

Clinical neurological characteristics of geriatric patients with Coronavirus disease 2019 (COVID-19)

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ABSTRACT

Background and objectives. Coronavirus Disease-2019 (COVID-19) is a respiratory infection caused by the severe acute respiratory syndrome coronavirus (SARS-CoV-2). The COVID-19 associates multi clinical symptoms such as neurological manifestations with mild to advanced progression. This study aimed to determine the clinical neurological characteristics of geriatric patients with COVID-19.

Methods. The study was an observational and descriptive study on 27 geriatric patients with COVID-19. All patients' age was over 60 years old who treated in the In-patient Department of Sanglah General Hospital, Denpasar, on July 2020 to January 2021. The data had taken from medical records.

Outcomes. The mean age of all patients was 70.41 (\pm 8.902) years which dominated by the male (51.9%). The majority of manifestations in this study were fever in 13 people (48.1%), unconsciousness in 10 people (37%), and hemiparesis in 10 people (37%), and cough in 9 people (33.3%).

Conclusion. The clinical neurology characteristics of geriatric patients with COVID-19 vary, which may involve general and neurological manifestations. Promptly accurate diagnosis is necessary for further management.

Keywords: Covid-19, geriatric, neurological manifestation

BACKGROUND

Coronavirus Disease-2019 (COVID-19) is a respiratory infection caused by the severe acute respiratory syndrome coronavirus (SARS-CoV-2) and first discovered in Wuhan, China. Clinical symptoms of COVID-19 vary from mild to advanced progression [1]. Neurological manifestations can be caused by infection of SARS-CoV-2 directly in the nervous system or indirectly through the immune response [2].

A study of 214 COVID-19 patients in Wuhan, China, conducted 53 patients (25%) had symptoms related to the central nervous system: dizziness (17%), headache (13%) and decreased consciousness (17%). Some of the other neurological clinical manifestations found include encephalopathy, encephalomy-

elitis, ischemic stroke, intracerebral hemorrhage, anosmia and neuromuscular disorders [1].

Appropriate treatment requires a proper diagnosis. Demographic data is necessary to consider the clinical diagnosis. Research on demographics data (including onset, age, gender, clinical symptoms and treatment durations) has not been establishing widely. Therefore, our study aimed to determine the clinical neurological characteristics of geriatric patients with COVID-19.

METHOD

This research was a retrospectively descriptive observational study. The data took from medical records of patients who were admitted in the inpatient department in Sanglah General Hospital, Den-

pasar, from July 1, 2020 to January 31, 2021. Inclusion criteria were COVID-19 sufferers aged more than 60 years with neurological manifestations. The diagnosis of COVID-19 is based on World Health Organization clinical guidelines, which had been proven from the results of the history, physical examination and support tests. The exclusion criteria were COVID-19 sufferers whose data in their medical records were incomplete. The data includes age, gender, comorbid factors, clinical manifestations, patient outcomes and laboratory tests.

Sample selection used all COVID-19 patients who had met the inclusion and exclusion criteria during a predetermined period without a specific sample size. The ethical approval number 2021.02.1.0246 was taken from the ethics committee of Sanglah General Hospital Denpasar.

The data collected is then processed using the International Business Machine Statistical Package for the Social Sciences (IBM SPSS) Statistics version 20 software. The descriptive analysis had performed to

determine the proportion and clinical neurological characteristics of geriatric patients with COVID-19 at Sanglah General Hospital Denpasar as a source for further research.

RESULT

Twenty-seven geriatric patients (over 60 years) with COVID-19 and clinical neurological manifestations had treated at Sanglah Hospital from July 1, 2020, to January 31, 2021. The demographic and clinical characteristics of the research sample showed in Table 1.

The mean age of all patients was 70.41 (\pm 8.902) years, with the male gender dominates (n =14, 51.9%) females (n =13, 48.1%) respectively. Comorbid factors included hypertension (n=19, 70.4%), diabetes mellitus (n=11, 40.7%), and chronic kidney disease (n=4, 14.8%). The risk factors included smoking (n=3, 11.1%) and alcohol consumption (n=1, 3.7%). General manifestations found fever in 13 peo-

TABLE 1. Demographic and Clinical Characteristics of Geriatric Patients with COVID-19 and neurologic manifestations

