



## **Factors Related to Clinical Outcome of Patients with Stroke and COVID-19 Pneumonia in Dr. Mohammad Hoesin General Hospital Palembang**

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### **ABSTRACT**

COVID-19 infection may predispose thrombotic complications mediated by inflammation, endothelial dysfunction, and platelet activation. Several studies have reported that infection with COVID-19 is associated with both ischemic and hemorrhagic stroke. Stroke with COVID-19 Pneumonia is associated with increased morbidity and mortality. This study aimed to describe factors related to clinical outcomes in stroke patients comorbid with COVID-19 pneumonia. This study was an observational study with a cross-section approach. The population of this study is the medical records of stroke patients with pneumonia due to COVID-19 who were treated at Dr. Mohammad Hoesin General Hospital Palembang. Sample inclusion criteria in the form of medical record data for stroke patients with COVID-19 pneumonia and treated from January to June 2021. It was found that the most demographic characteristics were age (30-60 years), female, and comorbid hypertension. The most clinical characteristics were hemorrhagic stroke with severe NIHSS category and hypercoagulable conditions, and respiratory failure. From the bivariate analysis, it was found that the use of a ventilator was significantly associated with the incidence of death from stroke with COVID-19 pneumonia.

### **1. Introduction**

Stroke is one of the etiology of brain dysfunction, which has become the second most common cause of death in many countries after heart disease. Coronavirus disease 2019 (COVID-19) infection is an emerging infectious disease caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and has become a worldwide pandemic.<sup>1</sup> The incidence of stroke with COVID-19 pneumonia is rapidly increasing worldwide. A previous study stated that the proportion of stroke patients with COVID-19 pneumonia who received treatment at the hospital was estimated at about 4.9%. Stroke with COVID-19

Pneumonia is associated with increased morbidity and mortality rates. Early identification of factors affecting the outcome of stroke patients with COVID-19 pneumonia is needed for early treatment and improving the outcomes. This study aimed to describe factors related to clinical outcomes in stroke patients comorbid with COVID-19 pneumonia.

### **2. Methods**

This study was an observational study with a cross-sectional approach. The population of this study was medical records of stroke patients with pneumonia due to COVID-19 who were treated at Dr.

Mohammad Hoesin General Hospital Palembang. The sample inclusion criteria consisted of medical records of stroke patients with COVID-19 pneumonia who were treated from January to June 2021. The data collected included patient demographic data, clinical data and other co-morbidities, and patient survival outcomes. The sampling was done by total sampling method and analyzed with univariate and bivariate using the SPSS Chi-square method. This research has received ethical approval from the research ethics committee of Dr. Mohammad Hoesin General Hospital.

### 3. Results

A total of 30 medical records of stroke patients accompanied by COVID-19 were included in this study. Most of the patients were aged 30-60 years, women, with hypertension as the most common co-morbidity (Table 1). The most common types of stroke in stroke patients with COVID-19 were hemorrhagic strokes with severe NIHSS, hypercoagulable conditions, and the use of mechanical ventilators (Table 2). Based on the outcome, most of the patients died after treatment (Table 3).

Table 1. Patient characteristic.

| Characteristics   | Total (n) | Percentage (%) |
|-------------------|-----------|----------------|
| Age               |           |                |
| < 30 years        | 0         | 0              |
| 30- 60 years      | 18        | 60             |
| > 60 years        | 12        | 40             |
| Gender            |           |                |
| Male              | 11        | 36.7           |
| Female            | 19        | 63.3           |
| Hypertension      | 21        | 70             |
| Diabetes mellitus | 8         | 26.7           |
| Prior stroke      | 8         | 26.7           |
| Lung disease      | 1         | 3.3            |
| Heart disease     | 2         | 6.7            |

Table 2. Clinical characteristics of patients.

