CORRELATION OF STROKE RISK FACTORS ON STROKE EVENTS IN PROF. DR. H. ALOEI SABOE GORONTALO HOSPITAL PERIOD MARCH -DECEMBER 2018

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ABSTRACT

Stroke is a health problem which has a high mortality rate that can cause long-term disability. In Gorontalo province, the prevalence of stroke based on diagnosis by health workers was 10.9%. Stroke risk factors are divided into two that can be modified and cannot be modified. This study aims to find out a description of the characteristics and an analysis of the factors that influence the incidence of stroke in Prof. dr. H. Aloei Saboe Gorontalo Hospital Period March - December 2018. The research design was descriptive analytic observational with a cross sectional retrospective approach. The sample in this study was all patients with ischemic stroke and hemorrhagic stroke who were treated in the neurology inpatient of Prof. dr. H. Aloei Saboe Hospital by using consecutive sampling techniques that fulfill the inclusion criteria. In this study, a sample of 115 patients was obtained, with the highest proportion is male (62.6%), age classification 56-65 years old (33%), elementary school certificate (40.9%), with onset <24 hours (33.9%). Based on risk factors, those with a history of hypertension (78,3) %, grade 2 hyper tension (32.2) %, and uncontrolled (72.2%). Total cholesterol ≥ 200 (59,1%), LDL <160 (68.7%), HDL ≥ 30 (98.3%), triglycerides ≤ 160 (73.9%), received dyslipidemia therapy (61.7%), heart disease (66,1%) and cardiomegaly (34,8%). History of diabetes mellitus 23,5%, with RPG <200mg / dL 73,9% and 67,8% never received diabetes therapy. In kidney disorders, it was only found 7,8%. Significant risk factors for stroke (p < 0.005) are age (p < 0.001), hypertension (p=0.044), heart disease (p=0.034), total cholesterol (p=0.047), LDL (p < 0.001), HDL (<0.012) and triglycerides (p <0.038), whereas diabetes mellitus, and kidney disorders have no significant relationship with the incidence of stroke. It can be concluded that most stroke patients are found in the age criteria 56-65 years with male gender, elementary school certificate, and less than 24 hours of onset. The most common risk factors found was hypertension who are not controlled by the drug, dyslipidemia with a total cholesterol component >200mg/dL and cardiomegaly. There is a significant relationship between age, heart disease, hypertension, LDL, HDL, triglycerides and total cholesterol on the incidence of stroke.

Keyword: Stroke, risk factors, characteristics.

INTRODUCTION

Stroke is a health problem that has a high mortality rate which can cause long-term disability. Research estimates that by 2030 more than 4 million people will have a stroke or 24.9% increase from the preva-lence in 2010.¹ The American Heart Asso-ciation (AHA) estimates that there are about 795 000 people in the United States have a stroke each year, of which about 610 000 are a first attack; and 6.4 million Ame-ricans are stroke

survivors.²The prevalence of stroke in Indonesia based on a doctor's diagnosis in the Basic Health Research (Riskesdas) in 2018 was 10.9%. Whereas in Gorontalo Province, the prevalence of stro-ke increased compared to Riskesdas 2013 which was 7% to 10.9%.³ Based on the process, the stroke is divided into 2, that is, hemorrhagic stroke and non-hemorrhagic stroke. Ischemic stroke is more frequent than bleeding stroke and it is about 87% of all stroke cases.⁴ Risk factors that trigger a high rate of stroke are factors that cannot be modified such as age, sex and race, gender, genetic. While the factors can be mo-dified that are hypertension, smoking, heart di-sease, kidney disease, diabetes, and dysli-pidemia [4][5].

METHODS

Research Design

The research design was a descriptive analytic observational research method by using a cross sectional approach which is retrospective, that is the type of research that measures the variables carried out at one time without a follow up.

