

## Differences in blood sugar levels during ischemic stroke and hemorrhagic stroke at RSU UKI Jakarta

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### Abstract

Stroke is the second leading cause of death globally; stroke is more severe in patients with hemorrhagic stroke than ischemic stroke. Nearly 2 out of 3 patients with acute stroke have a high blood glucose level as a physiological response from an acute disease. Poor clinical outputs are often found in acute stroke patients with hyperglycemia. This study aims to determine the differences in blood glucose levels in ischemic stroke and hemorrhagic stroke patients in RSU UKI Jakarta. It is descriptive observational research with the cross-sectional method. The sample is 132 patients, using total sampling with specified inclusion and exclusion criteria. The data used is secondary data. Data processing was performed using SPSS. The study revealed that from 108 ischemic stroke patients, 79 patients (73,1%) show an increase in blood glucose level and out of 24 hemorrhagic stroke patients, all the patients show an increase in blood glucose level. The mean value in blood glucose level during ischemic stroke is 129,83mg/dL and in hemorrhagic stroke is 151,12mg/dL. This study concludes that there is a significant difference ( $= 0,001$ ) in blood glucose level, which means the mean value of blood glucose level in hemorrhagic stroke is higher than ischemic stroke.

**Keywords:** random blood glucose, ischemic stroke, hemorrhagic stroke, RSU UKI Jakarta

### Introduction

According to WHO, stroke is a clinical sign that develops rapidly due to a focal or global disturbance of brain function, which lasts for 24 hours or more and causes death without causes other than vascular causes [1]. Stroke is the second leading cause of death globally, with a mortality rate of about 5.5 million people [2]. The prevalence of stroke in Indonesia based on Basic Health Research (Riskesdas) increases over time. In 2013, 7 out of 1000 people had a stroke, and in 2019, 10.9 out of 1000 people had a stroke. The highest prevalence of stroke in Indonesia is in East Kalimantan, where 15 out of 1000 people suffer from stroke and the prevalence of stroke also increases with age, namely at the age of 75 years and over, 50 out of 1000 people suffer from stroke and the prevalence of stroke by gender is higher. Experienced by men, namely 11 out of 1000 people are male compared to women.

Stroke is broadly divided into two categories, namely hemorrhagic stroke and ischemic stroke [3]. Ischemic stroke occurs because of thrombosis and embolus in blood vessels, causing obstruction and will cause a decrease in blood flow to the brain. Hemorrhagic stroke occurs due to intracerebral haemorrhage or subarachnoid haemorrhage, where this bleeding will damage the brain at the site of bleeding by pressing the surrounding tissue [4, 5]. About 80% of stroke cases are ischemic stroke, and another 20% are hemorrhagic stroke. The risk factors for stroke are divided into two, namely non-modifiable risk factors and modifiable risk factors. Non-modifiable risk factors consist of age, gender, ethnicity and genetics. Modifiable risk factors are hypertension, diabetes mellitus, hyperlipidemia and smoking [7].

People with diabetes mellitus have a higher risk of stroke than those without diabetes mellitus [8]. Almost 2 (two) of 3 (three) patients with acute stroke experience an increase in

blood sugar [9]. In acute stroke patients, hyperglycemia is often found, where patients with hyperglycemia mostly have a history of diabetes mellitus but can also be found in patients who are not diagnosed with diabetes mellitus. During the 12 hours after stroke, the hyperglycemic state will continue to increase and decrease over the next week or so [10]. Hyperglycemia occurs in almost 30-40% of ischemic stroke patients and 43-59% in hemorrhagic stroke patients [11]. Hyperglycemia in stroke patients can occur due to poor diabetes mellitus control, or as a physiological response to the disease at that time, or a combination of both [12]. Intracerebral hemorrhagic stroke usually has more severe disorders and even causes death. The severity of intracerebral hemorrhagic stroke reaches 40% at one month and 54% at one year, and only 12-39% of patients still have long-term functional independence [13]. In addition, disturbances and poor outcomes can also be found in acute stroke patients with hyperglycemia without a history of diabetes mellitus compared to stroke patients with hyperglycemia with a history of diabetes mellitus. In addition to causing poor outcomes, acute stroke patients with hyperglycemia without a history of diabetes mellitus also increase mortality and length of hospital stay [10].

Based on the data above, there was a higher incidence of hyperglycemia in hemorrhagic stroke than ischemic stroke and a higher degree of severity in hemorrhagic stroke. This study has not been carried out at RSU UKI before. Therefore, the researchers are interested in researching "Differences in Blood Sugar Levels in Ischemic Stroke and Hemorrhagic Stroke at RSU UKI Jakarta". Based on the background of the research background, the researcher formulates the research problem, namely "Are there differences in blood sugar levels during ischemic stroke and hemorrhagic stroke patients at RSU UKI?" with the aim of research to determine differences in blood sugar levels

while in ischemic stroke and hemorrhagic stroke patients at RSU UKI.

### Literature Review

Stroke is characterized by a neurological decline resulting from acute focal damage to the central nervous system (CNS), and this damage is caused by blood vessels such as cerebral infarction, intracerebral haemorrhage, and subarachnoid haemorrhage. Stroke is the most significant cause of disability and death in the world [14]. In America, of the entire population, it is estimated that 6.8 million (2.8%) of the population are patients who have had a stroke, of which 3.8 million are women, and 3 million are men. Of the patients who had had a stroke, almost half survived but experienced decreased physical abilities, such as weakness or cognitive impairment six months after stroke [15]. Stroke is classified into two: Hemorrhagic stroke, which is caused by bleeding in the brain, namely subarachnoid haemorrhage, which accounts for about 5% of all strokes, and intracerebral haemorrhage, which accounts for about 10% of all strokes. Subarachnoid haemorrhage is bleeding that occurs between the arachnoid layer and the pia mater. Subarachnoid haemorrhage can be caused by several things: vascular aneurysms, cerebral vascular bleeding, and vascular malformations [16].

