

Characteristics of Stroke Patients with Covid 19 at Dr. H Koesnadi Bondowoso General Hospital

Senoadji Pratama^a, Kamilka Taufiq^b, Eko Aprilianto Handoko^c

^asenoadjipratama@gmail.com

Department of Neurology Dr. H Koesnadi Bondowoso General Hospital , Indonesia

Abstract

Covid 19 has been linked to hypercoagulability which causes cerebrovascular complications. One of the cerebrovascular complications that occurs in Covid 19 infection is stroke. The purpose of this study is to provide an overview of the characteristics of stroke patients confirmed Covid 19 in the emergency department of Dr.H. Koesnadi Bondowoso General Hospital in February 2022. The research method is a retrospective study from medical record data at the Emergency Department of dr.H Koesnadi Bondowoso General Hospital, Indonesia. The results of this study showed that three stroke patients with Covid 19 infection had risk factors for hypertension, history of stroke and diabetes mellitus. Clinical manifestations occurred in the form of seizures, weakness of one-sided limbs, speech disorders (Brocca's aphasia) and dysarthria. There were also abnormalities from laboratory tests in the form of an increase in creatinine, urea, blood sugar, hyperkalaemia and an increase in the number of leukocytes.

Keywords: Stroke, Hypercoagulation, Covid 19

1. Introduction

Corona virus disease 2019 (COVID 19) is an acute respiratory disease caused by infection with the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV 2).¹ This disease was first reported in the city of Wuhan, Hubei Province, China at the end of December 2019.² Coronavirus is a single-stranded RNA virus and has 4 types, namely: α coronavirus, β coronavirus, γ coronavirus, and δ -coronavirus. SARS-CoV-2 belongs to the β -coronavirus family which also includes SARS-CoV-1, Human Coronavirus (HCoV)-OC43, Middle East Respiratory Syndrome (MERS)-CoV, and HCoV-HKU1.¹ SARS-CoV-2 virus has spread widely in more than 250 countries and on March 12, 2020 COVID-19 was declared a global pandemic by the World Health Organization (WHO) with a worldwide mortality rate of 5.28%.³ Meanwhile, it was reported that there were daily cases COVID-19 in Indonesia in July 2021 reaching 51,000 new cases with a death rate reaching 2000 cases per day.⁴

Common symptoms of COVID-19 include fever, dry cough, fatigue, myalgia, and dyspnea.⁵ Although COVID 19 is a disease mainly in the respiratory tract, currently, its clinical manifestations are diverse, including manifestations of neurological/neurological disorders. Invasion of the virus into the human body causes cytokines of the immune system to against the virus, with the impact of increasing the permeability of the blood-brain barrier so that the virus can invade the central nervous system.⁶ COVID-19 has been linked to hypercoagulation which causes cerebrovascular complications. One of the cerebrovascular complications that occurs in COVID-19 infection is stroke.⁷ Meanwhile, from a retrospective study of data from the COVID-19 outbreak in Wuhan, China, it was found that there was an approximately 5% incidence of stroke among hospitalized patients with COVID-19; the youngest patient in the case series were 55 years old. The risk factors for stroke in COVID-19 patients are older age, history of hypertension, and high D-dimer values.⁸⁻¹⁰

Due to the limited number of case studies regarding stroke with COVID 19 infection in Indonesia, this study aims to provide an overview of the characteristics of stroke patients confirmed COVID 19 in the emergency department of Dr.H. Koesnadi Bondowoso General Hospital in February 2022.

2. Case series

During the research in February 2022 at the Emergency Department, Dr. H Koesnadi Bondowoso General Hospital, we report 3 cases of ischemic stroke with COVID 19 infection, aged 42-67 years consisting of 2 male patients and 1 female patient. All patients had comorbid hypertension and stroke, and 1 patient had a history of Diabetes Mellitus. Since the limitation in using CT Scans in our Hospital due to the Covid 19 pandemic, these three patients were assessed with Siriraj Score and the results were all below minus 1, which means that these three patients were classified as non-haemorrhagic strokes. Of the three patients, only 2 patients were treated with antiplatelet. During the treatment in the ward, the three patients showed a good outcome by leaving the sequelae of stroke.

