

Neurological manifestations in COVID-19 patients at the Husada Utama hospital emergency room

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Abstract

COVID-19 is a respiratory disease that spreads rapidly starting at the end of 2019. The resulting manifestations vary from respiratory symptoms to neurological symptoms. The variety of neurological symptoms found when coming to the Emergency Department triggered a study to examine the neurological features of COVID-19 patients. A retrospective descriptive examination of 2,659 patients hospitalized to the emergency department between March 1, 2020, and March 31, 2022, constitutes the basis of our study. There were patients of every age and gender represented. The study considered all clinical factors, such as comorbidities, clinical presentation, and neurologic manifestations such as cephalgia, vertigo, stroke, hypoxic encephalopathy, a disorder of consciousness, seizure, myalgia, ageusia/dysgeusia, and anosmia. The study results showed 2,659 confirmed COVID-19 patients at the Husada Utama Hospital and 1,484 COVID-19 patients with neurological manifestations, or 55.8%, were found. The most common neurological manifestations are cephalgia, and the least are seizures.

Keywords: COVID-19; Neurological Manifestations; Disorder of Consciousness; Emergency Department

1. Introduction

The first COVID-19 case in Indonesia was announced on March 2, 2020, about four months after the first case in Wuhan, China. The peak of the first COVID-19 cases occurred in January 2021, with daily cases reaching 14,000 new cases. The second peak of cases occurred in July 2021, with the daily number of new cases reaching 51,000 new cases with the death rate reaching 2000 cases per day, so it reached more than 4 million cases⁽³⁾. According to WHO, as of October 29, 2021, more than 249 million people worldwide have been diagnosed with COVID-19. More than 4.9 million people have died as a result of the pandemic. Even in already vaccinated individuals, there is uncertainty about the duration of protection and efficacy of current vaccines against the emerging SARS-CoV-2 variant. COVID-19 is also associated with mental and neurological manifestations, including anxiety, depression, sleep problems, headache, dizziness, impaired sense of smell or taste, myalgia, delirium/encephalopathy, agitation, stroke, hypoxic-ischemic brain injury, seizures, coma, meningoencephalitis, and Guillain-Barré syndrome. In some cases, neurological manifestations are also found without any disturbances in the respiratory system⁽²⁰⁾. From the many clinical pictures caused by COVID-19 when they first arrived at the Emergency Department, it is, therefore, essential to research to find out the description of the neurological manifestations of COVID-19 patients when they arrive at the Husada Utama Hospital Emergency Installation.

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2. Material and methods

We performed this retrospective descriptive study for two years, from March 1, 2020, until March 31, 2022. The data is based on electronic and paper medical in Husada Utama Hospital. A retrospective descriptive examination of 2,659 patients admitted to the emergency department between March 1, 2020, and March 31, 2022, constitutes the basis of our study. Patients of all age groups, comorbid, and gender were included. All clinical parameters were included in the study, including Covid-19 with the manifestation of neurology including cephalgia, vertigo, stroke, hypoxic encephalopathy, the disorder of consciousness, seizure, myalgia, ageusia/dysgeusia, anosmia, comorbidities, clinical presentation

3. Results and discussion

From the study results, 2,659 confirmed COVID-19 patients at Husada Utama Hospital, and 1,484 COVID-19 patients with neurological manifestations (55.8%) were found. An overview of the demographic characteristics of COVID-19 patients divided by age and gender can be seen in the table below.

Table 1 Distribution of COVID-19 Patient Characteristics

No	Age (Year)	Amount	Percentage
1	0-5	62	2.3%
2	6-11	58	2.2%
3	12-17	44	1.7%
4	18-44	990	37.2%
5	45-54	540	20.3%
6	55-65	525	19.7%
7	66-74	294	11.1%
8	75-95	148	5.6%
Gender			
1	Man	1368	51.4%
2	Woman	1291	48.6%

