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Relationship between Lipid and Blood Glucose Levels with Stroke Risk in Dupak Surabaya

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Abstract

Background: Stroke is a syndrome characterized by rapidly developing symptoms and/or clinical signs in the form of focal or global brain functional disorders lasting more than 24 hours which are not caused by causes other than vascular. Stroke is the number one cause of disability and the main cause of death in Indonesia (19.42% of total deaths). Dyslipidemia and diabetes mellitus are two-fold risk factors for stroke. **Objective**: This research aims to determine the relationship between lipids and blood glucose and a high risk of stroke. **Methods:** This research uses descriptive analytical methods with a cross-sectional approach. The population is residents in Dupak Surabaya. The sampling method is a random sampling technique. The total research sample was 53 participants. The statistical test used is Chi-Square. **Result:** Statistical results show that there is no relationship between high cholesterol levels and the risk of stroke and there is a relationship between high triglyceride and blood sugar levels and the risk of stroke. **Conclusion**: This research concluded that there was a significant relationship between high levels of triglycerides and blood glucose and the risk of stroke and there was no significant relationship between high cholesterol levels and the risk of stroke. This lack of significant association could be due to the heterogeneous population and the presence of previous anti-cholesterol medication.

Keywords: lipid profile, blood glucose level, risk of stroke

Original Research Article

INTRODUCTION

The definition of stroke is mainly focused on focal or global brain functional disorders endured more than 24 hours, accompanied by rapidly developing symptoms and/or clinical signs, with vascular disease as the only cause. Stroke is the first disease to cause disability and the third disease to cause death globally (WSO, 2022).

Based on data from the Institute for Health Metrics and Evaluation (IHME) in 2019, stroke is the main cause of death in Indonesia (19.42% of total deaths). Based on Riskesdas, the prevalence of stroke in Indonesia increased by 56% from 7 per 1000 population in 2013, to 10.9 per 1000 population in 2018. Globally, there are 12.2 million new stroke cases per year, where a quarter of people over the age of 25 can suffer a stroke. 47% of the new cases are men and 53% are women (WSO, 2022).

Stroke can happen to anyone regardless of age and can have very broad and complex negative impacts. The direct impact on sufferers is disability in the form of impaired motor function and even death (Obrig, 2014). More than 50% of stroke survivors experience disability, resulting in loss of

independence, work and hopelessness, resulting in a decrease in productivity and quality of life for sufferers (Donkor, 2018)(Ananda et al., 2017). Ignorance of risk factors and Stroke symptoms are one of the causes of the serious impact of stroke, hampering preventive efforts, and delays in examination and immediate treatment at health facilities. Knowledge about risk factors (especially hypertension) and stroke symptoms (especially paralysis and hemiplegia) in developing countries is generally less than 50%.3This situation can be prevented early by identifying and controlling stroke risk factors(Kementrian Kesehatan Indonesia, 2019).

The American Stroke Association (ASA) issued a stroke risk detection model, namely the Stroke Risk Scorecard / stroke risk card that includes 8 stroke risk factors. The data for each factor is grouped into 3 categories which are high risk, caution and low risk. The determination is classified based on the value of each criteria, and the results are determined based on the number of risk factors in the high risk, careful and low risk groups (Boehme et al., 2017). With the stroke risk card, it is hoped that we can find out early whether someone is at high risk or not based on the presence of signs and symptoms in the person. The aim is to prevent stroke incidence and improve the prognosis in high-risk individuals (Tarwoto et al., 2023).

One of the risk factors for stroke that we can modify is dyslipidemia and diabetes mellitus. Dyslipidemia is characterized by a disturbance in lipid circulation, where there is an increase in levels of low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), and total cholesterol (TC) levels as well as low levels of high-density lipoprotein cholesterol (HDL-C) (Kopin & Lowenstein, 2010). An increase in total cholesterol, triglycerides, and blood sugar levels is said to double the risk of stroke and result in a death rate of 20% (Lindenstrom et al., 1994) (Banerjee et al., 2012). High cholesterol concentration is associated with a significantly higher risk of hemorrhagic stroke. This relation is due to the incapacitation of reverse transport via HDL-C from tissue that caused the acceleration of atherosclerotic vascular changes. The ischaemic stroke risk increased with plasma cholesterol over 8 mmol/l. The dietary modification would only lower the triglyceride concentration, but not significantly lower the risk of hemorrhagic or ischaemic stroke (Lindenstrom et al., 1994).

