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Magnetic Resonance Imaging (MRI) and neurological manifestations in SARS-CoV-2 patients

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Abstract. – OBJECTIVE: The "Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)" disease caused a challenging and threating pandemic (COVID-19) worldwide with a great loss to life and the global economy. SARS-CoV-2 mainly involves the respiratory system, however, with Magnetic Resonance Imaging (MRI), neurological and special senses clinical manifestations have been reported rarely. The present study aims to investigate the MRI findings, clinical manifestations of neurological and special senses involvement in SARS-CoV-2 patients.

METHODS: In this study, 284 articles from the databases "Pub-Med, Web of Science-Clarivate Analytics, Embase and Google Scholar" were identified. The keywords, coronavirus, SARS-CoV-2, COVID-19 pandemic, MRI, brain, special senses, neurological involvement were entered into the search engines and the concerned documents were selected and reviewed. The descriptive information was recorded from the particular studies; finally, we included 48 publications.

RESULTS: The common neurological manifestations in SARS-CoV-2 patients were headache, impaired consciousness, acute cerebrovascular disease, ataxia, tremors, meningitis, encephalitis, cerebral bleeding, subarachnoid hemorrhage, frontal lobe, temporal lobe and intracerebral hematoma, hemiparesis and seizures. However, common special senses manifestations in SARS-CoV-2 patients were olfactory, auditory and gustatory disorders including red eyes, painless monocular visual disturbance, anosmia, ageusia, dysgeusia, dysosmia and hypoacusis. Moreover, the MRI findings identified in SARS-CoV-2 patients were isolated oval-shaped lesion in the corpus callosum, bilateral basal ganglia hemorrhage, ischemic lesions involving the corpus callosum, basal ganglia, cerebellum and vasogenic edema extending to the cerebral peduncles, pons and ventricles.

CONCLUSIONS: The neurologic manifestations of SARS-CoV-2 patients are highly variable. The SARS-COV-2 exerts its damaging effects on the nervous system and special senses by developing determinant numerous neurological and special senses' clinical manifestations. Physicians with the help of MRI must rule out the neurological and special senses manifestations among SARS-CoV-2 patients.

Key Words:
SARS-CoV-2, MRI, Brain, Special senses, Neurological manifestations.

Introduction

The "Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2)" disease caused a challenging and threating pandemic globally (COVID-19). It has various key epidemiological and biological features, causing it to be more contagious than previous pandemics[1]. The viral infections spread rapidly and frequently provoke major health and socio-economic harms[1]. The trends in the prevalence and mortality rate of SARS-CoV-2 are changing on a daily basis[2]. On Dec 16, 2020, on the date of submission of this manuscript, COVID-19 pandemic involved 216 countries, and had, to date, affected 72,851,747 people with a fatality of 1,643,339 (2.25%)[3].

The most common clinical manifestations in SARS-CoV-2 patients are related to the respiratory system. However, limited number of studies are now available and are revealing neurologic manifestations too. The SARS-CoV-2 is not only affecting the respiratory system but it also involves the other body systems including the nervous system. However, the neurological manifestations of SARS-CoV2 are variable, and literature is acutely lacking. Therefore, this study aims at

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investigating the various clinical manifestations and evidence of neurological and special senses involvement in SARS-CoV-2 patients.

Materials and Methods

This study was performed in the "Department of Physiology, College of Medicine, King Saud University, Riyadh, Saudi Arabia". In this study, 284 published studies were identified through a systematic database with searches including "Pub-Med[4] "Web of Science-Clarivate Analytics[5], Embase and Google Scholar" from Dec 29, 2019 to Dec 2, 2020. The literature was searched by using the key-terms including Coronavirus, SARS-CoV-2, COVID-19 pandemic, brain, special senses and neurological manifestations. The study heading, abstract was appraised to determine the admissibility for the documents. All studies in which SARS-CoV-2, COVID-19 pandemic, brain, special senses, neurological manifestations were conferred, were eligible for inclusion. No limitations on publication status, study design or language of publication were imposed. The descriptive information was retrieved from the selected literature. Two co-authors reviewed articles, including, original articles, case series and case reports, for neurologic manifestations of SARS-CoV-2 and organized them into tabular form. After that, third co-author rechecked the literature and their findings. We reviewed 284 documents, finally we included 48 publications.

