lungs in chest CT during infection with SARA-CoV-2, Choi and Lee proposed a method called total severity score (TSS). The radiologist and pulmonologist evaluate all five lung lobes and score them according to the degree to which COVID-19 affects each lobe. Scores 0-4 represent the level of involvement, which is classified as 0 (none), 1 (1%-25%), 2 (26%-50%), 3 (51%-75%), and 4 (76%-100%). By summing the scores for each lobe, the overall score is calculated.¹² In our study, 7.5 was used as the cut-off value for determining severe TSS with a specificity of 80 and a sensitivity of 80 according to previous studies. The abnormalities and the final impression of brain CT scans were recorded in a questionnaire. Brain CT scans were finally labeled as abnormal and normal. The abnormal CT scans were also categorized as "atrophy or old stroke as the main abnormality", "without atrophy with other abnormality", and "atrophy or old stroke with other abnormality".

Comparisons between the 2 study groups were made using the Student's t-test for Gaussian continuous variables, the Mann-Whitney U test for non-Gaussian continuous variables, and the chi-square test (χ^2) (or Fisher's exact test when the expected cell frequency was < 5) for categorical variables, as appropriate. All analyses were done with SPSS software (version 22, IBM Corporation, Armonk, NY, USA) and a significance level of 0.05.

The current study was performed in accordance with the Declaration of Helsinki and was approved by the Ethical Committee of Shahid Beheshti University of Medical Sciences (code: IR.SBMU.RETECH.REC.1399.505). In addition,

the committee waived the requirement for informed consent.

Results

Demographics and history of patients: A total of 161 patients were enrolled in this study, including 63 women (39.1%) and 98 men. The mean age of patients was 60.84 [standard deviation (SD) = 19.74 with a median age of 63 and interquartile range (IQR) of 30], with 67.7% of them being over 55 years old (n = 109). 121 (75.2%) and 35 (21.7%) patients were admitted to the internal ward and intensive care unit (ICU), respectively. The mortality rate was estimated to be 35.4% (n = 57) (Table 1). Twenty-two patients (13.7%) were intubated. The supplementary oxygen was administered via nasal cannula, facial mask, facial mask with reserved bag, venture mask, and noninvasive positive pressure ventilation for 24.8%, 38.5%, 17.4%, 1.9%, and 1.2% of patients, respectively.

Patients with normal brain CT and those without were compared concerning their demographics and admission to the ward/ICU. Demographic indices and admission rates did not differ between the two groups ($P < 0.05$) (Table 1).

Seventeen patients (10.6%), eleven patients (6.8%), and four patients (2.5%) had a history of smoking, opium, or alcohol consumption, respectively. Drugs related to cardiovascular diseases (CVDs), including angiotensin receptor blockers (ARBs), angiotensin-converting enzyme inhibitor (ACEi), acetylsalicylic acid (ASA), or atorvastatin were prescribed for 15.5% of participants (Table 2).

The consumption of cardiovascular drugs such as ARBs, ACEis, ASA, and atorvastatin was compared between patients with normal brain CTs and those without. Comparing the two groups revealed no differences ($P < 0.05$) (Table 2).

Table 1. Patients' demographics

	All patients (n = 161)	Patients with normal brain CT (n = 119)	Patients with abnormal brain CT (n = 42)
Age (year)	60.84 ± 19.74	60.80 ± 20.30	60.90 ± 18.10
Patients with the age < 55	52 (32.3)	37 (31.1)	15 (35.7)
Patients with the age > 55	109 (67.7)	82 (68.9)	27 (64.3)
Sex (female/male)	63 (39.1)/98 (60.9)	46 (38.7)/73 (61.3)	17 (40.5)/25 (59.5)
Ward admission	121 (75.2)	95 (79.8)	26 (61.9)
ICU admission	35 (21.7)	28 (23.5)	7 (16.7)
Death	57 (35.4)	42 (35.3)	15 (35.7)
Duration of hospitalization (day)	5.60 ± 7.80 (median = 3.0, IQR = 6.0)	4.90 ± 6.30 (median = 3.0, IQR = 6.0)	7.70 ± 11.00 (median = 5.0, IQR = 6.5)

