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Ischemic Stroke Risk Factor Profile at Prof. Dr. W. Z. Johannes Hospital, Kupang, East Nusa Tenggara

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ABSTRACT

Introduction: In Indonesia, ischemic stroke is a major public health issue. Clinical data correlates with an ischemic stroke patient's prognosis. **Objective:** This study aimed to provide an overview of clinical data in ischemic stroke patients from October 2020 to December 2021. **Methods:** This was a retrospective, descriptive study using medical records. A non-probability purposive sampling strategy with a total sampling method is used in this study. Age, gender, cardiac comorbidities, diabetes, repeated strokes, blood laboratory exams, electrolyte tests, alcohol consumption, and smoking habits were all observed variables. **Results:** The sample consisted of 242 ischemic stroke patients. The majority of patients (32.23%) were in the 61 to 70 age group, and men (57.4%) made up the majority of the sex group. Then, cardiac comorbidities were dominated by coronary artery disease (CAD), with 33 patients (57.4%) with 4 deaths (12.1%), while 15 patients (6.19%) were found with atrial fibrillation (AF), with 7 deaths (46.67%). Hypertension was found in 81.40% of patients, diabetes in 26.03% of patients, and recurrent stroke in 31.40% of patients. Active smokers make up 52.06% of all patients, and 18.18% are heavy alcohol drinkers. The majority of patients showed blood and electrolyte levels within the normal range, except for an increased leukocyte count and a decreased potassium level. **Conclusion:** The main risk factors obtained sequentially are hypertension, coronary artery diseases, active smokers, diabetes, and excessive alcohol consumption.

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INTRODUCTION

Stroke is a major public health concern in Indonesia, as it is in many other countries worldwide. According to the World Health Organization, stroke is the second leading cause of death and the third leading cause of disability around the world. In Indonesia, stroke is also a significant cause of morbidity and mortality. According to the Ministry of Health's Basic Research conducted in 2018, the prevalence of stroke in Indonesia was 10.6% of the entire population (>15years old), or around seven hundred thousand people. Stroke prevalence was higher in rural areas than in urban areas, with 0.7% and 0.5%, respectively. Moreover, stroke was more prevalent in people aged 55 years and older, with a prevalence of more than 30% in this age group. In Indonesia, several risk factors contribute to the development of stroke. The major risk factors include hypertension, smoking, diabetes mellitus, hypercholesterolemia, obesity, physical inactivity, and an unhealthy diet. In Indonesia, a lot of people have these risk factors, which makes the chance of having a stroke higher. According to 2018 Basic Health Research, hypertension prevalence was 34.1% and diabetes mellitus prevalence was 6.9%. Furthermore, the prevalence of smoking was 26.9%, and the prevalence of obesity was 6.1%.[1]

A stroke, also known as a cerebrovascular accident (CVA), occurs when there is a sudden disruption in the blood supply or blood vessels in the brain. About 85% of strokes are caused by a lack of blood flow (ischemic), while the remaining cases involve bleeding in the brain (hemorrhagic).[2] There are several risk factors for stroke, which can be classified as non-modifiable and modifiable factors. Age, race, gender, and genetics are non-modifiable risk factors that cannot be changed. Modifiable risk factors, on the other hand, include hypertension, alcohol consumption, hyperlipidemia, diabetes, and smoking habits, all of which can be controlled or treated through lifestyle changes or medical intervention.[3]