Inclusion and Exclusion Criteria

The inclusion criteria were cohort, cross sectional studies, case series, case reports which reported the coronavirus, SARS-CoV-2, COVID-19 pandemic, MRI, brain, special senses, neurological manifestations. The studies published without clinical manifestation were excluded.

Data Extraction and Ethics Satement

MRI findings, neurological and special senses allied clinical manifestations of SARS-CoV-2 patients were thoroughly reviewed by investigators; the findings were documented by using a standardized form including a full description of the study characteristics. In this study, we recorded publicly available data base literature on coronavirus, SARS-CoV-2, COVID-19 pandemic, MRI findings, brain, special senses, neurological manifestations hence we did not require the ethical approval.

Results

Table I demonstrates the neurological manifestations in SARS-CoV-2 patients. The most frequent neurological clinical manifestations have shown to be headache, impaired consciousness, acute cerebrovascular disease, ataxia, tremors, meningitis, encephalitis, cerebral bleeding, subarachnoid hemorrhage, frontal lobe, temporal lobe and intracerebral hematoma, hemiparesis and seizures (Table I Figure I). The common special senses manifestations in SARS-CoV-2 patients are olfactory, auditory and gustatory disorders and include: red eyes, painless monocular visual disturbance, anosmia, ageusia, dysgeusia, dysosmia, ear hypoacusis (Table II, Figure I). The magnetic resonance imaging (MRI) based neuro-radiological findings in SARS-CoV-2 patients are presented in Table III.

Discussion

The novel coronavirus SARS-CoV-2 infection is an emerging global health concern and has infected a significant portion of the world's population[2]. In this study, it was identified that SARS-CoV-2 infection exerts damaging effects on the nervous system and special senses by developing determinant numerous neurological and special senses clinical manifestations. Moreover, the brain MRI findings also indicate a strong evidence of the involvement of various regions of brain (Tables I-III). SARS-CoV-2 patients primarily suffer from respiratory illnesses, which are occasionally accompanied by other body systems[54]. The severity can range from mild respiratory symptoms to severe acute respiratory distress syndrome, which also involves the nervous system[54].

Mao et al[25] reported the numerous central nervous system symptoms in patients with SARS-CoV-2. The authors found that 36.4% of patients had headache, dizziness, impaired consciousness, acute cerebrovascular disease, ataxia and seizures. Moreover, 8.9% patients have the involvement of special senses manifestations, such as taste, smell, vision impairment, and nerve pain. Similarly, in the present study, we identified nervous system and special senses associated clinical manifestations.

Brouwer et al[55] demonstrated that more than 10% of SARS-CoV-2 patients had complaints of headache, loss of smell and taste disturbance.

Table I. Neurological clinical manifestation among SARS-CoV 2 patients.