Data are presented as mean ± standard deviation (SD) or number and percent
IQR: Interquartile range; ICU: Intensive care unit; CT: Computed tomography

Table 2. Drug history of patients and prescribed medications in hospital

Drugs	All patients (n = 161)	Patients with normal brain CT (n = 119)	Patients with abnormal brain CT (n = 42)
Drugs related to CVDs*	23 (14.2)	17 (14.2)	6 (14.2)
Antibiotics	107 (66.5)	81 (68.0)	26 (61.9)
Antivirals	100 (62.1)	73 (61.3)	27 (64.2)
Glucocorticoids	25 (15.5)	19 (15.9)	6 (14.2)
Others (dimenhydrinate, diphenhydramine, IVIG, pantoprazole)	55 (34.1)	39 (32.7)	16 (38.0)

Data are presented as number and percent

*These drugs were used by patients before their admission.

CVD: Cardiovascular diseases; IVIG: Intravenous immunoglobulin; CT: Computed tomography

Patients with normal brain CT and those without were compared concerning their past medical history and comorbidities. In this comparison, no specific disease made patients more susceptible to COVID-19 neurological complications ($P < 0.05$) (Table 3).

Chest CT findings: In patients with COVID-19, TSS was used to assess lung involvement.¹² In our study, 7.5 was used as the cut-off value for determining severe TSS with a specificity of 80 and a sensitivity of 80 according to previous studies. In 16 patients (10%), the TSS was higher than 7.5. Only three of the patients with high TSS had abnormal brain CTs.

Brain CT findings: In the 161 patients included, brain CT detected abnormalities including injury and cortical atrophy or evidence of remote cerebrovascular accident (CVA) in 80 patients (49.7%). To compare patients with and without abnormalities on brain CT, brain CT scans showing "atrophy or old stroke as main abnormality" were considered normal findings due to the chronic nature of brain atrophy, patients' age, and irrelevance of brain atrophy to COVID-19. Thirty-eight patients (23.6%) had cortical atrophy on the brain CT. The mean age of patients with atrophy was 65.7 (SD = 18.45), the median age was 71, and the IQR was 18.3. Among the 38 patients who had

cortical atrophy, only five patients (13.2%) had chronic neurological disorders. According to neurologist consultations, brain magnetic resonance imaging (MRI) was performed on patients who had lateralized neurologic signs. Of 26 patients who underwent MRI, sixteen (61.5%) confirmed the abnormalities found on brain CT.

CT imaging of the brain identified thirteen cases of ischemic stroke (8). Brain CT revealed a subdural hematoma in one patient. There was one case of subdural effusion, and one of the patients was diagnosed with subarachnoid hemorrhage. There were also four cases of intracranial hemorrhage (ICH) and intraventricular hemorrhage (IVH). Encephalomalacia, periventricular hypodensity, microvascular abnormalities, hyperdensity of basal ganglia, post-ischemic abnormalities, and hydrocephalus have all been observed on brain CT scans of two patients, two patients, one patient, and one patient, respectively.

Nine out of thirteen patients with ischemic stroke were women (69.23%). Patients with ischemic stroke had a mean age of 68.92 (SD = 13.24). The average oxygen saturation (SpO₂) in patients with ischemic stroke at the time of their hospital admission was 89.08 on room air (SD = 7.59). The average age of patients with and without abnormal brain CTs was similar [$t(159) = -0.25, P < 0.05$].