Characteristics	No. (%)			
	Total (n=27)	Severe (n=18)	Mild (n=9)	p value
Age				
Mean (\pm standard deviation)	70.41 (8.902)	69.72 (9.627)	71.78 (7.579)	0.58
Gender				
Female	13 (48.1%)	8 (57.1%)	6 (42.9%)	0.49
Male	14 (51.9%)	10 (76.9%)	3 (23.1%)	
Comorbid Factors				
Hypertention	19 (70.4%)	13 (72.2)	6 (66.7%)	1.000
Diabetes Mellitus	11 (40.7%)	8 (44.4%)	3 (33.3%)	0.89
Dyslipidemia	1 (3.7%)	1 (5.6%)	0	1.000
Smoking	3 (11.1%)	1 (5.6%)	0	0.51
Malignancy	2 (7.4%)	1 (5.6%)	1 (11.1%)	1.000
Chronic Kidney Disease	4 (14.8%)	2 (11.1%)	2 (22.2%)	0.84
Alcohol consumption	1 (3.7%)	1 (5.6%)	0	1.000
General manifestations				
Fever	13 (48.1%)	10 (55.6%)	3 (33.3%)	0.49
Cough	9 (33.3%)	8 (44.4%)	1 (11.1%)	0.19
Shortness of breath	4 (14.8%)	3 (16.7%)	1 (11.1%)	1.000
Anorexia	2 (7.4%)	1 (5.6%)	1 (11.1%)	1.000
Vomit	1 (3.7%)	0	1 (11.1%)	0.71
Nausea	2 (7.4%)	1 (5.6%)	1 (11.1%)	1.000
Neurological manifestations				
Unconsciousness	10 (37%)	8 (44.4%)	2 (22.2%)	0.48
Headache	7 (25.9%)	4 (22.2%)	3 (33.3%)	0.87
Hemiparesis	10 (37%)	5 (27.8%)	5 (55.6%)	0.32
Slurred speech	7 (25.9%)	4 (22.2%)	3 (33.3%)	0.87
Dizziness	1 (3.7%)	0	1 (11.1%)	0.71
Blurred vision	1 (3.7%)	0	1 (11.1%)	0.71
Seizure	1 (3.7%)	1 (5.6%)	0	1.000
Drooped face	2 (7.4%)	1 (5.6%)	1 (11.1%)	1.000
Outcome				
Dead	7 (25.9%)	6 (33.3%)	1 (11.1%)	0.43
Alive	20 (74.1%)	12 (66.7%)	8 (88.9%)	

ple (48.1%), cough in 9 people (33.3%) and shortness of breath in 4 people (14.8%). Neurological manifestations found unconscious in 10 people (37%), headache in 7 people (25.9%), hemiparesis in 10 people (37%) and slurred speech in 7 people (25.9%). The clinical outcome obtained as many as 7 (25.9%) patients who died.

The outcome of this study had divided by severity degree of COVID-19 infection into 18 (67.7%) patients with severe and 9 (33.3%) patients with mild. There were no significant differences in determining the age, gender, comorbid factors, general clinical symptoms, neurological symptoms and clinical

outcomes between patients with mild and severe COVID-19 infection.

Table 2 showed the laboratory characteristics of COVID-19 patients aged over 60 years with neurological clinical manifestations. Patients with severe COVID-19 infection had a higher inflammatory response, characterized by higher CRP levels than those with low-grade COVID-19 infection (CRP: 100.9 mg/l [10.04-290]; $p < 0,01$). Patients with severe COVID-19 infection also had higher levels of SGOT/Aspartate aminotransferase (AST) (SGOT: 38.55 [14.9-644]; $p < 0.01$). Patients with severe COVID-19 infection also had lower uric acid levels (uric acid:

TABLE 2. Laboratory Characteristics of Geriatric Patients with COVID-19 and neurologic manifestations