The relationship between dyslipidemia and stroke risk is complex. The risk of stroke increases with an increase in total cholesterol. The risk of stroke decreases with increasing high-density lipoprotein (HDL) cholesterol. Obese individuals have large levels of adipokines in the body. This results in an increase in free fatty acids as a result of fat metabolism which triggers inflammation and then triggers the involvement of leukocytes in endothelial cells which will contribute to the formation of atherosclerosis (Kopin & Lowenstein, 2010). There's also a strong relationship between plasma triglycerides and non-hemorrhagic stroke, therefore plasma triglyceride is a better predictor of stroke than plasma total cholesterol. The high postprandial concentration of triglyceride is proven to cause atherosclerosis in the extracranial carotid arteries. A negative association is found between HDL-C concentration and risk of coronary heart disease, including stroke, due to HDL-C's responsibility in the reverse transport of cholesterol from tissue to the liver for bile formation (Lindenstrom et al., 1994).

Diabetes mellitus is a strong risk factor for all clinical manifestations of atherosclerotic vascular disease. Diabetes mellitus doubles the risk of stroke and results in a mortality rate of 20% (Sui et al., 2011). Mechanisms of increased atherogenesis in DM patients include lipid profile disorders, arachidonic acid metabolism disorders, increased platelet aggregation, increased fibrinogen levels, impaired fibrinolysis, and endothelial dysfunction (Aninditha & Wiratman, 2017). Other research presented several other potential mechanisms that built connections between diabetes and stroke. Intimal medial thickness and thin cap fibroatheromas became the association evidence between diabetic duration and atherosclerotic lesions. Hypertension which occurs twice as many as in diabetic patients than non-diabetic patients, also became one of the mechanisms, as chronic hypertension increased the macro and microvascular effects in diabetic patients. Microalbuminuria which occurs in long-term diabetes, is a strong and independent risk factor for stroke to happen in diabetic patients.

Dysfunctional endothel, fibrinogen and clotting process abnormality also contributes to the association between diabetes and stroke (Banerjee et al., 2012).

This research aimed to determine the relationship between lipids and blood glucose levels, and the high risk of stroke. The lipid and blood glucose levels were examined through laboratory processes with certain appropriate tools and materials. The result obtained were quantitative data. The stroke risk cards were filled by interviewing the research subjects and direct examination to fulfil the rest of the data needed. The result of the stroke risk cards were classified into 3 groups: low, moderate and high. This research did a statistic data analysis between the high lipids and blood glucose levels with the high result of stroke risk card, to evaluate the relations between those parameters.

MATERIALS AND METHODS

This research design uses descriptive analytical methods with a cross sectional approach. The population is residents in Dupak Surabaya, which consists of 167 households and spread into 11 regions of 45,600 m2 area . The sampling method is random sampling technique. This research samples were taken from all of the 11 regions. The number of participants from each regions were decided based on the proportion of total population in the region itself. The final total research samples were 53 participants. The inclusion criteria were age above 40 years old, living in the area of Dupak, were selected as the participant by the local research partner. The data from the participants were included if they aprroved to participate in the research by signing the informed consent letter and if they had fasted at least 10 hours before blood sampling. The data from the participant were excluded if they refused to be examined or refused their blood to be taken.

The data used in this research are primary data in the form of total cholesterol, triglyceride and fasting blood sugar examination results from laboratory examinations at Wijaya Kusuma University, Surabaya, as well as secondary data from the total score in the stroke risk cards. Taking patient blood samples using a 3cc syringe, tourniquet, vacuum tube, needle, cotton wool, and alcohol. The blood in the syringe is then put into a tube and incubated for ± 30 minutes. After incubation, the blood was put into a centrifuge and spun at 3000 RPM for 15 minutes. Next, the serum is separated from the blood cells red with the help of a micro pipette and placed in the sample cuvete then inserted into the tool which is ready to be used. The blood samples are then analyzed using reagents for blood glucose and lipid concentrations, then measured with spectrophotometer in a photometric method.