Due to its effect on blood-related factors, alcohol consumption may increase the risk of both ischemic and hemorrhagic strokes. Alcohol impacts several blood clotting and fibrinolysis factors, including plasminogen activator, platelet count, platelet aggregability, and fibrinogen levels. These alcohol-induced effects may lead to the formation of blood clots in some cases and increase the risk of bleeding in others. However, few clinical studies have looked into these effects and their relationship to the occurrence of strokes.[4] A recent study showed a J-shaped relationship between consumption of alcohol and stroke risk, indicating that alcohol can both elevate blood pressure and increase high-density lipoprotein cholesterol levels, which have opposing effects on stroke risk. Continuous excessive drinking increases stroke risk, but moderate drinking lowers it. Acetate's role in energy metabolism and insulin sensitivity may contribute to moderate alcohol consumption's protective effect.[5] An ischemic stroke happens when the blood supply to the brain is reduced due to a thrombotic or embolic event. During a thrombotic event, the blood vessel itself becomes dysfunctional due to conditions like atherosclerotic disease, arterial dissection, fibromuscular dysplasia, or an inflammatory condition. This results in an obstruction of the blood flow to the brain. On the other hand, an embolic event occurs when foreign material, usually from another region of the body, obstructs blood flow through the affected vessel.

According to a clinical profile of stroke patients at Sanglah Hospital, Bali, the most affected age group is 50–59 years, with ischemic stroke being the most prevalent type encountered.[6] A recent study on COVID-19-positive patients with ischemic stroke at the University of Indonesia Hospital in Depok found that the majority of patients are over the age of 55.[7] Several clinical studies showed that blood laboratory examinations may be correlated to a patient's prognosis. An increased white blood cell (WBC) count on admission has been correlated with increased mortality in stroke patients and could be used as a risk factor marker.[8,9] A study on electrolyte levels has also found that they can predict a patient's prognosis by preventing complications related to electrolyte imbalance.[10] In ischemic stroke patients, the blood is associated with a poor prognosis at 30 days.[11] Ischemic stroke patients also tend to have a greater NIHSS if they have a higher platelet count or platelet index.[12] Other clinical risk factors, such as cardiovascular disease, have been proven to worsen patient prognosis, particularly in atrial fibrillation (AF), coronary artery diseases (CAD), valvular heart diseases (VHD), and premature ventricular contraction (PVC).

OBJECTIVE

The objective of this study was to learn about the clinical and laboratory examination values of ischemic stroke patients, as well as to determine the profile of ischemic stroke risk factors at Prof. Dr. W. Z. Johannes Hospital, Kupang, East Nusa Tenggara, Indonesia.

METHODS

This was a descriptive observational study with retrospective medical record data from ischemic stroke patients at Prof. Dr. W. Z. Johannes Hospital, Kupang, from October 2020 to December 2021. The population of this study was all ischemic stroke patients at Prof. Dr. W. Z. Johannes Hospital, Kupang, for the period

October 2020 to December 2021. The stroke patients in the inpatient units were chosen for this study using total sampling, which is the method of collecting all samples that meet the inclusion and exclusion criteria between October 2020 and December 2021. Patients with a diagnosis of ischemic stroke met the inclusion criteria, while patients with a diagnosis of a non-ischemic stroke (hemorrhagic stroke, subarachnoid hemorrhage, or mimic stroke) did not.

The non-random sampling method was used to acquire data for this study. The study focused on four variables: gender, age, cardiac comorbidity, and blood laboratory studies. Medical records of stroke patients who got treatment between October 2020 and December 2021 were collected for the purpose of data collection. The acquired data will be processed, which includes coding, entering, and cleaning. To help in data capture and analysis, each variable was assigned a unique code. The data was subsequently entered into a computer or laptop via software such as Microsoft Office. During the cleaning stage, errors that may have happened through the analysis are identified and corrected. The data is then sorted by study variables, and a table is created to make the data easier to present.

RESULTS

The medical records of 242 patients were obtained. Patient data including name, gender, age, address, blood test results, hospital admission and discharge dates, medical record number, and cardiac morbidity type were recorded.

Sample distribution by age

Based on the obtained data (Table 1), the highest percentage of smokers among stroke patients was found in those between the ages of 61 and 70 (32.23%), while the lowest percentage was found in those between the ages of 21 and 30 (0.4%). A total of 242 patients were included in the study for these results, and their ages ranged from 23 to 100 (mean = 60.5, median = 61).