Ischemic stroke causes infarction of the brain, spine, and retina to cause neurological dysfunction. Symptoms may last 24 hours or more. Infarcts occur due to embolus (cardioembolic as in the atrial fibrillation case) or atherothrombosis (due to atherosclerosis of the arteries) [17]. Risk factors for stroke are divided into non-modifiable risk factors and modifiable risk factors: a) Non-modifiable risk factors - Non-modifiable risk factors, namely age, gender, ethnicity, and genetics. Age factor is very influential on the incidence of stroke, along with increasing age, the incidence of stroke will increase to double every decade after the age of 55 years. In addition, gender also affects, and stroke can also be influenced by genetic factors that come from the family and cannot be changed [18]; and b) Modifiable Risk Factors - Modifiable risk factors are important because early identification of risk factors and modification can prevent stroke. This risk factor is hypertension [19; 20], diabetes mellitus [18, 21], atrial fibrillation, dyslipidemia, inactive behavior, diet, obesity and metabolic syndrome.

Pathophysiology Stroke is divided into two types: a) Hemorrhagic Stroke, which consists of 1) intracerebral bleeding - Most intracerebral bleeding is caused by hypertension. When blood pressure increases, it will cause leakage in the arterioles. Intracerebral haemorrhage occurs only in local areas of the brain. The degree of damage inflicted according to the location, the bleeding volume, and the pressure generated by the bleeding. Intracerebral haemorrhage will be in the brain's white matter and enter the brain's ventricles, causing an increase in intracranial pressure. Bleeding causes the blood to clot over time, and causes swelling of the surrounding brain tissue and causes nerve cell damage. In addition, the haemoglobin contained in the blood, which consists of heme and iron, is toxic to mitochondria in brain cells, so that it can cause cell death [20] and 2) Subarachnoid haemorrhage - Subarachnoid haemorrhage is bleeding that is sudden onset in the subarachnoid space between the arachnoid mater and pia mater. The cause of subarachnoid haemorrhage is the presence of aneurysms and malformations in blood vessels

that trigger bleeding in the brain; b) Ischemic Stroke - The mechanism of ischemic stroke can be divided into three, namely thrombosis, embolus, and tissue hypoperfusion. Thrombosis is an obstruction in the blood vessels that form in the area of resistance itself. An embolus is an obstruction in a blood vessel formed and originates from another place, while tissue hypoperfusion is caused by decreased blood flow in the circulatory system [22, 23, 24].

Stroke Diagnosis - For stroke, the biomarker in the diagnosis is imaging. All patients with symptoms of a stroke are required to perform imaging examinations of the brain and neurovascular. The imaging used is non-contrast CT (Computed Tomography) and MRI (Magnetic Resonance Imaging). This imaging helps distinguish between the two strokes, namely hemorrhagic stroke consisting of intracerebral hemorrhagic stroke and subarachnoid hemorrhagic stroke with ischemic stroke. Non-contrast CT is more sensitive for detecting masses, such as abscesses and acute bleeding. Non-contrast CT examination can be performed within 24 hours after the patient is admitted to the hospital. CT can detect extensive lesions in the cortical area and basal ganglia. The non-contrast CT results showed hyperdense areas (white) in hemorrhagic strokes and hypodense areas (black) in infarct areas in ischemic strokes. In patients with acute stroke who have had a non-contrast CT examination, CT angiography is also expected. With CT angiography, blood vessels can be seen both extracranial and intracranial. CT angiography aims to identify blocked blood vessels in ischemic stroke, and identify the cause of bleeding, such as the presence of an aneurysm, and also determine the source of bleeding. Imaging can also be done with MRI (Magnetic Resonance Imaging). MRI has a higher sensitivity than CT. MRI also has better resolution than non-contrast CT. In lesions in the brain stem, the examination that can be done is an MRI. But non-contrast CT has several advantages, namely non-contrast CT is faster, more common and cheaper [25].

Glucose is a monosaccharide, and blood glucose is glucose in the blood, while glucose is the primary energy for cells in the body. The balance of blood glucose is regulated through its production and use. Glucose is obtained from food that has been absorbed and digested by the intestines and distributed to body tissues. Glucose in the blood is produced by 85% of the liver, and the other 15% comes from the kidneys. Glucose is needed by body cells, especially the brain. The brain requires 50% of the total body glucose level, another 25% is distributed to the liver and gastrointestinal system, and the remaining 25% is in muscle and adipose tissue [26]. Mechanism of blood sugar regulation - In healthy adults, glucose in the blood is around 70-99 mg/dl and will be maintained by certain hormones (insulin, glucagon) and the central and peripheral nervous systems. The insulin hormone that is secreted will bind to insulin receptors in the hypothalamus. Insulin that binds to the hypothalamus will stimulate brain neurons, which will then stimulate the release of IL-6 in the liver. The function of IL-6 is to activate STAT3 (Signal Transducer and Activator of Transcription 3) is activated by the phosphorylation process, which will cause a decrease in the gluconeogenesis process through a decrease in the production of glucose-6 phosphate and phosphoenolpyruvate kinase in the liver, resulting in a decrease in glucose production and a decrease in blood levels, and adipose tissue, which will play a role in the excretion, storage, and metabolism of glucose [27].

The most important hormones are insulin and glucagon, and both are produced by the islets of Langerhans in the pancreas. In the islets of Langerhans in the pancreas,  $\beta$ -cells produce insulin, and  $\alpha$ -cells produce glucagon. The hormone insulin reduces blood sugar levels by increasing blood sugar transport to insulin-sensitive cells and storing it through glycogenesis (change from glucose to glycogen) and lipogenesis (fat). Insulin also inhibits the secretion of glucagon. The hormone glucagon plays a role in low blood sugar, or called hypoglycemia. The role of the hormone glucagon is to increase glycogenolysis (change from glycogen to glucose) and increase gluconeogenesis (change from protein, fat to glucose).

Glucose levels influence insulin secretion from pancreatic pancreas  $\beta$ -cells. High glucose levels are needed, which is about 5 Mm/I, to be able to secrete insulin. Glucose will enter the liver through glucose transporter 2 (GLUT-2) and converted into glucose 6-phosphate, the enzyme glucokinase. This phosphorylation process releases ATP so that ATP levels are low, and low ATP levels result in the closure of  $K^+$  ATP channels, inhibition of potassium transfer, and depolarization of the plasma membrane. Closure of  $K^+$  ATP channels causes potassium to be retained in the intracellular space and causes depolarization.

