

Profile of Risk Factors for Hemorrhagic Stroke in Patients at the Neurological Inpatient Installation of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January to June 2022

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ABSTRACT

Introduction: Stroke is one of the top ten causes of death worldwide. Hemorrhagic strokes are more common in men, and their risks increase with age. This study aimed to determine the risk factor profile for hemorrhagic stroke (intracerebral hemorrhage/ICH and subarachnoid hemorrhage/SAH) among patients in the neurological inpatient installation of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January to June 2022.

Methods: This study employed a descriptive observational method, utilizing secondary data obtained from the medical records of patients with hemorrhagic stroke at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January to June 2022. The data calculations were performed using the International Business Machines Corporation (IBM) Statistical Package for Social Sciences (SPSS) version 26. The variables examined in this study included the type of hemorrhagic stroke, non-modifiable risk factors, modifiable risk factors, and other risk factors.

Results: In total, 50 medical records were retrieved. The type of hemorrhagic stroke was dominated by intracerebral hemorrhage. Among them, 29 (58%) patients were males, 35 (70%) patients were 46-65 years old, 41 (82%) patients had hypertension, 16 (32%) patients had diabetes mellitus (DM), 19 (38%) patients had dyslipidemia, 8 (16%) patients had a history of smoking, 14% of patients had aneurysms. Only 2% of patients had arteriovenous malformation (AVM).

Conclusion: The dominant risk factors for hemorrhagic stroke were gender, age 46-65 years old, and hypertension.

Highlights:

1. Modifiable risk factors of hemorrhagic stroke were hypertension, DM, dyslipidemia, and smoking history.
2. Non-modifiable risk factors of hemorrhagic stroke were gender and age.

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Introduction

Stroke is a neurological emergency with an incidence that continues to rise annually. In 2019, stroke was one of the top ten causes of death in the world, with a percentage of 11%.¹ The number of stroke patients in Indonesia has been increasing, with the prevalence rising from 7% in 2013 to 13% in 2018.² According to a report by the Centers for Disease Control and Prevention (CDC) in 2022, stroke is the fifth leading cause of death for females in the United States (US).³ Approximately one in five women aged 55 to 70 years old experiences a stroke.³ Overall, this leads to stroke becoming the fifth leading cause of death and the primary cause of neurological disability in the US.³

Stroke is a medical condition that occurs when a blood vessel in the brain becomes blocked or ruptures, leading to an insufficient blood and oxygen supply to the brain and causing the death of brain cells.^{2,3} It can be classified into ischemic or blockage stroke and hemorrhagic or bleeding stroke.⁴ In ischemic stroke, blockage of blood vessels can disrupt blood flow to some regions of the brain.⁵ According to a previous study, ischemic stroke was more common than hemorrhagic stroke, with a percentage of 72.60% for ischemic stroke and 27.39% for hemorrhagic stroke.⁶

Hemorrhagic stroke is a subtype of severe stroke with high morbidity and mortality rates. It occurs when blood vessels in the brain rupture, resulting in bleeding within the brain.⁷ It can be further classified into intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH). Intracerebral hemorrhage occurs within the brain parenchyma, whilst SAH occurs within the subarachnoid space.⁵

An intracerebral hemorrhage causes symptoms by damaging or compressing brain tissue, often resulting in more severe headaches.⁵ Spontaneous ICH, also known as hemorrhagic stroke, is a significant cause of death and disability in Indonesia.⁷ On the other hand, SAH can cause cerebral dysfunction due to increased intracranial pressure, resulting in hypoperfusion, direct tissue damage, and toxic constituents from subarachnoid blood.⁵ Subarachnoid hemorrhage often occurs more in females compared to males.⁸