2.1 First Patient

A 42-year-old man came to the emergency department at Dr.H.Koesnadi Bondowoso General Hospital with decreased consciousness after having one seizure at his home for 5 minutes. After the patient arrived at the emergency department, a second seizure occurred for 3 minutes and the seizures stopped after intravenous diazepam was given. The patient has a history of hypertension and stroke since 5 months of SMRS and has never been under control for 3 months. On examination of vital signs at the time of arrival, Glasgow Coma Scale (GCS) was E2V2M4, blood pressure 138/76, pulse 117 times per minute adequately palpable, respiratory rate 28 times per minute, temperature 36.4 C and oxygen saturation 94% in air. room. There were right lateralization and dysarthria on neurological examination. The result of Siriraj Score was <-1. The radiological examination of the thorax was normal. From the laboratory examination, it was found an increase in the number of leukocytes, an increase in creatinine, an increase in urea, an increase in potassium. The SARS-CoV-2 RT PCR was confirmed positive.

2.2 Second Patient

A 69-year-old man came to the emergency department of Dr. H. Koesnadi Bondowoso General Hospital with sudden weakness in the right limb since 2 hours of SMRS. The patient had no complaints of headache and vomiting, but the patient complained of fever since 1 day. The patient had a history of hypertension and 2 strokes. On examination of vital signs, Glasgow Coma Scale (GCS) was E4V5M6, blood pressure 133/78, pulse 92 beats per minute adequately palpable, respiratory rate 20 breaths per minute, temperature 38.2 C and oxygen saturation 99% in room air. On neurological examination, there was right hemiparesis. The result of Siriraj Score was <-1. Cardiomegaly was found on chest radiography. From the laboratory examination, creatinine increased and the RT PCR for SARS-CoV-2 was confirmed positive.

2.3 Third Patient

A 62-year-old woman came to the emergency department of Dr.H.Koesnadi Bondowoso General Hospital with difficulty speaking after waking up one day ago. Although the patient had difficulty speaking, she was able

to understand and follow orders. The patient had no complaints of headache and vomiting, but the patient complained of coughing since 1 day. The patient has a history of hypertension, diabetes, stroke. On examination of vital signs, the Glasgow Coma Scale (GCS) was E4VXM6, blood pressure 132/90, pulse 89 beats per minute adequately palpable, respiratory rate 18 times per minute, temperature 36.7 C and oxygen saturation 99% in room air. On neurological examination there was Broca's aphasia. The result of Siriraj Score was <-1. Pulmonary infiltrates was found on thorax xray. From the laboratory examination, blood sugar increased and the RT PCR of SARS-CoV-2 was confirmed positive.

| Demographic Characteristics | Patient I | Patient II | Patient III |
|-----------------------------|--|--|--|
| Age | 42 year old | 69 year old | 62 year old |
| Gender | Male | Male | Male |
| Covid 19 Vaccine status | Not vaccinated | Not vaccinated | Not vaccinated |
| Past medical history | Stroke and hypertension | Stroke and hypertension | Stroke, hypertension dan DM |
| Covid 19 symptoms | Common cold | Fever | cough |
| Early symptoms of stroke | Seizures, unconsciousness and weakness in the right limb | Weakness in the right limb | Difficulty speaking |
| Siriraj score | <-1 | <-1 | <-1 |
| Laboratory tests | | | |
| Hb | 12.5 | 13.7 | 13.3 |
| WBC | 19.200 | 8.700 | 6.400 |
| PLT | 341.000 | 213.000 | 287.000 |
| SGOT | 36 | 25 | 30 |
| SGPT | 50 | 19 | 19 |
| Creatinine | 6.70 | 2.06 | 0.90 |
| Urea | 196 | 21 | 31 |
| Blood sugar | 134 | 107 | 388 |
| Natrium | 134 | | |
| Kalium | 5.8 | | |
| Chloride | 91 | | |
| RT PCR | Confirmed SARS-COV2 | Confirmed SARS-COV2 | Confirmed SARS-COV2 |
| Thorax | Cardiomegaly | Cardiac and lungs in normal range | Pulmonary Infiltrate |
| Initial Treatment | oxygen, anti-seizure and Supportive | Antiplatelet, statin and Supportive | Antiplatelet, RCI, and Supportive |
| Covid Treatment | Remeva iv 1x200mg | Remeva iv 1x200mg | Remeva iv 1x200mg, ZINC, Vit D 5000 iu |
| Result | Out of hospital in 5 th day | Out of hospital in 6 th day | Out of hospital in 5 th day |