Table 3. Past medical history of patients

	All patients (n = 161)	Patients with normal brain CT (n = 119)	Patients with abnormal brain CT (n = 42)
Chronic lung disease	26 (16.1)	22 (18.5)	4 (9.0)
Diabetes	40 (24.8)	31 (26.1)	9 (21.4)
IHD	26 (16.1)	19 (16.0)	7 (16.7)
HTN	27 (16.8)	21 (17.6)	6 (14.3)
Chronic kidney disease	24 (14.9)	20 (16.8)	4 (9.5)
Chronic liver disease	3 (1.9)	3 (2.5)	0 (0)
Immunocompromised state	7 (4.3)	6 (5.0)	1 (2.0)
History of cancer	5 (3.1)	3 (2.5)	2 (4.8)
Chronic neurological disorder	17 (10.6)	13 (10.9)	4 (9.5)
History of CVA	16 (9.9)	8 (6.7)	8 (19.0)

Data are presented as number and percent

IHD: Ischemic heart disease; HTN: Hypertension; CVA: Cerebrovascular accident; CT: Computed tomography

Table 4. Laboratory findings in patients

	All patients (n = 161)	Patients with normal brain CT (n = 119)	Patients with abnormal brain CT (n = 42)
ESR (mm/h)	38.8 (2.0-115.0)	40.3 (2.0-115.0)	34.5 (3.0-110.0)
CRP (mg/l)	48.6 (0.1-179.3)	47.8 (0.9-179.3)	50.8 (0.9-179.3)
LDH (U/l)	615.6 (262.0-3010.0)	596.3 (262.0-1533.0)	669.6 (284.0-3010.0)
WBC ($\times 10^9/l$)	8.9 (2.3-26.0)	8.5 (2.3-22.5)	10.0 (3.4-26.0)
PLT ($\times 10^9/l$)	188.7 (22.0-517.0)	189.1 (67.0-499.0)	187.5 (45.0-517.0)
Hb (g/dl)	13.2 (4.5-20.7)	13.5 (4.5-17.3)	12.6 (8.0-16.3)
PaO ₂ (mmHg)	31.6 (3.6-187.6)	28.9 (3.6-58.7)	40.1 (11.0-187.6)

Data are presented as min-max

ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; LDH: Lactate dehydrogenase; WBC: White blood cell; PLT: Platelet; Hb: Hemoglobin; PaO₂: Partial pressure of oxygen; CT: Computed tomography

Brain CT abnormalities did not differ significantly between male and female sex [χ^2 (N = 161) = 0.43, P = 0.835]. Moreover, abnormal brain CT was not associated with death rate [χ^2 (N = 161) = 0.002, P = 0.961]. In the TSS analysis, no significant differences were found between the groups [χ^2 (N = 161) = 0.128, P = 0.721]. We also categorized the patients to over 55 and under 55 groups to further evaluate the correlation of brain CT scan abnormalities and lung involvement but did not find a significant correlation [χ^2 (N = 161) = 0.303, P = 0.582]. Among laboratory tests including plasma electrolytes, arterial blood gas (ABG), complete blood count (CBC), renal function tests, lactate dehydrogenase (LDH), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP), plasma potassium was higher in patients with normal brain CT [t(141) = 2.295, P = 0.023] and blood urea nitrogen (BUN) was higher in patients with normal brain CT [t(144) = 2.219, P = 0.28] (Table 4).

Comparing laboratory findings between patients with abnormal brain CT and those without suggested no difference (P > 0.05) (Table 4).

Vital signs and clinical manifestations: Vital signs for all patients are summarized in table 5. A comparison was made between two groups of patients regarding their brain CT results. Both groups of patients had similar systolic blood pressure (SBP), respiratory rate, heart rate, and body temperature. There were no differences

between the two groups in terms of clinical findings (P > 0.05).

Myalgia (15.5%), headache (11.8%), dizziness (13.0%), and loss of smell (11.2%) were the most common neurologic symptoms among patients (Table 6). The prevalence of symptoms did not differ between the two groups (P > 0.05).

Discussion

COVID-19, caused by the novel coronavirus SARS-CoV-2, may present with neurological symptoms such as headache, dizziness, loss of consciousness (LOC), hemiparesis, ataxia, and loss of smell or taste. In a meta-analysis of 21 studies, Choi and Lee found that 42.6% of patients with COVID-19 had abnormal neuroimaging findings.¹² In our study, 42 patients (26%) had abnormalities in brain CTs that could be contributed to their acute illness, and 38 patients (23.6%) showed cortical atrophy.