Based on age classification, the majority of hemorrhagic stroke patients were under 65 years old (85%), and more hemorrhagic strokes occurred in male patients (60%).⁶ When classified based on modifiable risk factors, more patients do not smoke than those who do. Additionally, there is only a small percentage of hemorrhagic stroke patients with a history of hypertension (20%) and a history of diabetes mellitus/DM (5%).⁶ Moreover, hemorrhagic stroke patients who have a history of dyslipidemia have a percentage of 26.7%.⁹ Studies related to risk factors for hemorrhagic stroke, especially ICH and SAH, have not been widely conducted. More studies are needed to determine the risk factors that

can affect both types of hemorrhagic stroke. Hemorrhagic stroke is one of the most severe subtypes of stroke, with a relatively high morbidity and mortality rate. More studies are needed to identify the risk factors involved in the occurrence of hemorrhagic stroke, particularly its two primary forms: ICH and SAH. By identifying the most common risk factors, it is expected that the findings of this study can serve as a basis for preventive efforts, thereby reducing the incidence of hemorrhagic stroke and minimizing the burden of long-term complications in patients.

Methods

This was a descriptive observational study with a retrospective method. A descriptive observational study is a type of research that only describes the data or characteristics of the object under study, without intervening or influencing the researcher.¹⁰ Meanwhile, a retrospective study analyzes already collected data before the study begins, involving existing records related to patient demographics, treatment received, and observed outcomes.¹⁰ Data were collected from the medical records of patients in the neurologic inpatient installation of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia. All statistical tests were performed using the International Business Machines Corporation (IBM) Statistical Package for Social Science (SPSS) version 26 for Windows.¹¹

The population or sample of this study was patients in the neurologic inpatient installation of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, who suffered from hemorrhagic stroke from January to June 2022. Inclusion criteria include patients in the neurologic inpatient installation at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, who had hemorrhagic stroke (ICH and SAH) on the first attack and who have complete medical records. Exclusion criteria included patients with non-hemorrhagic strokes and those with incomplete medical records.

The sampling technique used in this study was total sampling, utilizing secondary data obtained from the medical records of patients with hemorrhagic stroke at the neurologic inpatient unit of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, who met the inclusion and exclusion criteria. This study received ethical approval from the Research Ethics Committee of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia (No. 1253/LOE/301.4.2/III/2023).

Results

From the medical record data of patients admitted to the neurologic inpatient installation from 1 January to 31 June 2022, there were 50 patients suspected of hemorrhagic stroke.

Table 1. Type of stroke and site of bleeding distribution

Type of Stroke	n (%)
ICH	29 (58%)
SAH	9 (18%)
ICH+IVH	5 (10%)
SAH+IVH	3 (6%)
ICH+IVH+SAH	3 (6%)
ICH+SAH	1 (2%)
Site of Bleeding	n (%)
Basal ganglia	9 (18%)
Parietal lobes	7 (14%)
Pons	2 (4%)
Temporal lobes	2 (4%)
Corona radiata	2 (4%)
Nucleus caudatus	2 (4%)
Thalamus	2 (4%)
Basal cisterns	2 (4%)
Sylvian fissure	2 (4%)
Brain parenchyma	1 (2%)
Anterior interhemispheric	1 (2%)
Frontal lobes	1 (2%)
Frontoparietal lobes	1 (2%)
Temporoparietal lobes	1 (2%)
Putamen	1 (2%)
Midbrain	1 (2%)
Internal capsule	1 (2%)
No data	12 (24%)
Total	50 (100%)

ICH: intracerebral hemorrhage; IVH: intraventricular hemorrhage; SAH: subarachnoid hemorrhage

Source: Research data, processed

Based on Table 1, it can be seen that ICH stroke patients amounted to 29 people (58%), SAH stroke patients amounted to nine people (18%), ICH+intraventricular hemorrhage (IVH) patients amounted to six people (10%), SAH+IVH patients amounted to three people (6%), ICH+IVH+SAH patients amounted to three people (6%), whilst ICH+SAH patients amounted to only one person (2%). The most common type of stroke in patients within the neurological inpatient installation of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, between January and June 2022 was ICH.

Based on Table 1, it can be seen that the location of hemorrhage in patients with hemorrhagic stroke in the neurological inpatient installation was mainly in the basal ganglia of as many as nine patients (18%). However, 12 patients had no data regarding the location of their bleeding (24%).