Authors and study year	Sample size	Age (years)	Type of study	Study findings
Moriguchi et al 2020[6]	M:1	24	Case report	Meningitis, encephalitis, mainly involved the right lateral ventriculitis and encephalitis on right mesangial lobe and hippocampus
Bernard-Valnet et al 2020[7]	F:2	64, 67	Case report	Patient 1: Acute meningoencephalitis, tonico-clonic seizure. Patient 2: Intense wake-up headache and disorientation, left hemianopia, sensory hemineglect.
Ye et al 2020[8]	M:1		Case report	Encephalitis, meningeal including nuchal rigidity
Lyons et al 2020[9]	M:1	20	Case report	Lightheadedness and seizures
Al-olama et al 2020[10]	M:1	36	Case report	Meningoencephalitis with "right frontal intracerebral hematoma, subarachnoid hemorrhage, frontal and temporal lobes thin subdural hematoma"
Huang et al 2020[11]	F:1	40	Case report	Encephalitis, CSF positive for SARS-CoV-2
Hayashi et al 2020[12]	M:1	75	Case report	Mild encephalitis/encephalopathy
Beach et al2020[13]	M:3; F:1	≥ 68	Case series	Delirium with change in mental status
Morassi et al 2020[14]	M:5, F:1	≥ 57	Case series	Stroke, ischemic and hemorrhagic stroke
Wong et al 2020[15]	M:1	40	Case report	Encephalitis, acute brainstem dysfunction
Panariello et al 2020[16]	M:1	23	Case report	Encephalitis
Efe et al 2020[17]	F:1	35	Case report	Encephalitis, mimicking glial tumor
Afshar et al 2020[18]	F:1	39	Case report	para-infectious encephalitis
Lu et al 2020[19]	MF: 304	15-49	Retrospective	Seizures during acute phase of the disease.
Sedaghat et al 2020[20]	M:1	65	Case report	GBS neurological complication of COVID-19
Haddadi et al 2020[21]	M:1	65	Case report	COVID-19 effect basal ganglia
Avula et al 2020[22]	MF:4	-	Retrospective	COVID-19 patients can present with CVA
El Otmani et al 2020[23]	F:1	70	Case report	SARS-Cov-2 can trigger GBS.
Zhao et al 2020[24]	F:1	61	Case report	A linkage between GBS and COVID-19
Mao et al 2020[25]	214 M,F	52.7	Retrospective	36.4% patients had headache, dizziness, impaired consciousness, cerebrovascular disease, ataxia and seizures

M = Male; F = Female.

Moreover, acute cerebrovascular events were also identified in about 3% of the patients, and 6% of patients with severe manifestations had cerebrovascular events. Similarly, Tsai et al[56] reported the various neurologic manifestations, including "olfactory taste disorders, headache, acute cerebral vascular disease, dizziness, altered mental status, seizure, encephalitis, neuralgia, ataxia, Guillain-Barre syndrome, Miller Fisher syndrome, intracerebral hemorrhage, polyneuritis and dystonic posture".

Al-olama et al[10] found that SARS-CoV 2 infection can cause meningoencephalitis in the right frontal intracerebral hematoma, subarachnoid hemorrhage, frontal and temporal lobes thin subdural hematoma. Domingues et al[57] reported mild respiratory symptoms and neurological manifestations with demyelinating disease in SARS-CoV-2 patients.

Elkhaled et al[53] reported that SARS-CoV-2 patient can be presented with various neurological findings including auditory hallucinations, restlessness and rapidly developed systemic inflammatory response syndrome (SIRS). Brain MRI revealed an isolated oval-shaped lesion in the splenium of the corpus callosum, with hy-

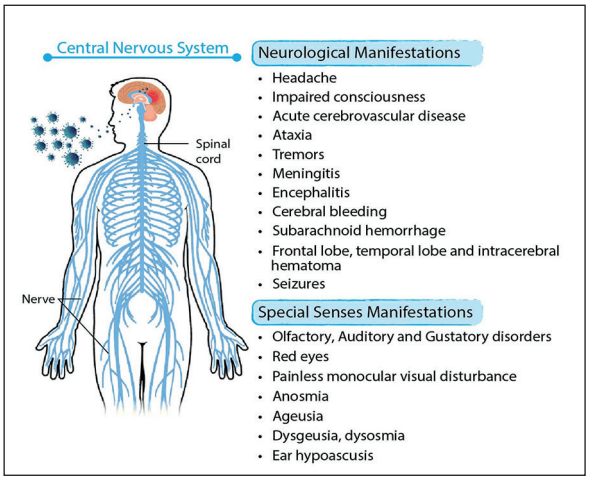

Figure 1. Neurological and special senses manifestations in SARS-CoV-2patients.