A thorough analysis of neurological symptoms, such as headache, ataxia, anosmia, and hemiparesis, can help identify the possible site of lesions. Anosmia can be the first symptom of COVID-19. It is explained by a direct olfactory invasion of SARS-CoV-2 or systemic inflammation.¹¹ In studies by Niesen et al.¹³ and Kas et al.,¹⁴ the olfactory bulb was shown to be involved in MRI and positron emission tomography (PET). In the current study, 10.2% of patients experienced a loss of smell; however, their CT or MRI scans were not sensitive enough to detect olfactory bulb involvement.

Table 5. Patients' clinical examinations

	All patients (n = 161)	Patients with normal brain CT (n = 119)	Patients with abnormal brain CT (n = 42)
SBP (mmHg)	115.7 (70.0-210.0)	116.7 (70.0-210.0)	113.2 (80.0-170.0)
Heart rate	88.4 (30.0-150.0)	89.4 (30.0-140.0)	85.7 (62.0-150.0)
Respiratory rate	19.5 (10.0-45.0)	19.4 (10.0-45.0)	19.7 (10.0-40.0)
Body temperature	37.2 (36.0-39.5)	37.2 (36.0-39.5)	37.1 (36.0-39.2)
LOC [n (%)]	89 (55.3)	66 (55.5)	23 (54.8)

SBP: Systolic blood pressure; LOC: Loss of consciousness; CT: Computed tomography

Data are presented as min-max

Table 6. Patients' initial symptoms

	All patients (n = 161)	Patients with normal brain CT (n = 119)	Patients with abnormal brain CT (n = 42)
Fever	50 (31.1)	33 (27.7)	17 (40.5)
Cough	35 (21.7)	28 (23.5)	7 (16.7)
Dyspnea	65 (40.4)	40 (49.4)	10 (23.8)
Sore throat	4 (2.5)	2 (1.7)	2 (4.8)
Myalgia	25 (15.5)	19 (16.0)	6 (14.3)
Weakness	65 (40.4)	51 (42.9)	14 (33.3)
Gastrointestinal manifestation	10 (6.2)	8 (6.7)	2 (4.8)
Headache	19 (11.8)	13 (10.9)	6 (14.3)
Confusion	18 (11.2)	13 (10.9)	5 (11.9)
Seizure	17 (10.6)	13 (10.9)	4 (9.5)
Dysarthria	5 (3.1)	3 (2.5)	2 (4.8)
Hemiparesis	12 (7.5)	7 (5.9)	5 (11.9)
Paresthesia	1 (0.6)	1 (0.8)	0 (0)
Dizziness	21 (13.0)	18 (15.1)	3 (7.1)
Ataxia	11 (5.9)	7 (5.9)	4 (9.5)
Loss of smell	18 (11.2)	13 (10.9)	5 (11.9)
Loss of taste	17 (10.6)	12 (10.1)	5 (11.9)

Data are presented as number and percent.

CT: Computed tomography

SARS-CoV-2 can also affect the prefrontal cortex, which is related to olfactory perception, as well as the olfactory bulb. Patients with COVID-19 have been shown to have involvement in the frontal cortex in several studies.¹⁴ Similarly, 23 (12%) of our study participants had abnormal brain CTs located in the frontal cortex. The clinical manifestations of COVID-19 vary among patients; therefore, different brain regions are likely involved during the infection. Further studies using MRI and PET will help demonstrate the involvement of brain regions, like the cerebellum and midbrain.

There was no difference in TSS mean between patients with and without abnormal brain CTs in the current study. Only three of the 16 patients with a high TSS score had abnormal brain CTs. Based on these findings, the extent of lung involvement during SARS-CoV-2 infection does not correlate with the likelihood of CNS involvement. Our results are in agreement with Lang et al.¹⁵ findings, but Mahammedi et al. declared that lung severity scores were higher among patients with abnormal brain imaging.¹⁶ We should emphasize that the main brain imaging that we used was brain CT which is not very sensitive in detecting different types of brain pathology.