Table 1. Sample distribution by age

Age (years)	n	%	Median (d/dL)
21-30	1	0.41	61
31-40	6	2.48	
41-50	46	19.01	
51-60	63	26.03	
61-70	78	32.23	
71-80	35	14.46	
81-90	11	4.55	
91-100	2	0.83	

Sample distribution by gender

Based on the obtained data (Table 2), the majority of the sample patients were male, with 139 patients (57.4%), while 103 patients were female (42.5%).

Table 2. Sample distribution by age

Gender	n	%
Male	139	57.43%
Female	103	42.56%

Sample distribution by clinical risk factors (hypertension status, diabetes status, and recurrent stroke)

Based on the obtained data (Table 3), the majority of patients (81.4%) were diagnosed with hypertension, while 45 patients (18.59%) were not. There was a history of diabetes type I and II in 63 patients (26.03%) and a history of recurrent stroke in 76 patients (31.40%).

Table 3. Sample distribution by clinical risk factors

Clinical risk factor	n	%
Hypertension	197	81.40%
Diabetes	63	26.03%
Recurrent stroke	76	31.40%

Sample distribution by cardiac comorbidities

Based on the obtained data (Table 4), there were 50 patients with comorbidities, dominated by CAD with 33 patients (57.4%) and 4 deaths (12.1%), while 15 patients (6.19%) were found with AF and 7 deaths (46.67%). There was one patient (2%) with valvular heart disease and one patient (2%) with premature ventricular contraction.

Table 4. Sample distribution by cardiac comorbidities

Cardiac comorbidities	n	%	Death	Mortality Rate (%)
AF	15	6.19	7	46.67
CAD	33	13.63	4	12.12
VHD	1	0.41	-	
PVC	1	0.41	-	

Sample distribution by habitual risk factor

Based on the obtained data (Table 5), 126 patients (52.06%) reported a history of smoking, while 44 patients (18.18%) reported a history of heavy (more than 3 drinks per day) alcohol consumption.

Table 5. Sample distribution by habitual risk factor

Habitual risk factor	n	%
Active smoker	126	52.06%
Heavy alcohol consumption	44	18.18%

Sample distribution by blood test result

Several data were acquired from the blood test, including hemoglobin levels, leukocyte levels, platelet count, platelet distribution width (PDW), blood urea

nitrogen, and creatinine. Hemoglobin levels were divided into three groups: 157 patients (64.8%) had levels ranging from 12 to 16 g/dL, 65 patients (26.8%) had levels ranging from 3 to 11.99 g/dL, and 20 patients (8.2%) had levels ranging from 16 to 20 g/dL (median = 13.4 g/dL) (Table 6).

Leukocyte level was raised in 125 patients (51.65%) with a range of 10.103–45.103/mm, 114 patients (47.11%) with a range of 4.103–10.103/mm, and decreased in 3 patients (1.24%) with a range of 1.103–3.99/mm (median = 10.120) (Table 6). The majority of the patients (86.36%) showed a thrombocyte count within the normal range of 150.103–400.103/µL; 13 patients (5.37%) showed a raised thrombocyte count of 400.103–800.103/µL; and 20 patients (8.26%) showed a decreased thrombocyte count (median = 250.103) (Table 6).

Platelet distribution width (PDW) increased in 97 patients (40.08%) within the range of 17.01–30 fL, 129 patients (53.31%) within the normal range of 9–17 fL, and 16 patients (0.06%) within the range of 1–8.99 fL (median = 12.9 fL) (Table 6). The majority of patients (69.01%) showed a normal range of 6–20 mmol/L BUN level, 65 patients (26.86%) showed an increased BUN level, and 10 patients (0.04%) showed a decreased BUN level (median = 14.5 mmol/L) (Table 6). The majority of patients (84.29%) showed a normal range of 0–1.4 mmol/L blood creatinine level, while 38 patients (15.7%) showed an increased blood creatinine level (median = 0.89 mmol/L) (Table 6).