3. Discussion

The type of acute stroke with COVID 19 infection in these case series based on the Siriraj score was ischemic stroke. This is in accordance with a retrospective study of 221 COVID-19 patients by Li Y et al (2020) which found 5.9% of patients had an acute stroke during hospitalization. The most common type of stroke was ischemic stroke (84.6%), followed by central venous thrombosis 17.25 (7.7%), and haemorrhagic stroke (7.7%)^{15,16} Based on the demographic characteristics of the three patients, there were more males than females with an age range of 42-67 years. The risk factors from these three patients were hypertension (100%), diabetes mellitus (33.33%) and a history of previous stroke (100%). This is in accordance with research conducted by Ntaios G et al (2020)

regarding the risk factors for stroke in COVID 19 infection, hypertension (68.4%), obesity (37.4%), and diabetes mellitus. Previous stroke history has been reported in 11.5% of patients.¹⁷ Diabetes mellitus has been recognized as one of the main risk factors for ischemic stroke due to vascular endothelial dysfunction, increased atherosclerosis, systemic inflammation and thickening of the capillary basement membrane.¹⁸ Atherosclerosis of the blood vessels is still the main basis of pathology. Other studies have shown that the prognosis of patients with hypertension accompanied by COVID-19 is poor, especially hypertensive patients taking ACE inhibitors and/or Angiotensin Receptor Blocker (ARB) therapy have a higher likelihood of developing more serious complications.¹¹ This is because SARS-CoV- 2 can cause disease through ACE2, which is found in human vascular endothelium. Therefore, when SARS-CoV-2 enters the human body through ACE2, it will not only cause hypertension but also cause Cerebrovascular disease. For COVID-19 patients with hypertension, the cerebrovascular risk is higher than in those without hypertension.

The first patient in this study had clinical manifestations of seizures. Patients with COVID-19 may have clinical features of recurrent seizures. There are factors inducing seizures include viral invasion in the CNS (Central Nervous System), metabolic factors, and other systemic diseases.⁸ Changes that occur due to infarction in the brain can cause seizures in the long term. Therefore, seizures should be considered as a result of stroke and long-term sequelae of COVID-19 infection.

In the second patient, there was a decrease in the number of lymphocytes. According to Xu P et al (2020) in his research, it was said that Coronavirus can infect bone marrow, resulting in inhibition of the haematopoiesis process and causes a decrease in the number of lymphocytes, thrombocytopenia, prolongation of partial activation of the thromboplastin time and an increase in the value of D-dimer. COVID 19 can also increase autoantibodies and immune complexes that result in the destruction of platelets by the immune system