As a consequence of depolarization of the cell membrane,  $Ca^{2+}$  channels will open, and calcium enters intracellularly. Calcium in the intracellular will stimulate exocytosis of insulin, and the function of the hormone insulin is to inhibit gluconeogenesis and glycogenolysis. Besides, it increases the process of glycogenesis. The process of gluconeogenesis is regulated by the enzymes phosphoenolpyruvate carboxykinase (PEPCK), fructose-1, 6-bisphosphatase (FP2ase) and glucose-6-phosphate (G6Pase). The role of insulin is to inhibit the activity of all three so that they cannot produce glucose from the gluconeogenesis process.

In non-hepatic tissues, insulin plays a role in increasing glucose uptake into body cells via plasma membrane via GLUT. Most glucose uptake is the striated muscle and adipose tissue. Glucose in striated muscle will be stored in glycogen and cannot be converted into glucose again. In the uptake of glucose in striated muscle and tissue, GLUT-4 plays a role. With the hormone insulin and contraction of striated muscles, an increase in GLUT-4 will be obtained, referring to an increase in glucose stores.

In contrast to striated muscle, only insulin in adipose tissue stimulates GLUT-4 levels. The increase in GLUT-4 is due to the activation of PI 3-kinase (Phosphatidylinositol 3-kinase) and TC10 by insulin, where both will cause the release of vesicles containing GLUT-4 from intracellular to the plasma membrane so that glucose transporters into cells will increase and the level in the blood will decrease.

In addition to the hormone insulin, the hormone glucagon also plays a role in regulating glucose levels in the body. Glucagon is produced by  $\alpha$ -cells in the islets of Langerhans in the pancreas. The hormone glucagon will be secreted in a state of hypoglycemia (reduced blood sugar levels). In contrast to insulin which is dependent on GLUT-2, the hormone glucagon is dependent on GLUT-1. There are many channels for regulating membrane potential in pancreatic cells, such as the  $K^+$ ATP channel and the tetrodotoxin-sensitive  $Na^+$ . When glucose levels in the blood decrease, the  $K^+$ ATP channel activity causes the membrane potential to be around -60mV, which will cause the T-type  $Ca^{2+}$  channel to open, and depolarization occurs.

Furthermore, the  $Na^+$  channel will open, and the N-type  $Ca^{2+}$  channel will also open, which causes the entry of calcium into the cell, and the exocytosis of the hormone glucagon occurs. The hormone glucagon will cause catabolism by stimulating glycogenolysis and gluconeogenesis to increase glucose levels in the blood. Enzymes that play a role in gluconeogenesis, such as glucose-6-phosphatase (G6P) and phosphoenolpyruvate carboxykinase (PCK2) and fructose-1,6-bisphosphatase (FBP1), which the hormone glucagon will activate through its activation in CAMP (cyclic AMP). The function of G6P is to produce glucose from glucose-6-phosphate. The function of FBP1 is to convert fructose-1,6-bisphosphate to fructose-6-phosphate. In addition, the hormone glucagon also plays a role in inhibiting glycolysis in the pyruvate kinase process. With the role of hormones, organs, and nerves, there can be homeostasis in blood sugar levels in the body [28].

**Blood Sugar Levels** - To measure blood sugar levels, several tests can be performed, namely, temporary blood glucose, fasting blood glucose, plasma glucose 2 hours after OGTT (Oral Glucose Tolerance Test), and HbA1c. According to the ADA (American Diabetes Association), hypoglycemic states are characterized by blood glucose less than (<70 mg/dL), and hyperglycemia states are characterized by blood glucose more than (>140 mg/dL) [29]. Differences in blood sugar levels in ischemic and hemorrhagic stroke - Based on several studies, hyperglycemia in stroke patients is a determinant to see the patient's disease prognosis. Of the total stroke patients, 60% had hyperglycemia, and 12-53% were patients who had never previously been diagnosed with diabetes mellitus [30]. Several things cause high blood sugar levels in stroke patients. High blood sugar levels in patients without a history of diabetes mellitus are referred to as stress hyperglycemia.

In acute critical illness, it will cause disturbances in the immunoneuroendocrine system. Critical illness activates the Hypothalamic Pituitary Adrenal (HPA) axis, a neuroendocrine system, activates the sympathetic nervous system, and causes the secretion of proinflammatory cytokines. In acute conditions, activation of the HPA axis is caused by Corticotropin-Releasing Factor (CRF), the hypothalamus will produce Adrenocorticotropic Hormone (ACTH), and trigger the adrenal kidneys to produce glucocorticoid hormones, cortisol hormones, and cause hypercortisolemia (increased cortisol levels). Cortisol plays a role in increased transcription of the PPECK gene (phosphoenolpyruvate carboxykinase), which is the main enzyme in gluconeogenesis, so that the process of gluconeogenesis will increase in the liver. Activation of the sympathetic nervous system causes the synthesis of catecholamine hormones (epinephrine, norepinephrine), glucagon, and growth hormone. Catecholamine plays a role in the transcription of PPECK, which triggers gluconeogenesis. It cooperates with the hormone glucagon in the process of glycogenolysis in muscle tissue and gluconeogenesis. Epinephrine hormone will inhibit insulin receptor substrate (IRS)-1, causing insulin resistance. In addition to the inhibition of IRS and interference with tyrosine kinase, it will cause the failure of transcription of GLUT-4, which plays a role in glucose uptake in peripheral tissues so that glucose uptake will decrease.

In addition, the secretion of proinflammatory cytokines, such as tumour necrosis factor (TNF- $\alpha$ ), interleukin (IL)-1,

IL-6 and IL-8, will also cause insulin resistance and increase glucose levels. IL-6 will increase the Corticotropin-Releasing Factor (CRF) and Adrenocorticotrophic Hormone (ACTH) to increase the hormone cortisol. TNF- plays a role in insulin receptor inhibition and tyrosine kinase and inhibition of PI3K (phosphatidylinositol three kinases) activation, which plays a role in insulin signalling, thereby interfering with GLUT-4 translocation. The presence of hormones and inflammatory cytokines and their role in eating will cause blood glucose levels to increase [31].