Research Subject

The sample in this study were all ischemic and hemorrhagic stroke patients who were treated in the neurology inpatient of Prof. dr. H. Aloei Saboe Gorontalo Hospi-tal with consecutive sampling techniques by selecting inclusion and exclusion cri-teria. Inclusion criteria: The patients with a stroke diagnosis which was confirmed by neurological examination and supported by brain CT scan results and CT head examination was performed with or without contrast, carried out laboratory tests of lipid profiles, blood sugar, blood pressure, urea, creatinine, and electrocardiography and Xray photo. Whereas the exclusion criteria were patients with blood disorders, brain tumors, brain infections, head trauma, stroke patients who died during treatment, and there were no support investigations which were carried out as in the inclusion criteria.

Data Retrieval

Examination was conducted on this research subjects consist of several types of examinations. Blood pressure checks were performed with a mercury sphygmomanometer in the reclining position, the cuff was positioned at 2.5cm above the cubital fossa and examined twice.

In laboratory tests, samples were taken using venous blood plasma to measure random plasma glucose (RPG) levels, lipid profile, ureum and creatinine. Lipid profile examination was carried out in the morning after fasting for 8 hours at night.

Other data regarding characteristics such as age, sex, onset, level of education, history of the disease and treatment were obtained from medical records and inter-views using the stroke registry form.

RESULTS

Based on the data obtained, there were 115 respondents who suffered a stroke in the period March - December 2018. From the total number patients, 102 (88.7%) patients had an ischemic stroke and 13 (11.3%) others suffered from hemorrhagic strokes based on CT-Scan results. From the total patients, 72 (62.6%) respondents were male and 43 (37.4%) respondents were female. Based on age classification, there were 38 (33%) respondents in middle-old group (56-65 years), then 33 (28.7%) respondents in the youngest-old group (46-55 years), 25 (21.7%) respondents in the oldest group (>65 years), 13 (11.3 %) respondents in adults (36-45 years), 5 (4.3%) respondents in early adults (26-35 years), teenagers (12-16 years) (0.9%) respondents only 1 and no respondents between 17-25 years old. Based on the level of education, the graduation from elementary school showed the highest frequency was 47 (40.9%) respondents, then from senior high school similar to junior high graduation was 29 (25.2%) respondents, 7 respondents college degree (6.1%)respondents, and thosewho uneducated were 3(2.6%) respondents. In accordance with the classification of onset, that is when patients experience symptoms until coming to the

hospital, mostly it was found at the onset <24 hours by 39 (33.9%) respondents, the onset <12 hours by 33 (28.7%), the onset <48 hours 14 (12.2%), the onset> 48 hours were 12 of total number (10.4%), the onset <3 hours was 10 (8.7%), and the onset <1 hour was 7 (6.1%) respondents.

Based on hypertension risk factors, 90 (78.3%) respondents had a history of hypertension, 25 (21.7%) respondents had no history of hypertension. From the classification of hypertension, 37 respondents (32.2%) had grade 2 hyper tension, grade 3 hypertension had then 35 respondents (30.4%), grade 1 hypertension had 16 respondents (13,9%), high-normal blood pressure were 14 respondents (12.2%), optimal blood pressure were 7 respondents (6.1%), and normal blood pressure were 6 respondents (5.2%). From the history of hypertension control. 83 (72.2%)respondents were uncontrolled, 23 (20.0%) respondents were controlled, and 9(7.8%)respondents were never receiving hypertension therapy before.

About 76 (66.1%) of respondents did not have history of diabetes mellitus, 27 (23.5%) respondents had diabetes mellitus, and 12 (10.4%) other respondents did not know whether there was a history of diabetes mellitus or not. According to blood sugar levels when the respondent first performed an examination, 30 (26.1%) respondents had RPG (random plasma glucose) levels >200mg/dL, while 85 (73.9%) other respondents had RPG levels <200mg / dL. From a history of diabetes mellitus therapy, 78 (67.8%) respondents were never receiving diabetes therapy, 27 (23.5%) respondents were not controlled, and 10 (8.7%) respondents were controlled.