Table 6. Sample distribution by blood test

Blood test	Frequency	%	Median
Hemoglobin (g/dL)			
16.01–20	20	8.26%	13.4 (g/dL)
12–16	157	64.88%	
3–11.99	65	26.86%	
Leukosit (cells/mm)			
10.01–45	125	51.65%	10.12 (cells/mm)
4–10	114	47.11%	
1–3.99	3	1.24%	
Thrombocyte (cells/µL)			
400.01–800	13	5.37%	250 (cells/µL)
150–400	209	86.36%	
0–149.9	20	8.26%	
PDW (fL) range			
17.01–30	97	40.08%	12.9 (fL)
9–17	129	53.31%	
1–8.99	16	6.61%	
BUN (mmol/L) range			
20.01–150	65	26.86%	14.5 (mmol/L)
6–20	167	69.01%	
0–5.99	10	4.13%	
Creatinine (mmol/L) range			
1.41–30	65	26.86%	0.89 (mmol/L)
0.001–1.4	167	69.01%	

Sample distribution by electrolyte study

The majority of the patients' sodium levels (88.43%) were within the normal acceptable range of 132–147 mmol/L; 13 patients (5.37%) showed an increased sodium level; and 15 patients (6.2%) showed a decreased sodium level (median = 139 mmol/L) (Table 7). Potassium levels in 123 patients (50.83%) showed a normal acceptable range of 3.5–4.5 mmol/L; 102 patients (42.15%) showed decreased potassium levels; and 17 patients (0.07%) showed an increased potassium levels (median = 3.535 mmol/L) (Table 7). Chloride levels in 189 patients (78.10%) showed a normal acceptable range of 96–111 mmol/L; 36 patients (14.88%) showed increased potassium level, while 7 patients (0.07 %) showed decreased sodium level (median = 105 mmol/L) (Table 7). Calcium level in 113 patients (46.69 %) showed normal acceptable range of 2.2-2.55 mmol/L, 89 patients (36.78 %) showed increased calcium level, while 40 patients (16.53%) showed decreased calcium levels (median = 2.5 mmol/L) (Table 7).

Table 7. Sample distribution by electrolyte level

Electrolyte	Range (mmol/L)	Frequency	%	Median (mmol/L)
Sodium (Na)	147.1–170	13	5.37	139
	132–147	214	88.43	
	110–131.99	15	6.2	
Potassium (K)	4.51–6	17	7.02	3.553
	3.5–4.5	123	50.83	
	1–3.49	102	42.15	
Chloride (Cl)	111.01–160	36	14.88	105
	96–111	189	78.10	
	70–95.99	17	7.02	
Calcium (Ca)	2.56–5	89	36.78	2.5
	2.2–2.55	113	46.69	
	0.1–2.19	40	16.53	

DISCUSSION

This study found that ischemic stroke most commonly occurs in patients between the ages of 61 and 70, which is consistent with a previous study showing that stroke is more common in patients over the age of 65, accounting for about three-quarters of all strokes.[13] The majority of the 242 samples who suffered an ischemic stroke were male. Previous studies have shown that women have a lower risk of suffering an ischemic stroke.[14] This feat of lower risk could be explained by estrogen's ability to increase nitric oxide production, which helps widen blood vessels and prevents blood clots from forming; its ability to reduce inflammation and oxidative stress in blood vessels; its ability to increase production of high-density lipoprotein (HDL) and decrease production of low-density lipoprotein (LDL); and its neuroprotective effects on the brain.[15]

According to our study, CAD has a mortality rate of 12.12% and is the most common cardiac comorbidity. Similar to this finding, a previous study estimated that about a third of all ischemic strokes are associated with underlying CAD.[16] CAD has been known to increase mortality in patients with a higher recurrence rate of ischemic stroke and an increased prevalence of other cardiovascular and non-cardiovascular complications caused by plaque buildup in the arteries.[17]