Table 2. Gender and type of stroke by gender distribution

	Male n (%)	Female n (%)	Total
Stroke patients	29 (58%)	21 (42%)	50 (100%)
Type of Stroke			
ICH	20 (69%)	9 (31%)	29 (100%)
SAH	3 (33%)	6 (67%)	9 (100%)
ICH+IVH	2 (40%)	3 (60%)	5 (100%)
SAH+IVH	0 (0%)	3 (100%)	3 (100%)
ICH+IVH+SAH	3 (100%)	0 (0%)	3 (100%)
ICH+SAH	1 (100%)	0 (0%)	1 (100%)
Total	29 (58%)	21 (42%)	50 (100%)

ICH: intracerebral hemorrhage; IVH: intraventricular hemorrhage; SAH: subarachnoid hemorrhage

Source: Research data, processed

Based on Table 2, the total number of patients was 50, comprising 29 males (58%) and 21 females (42%). It can be concluded that the most common gender found in hemorrhagic stroke patients within the neurologic inpatient

installation of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January to June 2022 was males.

Based on Table 2, there were 29 patients with ICH and nine patients with SAH. Most ICH patients were males, with a total of 20 people (69%). Meanwhile, SAH was predominantly female, with a total of six patients (67%). Both ICH and IVH patients were predominantly female, accounting for 60% of the total. The same can be said about SAH and IVH patients, who were also dominated by females, with a percentage of 100%. Lastly, patients with ICH, IVH, and SAH were predominantly male, with a percentage of 100% for ICH and SAH.

Table 3. Age distribution

Age Group	n (%)
26-45 years old	10 (20%)
46-65 years old	35 (70%)
>65 years old	5 (10%)
Total	50 (100%)

Source: Research data, process

In this study, the age of hemorrhagic stroke patients was grouped into three age groups: adults (26-45 years old), elderly (46-65 years old), and seniors (>65 years old). From the data obtained, the youngest hemorrhagic stroke patient was 26 years old, while the oldest was 75 years old. Based on Table 3, 10 patients fell into the 26-40 years old age group, 35 patients fell into the 46-65 years old age group, and five patients fell into the >65 years old age group. Therefore, it can be concluded that most hemorrhagic stroke patients were in the age group of 46-65 years old (elderly), with 35 patients (70%).

Table 4. Modifiable risk factors of hemorrhagic stroke distribution

Risk Factors	Yes	No	No Data	Total
Hypertension	41 (82%)	9 (18%)	0 (0%)	50 (100%)
Diabetes mellitus	16 (32%)	34 (68%)	0 (0%)	50 (100%)
Dyslipidemia	19 (38%)	31 (62%)	0 (0%)	50 (100%)
Smoking history	8 (16%)	42 (84%)	0 (0%)	50 (100%)

Source: Research data, process

Based on Table 4, there were 41 patients with hypertension (82%) and nine patients without hypertension (18%). Hemorrhagic stroke patients in the neurologic inpatient installation of Dr. Soetomo General Academic Hospital from January to June 2022 were dominated by patients with hypertension (41 patients). Sixteen patients suffered from DM (32%), and 34 patients did not suffer from DM (68%). This shows that most hemorrhagic stroke patients in the neurologic inpatient unit at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January to June 2022 did not suffer from DM.

Based on Table 4, there were 19 patients with dyslipidemia (38%) and 31 patients without dyslipidemia (62%). This shows that hemorrhagic stroke patients in the neurologic inpatient installation of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January to

June 2022, who suffered from dyslipidemia, were only 38% and the majority of patients did not suffer from dyslipidemia, as much as 62%.

Based on Table 4, eight patients had a history of smoking, and 42 patients did not have a history of smoking. Therefore, it can be concluded that the majority (84%) of hemorrhagic stroke patients in the neurologic inpatient installation of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January to June 2022 did not have a history of smoking.