Laboratory characteristics	Median			p value
	Total	Severe	Mild	
Haemoglobin	13.37 (8.69-15.37)	13.17 (11.03-15.37)	13.57 (8.69-14.38)	0.50
Hematocrite	41.24 (23.67-47.86)	41.21 (33.56-44.64)	41.24 (23.67-47.86)	0.60
White blood cell	8.99 (4.98-32.57)	9.9 (4.98-32.5)	8.87 (5.26-30.64)	0.79
Platelet count	210 (108-505)	209 (108-557)	249 (125-490)	0.53
Neutrophil to Lymphocyte ratio (NLR)	9.11 (1.20-31.94)	7.72 (1.88-31.94)	6.15 (1.2-11.59)	0.143
Random blood glucose	117 (70-489)	139 (79-349)	109 (70-489)	0.47
C-Reactive Protein (CRP)	48.5 (1.30-290)	100.9 (10.04-290)	7.53 (1.30-59.65)	0.003*
D-dimer	1.21 (0.34-20)	1.37 (0.34-20)	1.03 (0.73-2.85)	0.071
Blood Urea Nitrogen (BUN)	19.1 (6.70-64.7)	15.5 (6.70-64.7)	20.9 (8.1-37)	0.41
Creatinine	0.85 (0.42-4.92)	0.85 (0.42-4.92)	0.76 (0.56-2.4)	0.53
Glomerular Filtration Rate	73.38 (12.82-101.85)	74.5 (12.8-101.8)	72.7 (26.3-96.3)	0.82
Serum Glutamic Oxaloacetic Transaminase (SGOT)	33.8 (14.10-644)	38.55 (14.9-644)	27.6 (14.1-50.7)	0.018
Serum Glutamic Pyruvic Transaminase (SGPT)	24.5 (5.00-413)	27.2 (12-413)	14.4 (5-53.2)	0.08
Natrium	133 (109-149)	133 (109-146)	135 (131-149)	0.188
Kalium	3.63 (2.80-5.22)	3.72 (2.8-5.22)	3.52 (3.03-4.07)	0.24
Total Cholesterol	132 (62-281)	129.5 (62-281)	141 (96-153)	0.77
Low density level (LDL) of Cholesterol	88 (27-218)	82 (27-218)	90 (37-122)	0.979
High density level (HDL) of Cholesterol	35 (20-51)	35.5 (20-51)	32 (25-48)	0.92
Tryglyceride	111 (47-238)	116.5 (47-238)	109 (65-157)	0.537
Uric acid	4.3 (1.7-7.00)	4.15 (1.7-5.3)	5.3 (2.6-7)	0.026
Albumin	3.5 (2.60-4.70)	3.4 (2.6-4.7)	3.6 (3.1-4.4)	0.12

4.15 [1.7-5.3]; $p < 0.05$). The statistical data analysis found that patients with mild and severe COVID-19 infection have insignificant differences in laboratory tests such as routine blood tests (hemoglobin, hematocrit, white blood cell, platelet), D-dimer, kidney function tests (urea, creatinine) albumin, lipid profile (total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides).

DISCUSSION

This study used a descriptive design to show the proportion and mean of the sample. Twenty-seven samples were obtained, with a mean age of 70.41 (± 8.902) years old. This result is in line with Guo et al., study in 2020 that found an average age of 67 years [3].

The gender sample of this study dominated by the male (51.9%) to female (48.1%) is similar to a study conducted by Chen et al., in 2020 from Wuhan, which found that male results were 54.3-68% [3,4].

The dominant comorbid factors were hypertension as many as 19 people (70.4%) and diabetes mellitus as many as 11 people (40.7%). This is following a study that explained that geriatric patients (>60 years) had higher risk factors, including hypertension, diabetes mellitus, hyperlipidemia and vascular disease [2]. The risk factors for smoking were 3 people (11.1%) and alcohol consumption was 1 person (3.7%).

The general manifestations included fever in 13 people (48.1%) and cough in 9 people (33.3%). This result was similar with research conducted by Liu et al., in 2020, the main symptoms that are commonly found are fever and cough [5,6]. The upper respiratory tract is the entry point for SARS-CoV-2. The main target of SARS-CoV-2 is respiratory and digestive tract epithelial cells which have angiotensin converting enzyme 2 (ACE2). Decreased airway particle clearance function, and the number of cilia found in the elderly This causes factors that cause respiratory symptoms to be found more in the elderly [6]. Based on a retrospective study conducted by Mao et al., in 2020, it was found that COVID-19 predominantly affects the respiratory system, with common symptoms that are often found to be fever (61.7%), cough 50%, and decreased appetite (31.8%). Other common symptoms include fatigue, myalgia and shortness of breath [7].

The most common neurological clinical symptoms were unconsciousness in 10 people (37%) and hemiparesis in 10 people (37%). Based on the research data of Mao et al., in 2020, there were 214 COVID-19 patients, and as many as 36.4%, of which 39 people (31%) decreased consciousness and 77 people (62%) with cerebrovascular disease [2,7].

Several cases of COVID-19 with neurological symptoms reported encephalitis (10-70%), headache (13%), dizziness (17%), neuralgia (2%), seizures (1%), ataxia (1%), and acute neurologic deficits (3%) [1]. SARS-CoV-2 has a high affinity for the ACE2 receptor. The ACE2 receptor is a SARS-CoV-2 receptor found in various organs. The distribution and expression of ACE2 receptors involving the nervous system can lead to neurologic manifestations through direct and indirect mechanisms [7,8]. Mechanism of the spread of SARS-CoV-2 to the nervous system through the hematogenous distribute to the cribriform plate and olfactory bulb [8]. The ACE2 receptor is also expressed by neurons and glial cells, making the nervous system a potential target for SARS-CoV-2 [7].