The stroke risk cards contains indicators of stroke risks, which are obesity, blood pressure, atrial fibrillation, smoking habit, stroke history, history of cholesterol concentration and diabetes, life style (exercise habit) and family health history. The total score is classified into 3 groups. If 6 or 8 indicators in the low risk result, means the person is in a good job in maintaining his/her health. If 4 to 6 indicators in the middle risk result, means the person should start to concern about his/her condition. If there are 3 or more indicators are in the high risk result, means the person should get medical advice to prevent stroke. The data that has been obtained from the results of laboratory examinations and stroke risk cards are then analyzed using the Normality test which is continued to the correlation test. If the data obtained is normal then the Pearson Rank correlation test is used. If the data obtained in the normality test is not normal, use the alternative Spearman Rank test using the SPSS statistical application program.

This research has been declared ethically appropriate under the number: No 93/SLE/FK/UWKS/2023, published by the Ethics Commission of the Faculty of Medicine, Wijaya Kusuma University, Surabaya.

RESULTS

Cholesterol is one of the main lipid components in the plasma membrane. Most of the cholesterol produced by the human body comes from foods containing animal products. Apart from food, genetic factors also play an important role in determining cholesterol levels. Adequate cholesterol levels are important in maintaining blood vessel integrity and resistance to rupture. High cholesterol levels

(hypercholesterolemia) play a major role in the formation of atheroscelosis (Yi et al., 2018). In ischemic stroke patients, brain blood vessels are blocked due to atherosclerosis, causing hypoxia in brain tissue and death of brain cells due to inadequate oxygen supply to these cells (Wang et al., 2017). According to the stroke risk card results, there are 25 samples that have high risk and 28 samples that have low risk of stroke. The total cholesterol concentrations laboratory results show that there are 15 people with normal value, 25 people with above normal value and 13 people with high value. The results of this study obtained a value of asymp.sig (2-sided) > 0.05, namely 0.516, which means there is no significant relationship between cholesterol levels and the risk of stroke (Table 1).

Table 1. Relationship between Cholesterol Levels and Stroke Risk

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	1.324	2	.516
Likelihood Ratio	1.3	2	.511
Linear-by-Linear Association	.515	1	.473
N of Valid Cases	.53		

Triglycerides consist of 90% of vegetable and animal fats in food. In the body, triglyceride levels are stored in fat cells for energy. If the amount of triglycerides is too much without exercise, the triglyceride levels will increase. An increase in triglycerides is said to double the risk of stroke and result in a death rate of 20% (Lindenstrom et al., 1994) (Banerjee et al., 2012). Increased triglyceride levels will result in fat deposits in the blood vessels, which will further cause atherosclerosis, which is the beginning of stroke (Soeharto, 2004). Blood vessels the brain that is blocked due to atherosclerosis will cause hypoxia in brain tissue and death of brain cells due to inadequate oxygen supply to these cells (Wang et al., 2017). Other studies say that high triglyceride levels do not always increase the risk of atherosclerosis or coronary artery disease. In relation to the incidence of stroke, triglycerides cannot stand alone as a causal factor because there are still causal factors that support the occurrence of stroke such as age and obesity. The triglyceride concentrations laboratory results show that there are 33 people with normal values, 8 people with above normal values, and 12 people with high values. The results of this study obtained a value of asymp.sig (2-sided) < 0.05, namely 0.016 which means that there is a significant relationship between triglyceride levels and the risk of stroke (Table 2).

Table 2. Relationship between Triglyceride Levels and Stroke Risk

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	8.223	2	.016
Likelihood Ratio	8.435	2	.015
Linear-by-Linear Association	7.817	1	.005
N of Valid Cases	.53		

Caption: day in indicates …, variable 1 indicates…., variable 2 indicates…..