Table II. Special senses clinical manifestation among SARS-CoV-2 patients.

Authors and study year	Sample size	Age (years)	Type of study	Study findings
Lechien et al 2020[26]	N:417	---	Multi-center cross sectional	The olfactory and gustatory disorders are prevalent symptoms in SARS-CoV-2 patients
Vaira et al 2020[27]	N:72	--	Case series	Olfactory and gustatory dysfunctions findings in SARS-CoV-2 patients
Haldrup et al 2020[28]	M:1	30	Case report	Anosmia and ageusia in COVID-19 patients
Lee et al 2020[29]	N:3191		Observational	Female patients with anosmia or ageusia
Gilani et al 2020[30]	N:8	22-39	Case series	Anosmia
Melley et al 2020[31]	N:1	59	Case report	Hypogeusia an initial presentation of COVID-19
Zhang et al 2020[32]	N:1	60	Case report	Anosmia and ageusia could be the only symptoms.
Gane et al 2020[33]	N:1	----	Case report	Anosmia in their current COVID-19
Vijairam et al 2002[34]	1 F:1	50	Case report	Acute painless right eye, visual disturbance, Dysgeusia, dysosmia, right ear hypoacusis and right hemiparesis.
Alex et al 2020[35]	134	57.1	Case control	Anosmia or dysgeusia, presence of blurred vision
Shane et al 2020[9]	M:1	20	Case report	Blurred and double vision
Mao et al 2020[25]	214 M,F	52.7	Retrospective	8.9 % patients had taste, smell impairment, vision impairment, and nerve pain, and skeletal muscular injury

M = Male; F = Female.

perintense signal on diffusion-weighted imaging (DWI) and hypointense on apparent diffusion coefficient (ADC) maps. The patient also developed multiple organ dysfunction syndrome and severe intra-abdominal and cerebral bleeding, and cardiac arrest.

Mao et al 2020[25] established the pathologic mechanism and reported that SARS-CoV-2 may enter into the brain through the hematogenous or retrograde neuronal route. The authors highlighted the evidence that patients with SARS-CoV-2 had smell impairment and the low lymphocyte numbers support the hypothesis of the entry of the virus into the nervous system. SARS-CoV2 can reach the nervous system from the bloodstream or olfactory pathway by binding with the ACE-2 receptor. Ahmed et al[58] established the hypothesis that SARS-CoV-2 enters into the CNS through direct infection injury, blood circulation pathway, neuronal pathway, immune mediated injury and hypoxic injury. We also believe that SARS-CoV-2 can enter into the CNS through the hematogenous or retrograde neuronal route and infect the nervous system and special senses. There is reliable MRI evidence that SARS-CoV-2 develops neurological manifestations (Table III). It enters into the brain through the blood and neuronal routes, and causes the breakdown of blood brain barriers and infects the meningeal layers and various parts of the brain.

Study Strengths and Limitations

This is the first study added in the literature to analyze the numerous neurological, special senses and MRI allied clinical manifestation in SARS-CoV 2 patients. This study has few limitations, no homogeneity in the study type, design and sample size.

Conclusions

The SARS-CoV-2 exerts its effects on the nervous system and special senses by developing determinant neurological and special senses clinical manifestations, including headache, meningitis, encephalitis, impaired consciousness, acute cerebrovascular disease, ataxia, tremors, cerebral bleeding, frontal lobe, temporal lobe and intracerebral hematoma, hemiparesis and seizures. It also causes olfactory, auditory and gustatory disorders including red eyes, painless monocular visual disturbance, anosmia, ageusia, dysgeusia, dysosmia and hypoacusis.

The neurologic manifestations of COVID-19 are highly variable and can occur at the initial stage of the diseases. The neurological manifestations alert the physicians to immediately rule out the high-risk patients. As the brain is a very vital and complex organ, hence its complications are also complex. There is an acute need to establish varying degrees of an

Table III. Magnetic resonance imaging (MRI) based neuro-radiological findings in SARS-CoV-2 patients.