Atrial fibrillation has been known as one of the leading risk factors for ischemic stroke. In this study, we found that AF is the second most prevalent cardiac comorbidity in 6% of 242 patients, with a mortality rate of 46.67%. The number of ischemic stroke patients diagnosed with AF in this study is similar to a study conducted in South Africa, where 2% of all strokes are related to AF, with 80% of these patients having ischemic stroke.[18] This study further emphasizes the important role of AF and its pathophysiology in ischemic stroke patients by causing blood turbulence and the formation of blood clots, which is a modifiable and manageable risk factor in ischemic stroke patients.[19]

Hypertension was determined to be the main clinical risk factor in this study, with 81.40% of patients having hypertension prior to admission. Hypertension, or high blood pressure, is a major risk factor for ischemic stroke, which occurs when a blood vessel supplying blood to the brain becomes blocked. Brain blood vessels can be damaged by chronic hypertension, rendering them more susceptible to constriction and blockage.[20]

Stroke treatment depends heavily on blood pressure management, as uncontrolled hypertension both increases the risk of stroke and worsens recovery results. The purpose of blood pressure management during a stroke is to lower blood pressure to a safe level without negatively affecting blood flow to the brain. Lowering blood pressure after an acute ischemic stroke can help minimize the chances of hemorrhagic transformation, which occurs when a previously ischemic region of the brain begins bleeding.[21]

Diabetes mellitus (DM) was identified in 26.03% of the patients. Diabetes is a major risk factor for stroke. People with diabetes are two to four times more likely to have a stroke than people who don't have diabetes. The mechanisms underlying this association involve the pathophysiological changes that occur in diabetes, including endothelial dysfunction, inflammation, oxidative stress, and changes in blood clotting factors, all of which can increase the risk of blood vessel damage and stroke.[22] However, the exact mechanisms behind this finding are still unknown.

In this study, the majority of patients showed a normal hemoglobin level. However, a considerable number of patients showed anemia and a high hemoglobin level, which is associated with a worse outcome.[23] Furthermore, more detailed and specific studies are needed to confirm and discover the underlying mechanism of this outcome in stroke

patients. Similar to previous studies, leukocyte levels were increased in the majority of patients and were related to a more severe outcome.[24] Leukocytosis may have been caused by several factors, including the underlying health status of the patients and the degree of inflammation triggered by the stroke alone, making the leukocyte count a considerable prognostic value.[25]

The majority of the patients had normal thrombocyte counts and platelet distribution widths (PDW). Increased thrombocyte count and PDW are also associated with a worse outcome due to the formation of thrombosis in the brain, which causes further damage.[26,27] Most patients also had normal BUN and creatinine levels. However, a considerable number of patients had an increased level, which is associated with a worse outcome. Rong Peng *et al.* showed an association between BUN and creatinine levels and an increased risk of stroke in recent study.[28]

Patients who had a history of stroke made up 31.40% of the sample in this study. Compared to the recurrence rates of 14.2% and 18.8% seen in several studies during a 5-year period, our findings showed a higher incidence of recurrent stroke.[29,30] However, our findings were similar with a systematic review study conducted by Kolmos *et al.* which found a 35.1% incidence rate after 5 years of initial stroke.[31] This high recurrent stroke incidence rate is associated with multiple risk factors; by managing risk factors, the incidence rate of recurrent stroke is expected to be reduced.[32]

The majority of patients had normal sodium, potassium, chloride, and calcium levels, according to the electrolyte study. However, there is a marked difference in decreased potassium levels. This finding is similar to a previous study by Fukaguchi *et al.* which showed that ischemic stroke patients have a considerable reduction in potassium levels.[33] Electrolyte imbalances, especially sodium and potassium levels, are associated with worse stroke outcomes. The relationship between electrolyte imbalances and stroke outcomes is complex and involves multiple factors, thus requiring further studies.