COVID-19 is also associated with life-threatening neurological conditions, including acute ischemic stroke (AIS), ICH, and IVH. Signs and symptoms similar to those described above were also found in the participants of the study.¹⁷ Our study's most frequent neuroimaging finding

was an ischemic stroke, accounting for 8% of cases. Previous studies have also found that AIS is the most prevalent neuro-radiologic finding among COVID-19 patients with neurological manifestations.^{10,18} In their studies, Tan et al.¹⁹ and Nannoni et al.²⁰ found a pooled ischemic stroke incidence rate of 1.2% and 1.4%, respectively, since the beginning of the pandemic. There is, however, a possibility of acute cerebrovascular disease occurring in patients with COVID-19 at a rate of 0.4%-8.1%.²⁰ Depending upon the demographic characteristics, the incidence of a stroke may vary. Furthermore, severe COVID-19 and ICU admission could increase the risk of AIS.^{4,18} Neuroimaging commonly reveals large vessel occlusions, emboli, or stenosis in these studies.²⁰

Studies have investigated the mechanisms by which COVID-19 can cause venous thrombosis and AIS through a hypercoagulability state. In association with SARS-CoV-2 infection, elevated levels of pro-inflammatory cytokines and activation of inflammatory cells are suggested to activate coagulation pathways and inhibit anti-thrombin.²¹ The patients with COVID-19-associated AIS also had antiphospholipid antibodies,²² as well as elevated levels of D-dimer and fibrinogen,²³ suggesting a condition of hypercoagulability associated with SARS-CoV-2. As SARS-CoV-2 enters the cell through ACE2 receptors, it can cause endothelial and myocardial injury and subsequent arrhythmias.²⁴ COVID-19 is also associated with cytokines storm, respiratory distress, sepsis, and disseminated intravascular coagulation (DIC). All

these conditions can prompt coagulation and thrombosis formation.²⁵

There has been no difference in sex between patients with and without AIS in previous studies. A majority of patients who had COVID-19-associated AIS were over 60. In addition, COVID-19-associated ischemic stroke was more common in persons with HTN, diabetes, and high plasma cholesterol.²⁰ These findings are in accordance with those in this study. The Lang et al. study found no difference in mortality rate between patients with and without acute neuroimaging findings,¹⁵ consistent with our findings. Contrary to Lang et al., the average length of hospitalization in patients with abnormal brain CTs was not significantly different from those without abnormal brain CTs.

In recent studies, a significant number of patients with COVID-19-associated AIS did not present with typical symptoms of stroke. AIS was also found in young patients with COVID-19 without or with few cardiovascular risk factors.²⁰ Additionally, AIS can occur in the early stages of COVID-19.^{26,27} Thus, SARS-CoV-2 should be included as a cause of AIS in cases where no rational explanation can be found.

A subdural hematoma, subdural effusion, subarachnoid hemorrhage, and ICH or IVH were detected in thirteen patients. Patients with COVID-19 are at risk for bleeding. The hypotheses suggest that COVID-19 is associated with hypoxia, thrombocytopenia,²⁸ endothelial injury caused by ACE2 receptor invasion,^{29,30} and DIC, which is defined as excessive consumption of coagulation factors. Micro hemorrhages were postulated to be caused by hypoxemia as a late complication of severe COVID-19.³¹ In addition, patients with COVID-19 admitted to the ICU receive prophylactic anticoagulants like low-molecular-weight heparin (LMWH) and unfractionated heparin (UFH), increasing the bleeding risk.³²

Limitations: Our study had many limitations. As it was a retrospective study, we faced significant missing data that resulted in a rather small sample

size. A single-center study is not enough for making conclusions about the prevalence of pathologies. Furthermore, we used brain CT which is not very sensitive to different types of brain pathologies, and future studies with better methodology and use of brain MRI are recommended.