Hemorrhagic stroke is a stroke with a higher mortality and morbidity rate than ischemic stroke. In hemorrhagic stroke, oxidative stress plays a significant role in brain damage after a hemorrhagic stroke. Oxidative stress responds to disturbances by producing Reactive active oxygen species (ROS) and Reactive Nitrogen Species (RNS). A hemorrhagic stroke will cause bleeding in the brain. In addition, the blood-brain barrier will also be disrupted and cause oedema in the brain parenchyma. Inflammatory cells such as microglia and neutrophils play a role in this inflammatory process. In hemorrhagic stroke, blood cells will break down into iron ions, heme and thrombin. The results of this degradation and neutrophils and microglia will trigger the production of free radicals. Free radicals will cause damage to nerve cells, starting from brain cells that contain lipids that will be sensitive to free radicals, which cause the lipid peroxidase process and cause disruption of cell membranes resulting in the influx of calcium ions into cells and increased levels in the cells. High calcium levels in cells will cause damage to both cell membranes and cell organelles. With the presence of oxidative stress, an increase in calcium ions in cells and perihematomal oedema, the inflammation that occurs will be very high and cause the release of proinflammatory cytokines such as TNF and interleukins, which have an impact on higher blood sugar levels in hemorrhagic strokes compared to ischemic strokes [32].

High blood sugar will cause disturbances in the nervous system. High blood sugar levels in patients will be toxic to the ischemic brain. The ischemic brain will produce lactic acid and increase intracellular acidosis (due to anaerobic glucose metabolism), which causes an increase in the peroxidation of lipids and the formation of free radicals and interferes with the function of cell mitochondria. Hyperglycemia as neurotoxic will affect the penumbra area around the ischemic area, where there are still nerves that can be saved from infarction. The presence of acidosis in the cells of the penumbral area will cause widespread infarction so that the neurons that were still able to be saved turn into infarcts, and also hyperglycemia will increase the synthesis of plasminogen activator in the tissue, which will cause the expansion of bleeding in intracerebral haemorrhage [33]. In several studies, hyperglycemia found in acute stroke revealed that hyperglycemia stems from a disturbance in neuroendocrine regulation in response to lesions in the brain cortex, caused by the release of the hormones cortisol and epinephrine. Hyperglycemia can also damage the blood-brain barrier and cause apoptosis in the vascular endothelium. High blood glucose will also cause brain oedema, widening bleeding volume, and expansion of infarction. Patients with Hyperglycemia usually have low insulin levels, which will lead to reduced uptake from surrounding organs and increased gluconeogenesis, with the expectation that glucose can diffuse to the brain more [34].

## Research Method

This study is a descriptive observational study using a cross-sectional design with content analysis, collecting data from medical records and carried out only at a specific time or period. The study used secondary data from stroke patients obtained at the Medical Record Unit of the RSU UKI Jakarta from January 2016 to January 2018. This data collection aimed to find differences in blood sugar levels in ischemic stroke and hemorrhagic stroke in stroke patients at RSU UKI Jakarta. This research was conducted at the Medical Record Unit of the RSU UKI in Jakarta and took place from August to November 2019. The subjects that became the population in the study were patients with ischemic stroke and hemorrhagic stroke who had been treated in the neurology ward of the RSU UKI in the period January 2016 to January 2018 as many as 177 patients. The sampling technique used is total sampling, where the number of samples is taken from the entire population based on the inclusion and exclusion criteria that the researcher has determined. This study uses document analysis techniques, with research instruments in medical records that store data on patients with ischemic and hemorrhagic stroke in January 2016 - January 2018 at RSU UKI Jakarta. The research data was obtained from the results of observations and data collection that had been carried out at RSU UKI. Data in secondary data from medical records of ischemic and hemorrhagic stroke patients in January 2016-January 2018. The tabulated research data were analyzed using Univariate analysis to determine the frequency distribution of each variable. Next, Bivariate analysis was carried out by cross-tabulating to determine the relationship between the two variables. An Independent T-test was conducted to determine the significance of the difference between the independent and dependent variables. The first was data normality test to determine the existing data description and as a condition for performing an independent t-test, on the results of an independent t-test (if the value of sig. (2-tailed) < 0.05, then Ho is rejected and Ha is accepted, and if the value of sig. (2-tailed) > 0.05, then Ho is accepted, and Ha is rejected.) Data analysis using the SPSS 17 application.

## Result and Discussion

This study was conducted to know the difference in blood sugar levels in ischemic stroke and hemorrhagic stroke patients. Sampling was carried out at the Medical Records Unit of the UKI RSU Jakarta from October 7, 2019, to October 11, 2019. The research sample used a total sampling technique to determine a sample from the entire population. The research subjects were patients with ischemic stroke and hemorrhagic stroke at RSU UKI from January 2016 to January 2018. The study population consisted of 177 patients consisting of 142 ischemic stroke patients and 35 hemorrhagic stroke patients. However, only 132 patients met the inclusion and exclusion criteria with details of 108 ischemic stroke patients and 24 hemorrhagic stroke patients, which were then used as research samples. The results of the study are described as follows:

**Table 1:** Distribution of Patient Frequency by Type of Stroke

Stroke Type	N	%
Ischemic Stroke	108	81,8
Hemorrhagic Stroke	24	18,2
Total	132	100

Based on table 1, obtained from 132 patients, 108 patients (81.8%) had an ischemic stroke, and 24 patients (18.2%) had a hemorrhagic stroke. From the results of the study, it was found that there were more patients with ischemic stroke than patients with hemorrhagic stroke.