Regarding to these results, all respondents who were previously diagnosed with dyslipidemia and who were just diagnosed with dyslipidemia had received dyslipidemia therapy. On examination of the lipid profile, the respondents with total cholesterol \geq 200 were 68 respondents (59,1%) and cholesterol <200 were 47 respondents (40.9%), LDL levels <160 were

79 respondents (68.7%), LDL levels ≥ 160 were 36 respondents (31.3%). The results of HDL examination showed that only 2 respondents (1.7%) had HDL levels <30, 113 respondents (98.3%) had HDL levels ≥ 30 . In the triglyceride examination, it had a level <160 were 85 respondents (73.9%), and ≥ 160 were 30 respondents (26.1%).

Based on the risk of heart disease, 76 respondents (66.1%) suffered from cardiac disease, and 39 respondents (33.9%) did not suffer from cardiac disease, with the most types of abnormalities that were cardiomegaly 40 (34.8%) respondents, 35 respondents (30.4%) were normal, 32 respondents (27.8%) suffered from coronary heart disease, and 8 (7.0%) respondents suffered arrhythmias.

In kidney disease, only 9 respondents (7.8%) who had kidney problems, while 106 respondents (92.2%) did not suffer kidney problems.

Table 1. Distribution of stroke patients in the neurology room of Prof. dr. H. Aloei Saboe Gorontalo Hospital based on characteristics and risk factors (N = 115)

		/			
Variable	F	%			
Onset					
< 1 hour	7	6,1			
< 3 hour	10	8,7			
< 12 hour	33	28,7			
< 24 hour	39	33,9			
< 48 hour	14	12,2			
> 48 hour	12	10,4			
Level of education					
Uneducated	3	2,6			
Elementary school certificate	47	40,9			
Junior high school certificate	29	25,2			
Senior high school certificate	29	25,2			
College Degree	7	6,1			
Sex					
Men	72	62,6			
Women	43	37,4			
Age					
12 - 16	1	0,9			
26 - 35	5	4,3			
36 - 45	13	11,3			
46 - 55	33	28,7			
56 - 65	38	33			
> 65	25	21,7			
History of Hypertension					
Yes	90	78,3			
No	25	21,7			
Hypertension Classification	•				
Optimal	7	6,1			
Normal	6	5,2			

Variable	F	%				
High-normal	14	12,2				
Grade 1 Hypertension	16	13,9				
Grade 2 Hypertension	37	32,2				
Grade 3 Hypertension	35	30,4				
Controlled Hypertension						
Yes	23	20,0				
No	83	72,2				
Not receiving therapy	9	7,8				
History of Diabetes						
Yes	27	23,5				
No	76	66,1				
Unknown	12	10,4				
RPG levels						
> 200	30	26,1				
< 200	85	73,9				
Controlled Diabetes						
Yes	10	8,7				
No	27	23,5				
Not Receiving Therapy	78	67,8				
Heart Disease						
Positive	76	66,1				
Negative	39	33,9				
Type of Heart Disease						
Normal	35	30,4				
Arrhythmia	8	7,0				
Coronary Heart Disease	32	27,8				
Cardiomegaly	40	34,8				
Kidney Disorders						
Positive	9	7,8				
Negative	106	92,2				
Total Cholesterol						
< 200	47	40,9				
\geq 200	68	59,1				
LDL						
< 160	79	68,7				
≥ 160	36	31,3				
HDL						
< 30	2	1,7				
\geq 30	113	98,3				
Triglycerides						
< 160	85	73,9				
≥ 160	30	26,1				
Received dyslipidemia therapy						
Yes	71	61,7				
No	44	38,3				
CT-Scan						
Ischemic Stroke	102	88,7				
Hemorrhagic Stroke	13	11,3				