Conclusion

Our experience revealed a wide range of imaging findings including ischemic stroke, effusion, hematoma, hemorrhage, encephalomalacia, periventricular hypodensity, microvascular abnormalities, hyperdensity of basal ganglia, post-ischemic abnormalities, and hydrocephalus in patients with COVID-19. These findings were not associated with a more severe lung involvement or increased rate of mortality. Patients with normal brain CT and those without were compared concerning their demographic indices, past medical history, comorbidities, and laboratory findings. Demographic indices and admission rates did not differ between the two groups. There was no specific disease that made patients more susceptible to COVID-19 neurological complications. Comparing laboratory findings between patients with abnormal brain CT and those without suggested no difference. There were no differences between the two groups in terms of clinical findings. The prevalence of symptoms did not differ between the two groups. CT imaging of the brain identified thirteen (8%) cases of ischemic stroke. Nine out of them were women. However, brain CT abnormalities did not differ significantly between the male and female sexes.

Conflict of Interests

The authors declare no conflict of interest in this study.

Acknowledgments

The authors of this paper thank Dr. Toktam Alirezaei M.D and Dr. Farzad Ashrafi M.D for their advice, guidance and motivation in regard to the analysis of data.

References

1. WHO Coronavirus (COVID-19) Dashboard. WHO Coronavirus (COVID-19) Dashboard with Vaccination Data [online]. [cited 2021 Nov 22]; Available from: URL: <https://covid19.who.int/>
2. Ellul MA, Benjamin L, Singh B, Lant S, Michael BD, Easton A, et al. Neurological associations of COVID-19. *Lancet Neurol* 2020; 19(9): 767-83.
3. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020; 382(18): 1708-20.
4. Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA Neurol* 2020; 77(6): 683-90.
5. Battaglini D, Brunetti I, Anania P, Fiaschi P, Zona G, Ball L, et al. Neurological manifestations of severe SARS-CoV-2 infection: Potential mechanisms and implications of individualized mechanical ventilation settings. *Front Neurol* 2020; 11: 845.
6. Kremer S, Lersy F, Anheim M, Merdji H, Schenck M, Oesterle H, et al. Neurologic