Table 5. Other risk factors for hemorrhagic stroke distribution

Risk factors	Yes	No	No Data	Total
Aneurysm	7 (14%)	4 (8%)	39 (78%)	50 (100%)
AVM	1 (2%)	10 (20%)	39 (78%)	50 (100%)

AVM: arteriovenous malformation

Source: Research data, process

Based on Table 5, it was found that there were only seven patients (14%) who experienced aneurysms and one patient (2%) who experienced an arteriovenous malformation (AVM) in the neurologic inpatient unit of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January to June 2022.

Discussion

Based on the data obtained from hemorrhagic stroke patients, the most frequent form of hemorrhagic stroke was ICH, with 29 (58%) patients, whilst there were only 9 (18%) patients with SAH. In the medical record data, there were several other patients with Siriraj score ≥ 1 , indicating a hemorrhagic stroke. However, further supporting examinations are required to confirm the diagnosis. These results are similar to the study conducted by Yunus, *et al.* (2024), where the most common type of hemorrhagic stroke was ICH (73.4%), while SAH patients had a percentage of 26.6%.⁹ In another study conducted by Muharram, *et al.* (2019), IVH was found to be more common than non-IVH, with 128 patients with IVH and 119 patients with non-IVH reported.¹²

In Table 1, five patients were reported to have both ICH and IVH, with a percentage of 10%. In a study by Irsyad, *et al.* (2020) conducted at Haji Adam Malik General Hospital, Medan, in 2018-2019, the study found 159 patients with ICH+IVH.¹³ Table 1 also presents results of the patients' computed tomography (CT) scan, where it can be seen that the location of hemorrhage in hemorrhagic stroke patients was mainly in the basal ganglia, with nine patients (18%), followed by bleeding in the parietal lobe (14%). In a study conducted by Mahayani, *et al.* (2019) at Prof. Dr. I Goesti Ngoerah Gde Ngoerah General Hospital, Denpasar, 17 patients with hemorrhagic strokes had their bleeding locations localized within the basal ganglia.¹⁴ This aligns with the study conducted by Melisa, *et al.* (2020), which found CT scan results of bleeding in the basal ganglia in 95 patients (45.89%).¹⁵ However, different results were found in another study conducted by Yusastra, *et al.* (2021),

where patients with bleeding in the basal ganglia were found to be only 16.6%.¹⁶ In this study, the most common location for bleeding was in the thalamus (66.6%).¹⁶

Hemorrhagic stroke commonly causes bleeding in the basal ganglia (50%), cerebral lobes (10-20%), thalamus (15%), pons and brainstem (10-20%), and cerebellum (10%).² Spontaneous hemorrhages located in the basal ganglia are primarily due to uncontrolled hypertension.¹⁷ Hemorrhage in the basal ganglia most commonly occurs in the putamen and internal capsule, as the lenticulostriate arteries that supply blood to the basal ganglia are susceptible to high blood pressure. Bleeding in the basal ganglia can be asymptomatic if the bleeding is minor and remains within the basal ganglia. However, widespread bleeding can cause hemiparesis on the contralateral side.⁴

Lestari, *et al.* (2020) stated that the majority of hemorrhagic strokes occurred in females, with an incidence rate of 10 out of the 17 patients.¹⁸ According to Rahayu (2023), out of 200 patient data, 52% of patients were males.¹⁹ A previous study also conducted at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January to October 2018 reported that hemorrhagic stroke patients were dominated by males, namely 12 patients (60%).⁵ Based on Table 2, the results obtained in this study align with those of several previous studies. It was found that males suffered more hemorrhagic strokes, with 29 patients (58%), while females were only 21 patients (42%). Based on Table 2, it was found that the prevalence of ICH was higher in males, specifically 20 patients. Men who have unhealthy lifestyles, such as frequent smoking and consuming alcohol, can affect their health conditions.¹⁹

In contrast, SAH was dominated by females, as many as six people. This is similar to a systematic review conducted by Bolouki, *et al.* (2019), where the prevalence of subarachnoid hemorrhage in females was 1.24 times higher than that of males.²⁰ The cause of the higher occurrence of SAH in females might be due to hormonal factors such as estrogen.²⁰ During menopause, estrogen levels will decrease naturally, likely playing a role in the pathogenesis of the formation and rupture of blood vessels found in aneurysm cases.⁷