**Table 2:** Frequency Distribution of Sex by Type of Stroke

Gender	Ischemic Stroke		Hemorrhagic Stroke		Total	
	N	%	N	%	N	%
Male	61	46,2	15	11,4	76	57,6
Female	47	35,6	9	6,8	56	42,4
Total	108	81,8	24	18,2	132	100

Table 2 shows the number of patients with ischemic stroke and hemorrhagic stroke in both male and female sexes. Based on the study, 132 ischemic and hemorrhagic stroke patients at RSU UKI Jakarta, consisting of 76 male patients (57.6%), of which 61 patients (46.2%) had an ischemic stroke, and 15 patients (11.4 %) had a hemorrhagic stroke. In a total of 56 female patients (42.4%), there were 47 patients (35.6%) who had an ischemic stroke, and nine patients (6.8%) had a hemorrhagic stroke. Based on the research, it was found that in men and women, more patients suffered from ischemic stroke (81.8%) than hemorrhagic stroke (18.2%).

**Table 3:** Frequency Distribution of Patient Age by Type of Stroke

Patients Age (year)	Ischemic Stroke		Hemorrhagic Stroke		Total	
	N	%	N	%	N	%
45-54	28	21,2	8	6,1	36	27,3
55-64	43	32,6	11	8,3	54	40,9
65-75	28	21,2	3	2,3	31	23,5
>75	9	6,8	2	1,5	11	8,3
Total	108	81,8	24	18,2	132	100

Table 3 shows that in the age range of 45 to 55 years, there were 36 patients (27.3%), consisting of 28 patients (21.2%) having an ischemic stroke and eight patients (6.1%) having a hemorrhagic stroke. In the age range of 55-64 years, there were 54 patients (40.9%), consisting of 43 patients (32.6%) having an ischemic stroke and 11 patients (8.3%) having a hemorrhagic stroke. In the age range of 65-75 years, 31 patients (23.5%), consisting of 28 patients (21.2%), had ischemic stroke and three patients (2.3%) had a hemorrhagic stroke. Furthermore, at the age of more than 75 years, there were 11 patients (8.3%) consisting of 9 patients (6.8%) with ischemic stroke and two patients (1.5%) with hemorrhagic stroke. The study results found that the age group of 55-64 years had a higher risk for ischemic and hemorrhagic stroke.

**Table 6:** Distribusi Frekuensi LDL Berdasarkan Jenis Stroke dan Riwayat Diabetes Melitus

LDL (mg/dL)	Category	Ischemic Stroke				Hemorrhagic Stroke				Total	
		DM History		No DM History		DM History		No DM History		N	%
		N	%	N	%	N	%	N	%		
<100	Normal	3	2,3	4	3	1	0,75	3	2,3	11	8,3
100-129	Medium	4	3	20	15,2	2	1,5	4	3	30	22,7
130-159	High Limit	5	3,8	20	15,2	1	0,75	8	6	34	25,8
160-189	High	11	8,3	23	17,4	1	0,75	3	2,3	38	28,8
>190	Very high	6	4,5	12	9	0	0,0	1	0,8	19	14,4
Total		29	22,0	79	59,8	5	3,8	19	14,4	132	100,0

Based on table 6, it was obtained from 132 stroke patients, there were 11 patients (8.3%) who had normal LDL levels, namely <100mg/dL, 30 patients (22.7%) had moderate LDL

**Table 4:** Frequency Distribution of Blood Sugar Levels During Diabetes by Type of Stroke and History of Diabetes Mellitus

GDS (Md/Dl)	Ischemic Stroke				Hemorrhagic Stroke				Total	
	DM		No DM		DM		No DM		N	%
	N	%	N	%	N	%	N	%		
<100	1	0,8	18	13,6	0	0,0	0	0	19	14,4
100-140	10	7,6	36	27,3	1	0,8	11	8,3	58	43,9
>140	18	13,6	25	18,9	4	3	8	6,1	55	41,7
Total	29	22,0	79	59,8	5	3,8	19	14,4	132	100,0

Based on table 4, from a total of 132 stroke patients, 19 patients (14.4%) had a stroke who had blood sugar levels <100 mg/dL, 58 patients (43.9) had temporary blood sugar levels between 100-140 mg/dL, and 55 patients (41.7%) with blood sugar levels when >140mg/dL. Patients with blood sugar levels above 100 totalled 113 patients (85.6%). It consists of 28 patients (21.2%) ischemic stroke with a history of DM, of which there were ten patients (7.6%) with blood sugar between 100-140mg/dL, and 18 patients (13.6) with blood glucose levels >100mg/dL and 61 patients (46.2%) ischemic stroke without a history of diabetes mellitus, consisting of 36 patients (27.3%) with levels of 100-140mg/dL, and 25 patients (18.9%) with blood sugar levels >140mg/dL. Furthermore, there were five patients (3.8%) of hemorrhagic stroke with diabetes mellitus, of which one patient (0.8%) had blood sugar levels between 100-140mg/dL and four patients (3.0%) with blood sugar levels >140mg/dL, in 19 patients (14.4%) hemorrhagic stroke without a history of diabetes mellitus there were 11 patients (8.3%) with blood sugar levels between 100-140mg/dL and 8 patients (6.1%) with blood sugar levels >140 mg/dL. It shows an increase in blood sugar levels in acute stroke patients, both ischemic and hemorrhagic, whether accompanied by diabetes mellitus or not.

**Table 5:** Frequency Distribution of Diabetes Mellitus History by Type of Stroke and History of Diabetes Mellitus

DM History	Ischemic Stroke		Hemorrhagic Stroke		Total	
	N	%	N	%	N	%
Yes	29	22,0	5	3,8	34	25,8
No	79	59,8	19	14,4	98	74,2
Total	108	81,8	24	18,2	132	100

Berdasarkan tabel 5, didapatkan bahwa terdapat 34 pasien stroke (25,8%) memiliki riwayat diabetes melitus, dimana 29 pasien (22,0%) merupakan pasien stroke iskemik dan 5 pasien lainnya adalah pasien stroke hemoragik (3,8%).

levels, which were between 100-129mg/dL, 34 patients (25.8%) had high LDL levels of 130-150mg/dL, 38 patients (28.8%) had high LDL levels of 160-189mg/dL, and 19

patients (14.4%) with LDL levels are very high, namely > 190 mg/dL. In ischemic stroke patients with a history of diabetes mellitus, 29 patients (22.0%) had 22 patients (16.6%) with LDL levels in the high, high and very high limits. In 79 patients (59.8%) of ischemic stroke without a history of diabetes mellitus, 55 patients (41.7%) had high, high, and very high LDL levels. In 5 patients (3.8%) of ischemic stroke with diabetes mellitus, there were two patients (1.5%) who had LDL levels in the high and high range, and in 19 (14.4) patients with hemorrhagic stroke without diabetes mellitus, there were 12 patients (9.0%) had LDL levels in the high, high and very high limits. So that it can be found that from 98 patients (74.2%) of ischemic and hemorrhagic stroke who did not have a history of diabetes, 67 patients (50.8%) had elevated LDL levels in the high, high and very high limits. Ischemic stroke and hemorrhagic stroke patients with a history of diabetes and those without both had more elevated LDL levels.