Poor blood sugar control also plays a role in the formation of atherosclerosis. Poor circulation to most organs causes hypoxia and tissue injury, and stimulates an inflammatory reaction in the walls of blood vessels resulting in the accumulation of fat in the lumen of blood vessels. The consequence of atherosclerosis is narrowing of the lumen of blood vessels and a decrease in blood flow velocitywhich can then increase the risk of stroke.28 The blood glucose concentrations laboratory results show that there are 31 people with normal value, 11 people with prediabetic value and 11 people with diabetic value. The results of this study obtained a value of asymp.sig (2-sided) < 0.05, namely 0.003, which means that there is a significant relationship between blood glucose levels and stroke risk (Table 3).

Table 3. Relationship between blood sugar levels and stroke risk

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	11.434	2	.003
Likelihood Ratio	11.816	2	.003
Linear-by-Linear Association	9.427	1	.002
N of Valid Cases	.53		

Caption: day in indicates …, variable 1 indicates…., variable 2 indicates…..

DISCUSSION

Stroke can happen to anyone regardless of age and can have very broad and complex negative impacts. More than 50% of stroke survivors experience disability, resulting in loss of independence, work and hopelessness, as a decrease in productivity and quality of life for sufferers (Donkor, 2018) (Ananda et al., 2017). Knowledge about risk factors and symptoms of stroke in developing countries is generally less than 50%. We can prevent it by identifying and controlling stroke risk factors. The diagnosis can only be made after signs and symptoms appear, even though a disease already exists long before signs and symptoms appear (Kementrian Kesehatan Indonesia, 2019).

The stroke risk card issued by the American Stroke Association (ASA) contains eight stroke risk factors (blood pressure, atrial fibrillation, diabetes, smoking, exercise, diet, cholesterol, and family history of stroke). Each risk factor is categorized based on the value of the risk factor criteria, and the results are determined based on the number of risk factors in the high-risk, careful, and low-risk groups (Boehme et al., 2017). With the stroke risk card, it is hoped that we can find out early whether someone is at high risk. stroke or not based on the presence of signs and symptoms in the person so that we can help prevent stroke and improve the prognosis in high-risk individuals. The sensitivity, specificity and accuracy values of this stroke risk card were 91.67%, 77.78%, 83.33%. One of the risk factors for stroke that we can modify is dyslipidemia (increased cholesterol and triglycerides) and diabetes mellitus (Tarwoto et al., 2023).

As a person gets older, lipid profile levels tend to be higher because uncontrolled diet and reduced physical activity result in the body becoming fatter and at risk of experiencing hyperlipidemia. As you get older, your metabolism will decrease and your physical activity will also decrease. Therefore, the energy required by the body is also lower. In such a body condition, if the quality and quantity of food intake does not change during old age, there will be an excess of necessary calories. Eventually the body turns it into fat deposits, resulting in weight gain and if the condition is not controlled, disease will arise, one of the effects of which is hyperlipidemia. [Azwan Nurdin et al., 2020]. Hyperlipidemia is characterized by an increase in low-density lipoprotein cholesterol (LDL-C), triglyceride (TG) and total cholesterol (TC) levels (Kopin & Lowenstein, 2010).

The positive relationship between cholesterol levels and stroke risk has been proven in several studies. One study stated that total cholesterol is a risk factor for stroke, although the factor is less strong (Qizilbash et al., 1991). Retrospective observational cohort studies report that increasing cholesterol levels are associated with the risk of recurrent stroke (de la Riva et al., 2017). However, there are some inconsistencies regarding the relationship between high cholesterol levels and the risk of stroke. strokes. The Northern Manhattan study and a study in Japan did not find a relationship between high cholesterol and the risk of stroke (Willey et al., 2009) (Yokokawa et al., 2011). A prospective cohort study also stated that in their research there was no significant relationship between high cholesterol levels and the risk of stroke (Wang et al., 2017). The results of this study are in line with the results of the research we conducted, namely that there was no significant relationship between cholesterol levels and the risk of stroke. These discrepant findings may be due to a heterogeneous population, inaccurate data on stroke and also the possibility that participants in this study had previously received anti-cholesterol treatment (Liu et al., 2019). Anti-cholesterol treatments, mainly statins (atorvastatin, simvastatin, rosuvastatin, fluvastatin, lovastatin, pitavastatin and pravastatin), have been prescribed to hypercholesterolemia patients extensively. Statins have