Electrolyte imbalances can be a sign of problems with the fluidand electrolyte balance. These problems can affect blood pressure, blood chemical concentrations, and cerebral blood flow, all of which can lead to brain injury. Furthermore, electrolyte imbalances may also affect the function of platelets, blood clotting, and inflammation, all of which are involved in the development of stroke.[10]

Smoking has long been associated with cultural and heritage-related habits in Indonesia.[34] According to several studies, 39.5% of Indonesians aged 15 and over are active smokers in 2016 which is 7.4% higher than the global average.[35] In this study, a high proportion of patients (52.06%) are or were active smokers. It is important to emphasize the benefits of smoking cessation, as one study found that those who quit smoking had a 31% reduced risk of recurrent stroke and a 30% lower risk of death within the first year after a stroke than those who continued smoking. The results also suggest that the longer a person abstained from smoking after a stroke, the lower the risk of recurrent stroke and death.[36] Nicotine, a chemical present in cigarettes, accelerates the development of vascular disease by stimulating the release of catecholamines, which boosts both heart rate and blood pressure. These unfavourable changes in blood flow dynamics have been connected to the progression of atherosclerosis. Additionally, nicotine-induced catecholamine release enhances the tendency of platelets to clump together.[37]

In this study, around 18.18% of patients reported drinking more than three alcoholic beverages each day. The association between alcoholic beverage consumption and the risk of ischemic stroke has been uncertain over time. Mukamal *et al.* found that compared to abstainers, those who drank moderately (defined as one to two drinks per day) had a reduced risk of ischemic stroke, whereas those who drank more than three drinks per day had a higher risk of stroke.[38] This J-shaped association is thought to be caused by elevated blood pressure and increased high-density lipoprotein cholesterol levels, which have opposing effects on stroke risk and alcoholic beverage consumption. The impacts of alcohol intake on blood pressure appear to vary with the amount of alcohol consumed, with chronic heavy drinking association to an elevation in blood pressure, as shown in recent studies.[5] Another study on alcohol as one of the drug use disorders that it stimulates microglia, which changes the pattern of neuroinflammation.[39] Neuroinflammation contributes to brain damage during the early stages of ischemic stroke. In both animals and humans, post-ischemic inflammation is associated to the acute disruption of the blood-brain barrier (BBB), the development of vasogenic edema, hemorrhagic transformation, and worse neurological outcomes.[40]

Alcohol consumption and smoking are easier to reduce due to their modifiable nature but harder to prevent due to several challenges such as addiction and dependency to addictive substances as well as cultural and social factors that play a significant role in both of these habits. These risk factors are believed to be reduced by improved education and public awareness.

CONCLUSION

There are numerous clinical risk factors associated with ischemic stroke. Our study showed that most of the strokes occurred between the ages of 61 and 70, dominated by males, with CAD being the most prevalent cardiac comorbidity and patients diagnosed with AF showing a higher mortality rate. A small

number of patients have diabetes, but most of them had hypertension prior to admission, and the incidence rate of recurrent strokes was markedly high. More than half of the patients were active smokers, and a minority of the patients took more than three alcoholic drinks per day. Most patients showed a normal hemoglobin level, thrombocyte count, PDW, BUN, and creatinine level. The majority of the patients showed normal electrolyte levels with the exception of potassium, with a considerable number of patients showing a decreased level.

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Conflict of Interest
The author has no conflict of interest to disclose for this report

Ethic Consideration
This research has passed the ethical test and received a certificate with an ethic number 33/UN15.16/KEPK/2022 from the Health Research Ethics Committee of Faculty of Medicine and Veterinary Medicine, Universitas Nusa Cendana. Researchers protected the privacy of participants by ensuring that data is anonymized and confidential.

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Author Contribution
IP contributed to the conceptualization, resources, writing, review and editing.

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