**Table 7:** Frequency Distribution of Total Cholesterol Levels by Type of Stroke

Total Cholesterol Levels (mg/dL)	Category	Ischemic Stroke		Hemorrhagic Stroke		Total	
		N	%	N	%	N	%
<200	Normal	56	42,4	17	12,9	73	55,3
200-239	Sedang	39	29,5	6	4,5	45	34,1
≥240	tinggi	13	9,8	1	0,8	14	10,6
Total		108	81,8	24	18,2	132	100

Based on table 7, it was found that in all stroke patients, from 108 ischemic stroke patients, 56 patients (42.4%) had total cholesterol levels <200mg/dL, 39 patients (29.5%) had cholesterol levels between 200-239mg/dL, and 13 patients (9.8%) had high cholesterol levels of 240mg/dL. In 24 hemorrhagic stroke patients, 17 patients (12.9%) had a total cholesterol level <200mg/dL, 6 patients (4.5%) had a total cholesterol level between 200-239 mg/dL, and 1 patient (0.8 %) had a total cholesterol level of 240mg/dL. An analysis was carried out using the Independent T-test to determine the difference in blood sugar levels in ischemic stroke and hemorrhagic stroke. It previously had a regular distribution test as a condition for conducting the Independent T-test. Data normality test results are as follows.

**Table 8:** Data normality test results

One-Sample Kolmogorov-Smirnov Test	
Kolmogorov-Smirnov Z	1.227
Asymp. Sig. (2-tailed)	.099

Test distribution is Normal

Based on the table obtained p of 0.099 >: 0.05, it can be concluded that the data is usually distributed and meets the requirements for the Independent T-Test test. The results of the Independent T-Test are:

**Table 9:** Independent T-test results

When blood sugar	Stroke Type		N	M
	Ischemic Stroke		108	129.83
Hemorrhagic Stroke		24	151.12	

**Table 10**

Blood Sugar	Levene's test for equality of variances		T-test for quality of means			
	Equal variances assumed	f	sig	t	df	Sig (2-tailed)
			2.589	.110	-3.321	130

The results of the Independent T-Test test showed a sig. (2-tailed) of 0.001 < α: 0.05, where Ho was rejected, and Ha was accepted, which means a significant difference between current blood sugar levels in patients with ischemic stroke and hemorrhagic stroke in RSU UKI Jakarta. So it was found that blood sugar levels during hemorrhagic stroke patients were higher than ischemic stroke patients, with the average blood sugar during ischemic stroke was 129.83mg/dL and the average hemorrhagic stroke was 151.12mg/dL. Based on the results in the study, it was obtained from a total of 132 stroke patients at RSU UKI, as many as 108 patients (81.8%) had an ischemic stroke, and 24 other patients (18.2%) had a hemorrhagic stroke. The results of this study indicate that the number of patients with ischemic stroke is higher than that of hemorrhagic stroke, which is following the results of various studies that have been conducted previously. Based on an article compiled by Feigin Valery L on the Golden Burden of Stroke, it is stated that globally the incidence of ischemic stroke is higher than hemorrhagic stroke [35]. In addition, from another study conducted by Harris Salim at 18 hospitals in Indonesia, it was stated that of the 5,411 stroke patients, there were 3,627 patients (67.03%) with ischemic stroke and 1,784 patients (32.97%) with hemorrhagic stroke. It is often the case in Asian countries, where there is research that high rates of ischemic stroke are associated with high rates of hypertension, diabetes mellitus, and dyslipidemia, which are the highest risk factors for ischemic stroke [36].

From the study results obtained from 132 stroke patients at RSU UKI from January 2016 to January 2018, 76 patients (57.6%) were male, and 56 patients (42.4%) were female. In a total of 76 male patients, 61 people (46.2%) had an ischemic stroke, and 15 (11.4%) had a hemorrhagic stroke, and from 56 female patients, 47 people (35.6%) had an ischemic stroke, and nine others (6.8%) had a hemorrhagic stroke. These results indicate that both types of stroke, namely ischemic stroke and hemorrhagic stroke, are more common in men than women. These results are following research and studies that have been conducted previously. Based on a study on the Global Burden of Disease in 2013, it was found that the incidence of stroke in men was higher than in women, wherein men, the incidence of ischemic stroke occurred in 132 people out of 100,000 people, and hemorrhagic stroke occurred in 64 people out of 100,000 people, and hemorrhagic stroke occurs in 45 people out of 100,000 people [37]. Based on the American Heart Association (AHA) in 2008, it was stated that men mainly experienced the prevalence of stroke in the world. It is due to differences in risk factors in men and women. In men, risk factors such as smoking, atrial fibrillation, hypertension, diabetes mellitus, hypertension, metabolic syndrome were higher than in women. In addition, in premenopausal women, high content of 17-estradiol (E2) was found, which helps reduce the risk of stroke [38].

The results showed that from 132 stroke patients at RSU UKI, 36 patients (27.3%) in the age range of 45-54 years. 55-64 years there were 54 patients (40.9%), in the age range 65-75 years there were 31 patients (23.5%), and at the age of more than 75 years, 11 patients (8.3%), wherein each age range the number of ischemic stroke patients is higher than the number of hemorrhagic stroke patients. The study results found that those aged over 55 years had a higher risk of

experiencing an ischemic and hemorrhagic stroke. These results are consistent with previous studies that stated that ten years after 55 years, men and women were twice as likely to have a stroke [39]. In another study, it was also found that people aged 55 years had an approximately 5.8 times greater risk of having a stroke than those aged 15-44 [40]. Based on previous studies, it was stated that stroke could occur at any age, but at the age of 55-64 years, it was found that the risk factors for stroke were highest compared to other age ranges, so the risk for stroke was also higher. The risk factors are high blood pressure (hypertension), diabetes mellitus and atherosclerosis, which frequently increase with increasing age.