Kidney involvement in Covid-19 patients most often manifests as acute kidney injury, haematuria or proteinuria. In this study, renal involvement occurred in the first and second patients with increased serum creatinine and blood urea. The presence of high expression of ACE2 in the kidney allows SARS-Cov-2 to directly injure kidney cells. There are some evidences including the finding of viral nucleic acids in urine (Ling, et al 2020), the accumulation of SARS-CoV 2 NP antigen in the cytoplasm of the renal tubules (Diao, et al 2020), which indicates that SARS-CoV causes acute tubular necrosis by infecting the renal tubules. The incidence of Covid 19 is quite high, especially in critically ill patients, so AKI has been known as a common complication in Covid 19 patients (Nadim et al 2020). Pre-existing chronic kidney disease is an independent risk factor for AKI. However, based on the results of the regression analysis, Chronic Kidney Disease has not been shown to be an important prognostic factor for worse COVID-19 outcomes (Guan et al 2020). Meanwhile, hypertension has been independently associated with more severe COVID-19 (Palevsky et al 2020). Hypertension and diabetes are frequent causes of CKD. On the other hand, CKD is the most common cause of secondary hypertension.¹⁹⁻²¹

Antiplatelet agents (Aspirin and Clopidogrel) were given to the second and third patients of this study. Antiplatelet drugs, such as aspirin and clopidogrel, as well as anticoagulants (especially enoxaparin), have been used to treat acute stroke in patients with COVID-19.^{20,21,22} There are no studies reporting whether antiplatelet use is better than anticoagulants or vice versa, and some patients are given dual therapy prescriptions. Antiplatelet administration or a combination of aspirin and clopidogrel may be considered as a substitute for recombinant tissue plasminogen activator (rt-PA). Low molecular weight heparin (LMWH) is considered more effective than the combination of aspirin and clopidogrel. LMWH can reduce the activation of tissue factor-dependent

coagulation pathways and there is no interaction with antiviral drugs such as lopinavir/ritonavir due to the activation of cytochrome 450, so that the concentration of clopidogrel in the blood decreases.^{13,14}

4. Conclusion

Stroke patients with Covid 19 infection cause various neurological clinical manifestations, such as seizures, weakness of the limbs on one side, speech disorders (Broca's aphasia) and dysarthria; preceded "flu like syndrome" symptoms in the form of fever, cough and runny nose. This study found risk factors for hypertension, history of stroke and diabetes mellitus. The complex mechanism between stroke and Covid 19 infection requires further research to determine appropriate management decisions. Although controlling Covid 19 infection is the priority during this pandemic, we must not ignore the incidence of stroke due to Covid 19 complications with varied neurological clinical features.