| Clinical characteristics | Total (n) | Percentage (%) |
|--------------------------|-----------|----------------|
| Stroke type              |           |                |
| Hemorrhagic              | 19        | 63.3           |
| Ischemic                 | 11        | 36.7           |
| NIHSS                    |           |                |
| Mild                     | 7         | 23.3           |
| Medium                   | 11        | 36.7           |
| Severe                   | 12        | 40             |
| Very severe              | 0         | 0              |
| Hypercoagulation         |           |                |
| Yes                      | 27        | 90             |
| No                       | 3         | 10             |
| Mechanic ventilator      | 15        | 50             |

Table 3. Distribution of patients by the outcome.

| Outcome | Total (n) | Percentage (%) |
|---------|-----------|----------------|
| Alive   | 11        | 36.7           |
| Dead    | 19        | 63.3           |

The study showed that most of the dead stroke patients with COVID-19 pneumonia were in the age range of 30-60 years, female, and had hypertension

as the comorbid. Bivariate analysis was performed, but no significant correlation was found (Table 4).

Table 4. Distribution of demographic characteristics based on the patient's clinical outcome.

| Demographic characteristics | Dead |      | Alive |      | p     |
|-----------------------------|------|------|-------|------|-------|
|                             | N    | %    | n     | %    |       |
| Age                         |      |      |       |      |       |
| < 30 years                  | 0    | 0    | 0     | 0    | 0.643 |
| 30- 60 years                | 12   | 63.1 | 6     | 54.5 |       |
| > 60 years                  | 7    | 36.8 | 5     | 45.5 |       |
| Gender                      |      |      |       |      |       |
| Male                        | 8    | 42.1 | 3     | 27.2 | 0.417 |
| Female                      | 11   | 57.8 | 8     | 72.7 |       |
| Hypertension                | 14   | 46.6 | 7     | 23.3 | 0.563 |
| Diabetes mellitus           | 4    | 13.3 | 4     | 13.3 | 0.361 |
| Prior stroke                | 6    | 2    | 2     | 6.6  | 0.424 |
| Lung disease                | 1    | 3.3  | 0     | 0    | 0.439 |
| Heart disease               | 1    | 3.3  | 1     | 3.3  | 0.685 |

The study also showed that most of the dead stroke patients with COVID-19 pneumonia were caused by a hemorrhagic stroke with severe NIHSS, having hypercoagulable conditions, and using

ventilators. Bivariate analysis was performed using the Fisher exact test. It was found that the use of ventilators was significantly related to the incidence of death with a p-value of 0.000 (Table 5).

Table 5. Distribution of demographic characteristics based on the patient's clinical outcome.

| Clinical outcome    | Dead |      | Alive |      | p     |
|---------------------|------|------|-------|------|-------|
|                     | n    | %    | N     | %    |       |
| Stroke type         |      |      |       |      |       |
| Hemorrhagic         | 12   | 63.1 | 7     | 63.6 | 0.979 |
| Ischemic            | 7    | 36.8 | 4     | 36.3 |       |
| NIHSS               |      |      |       |      |       |
| Mild                | 3    | 15.7 | 4     | 36.3 | 0.158 |
| Medium              | 6    | 31.5 | 5     | 45.4 |       |
| Severe              | 10   | 52.6 | 2     | 18.1 |       |
| Very severe         | 0    | 0    | 0     | 0    |       |
| Hypercoagulation    |      |      |       |      |       |
| Yes                 | 16   | 84.2 | 11    | 100  | 0.165 |
| No                  | 3    | 15.7 | 0     | 0    |       |
| Mechanic ventilator |      |      |       |      |       |
| Yes                 | 15   | 78.9 | 0     | 0    | 0.000 |
| No                  | 4    | 21.0 | 11    | 100  |       |