Authors and year of study	Sample size	Age (years)	Type of study	MRI findings
Poyiadji et al 2020[36]	F = 1	58	Case report	The hemorrhagic rim enhancing lesions in the bilateral thalami, medial temporal lobes and sub insular regions
Zambreanu et al 2020[37]	F = 1	66	Case report	Hyperintensities in medial temporal lobe and medial thalami, lesser extent upper pons, as well as scattered subcortical white matter hyperintensities
Dixon et al 2020[38]	F = 1	59	Case report	Hemorrhagic lesions in the brain stem, amygdalae, putamina, and thalamic nuclei. It causes brain stem distension
Beyrouti et al 2020[39]	M = 5 F = 1	53-85	Case series	The findings show left vertebral artery occlusion, left posterior inferior cerebellar artery infarction with petechial hemorrhage, infarct and thrombus in the basilar artery, stenosis and multiple acute infarcts
Radmanesh et al 2020[40]	M = 9 F = 2	38-64	Case series	Microhemorrhasgic transformation, parenchymal hemorrhages, and thalamic expansile T2 hyperintensity
Radmanesh et al 2020[41]	N = 242	68.7 ± 16.5	Retrospective case series	Nonspecific white matter microangiopathy, acute or subacute ischemic infarct and hemorrhage
Mahammedi et al 2020[42]	M = 69 F = 39	69 ±1 5	Retrospective case series	Acute ischemic infarcts, and intracranial hemorrhages with subarachnoid hemorrhage being the most common.
Klironomos et al 2020[43]	M = 138 F = 74	62 ± 14	Retrospective case series	Corpus callosum ischemic changes and macro-hemorrhagic manifestations
Chougar et al 2020[44]	M = 48 F = 25	58.5 ± 15.6	Retrospective	Acute ischemic infarct, deep venous thrombosis, microhemorrhages, perfusion abnormalities, foci within the corpus callosum with cytotoxic lesions in corpus callosum, basal ganglia lesions
Kremer et al 2020[45]	M = 30 F = 7	8-78	Retrospective case series	Signal abnormalities in medial temporal lobe, hemorrhagic lesions, wide isolated white matter microhemorrhages and intracerebral hemorrhagic lesions
Forestier et al 2020[46]	M = 1	55	Case report	Brain MRI demonstrated cytotoxic lesion of the corpus callosum
Lin et al 2020[47]	M = 158 F = 1 20	50-75	Case series	Cranial nerve abnormalities including olfactory bulb abnormalities, and microhemorrhage pattern associated microbleeds
Hanafi et al 2020[48]	M = 1	65	Case report	Ischemic lesions involving the centrum semiovale, corpus callosum, basal ganglia, and cerebellum with patchy/punctuate enhancement
Chougar et al 2020[49]	M = 1	72	Case report	Marked vasogenic edema, extending to the right cerebral peduncle, pons and increased hemorrhagic changes involving the lateral ventricle
Aragão et al 2020[50]	N = 5	--	Case series	Small hyperintensity in the left olfactory bulb
Cavalcanti et al 2020[51]	M = 2 F = 1	38, 41,23	Case series	Reduced diffusion throughout the subcortical and deep hemispheric white matter bilaterally, left greater than right
Daci et al 2020[52]	F = 1	60s	Case report	Bilateral basal ganglia hemorrhage
Elkhaled et al 2020[53]	M = 1	23 year	Case report	Isolated oval-shaped lesion in the splenium of the corpus callosum, with hyperintense signal on diffusion-weighted imaging (DWI) and hypointense on apparent diffusion coefficient (ADC) maps

association between the medical and intensive care unit physicians, neurologists and neuro-radiologist for the treatment of SARS-CoV-2 patients. The team should consider the nervous system as a priority like considering the respiratory system.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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