In Table 2, there were five patients with both ICH and IVH, of whom the majority were females, accounting for as many as three people (60%). These results differ from a study conducted by Irsyad, *et al.* (2020), which found 159 patients with ICH and IVH, with 95 patients (60.4%) being males.¹³ The risk of stroke increases with age, as the aging process causes all organs of the body to experience a decrease in function, including cerebral blood vessels. The incidence of stroke in old age is higher than that of young adults. Age is one of the many non-modifiable risk factors. As age increases, the elasticity of blood vessels progressively declines.²

Based on Table 3, hemorrhagic stroke patients in the neurologic inpatient installation of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January to June 2022 were dominated by the age group of 46-65 years old (70%), and the least common age group was in the age group of >65 years old (10%). This aligns with a study conducted by Sibagariang (2023) at Haji Adam Malik

General Hospital, Medan, which reported that 52.7% of stroke hemorrhagic patients were in the 46-65 years old age group.²¹ Stroke prevalence varies significantly by age, with strokes occurring at a younger age having a higher risk of mortality. Risk factors for stroke at a young age can be influenced by lifestyle factors such as smoking habits.² At the age of >65 years old, hemorrhagic stroke is mainly caused by cerebral amyloid angiopathy (CAA), as the prevalence of CAA increases with age. Cerebral amyloid angiopathy occurs due to amyloid deposition, leading to blood vessel fragility and an increased risk of intracerebral hemorrhage.²²

Based on Table 4, it was found that 41 patients (82%) in the neurologic inpatient installation of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, between January and June 2022 suffered from hypertension. In a study conducted by Wong, *et al.* (2022), it was found that hemorrhagic stroke patients with hypertension had a percentage of 86.42%.²³ Meanwhile, in a study conducted at Prof. Dr. I Goesti Ngoerah Gde Ngoerah General Hospital, Denpasar, hypertension was the dominant risk factor in hemorrhagic stroke (77.8%).¹⁴ In a study conducted by Saputra, *et al.* (2019), it was also found that hypertension was the most influential risk factor for stroke.²⁴ Hypertension can cause rupture of blood vessels in the brain, causing bleeding within the brain.²⁴ Increased systolic and diastolic blood pressure is most closely related to the incidence of hemorrhagic stroke. Patients with untreated hypertension have a high incidence of hemorrhagic stroke. Although hypertension has been treated, it remains a significant risk factor for hemorrhagic stroke. Therefore, even if all hypertensive patients receive treatment, there may still be an increased risk of stroke.²⁴

According to a study by Sari, *et al.* (2021), DM is a state of hyperglycemia due to a deficiency in insulin secretion.²⁵ Hyperglycemia can cause damage to the walls of large blood vessels and peripheral blood vessels. In addition, it can enhance platelet aggregation, and both processes contribute to the development of atherosclerosis, which may lead to stroke due to vascular occlusion in the brainstem. Diabetes mellitus is present in an average of 26% of hemorrhagic stroke patients and 33% of ischemic stroke patients. It can increase the risk of ischemic and hemorrhagic stroke by 2.27 times and 1.56 times, respectively.

Based on Table 4, it was found that the number of hemorrhagic stroke patients in the neurologic inpatient installation of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, between January and June 2022, who suffered from DM was only 16 people (32%). This means that the majority of patients did not suffer from DM, with 34 people (68%). This is similar to a study conducted by Hartono, *et al.* (2019), where 14 hemorrhagic stroke patients (38.89%) were reported to have DM, whilst the other 22 patients (61.11%) were reported not to have DM.²⁶ Table 4 also shows that there were 16 people (38%) who had a history of dyslipidemia among the hemorrhagic stroke patients in the neurologic inpatient installation of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January to June 2022. The results of this

study align with a study conducted by Sibagariang (2023) at Haji Adam Malik General Hospital, Medan, where there were only 29% patients who had a history of dyslipidemia out of the 93 patients who suffered hemorrhagic stroke.²¹ In a different study conducted at Prof. Dr. I Goesti Ngoerah Gde Ngoerah General Hospital, Denpasar, hemorrhagic stroke patients who had a history of dyslipidemia had a percentage of 26.7%.¹⁴ Dyslipidemia is a more common risk factor for ischemic stroke than hemorrhagic stroke.¹⁴