Hypertension will cause atherosclerotic plaques, hypertrophy and changes in vascular smooth muscle. Another risk factor that increases in the elderly is diabetes mellitus; diabetes mellitus will cause changes in the structure of blood vessels. The result of both is a decrease in blood flow to the brain, and besides that, this will also cause rupture of blood vessels and cause bleeding. In addition, heart disorders, such as atrial fibrillation (AF), can also cause a stroke by causing fibrillation in the heart's left atrium, causing thrombus formation in blood vessels and causing an embolus in the brain disrupt cerebral blood flow [41]. Based on the risk factors described, people aged more than 55 years have a high risk for stroke. From the results of the study, obtained data from 132 stroke patients, there were only 34 patients (25.8%) who had a history of diabetes mellitus, consisting of 29 patients (22.0%) ischemic stroke and five patients (3.8%) stroke hemorrhagic. So it was found that more ischemic stroke patients had a history of diabetes mellitus than hemorrhagic stroke. These results are following the meta-analysis studies that have been carried out previously, which stated that of the total acute stroke patients there were about 20-33% of patients who had diabetes mellitus, and patients with diabetes mellitus had a higher chance of having an ischemic stroke than hemorrhagic stroke. People with diabetes mellitus will experience endothelial dysfunction, stiffness in the arteries, inflammation, and thickening of the basement membrane of blood vessels. Endothelial dysfunction occurs due to a decrease in NO (nitric oxide), which functions to vasodilate blood vessels. In people with diabetes mellitus, NO will decrease and cause endothelial dysfunction and a decrease in elasticity and cause stiffness of blood vessels, in addition to an increase in the inflammatory response in blood vessels, also plays a role in triggering the formation of atherosclerotic plaque, which is the leading cause of ischemic stroke. With this mechanism, it was found that having a history of diabetes mellitus would increase the incidence of ischemic stroke compared to hemorrhagic stroke.

From the results of the study, obtained data from 132 patients with ischemic stroke and hemorrhagic stroke, 11 patients (8.3%) had normal LDL levels of <100mg/dL, 30 patients (22.7%) had moderate LDL levels between 100-129 mg/dL, 34 patients (25.8%) had high LDL levels between 130-159 mg/dL, 38 patients (28.8%) had high LDL levels between 160-189 mg/dL, and 19 patients (14.4%) had very high LDL levels >190 mg/dL. In ischemic stroke patients with or without diabetes mellitus, LDL levels in both also increased more than the normal threshold. In ischemic stroke patients with a history of diabetes mellitus, from 29 patients (22.0%), 22 patients (16.6%) had LDL

levels in the high, high, and very high limits. In 79 patients (59.8%) of ischemic stroke without a history of diabetes mellitus, 55 patients (41.7%) had high, high, and very high LDL levels. In 5 patients (3.8%) of ischemic stroke with diabetes mellitus, there were two patients (1.5%) who had LDL levels in the high and high range, and in 19 (14.4%) patients with hemorrhagic stroke without diabetes mellitus, there were 12 patients (9.0%) had LDL levels in the high, high and very high limits. So it can be concluded that from 98 patients (74.2%) with stroke without a history of diabetes, there were 67 patients (50.8%) who had elevated LDL levels in the high, high and very high limits. It shows that the incidence of stroke has many risk factors. In addition to diabetes mellitus, hypertension, dyslipidemia is also a risk factor for stroke, especially in ischemic stroke. Following previous studies stated that people with dyslipidemia had more ischemic strokes (92.3% of all ischemic strokes) than hemorrhagic strokes (85.9% of all hemorrhagic strokes). Dyslipidemia is a condition with abnormal fat levels in the blood, one of which is an increase in LDL levels. Dyslipidemia, especially with elevated LDL, can lead to atherosclerotic plaques leading to stroke [42]. Increased blood cholesterol levels cause changes in the permeability of the endothelial walls of blood vessels which causes migration of lipids, especially LDL, to the arterial wall in the subendothelial layer and settles in the intima layer of blood vessels and will subsequently cause the release of VCAM-1 (vascular adhesion molecule-1), which results in the release of VCAM-1 (vascular adhesion molecule-1). It causes monocytes to adhere to the subendothelial space of blood vessels and become macrophages. LDL will be oxidized and bound to macrophages and form foam cells. Smooth muscle cells in the intima will also bind to oxidized LDL and make foam cells. The proliferation of vascular muscles will cause thickening and form sclerosis and become atherosclerotic plaques [23].

The table obtained in 132 patients with ischemic stroke and hemorrhagic stroke, 59 patients (44.7%) had cholesterol levels above normal, i.e. > 200 mg/dL. This study indicates that total cholesterol level is one of the risk factors for stroke. This research is in line with the research that has been done at Dr RSUP. Kariadi Semarang in 2013, with the result that 43.8% of stroke patients had a total cholesterol level above normal with an average total cholesterol of 202.45mg/dL. High cholesterol levels are associated with the formation of atherosclerotic plaques in blood vessels; high cholesterol levels can cause changes in blood vessel permeability, affecting the formation of atherosclerotic plaques that cause blockages in blood flow and cause an increased risk of stroke [43]. From the results of the study obtained, from a total of 132 stroke patients, there were 19 patients (14.4%) with stroke who had blood sugar levels <100 mg/dL, 58 patients (43.9%) had blood sugar levels between 100-140 mg. /dL, and 55 patients (41.7%) with blood glucose levels >140 mg/dL. Patients with blood sugar levels above 100, totalling 113 patients (85.6%), consisting of 33 patients (25%) of the total 34 (25.8%) patients with a history of diabetes mellitus and 80 patients (61%) of the total 98 patients (74.2%) without a history of diabetes mellitus. Based on the results of this study, it was found that blood sugar levels in patients with dominant ischemic and hemorrhagic stroke ranged between 100-140 mg/dL and > 140mg/dL. According to the American Diabetes

Association, based on previous research, hyperglycemia is characterized by blood sugar levels  $> 140$  mg/dL.