The study's results (Table 1) show that COVID-19 patients with productive age, i.e., ages 18 to 44 years at Husada Utama Hospital, are the largest age group, 990 patients (37.2%). Furthermore, the lowest age group is ages 6 to 11 years, namely 58 patients (2.2%). Most COVID-19 patients at Husada Utama Hospital were male, namely 1,368 out of 2,659 patients (51.4%). In this study, it was found that Covid-19 patients had the most comorbidities, namely hypertension by 640 people (24.07%), in the second position there was diabetes mellitus by 515 people (19.37%), followed by chronic heart failure by 127 people (4.78%). It was also found that 107 pregnant women (4.02%) could affect the prognosis and severity of Covid-19. Other comorbidities were also found in 81 people with stroke (3.05%), 70 people with coronary heart disease (2.63%), 61 people with asthma (2.29%), 33 people with Chronic Kidney Disease (1.24%), 30 people with hypercholesterolemia (1.13 people%), 23 people with arrhythmia (0.86%). There were also 16 people with tuberculosis (0.6%), 13 people with hepatitis (0.49%), 10 people with vertigo (0.38%), 8 people with hyperthyroidism (0.3%), 6 people with breast cancer (0.23%) and 4 people with liver cirrhosis (0.19%). Also found comorbid with nephrolithiasis, COPD, and cervical ca as much as 0.15%. Psoriasis-Arthritis, Benign Prostate Hyperplasia, Systemic Lupus Erythematosus, epilepsy, and leukemia were also found to be comorbid 0.11%, cerebral palsy, rheumatoid arthritis, and brain tumors were found in 0.08% which aggravated the patient's condition.

Table 2 Overview of Neurological Manifestations in Covid-19 Patients

No	Neurological Manifestation	Amount	Percentage	Gender		Age (Year)	Percentage
				Man	Woman		
1	Cephalgia	608	22.9%	47.6%	52.4%	18-44	42.2%
2	Anosmia	345	13%	44.3%	55.7%	18-44	51.9%
3	Myalgia	334	12.6%	50%	50%	18-44	45.5%
4	Ageusia/Dysgeusia	259	9.7%	53.7%	46.3%	18-44	38.6%
5	Disorder of Consciousness	196	7.4%	57%	43%	66-74	30.1%
6	Vertigo	192	7.2%	41.1%	58.9%	18-44	40.1%
7	Stroke	131	4.9%	60.3%	39.7%	66-74	30.5%
8	Seizure	35	1.3%	54%	46%	66-74	14.3%

3.1. Cephalgia in COVID-19

The findings of this investigation revealed that among 2,659 COVID-19, 608 patients (22.9%) experienced headaches (cephalgia), of which 148 (24.3%) had comorbid hypertension. Headaches that are felt also vary from migraine and tension-type headaches. The prevalence of headaches in COVID-19 patients varied across studies. The study found that the prevalence of headaches was 17.4% and 14.1% in the outbreak's epicenter, Hubei Province, respectively. Another study in European countries found that headaches were reported to occur in more than 40% of 417 COVID-19 patients. The global prevalence of headaches in a systematic review of previous studies was more than 25% of 104,751 cases of COVID-19 ⁽¹⁰⁾. SARS-direct CoV-2's invasion of trigeminal nerve terminals in the nasal cavity is the first plausible mechanism for COVID-19-associated headaches. Second, vascular pathogenesis through the involvement of endothelial cells with high ACE2 expression may play a role in trigeminovascular activation that causes headaches ⁽⁴⁾.