#### 4. Discussion

From this study, it was found that the socio-demographic characteristics of stroke patients with COVID-19 pneumonia were mostly in the age range of 30 to 60 years, with the lowest age being 37 years and the oldest age being 80 years. Female is found

more than male. This study is in line with research conducted by Anastasia et al., who found that the gender of the most acute ischemic stroke patients with COVID-19 who entered the intensive care unit was female, but the age range of most patients was 60 to 69 years.<sup>2</sup> Age more than 55 years is one of the

risk factors for acute ischemic stroke, and the age group which is more than 65 years is susceptible to being exposed to the SARS-CoV2 virus and has a fairly high mortality rate. This age group also has a severe level of severity of COVID-19, which causes many patients in this age group to have a high mortality rate.<sup>3,4</sup> Based on the physiological theory of the aging process that as you age, your physiological ability to deal with various changes that disrupt the body's homeostasis process will be reduced so that an elderly person is more susceptible to illness or death. In this study, it was found that the most common comorbid factors suffered by stroke patients with COVID-19 pneumonia were hypertension, followed by diabetes mellitus, and a history of the previous stroke.

In chronic hypertension, there is a series of pathological changes that include fibrinoid necrosis, lipohyalinosis, and the formation of Charcot-Bouchard microaneurysms. Blood vessels that have undergone pathological changes will lose their elasticity and can no longer adjust to fluctuations in systemic blood pressure, so a sudden increase in blood pressure can cause blood vessels to burst. In addition, hypertension triggers the stiffness/rigidity of blood vessels by increasing collagen content. Hardening of the walls of blood vessels can result in impaired autoregulation in the form of difficulty in contracting or dilating to changes in systemic blood pressure. If there is a sudden drop in systemic blood pressure, failure of the cerebral vessels to dilate causes inadequate cerebral perfusion, and brain tissue ischemia occurs. If there is an increase in systemic blood pressure, failure of cerebral vessels to contract causes excessive cerebral perfusion and hyperemia, edema and bleeding occur.<sup>5</sup>

In this study, the most common type of stroke in stroke patients with COVID-19 was a hemorrhagic stroke, with a high NIHSS score at the time of admission. Stroke severity which is measured by the NIHSS, is a quantitative measure of stroke-related neurological deficits that can predict long-term stroke

outcomes. This is in accordance with The Global COVID-19 Stroke Registry data, which states that an increase in the severity score of stroke patients with COVID-19 has a worse prognosis than non-COVID patients.

In this study, it was found that most of the patients had hypercoagulable conditions and used mechanical ventilators because of respiratory failure. Elevated D-dimer is often found in severe COVID-19 patients and becomes a predictor of ARDS, intensive care unit care, and mortality.<sup>6</sup> Increased fibrinogen is common in COVID-19 and correlates with inflammation and IL-6 levels, but in severe cases, there may be a decrease in fibrinogen levels as a result of worsening coagulopathy.<sup>7</sup>

The main causes of death in COVID-19 are acute respiratory distress syndrome and progressive respiratory failure. The mechanism of respiratory failure in COVID-19 is not only caused by inflammatory factors but also because of micro thrombosis. Primary viral infection can cause alveolar injury and significant production of proinflammatory cytokines in COVID-19 patients.<sup>8</sup> Activation and recruitment of mononuclear cells and neutrophils leads to increased lung tissue and vascular endothelial damage. Hypoxia, endothelial injury, and a sustained inflammatory response increase the procoagulant state that can lead to pulmonary vascular micro thrombosis, leading to respiratory failure.

From the results of the epidemiological study at the Medical Faculty of Indonesia University and Jakarta Health Service in 2020 regarding the predictor factors of death in COVID-19 patients, it was found that old age, history of pneumonia, shortness of breath and risk factors for hypertension were the most significant factors influencing the mortality rate. Patients with a history of pneumonia and shortness of breath can have acute respiratory distress syndrome, and the incidence of hypertension can be doubled in the risk of death in COVID-19 patients.

## 5. Conclusion

The most demographic characteristics of stroke patients with COVID-19 pneumonia are the age range of 30-60 years, being female, and having hypertension as the comorbid factor. The most clinical characteristics were hemorrhagic stroke with severe NIHSS, hypercoagulable conditions, and respiratory failure. The use of a ventilator was significantly associated with the incidence of death from stroke with COVID-19 pneumonia. The outcome of a stroke patient with pneumonia COVID-19 is not only affected by the severity of the stroke but also by pneumonia due to COVID-19 infections.

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