In this study, the majority of patients were not dyslipidemic. However, despite being less prevalent than hypertension, dyslipidemia must still be considered, as the instability of cholesterol levels can increase the fragility of the endothelial membrane. An increase in endothelial fragility can lead to angionecrosis and microaneurysm formation, which can then lead to hemorrhagic stroke.²⁷ Table 4 also shows that out of a total of 50 hemorrhagic stroke patients in the neurologic inpatient installation of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January 2022 to June 2022, 8 people (16%) had a history of smoking, and most did not have a history of smoking (84%). This is similar to a study conducted by Sibagariang (2023) at Haji Adam Malik General Hospital, Medan, where most hemorrhagic stroke patients did not have a history of smoking.²¹

Out of the eight patients who smoked, the most significant number of cigarettes consumed was one pack/day. A non-smoker is six times less likely to have a stroke than a person who smokes 20 cigarettes a day.²⁸ Cigarettes contain thousands of harmful chemicals that are absorbed into the bloodstream from the lungs. These chemicals alter and damage cells, affecting bodily functions. Carbon monoxide reduces the amount of oxygen in the blood, while nicotine increases heart rate and blood pressure.²⁹ The duration and quantity of smoking directly correlate with the amount of harmful chemicals and toxins that enter the body. The presence of toxic substances can damage the walls of blood vessels, possibly leading to the development of atherosclerosis or aneurysms.²⁸

Cerebral aneurysm is a recognized trigger for spontaneous SAH. Additionally, this condition often shows no symptoms. However, if a rupture occurs, it can result in severe complications.³⁰ Based on Table 5, it was found that hemorrhagic stroke patients in the neurologic inpatient installation of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January to June 2022, had only seven patients (14%) who suffered from aneurysms, most commonly occurring in SAH patients. A brain AVM is a condition characterized by irregular and weakened blood vessels. Arteriovenous malformations can lead to neurological problems through three main pathophysiological mechanisms. These abnormal blood vessels are prone to rupture, which can cause bleeding in areas such as the subarachnoid space, intraventricular space, or, most commonly, within the brain tissue.³¹ Based on Table 5, out of all the hemorrhagic stroke patients in the neurologic inpatient installation of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January to June 2022, only one ICH patient (2%) was reported to have AVM.³¹

Strengths and Limitations

The strength of this study lies in its comprehensive data collection through medical records. However, the sample used was not large enough because the data collected were limited to only one location, namely the neurologic inpatient unit of Dr. Soetomo General Academic Hospital in Surabaya, Indonesia.

Conclusion

It can be concluded that the type of hemorrhagic stroke in patients within the neurologic inpatient installation of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January to June 2022 was dominated by ICH. Among hemorrhagic stroke patients, ICH was more prevalent in males, whereas SAH was more common in females, particularly within the 46–65 years old age group. The location of bleeding was most commonly found in the basal ganglia. The majority of hemorrhagic stroke patients in the neurologic inpatient installation of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January to June 2022 had hypertension. It is recommended to conduct more research on other risk factors that may contribute to hemorrhagic strokes.

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Conflict of Interest

The authors declared there is no conflict of interest.

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Ethical Clearance

This study had received ethical clearance from the Ethical Committee for Health Research Dr. Soetomo General Academic Hospital, Surabaya, Indonesia (No.1253/LOE/301.4.2/III/2023) on 08/03/2023.

Authors' Contributions

Designed the study and drafted the manuscript: ANS and MSA. Collected data and performed background literature review: ANS and MSA. Results and discussion: ANS, MSA, MAP, and SS. All authors reviewed and approved the final version of the manuscript.

Data Availability

N/A.

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