3.2. Vertigo in COVID-19

Apart from cephalgia, other neurological manifestations were vertigo and dizziness, which were seen in 192 patients (7.2%). The manifestations of vertigo and dizziness experienced by COVID-19 patients were 92.8% without a history of vertigo or other balance disorders, of which 58 patients (30.2%) who complained of vertigo had comorbid hypertension. An online questionnaire was utilized to determine the existence of tinnitus and balance issues in 185 COVID-19 patients in an Italian multicentric research. According to the authors, 5.9% of the interviewers experienced acute vertigo, 94.1% felt dizziness, and 18.4% reported poor balance. Korkmaz et al. demonstrated that the incidence of vestibular symptoms was 31.8% for dizziness and 6% for vertigo. Chen et al. described dizziness in 8% of 274 confirmed COVID-19 patients, whereas Mao et al. found dizziness in 16.8% of 214 patients in two major case series from Wuhan ⁽¹³⁾. Vertigo and dizziness are other clinical manifestations of COVID-19. Given the anatomically widespread nature of the central and peripheral audiovestibular pathways, SARS-CoV-2 neurotropism can produce a broad spectrum of neuropathic effects, including effects on the neural network that regulates hearing and balance. Meniere's disease, vascular vertigo, and Benign Paroxysmal Positional Vertigo (BPPV) have also been associated with elevated IL-6 and TNF- cytokines suggesting inflammatory pathogenesis. Studies have shown that arteriosclerosis and the resulting reperfusion injury are associated with oxidative stress and inflammatory responses, potentially leading to vascular vertigo ⁽⁷⁾.

3.3. Stroke in COVID-19

It was also found that out of 2,659 Covid-19 patients, 131 patients (4.9%) had an ischemic or hemorrhagic stroke, of which 76 patients (60.3%) had comorbid hypertension. A World Stroke Organization panel review reports that ischemic stroke risk during COVID-19 is around 5%. Hemorrhagic strokes associated with COVID-19 are much less common than ischemic strokes, but few cases have been reported ⁽¹⁶⁾. In a previous study of 11 patients with acute stroke, 81.8% were ischemic and 18.2% hemorrhagic. Stroke occurrences occurred an average of 15.2 days following COVID-19 diagnosis, and 72.7% of patients presented with stroke during acute treatment ⁽⁹⁾. Activation of the coagulation pathway with increased D-dimer and fibrinogen is common in COVID-19 patients with severe symptoms. Sepsis-induced coagulopathy (Sepsis-Induced Coagulopathy) is associated with an infection-induced systemic inflammatory response and may contribute to an increased risk of thrombosis and stroke. Hypercoagulation can lead to ischemic stroke leading to venous thromboembolism and paradoxical embolism. SARS-CoV-2's affinity for the ACE2 receptor may allow the

virus to damage intracranial arteries, causing vessel wall rupture directly, and reducing RAS regulation can increase blood pressure and place patients already diagnosed with hypertension at risk a higher risk for hemorrhagic stroke. ⁽¹¹⁾.

3.4. Seizure in COVID-19

This study also found that 35 patients had seizures (1.3%), of which two or 5.7% had a history of work or epilepsy. Meanwhile, the most common previous medical history was hypertension, which was 22.9%. In a previous study, in 7 patients with Covid-19 seizures, 5 of them (71%) had generalized tonic-clonic seizures, while two patients had focal seizures characterized by visual deviation, head version, and unilateral motor symptoms. Four patients had focal postictal deficits ⁽¹⁾. There has been increased reporting of seizures associated with SARS-CoV2. Overload of ACE-2 receptors by SARS-CoV-2 results in downregulation of ACE-2 expression. This loss of ACE-2 receptors leads to dysfunction of the renin-angiotensin system and increased production of angiotensin II. Overproduction of angiotensin II results in interactions that eventually lead to severe acute lung injury, vasoconstriction, and oxidative processes that promote brain degeneration with possible seizures. Hypoxia can result in hypoxic encephalopathy, which can contribute to seizure manifestations. Ischemic brain injury also contributes to brain tissue hypoperfusion and can cause seizures ⁽¹²⁾.

3.5. Disorder of Consciousness in COVID-19

In addition, impaired consciousness was also found in 196 patients (7.4%), of which 78 or 39.8% had comorbid hypertension. Covid-19 patients who come to the Emergency Room with severe hypoxia can cause their condition to be restless until there is a decrease in consciousness. The study results found that 131 or 4.9% of COVID-19 patients with hypoxic conditions cause impaired consciousness. The most common age range occurs at the age of 66-74 years (30.5%), and this condition was found to be more common in 78 male patients (59.5%). The most common comorbid conditions in patients with hypoxia were hypertension (37.4%) and diabetes mellitus (36.6%). Impaired consciousness was common (19.6%), mostly in older patients and severe and advanced COVID-19 ⁽¹⁵⁾. Impaired consciousness, such as coma, is common in patients hospitalized for COVID-19 and is associated with length of hospital stay and death. Impaired consciousness has been reported in 15% of patients with severe COVID-19 ⁽²⁾. There is an increase in serum inflammation before the disturbance of consciousness occurs. This involves inflammation as a factor causing impaired consciousness in non-structural brain injuries, such as septic encephalopathy and delirium. Before the onset of the disturbance of consciousness, it was found that hypoxia was experienced by patients with decreased consciousness ⁽¹⁹⁾.