Acknowledgements

None

References

1. Franceschi AM, Arora R, Wilson R, Giliberto L, Libman RB, Castillo M. Neurovascular Complications in COVID-19 Infection: Case Series. *Am J Neuroradiol.* 2020 Jun 11;ajnr:ajnr.A6655v1.
2. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med.* 2020 Jan;382:727- 733
3. WHO. WHO Timeline – COVID 2019. Available online at: <https://www.who.int/newsroom/detail/27-04-2020-who-timeline---covid19>
4. Buku Panduan Tatalaksana COVID 19 di Indonesia tahun 2022
5. Wang LS, Wang YR, Ye DW, Liu QQ. A review of the 2019 Novel Coronavirus (COVID-19) based on current evidence. *International Journal of Antimicrobial Agents.* 2020 Mar:105948
6. Divani AA, Andalib S, Napoli M Di, Lattanzi S, Hussain MS, Biller J, et al. Coronavirus Disease 2019 and Stroke: Clinical Manifestations and Pathophysiological Insights. *J Stroke Cerebrovasc Dis.* 2020;29(8):1–12.
7. Reddy ST, Garg T, Shah C, Nascimento FA, Imran R, Kan P, Bowry R, Gonzales N, Barreto A, Kumar A, Volpi J, Misra V, Chiu D, Gadhia R, Savitz SI. Cerebrovascular Disease in Patients with COVID-19: A Review of the Literature and Case Series. *Case Rep Neurol.* 2020;12(2):199-209. doi: 10.1159/000508958.
8. Fifi JT, Mocco J. COVID-19 related stroke in young individuals. *Lancet Neurol.* 2020 Sep;19(9):713–5.
9. Oxley TJ, Mocco J, Majidi S, Kellner CP, Shoirah H, Singh IP, et al. Large-Vessel Stroke as a Presenting Feature of Covid-19 in the Young. *N Engl J Med.* 2020 May 14;382(20):e60.
10. Spence JD, de Freitas GR, Pettigrew LC, Ay H, Liebeskind DS, Kase CS, et al. Mechanisms of Stroke in COVID-19. *Cerebrovasc Dis.* 2020 Jul 20;1–8
11. Anand P, Al-Faraj A, Sader E, Dashkoff J, Abdennadher M, Murugesan R, et al. Seizure as the presenting symptom of COVID-19: A retrospective case series. *Epilepsy Behav* 2020;112:107335
12. Han H, Yang L, Liu R, et al. Prominent changes in blood coagulation of patients with SARS-CoV-2 infection. *Clin Chem Lab Med.* 2020;58(7):1116–1120. doi:10.1515/cclm-2020- 0188
13. Qureshi AI, Abd-Allah F, Al-Senani F, Aytac E, Borhani-Haghighi A, Ciccone A, et al. Management of acute ischemic stroke in patients with COVID-19 infection: Report of an international panel. *Int J Stroke.* 2020;15(5):540–54. doi: 10.1177/1747493020923234
14. Vivas D, Roldán V, Esteve-Pastor MA, Roldán I, Tello-Montoliu A, Ruiz-Nodar JM, et al. Recommendations on antithrombotic treatment during the COVID-19 pandemic. Position statement of the Working Group on Cardiovascular Thrombosis of the Spanish Society of Cardiology. *Rev Esp Cardiol.* 2020;73(9):749–57. doi: 10.1016/j.recesp.2020.04.006.
15. Pinzon RT, Wijaya VO, Buana RB, Al Jody A, Nunsio PN. Neurologic Characteristics in Coronavirus Disease 2019 (COVID-19): A Systematic Review and Meta-Analysis. *Front Neurol.* 2020;11:1–11. 25. Li Y, Wang M, Zhou Y, Chang J, Xian Y, Mao L, et al. Acute cerebrovascular disease following COVID-19: a single center, retrospective, observational study. *Lancet.* 2020
16. Li Y, Wang M, Zhou Y, Chang J, Xian Y, Mao L, et al. Acute cerebrovascular disease following COVID-19: a single center, retrospective, observational study. *Lancet.* 2020

17. Ntaios G, Michel P, Georgiopoulos G, Guo Y, Li W, Xiong J, et al. Characteristics and Outcomes in Patients With COVID-19 and Acute Ischemic Stroke: The Global COVID-19 Stroke Registry. *Stroke*. 2020;51(9):e254-e258. doi: 10.1161/STROKEAHA.120.031208.
18. Chen R, Ovbiagele B, Feng W. Diabetes and stroke: epidemiology, pathophysiology, pharmaceuticals and outcomes. *Am J Med Sci* 2016; 351(4):380-6. <https://org.doi/10.1016/j.amjms.2016.01.011>
19. Xu P, Zhou Q, Xu J. Mechanism of thrombocytopenia in COVID-19 patients. *Ann Hematol* 2020;15:1-4. <https://org.doi/10.1007/s00277-020-04019-0> 39. Avula A et al. COVID-19 presenting as stroke. *Brain Behav Immun*. 2020;87:115-9.
20. Baracchini C et al. Acute stroke management pathway during coronavirus-19 pandemic. *Neurol Sci*. 2020;41(5):1003-5.
21. Morassi M et al. Stroke in patients with SARS-CoV-2 infection: case series. *J Neurol*. 2020;267(8):2185-92.
22. Beyrouti R et al. Characteristics of ischaemic stroke associated with COVID-19. *J Neurol Neurosurg Psychiatry*. 2020;jnnp-2020-323586.