been found to prevent cardiovascular diseases such as CHD and stroke, in patients who have high-risk factors. It's even proven the efficacy of statin medication in the early stages of stroke as a secondary prevention. Statins are able to reduce plasma levels of LDL-C which is the main factor or lipid transport in the process of atherogenesis, and that has genetic effects in the atherosclerosis pathogenesis (Wang et al., 2017).

An increase in triglycerides is said to double the risk of stroke and result in a death rate of 20% (Lindenstrom et al., 1994) (Banerjee et al., 2012). The results of this study are in accordance with the results of the Quiziblash study which states that there is a strong relationship between triglycerides and the incidence of stroke (Qizilbash et al., 1991). Research conducted in the country Korea also found that high triglyceride levels were significantly associated with an increased incidence of stroke. Triglyceride is the strongest predictive value in adults, male sex, with obesity, unhealthy lifestyle behaviors (like smoking, drinking alcohol, and a sedentary lifestyle), family history of hypertension, diabetes mellitus, and cardiovascular diseases. Triglyceride is also the sole independent determinant of clinical events for early-onset stroke (Lee et al., 2020). Other studies also stated that triglyceride levels were associated with the risk of stroke (Soeharto, 2004). Qodriani's research also states that someone with high triglyceride levels has a 1.46 times greater risk of having a stroke. All of these previous researches implicate the importance of a healthy lifestyle that will eliminate high triglyceride concentration, thus lowering the risk of stroke incidence. However, the results of this study contradict the results of Sidharam's research which stated that there was no relationship between triglyceride levels and the risk of stroke (Sridharan, 1992). We suggested that the triglyceride level should be measured as a research data, before and after the stroke incidence, to get a clearer view of triglyceride level association with stroke outcome.

Hyperglycemia will cause total cholesterol levels to increase. Increased blood glucose levels will cause low glucose levels in cells, thus will decrease glucose oxidation and energy production. Low energy production will increase the lipid metabolism. Eventually, hypercholesterolemia will trigger an increase in LDL and a decrease in HDL levels. These three lipid fractions are called the lipid triad which plays an important role in the process of atherosclerosis (Ningsih & Ngarang, 2020). High blood glucose levels will initiate atherosclerosis by narrowing of the lumen of blood vessels and a decrease in blood flow velocity which can then increase the risk of stroke (Corwin. Elizabeth J, 2007). The results of this study show a significant relationship between blood glucose levels and the risk of stroke. This is in accordance with previous research that shows high blood sugar levels have a higher risk of having a stroke (Chrisna & Martini, 2016). Another study says that diabetes mellitus can increase the risk of stroke 2-4 times compared to people who do not have diabetes (Tarigan, 2011). But there are also other studies that do not match the results of this study, such as research conducted by Putri et al which said that there was no significant relationship between fasting blood sugar levels and the incidence of ischemic stroke. Other researchers stated that the majority of patients who suffer a stroke for the first time do so not only because they have diabetes mellitus (Nur Rahayu et al., 2020) (Nastiti, 2012). The discordant results may need further standardization on the diabetes duration, severity, treatment, and other factors in diabetic patients that may contribute to the stroke risk outcome. Future research should have limitations to other stroke risk factors that may influence stroke incidence, besides high blood glucose levels.

CONCLUSION

This study concluded that there is no relationship between high cholesterol levels and a high risk of stroke, but there is a relationship between high levels of triglycerides and blood sugar and a high risk of stroke in Dupak Bandarejo Surabaya. There are several limitations of this study that can be revised in future research on the same topic. Larger sample with strict inclusion criterias in age and health history/condition (disease and medication), additional quisionairre for data background and statistic analysis on other data gained from the research methods will provide a more accurate and established association between the parameters and the risk of stroke.

CONFLICT OF INTEREST

There is no conflict of interest in this article.

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