3.6. Myalgia in COVID-19

Myalgia is a common symptom among individuals with viral infections, including new coronavirus disease 2019 (COVID-19). Three hundred thirty-four patients, or 12.6%, have complaints of myalgia, of which 19.2% have hypertension. In COVID-19, musculoskeletal complaints have reached 15-36% of cases. In previous studies, 30% of COVID-19 cases were accompanied by musculoskeletal symptoms ⁽⁵⁾. Myalgia reflects a generalized inflammatory and cytokine response and can be an early symptom in 36% of patients with COVID-19. It was found that lactate levels increase due to excessive cell damage during COVID-19 infection. In hyperlactatemia, the ability of erythrocytes to carry oxygen and transport oxygen to tissues is significantly reduced. As with exercise, the musculoskeletal system may remain deoxygenated, and the muscles may become ischemic during COVID-19 infection. Also, during hypoxic ischemia, increased growth factors, cytokine levels, ischemic conditions, and microvascular changes can trigger pain with overexpression in the dorsal root ganglion ⁽⁸⁾.

3.7. Anosmia in COVID-19

Anosmia is also a manifestation that is quite often found in COVID-19 patients. It was found that 345 COVID-19 patients experienced anosmia (13%), of which 16.8% had a history of hypertension. A study by T. Klopfenstein et al. reported that 54 of 114 patients (47%) with confirmed COVID-19 reported anosmia. This study found that anosmia occurs in half of the European COVID-19 patients. The median duration of anosmia is seven days, and the results appear favorable in less than 28 days ⁽⁶⁾. Some of the possible pathophysiologies of anosmia are local infection of supporting cells and vascular pericytes in the nose and olfactory bulb, which can affect the function of bipolar neurons or mitral cells, damage to supporting cells in the sensory epithelium that can indirectly affect signaling pathways from sensory neurons to the brain, and finally Damage to sustentacular cells and Bowman's gland cells that can cause diffuse morphological damage to the olfactory sensory epithelium and changes in olfactory perception ⁽¹⁷⁾.

3.8. Ageusia/Dysgeusia in COVID-19

Of 2,659 COVID-19 patients, 259 were ageusia (9.7%), of which 20.8% had comorbid hypertension. According to Carrillo-Larco and Altez-Fernandez, in an analysis of six published studies with 2,757 patients with temporary

disturbances of taste, subclassification as dysgeusia and ageusia, and distorted taste sensations were present in 33%, 20%, and 21% of patients⁽¹⁴⁾. Angiotensin-converting enzyme 2 (ACE2) is the cellular receptor for SARS-CoV-2. ACE2 receptors are expressed diffusely on mucous membranes throughout the oral cavity, especially on the tongue. The mechanism by which ACE2 inhibitors cause taste disturbance is unclear but does not appear to be associated with changes in serum and salivary zinc levels. The possibility of taste disturbances due to the ability to feel the taste in these patients is influenced by the presence of concurrent olfactory disorders⁽¹⁸⁾.

4. Conclusion

From the study results, 2,659 confirmed COVID-19 patients at the Husada Utama Hospital and 1,484 COVID-19 patients with neurological manifestations, or 55.8%, were found. According to the study's findings, men were exposed to COVID-19 at higher rates than women. It was also found that the most neurological manifestations in COVID-19 patients at Husada Utama Hospital were cephalgia. With various comorbidities that were found to affect the degree of COVID-19 disease, it was found that the most comorbid patients suffered from was hypertension.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this document.

Statement of informed consent

Informed consent has been given and signed by the patient and obtained permission from the hospital.

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