- and neuroimaging findings in patients with COVID-19: A retrospective multicenter study. *Neurology* 2020; 95(13): e1868-e1882.
7. Lodigiani C, Iapichino G, Carenzo L, Cecconi M, Ferrazzi P, Sebastian T, et al. Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy. *Thromb Res* 2020; 191: 9-14.
 8. Chen B, Chen C, Zheng J, Li R, Xu J. Insights into neuroimaging findings of patients with coronavirus disease 2019 presenting with neurological manifestations. *Front Neurol* 2020; 11: 593520.
 9. Klironomos S, Tzortzakakis A, Kits A, Ohberg C, Kollia E, Ahoromazdae A, et al. Nervous system involvement in coronavirus disease 2019: Results from a retrospective consecutive neuroimaging cohort. *Radiology* 2020; 297(3): E324-34.
 10. Najt P, Richards HL, Fortune DG. Brain imaging in patients with COVID-19: A systematic review. *Brain Behav Immun Health* 2021; 16: 100290.
 11. Moonis G, Filippi CG, Kirsch CFE, Mohan S, Stein EG, Hirsch JA, et al. The spectrum of neuroimaging findings on CT and MRI in adults with COVID-19. *AJR Am J Roentgenol* 2021; 217(4): 959-74.
 12. Choi Y, Lee MK. Neuroimaging findings of brain MRI and CT in patients with COVID-19: A systematic review and meta-analysis. *Eur J Radiol* 2020; 133: 109393.
 13. Niesen M, Trotta N, Noel A, Coolen T, Fayad G, Leurkin-Sterk G, et al. Structural and metabolic brain abnormalities in COVID-19 patients with sudden loss of smell. *Eur J Nucl Med Mol Imaging* 2021; 48(6): 1890-901.
 14. Kas A, Soret M, Pyatigorskaya N, Habert MO, Hesters A, Le GL, et al. The cerebral network of COVID-19-related encephalopathy: A longitudinal voxel-based 18F-FDG-PET study. *Eur J Nucl Med Mol Imaging* 2021; 48(8): 2543-57.
 15. Lang M, Li MD, Jiang KZ, Yoon BC, Mendoza DP, Flores EJ, et al. Severity of chest imaging is correlated with risk of acute neuroimaging findings among patients with COVID-19. *AJNR Am J Neuroradiol* 2021; 42(5): 831-7.
 16. Mahammedi A, Ramos A, Bargallo N, Gaskill M, Kapur S, Saba L, et al. Brain and lung imaging correlation in patients with COVID-19: Could the severity of lung disease reflect the prevalence of acute abnormalities on neuroimaging? A global multicenter observational study. *AJNR Am J Neuroradiol* 2021; 42(6): 1008-16.
 17. Whittaker A, Anson M, Harky A. Neurological manifestations of COVID-19: A systematic review and current update. *Acta Neurol Scand* 2020; 142(1): 14-22.
 18. Vogrig A, Gigli GL, Bna C, Morassi M. Stroke in patients with COVID-19: Clinical and neuroimaging characteristics. *Neurosci Lett* 2021; 743: 135564.
 19. Tan YK, Goh C, Leow AST, Tambyah PA, Ang A, Yap ES, et al. COVID-19 and ischemic stroke: A systematic review and meta-summary of the literature. *J Thromb Thrombolysis* 2020; 50(3): 587-95.
 20. Nannoni S, de Groot R, Bell S, Markus HS. Stroke in COVID-19: A systematic review and meta-analysis. *Int J Stroke* 2021; 16(2): 137-49.
 21. Zuo Y, Yalavarthi S, Shi H, Gockman K, Zuo M, Madison JA, et al. Neutrophil extracellular traps in COVID-19. *JCI Insight* 2020; 5(11): e138999.
 22. Zhang Y, Xiao M, Zhang S, Xia P, Cao W, Jiang W, et al. Coagulopathy and antiphospholipid antibodies in patients with Covid-19. *N Engl J Med* 2020; 382(17): e38.
 23. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *J Thromb Haemost* 2020; 18(4): 844-7.
 24. Zhang S, Zhang J, Wang C, Chen X, Zhao X, Jing H, et al. COVID-19 and ischemic stroke: Mechanisms of hypercoagulability (Review). *Int J Mol Med* 2021; 47(3): 21.
 25. Majmundar N, Ducruet A, Prakash T, Nanda A, Khandelwal P. Incidence, pathophysiology, and impact of coronavirus disease 2019 (COVID-19) on acute ischemic stroke. *World Neurosurg* 2020; 142: 523-5.
 26. Fara MG, Stein LK, Skliut M, Morgello S, Fifi JT, Dhamoon MS. Macrothrombosis and stroke in patients with mild Covid-19 infection. *J Thromb Haemost* 2020; 18(8): 2031-3.
 27. Gunasekaran K, Amoah K, Rajasurya V, Buscher MG. Stroke in a young COVID-19 patient. *QJM* 2020; 113(8): 573-4.
 28. Xu P, Zhou Q, Xu J. Mechanism of thrombocytopenia in COVID-19 patients. *Ann Hematol* 2020; 99(6): 1205-8.
 29. Al Saiegh F, Ghosh R, Leibold A, Avery MB, Schmidt RF, Theofanis T, et al. Status of SARS-CoV-2 in cerebrospinal fluid of patients with COVID-19 and stroke. *J Neurol Neurosurg Psychiatry* 2020; 91(8): 846-8.
 30. Zubair AS, McAlpine LS, Gardin T, Farhadian S, Kuruvilla DE, Spudich S. Neuropathogenesis and neurologic manifestations of the coronaviruses in the age of coronavirus disease 2019: A review. *JAMA Neurol* 2020; 77(8): 1018-27.
 31. Radmanesh A, Derman A, Lui YW, Raz E, Loh JP, Hagiwara M, et al. COVID-19-associated Diffuse Leukoencephalopathy and Microhemorrhages. *Radiology* 2020; 297(1): E223-7.
 32. Dorgalaleh A. Bleeding and bleeding risk in COVID-19. *Semin Thromb Hemost* 2020; 46(7): 815-8.