Elevated blood sugar levels are often found in the early stages of stroke. This statement follows the results of this study where blood sugar levels were found when the patient was more dominant in the range of 100-140mg/dL and  $>140$ mg/dL. Based on the table, it was also found that the incidence of an increase in blood sugar levels equally occurred in stroke patients with diabetes mellitus or without diabetes mellitus. It is following research that states that an increase in blood sugar levels like this is often found in acute stroke patients, whether with diabetes mellitus or not, where the presence of diabetes mellitus does not always cause the state of hyperglycemia in acute stroke patients, but can also be caused as a response. from stress with the release of the hormones cortisol and norepinephrine <sup>[44]</sup>. This increase in blood sugar levels occurs due to a stress reaction caused by a stroke. This stress reaction will activate the Hypothalamic-Pituitary-Axis (HPA), so that serum glucocorticoid levels will increase, increase the release of catecholamines and also cause activation of the autonomic sympathetic nervous system. Increased levels of this hormone will cause an increase in the process of glycolysis, gluconeogenesis and glycogenolysis, and cause insulin inhibition. As a result, blood sugar levels will increase. Elevated glucose levels in acute stroke may be associated with high mortality and poor outcome.

Based on the analysis results, it was found that the average blood sugar level in hemorrhagic stroke patients was higher than in ischemic stroke patients. The average temporary blood sugar in hemorrhagic stroke patients was 151.12 mg/dL, and the average temporary blood sugar in ischemic stroke patients was 129.83mg/dL. The difference between the two types of stroke was 21.28. Based on the results of the independent t-test, the value of sig. (2-tailed) = 0.001  $<$  0.05, so  $H_0$  is rejected, and  $H_a$  is accepted, and there is a significant difference between blood sugar levels during ischemic stroke and hemorrhagic stroke. The results of this study are following previous studies—research conducted by Indrayarti in 2002 at Dr RSUPN. Cipto Mangunkusumo found that blood sugar levels during hemorrhagic stroke have higher levels than ischemic stroke. In this study, the average blood sugar during ischemic stroke was 107.2 mg/dL, and the average blood sugar was 134.3 mg/dL during ischemic stroke, so there was a significant difference between blood sugar levels during hemorrhagic and ischemic stroke. In another study conducted by Dwiputra in 2015 at RSAU, Dr M. Salamun found the median value of blood sugar levels during hemorrhagic stroke was 125mg/dL and 110.5mg/dL in ischemic stroke. So that the results obtained are significant differences in blood sugar levels during ischemic stroke and hemorrhagic stroke. Based on previous studies, hyperglycemic states are shared in acute stroke in diabetic and nondiabetic patients. This condition is referred to as a hyperglycemic stress state (a hyperglycemic state caused as a stress response from the inflammatory reaction. Stress hyperglycemia is characterized by blood sugar levels of 140mg/dl in the first 72 hours of acute stroke <sup>[45]</sup>.

One of the causes of higher transient blood sugar levels in hemorrhagic stroke is the inflammatory reaction, which was more severe in hemorrhagic stroke than in ischemic stroke. In hemorrhagic stroke, the expansion of the hematoma area can immediately be seen and causes an increase in

intracranial pressure. In effect, severe inflammation is characterized by the accumulation and activation of inflammatory cells and inflammatory mediator cells. In addition, in hemorrhagic stroke, there is direct infiltration of blood components such as red blood cells, leukocytes, macrophages, plasma proteins in the area where bleeding occurs. So there is a high inflammatory response following the infiltration of blood components, the inflammatory response in the form of the release of inflammatory mediators, activation of proteases, microglia cells and astrocyte cells in response to nerve tissue damage <sup>[46]</sup>. It is a more significant inflammatory reaction that will trigger a more excellent stress response as well. This high-stress response will trigger the activation of the Hypothalamic Pituitary Adrenal Axis (HPA Axis) and trigger the release of hormones that can cause hyperglycemia, namely cortisol and catecholamines. The release of these hormones will trigger an increase in gluconeogenesis and insulin resistance due to disturbances in insulin receptor binding and signal transduction in the liver and a decrease in peripheral glucose uptake. As a result, blood sugar levels will increase.

Based on previous studies, it was found that high blood sugar levels in hemorrhagic stroke correspond to the severity of nerve damage <sup>[47]</sup>. In a state of hyperglycemia, it will cause apoptosis in nerve cells which are caused because, in a state of hyperglycemia, it will trigger the formation of free radicals from the inflammatory response and the formation of toxins for nerve cells. Due to the increase in free radicals in the body, superoxide (antioxidants) will increase, resulting in disruption of the blood-brain barrier and cerebral oedema. As a result, hyperglycemia will lead to poor outcomes than stroke patients without hyperglycemia.

## Conclusion

Based on the results of the research and discussion described in the previous chapter, the following conclusions can be drawn: a) Based on the study results, the number of ischemic stroke patients is higher than hemorrhagic stroke patients. In a total of 132 ischemic and hemorrhagic stroke patients, 108 patients (81.8%) had an ischemic stroke, and 24 patients (18.2%) had a hemorrhagic stroke; b) Based on the results of the study, it was found that blood sugar levels during ischemic stroke patients who had blood sugar levels between 100-140 mg/dL were 46 patients (34.8%), and those who had blood sugar levels more than 140 mg/dL were 43 patients (32.6%). In a total of 24 patients with hemorrhagic stroke, 12 patients (9.1%) had blood glucose levels between 100-140mg/dL and 12 patients (9.1%). Based on these results, there were 55 patients (41.7 %) who had hyperglycemia with blood sugar  $>140$ mg/dL; and c) Based on the results of statistical tests using the independent T-test, there was a significant difference between blood sugar levels during ischemic stroke and hemorrhagic stroke, as evidenced by the sig. (2-tailed) value of 0.0010  $<$  :0.05. The average blood sugar while in ischemic stroke is 129.83mg/dL and in hemorrhagic stroke is 151.12mg/dL.

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