The unconsciousness may be caused by encephalopathy related to hypoxia, drugs, toxins and metabolism. Consideration of the cause of encephalitis must be associated with the presence of brain inflammation characterized by other neurologic deficits [2].

In this study, headache manifested in only 7 (25.9%) of 27 patients. These differ from a study conducted by Rahman et al., in 2020, where reported headache as the most common neurological symptom. The underlying mechanism of headache is related to infection of the nervous system and other factors related to stress, fear and anxiety [9].

Cerebrovascular disease is associated with damage to blood vessels (specifically large blood vessels) accompanied by risk factors. Increased inflammatory response and hypercoagulable conditions characterized by increased levels of C-Reactive Protein (CRP) and D-dimer. The ischemic stroke resulted from a cytokine storm, which damage the vascular endothelium, disseminated intravascular coagulation and impair autoregulation. The binding of the virus to the ACE2 receptor found on the endothelium of blood vessels will cause extensive, which will increase the risk of thrombosis and cause ischemic stroke. In hemorrhagic stroke, the SARS-CoV-2 virus will reduce the expression and function of the ACE2 protein resulted in uncontrolled hypertension, rupture of artery walls and cerebral hemorrhage. Thrombocytopenia and hypercoagulation can also cause cerebral hemorrhage [10]. The dead clinical outcome obtained as many as 7 (25.9%) patients.

From the results of the study, there was an increase in CRP with an average of 48.5 mg/l ($\pm 1.3-290$). This is in line with a meta-analysis study conducted by An et al. in 2020, from 14 studies an increase in CRP was found, with an average of 75.47 mg/dL. SARS-CoV-2 infection is an inflammatory response characterized by increased levels of interleukin (IL)-6, Granulocyte Colony-Stimulating Factor (GCSF), Interferon gamma-induced protein 10

(IP10), and Tumor Necrosis Factor- α (TNF α). In the condition of COVID-19 infection, cytokine storms were involved which were characterized by the secretion of Interleukin-6, Interleukin-1, Interleukin-12 and other inflammatory markers. C-reactive protein (CRP) is elevated in inflammatory conditions such as cardiovascular disease, rheumatoid arthritis and infections. CRP levels can be used as an early marker of inflammation and pneumonia. Severe pneumonia has higher CRP levels, because severe inflammation is associated with higher production of pro-inflammatory markers [11]. Patients with severe COVID-19 infection had a higher inflammatory response, characterized by higher CRP levels, than low-grade COVID-19 infection (CRP: 100.9 mg/l [10.04-290]; $p < 0.01$). CRP levels are related to the degree of inflammation which not affected by age and gender [3,12].

Glutamic Oxaloacetic Transaminase (SGOT: 38.55 [14.9-644]; $p < 0.01$). Impaired liver function caused by direct viral infection, activation of the immune system (cytokine storm), hypoxia caused by pneumonia or hypovolemic shock, and side effects of drug use at an advanced stage. The extent of liver damage depends on the severity of the COVID-19 infection. In a study conducted by Afra et al., in 2020, levels of SGOT, Serum Glutamic Pyruvic Transaminase (SGPT), Lactate Dehydrogenase (LDH), and total bilirubin increased significantly in severe COVID-19 infection. Liver function impairment was found in 59-78% of patients with severe COVID-19

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infection. High levels of liver enzymes indicate the severity of COVID-19 infection. Based on a study conducted by Zheng et al. in 2021, some markers of tissue damage such as LDH, SGOT SGPT, and ferritin increased in severe COVID-19 infections or COVID-19 patients who died [13-15].

Patients with severe COVID-19 infection had lower uric acid levels (uric acid: 4.15 [1.7-5.3]; $p < 0.05$). This result was different from the study conducted by Zheng et al. in 2021, where hyperuricemia is found in severe COVID-19 infections or COVID-19 patients who died. In tissue damage, intracellular uric acid reserves will be released, which will cause uric acid levels in the area to increase and form crystals. The crystal form of uric acid will stimulate the production of inflammatory cytokines (such as IL-1, TNF-, and IL-6). A positive correlation was found between uric acid levels and markers of inflammation in COVID-19 patients [15].

CONCLUSION

This retrospective study used 27 of geriatric COVID-19 sufferer data which collected during a year at Sanglah Hospital. The characteristics of the study sample obtained an average sample age of 70.41 (± 8.902) years, dominated by the male gender. The most common comorbid factor is hypertension. This study is a preliminary study with a small sample size, therefore, a larger population and longer period is needed in future study.