Data obtained from the study show the prevalence of ischemic stroke from a total of 102 respondents was frequently found in the middle-old group with 37 (26.3%)respondents, then the youngest-old group 29 (28.4%) respondents, the oldest group was 25 (24.5%) respondents, adult 7 was (6.9%) respondents. early adults 3 (2.9%)respondents and teens 1 (1%) respondent. Meanwhile, from a total of 13 hemorrhagic stroke respondents, there were 6 (46.2%) respondents in the adult, then the youngestold group 4 (30.8%) respondents, early adult 2 (15.4%) respondents, middle-old group 1 (7, 7%), whereas the teenager and the oldest group, no one suffered a hemorrhagic stroke. After analyzing the test, p value <0.001 is obtained so that there is a significant relationship between age and stroke.

The highest number of respondents who suffered ischemic stroke was men with 65 of total number (63.7%) respondents, while women with 37 total number of respondent (36,3%) respondents. In hemorrhagic stroke, there were 8 (61,5%) are women and 5 (38,5%) are men respondents. Based on the results of the analysis with a p value of 0,07 it can be concluded that there is no significant relationship between gender and stroke.

Patients with ischemic stroke who had a history of hypertension were 77 (75.5%) respondents, and 25 (24.5%) respondents did not have a history of hypertension. Respondents with hemorrhagic stroke who had a history of hypertension were 13 (100%) and who did not have a history of hypertension was 0 (0%) respondents. After being analyzed, the p value was 0.044 so that it can be concluded that there is a significant relationship between the history of hypertension and the incidence of stroke.

Patients with ischemic stroke who did not have a history of diabetes mellitus were 64 (62.7%) patients, had a history of diabetes mellitus were 27 (26.5) patients, and who were not known to have a history of diabetes mellitus were 11 (10.8%) patients. Patients with hemorrhagic stroke who did not have a history of diabetes mellitus were 12 (92.3%). patients who were not known to have a history of diabetes mellitus were 11 (7.7%), and none of the respondents had a history of diabetes mellitus. After being analyzed, the p value of 0.079 was obtained so that it is concluded that there is no a significant relationship between the history of diabetes mellitus and the incidence of stroke.

Patients with ischemic stroke who had heart disease were 64 (62.7%) patients, and did not have heart disease were 38 (37.3%).

Patients with hemorrhagic stroke who had heart disease were 12 (92.3%) patients, and did not have heart disease were 1 (7.7%) patient. After analysis, p values of 0.034 were obtained so that it is concluded that there is a significant relationship between heart diseasesand stroke.

Patients with ischemic stroke who did not have kidney disorder were 93 (91.2%) patients and 9 patientshad kidney disorder (9.88%). Patients with hemorrhagic stroke who did not have kidney disorder were 13 (100%) respondents, and none had kidney disorders. After analyzing, the p value was 0.595, so it can be concluded that there is no a significant relationship between kid-ney disorders and the incidence of stroke.

number of 57 (55.9%)А total respondents who suffered from ischemic stroke had cholesterol levels >200mg/dL, and 45 (44.1%) others had cholesterol levels <200mg/dL. Respondents who suf-fered hemorrhagic stroke were 11 (84.6%) and had cholesterol levels \geq 200mg/dL and 2 (15.4%) respondents had cholesterol levels <200mg/dL. After analyzing the tests using the Pearson chi square method, p value was 0.047, it can be concluded that there is a significant relationship between total cholesterol and stroke.

Respondents with ischemic stroke who had LDL levels <160 mg/dL were 68 (66.7%) respondents, and LDL levels L \geq 160mg/dL were 34 (33.3%) respondents. Respondents with hemorrhagic stroke who had LDL levels <160mg/dL were 11 (84.6%) respondents, and 2 (15.4%) respondents had LDL levels \geq 160mg / dL. After analyzing the test, p value <0.001 so it can be concluded that there is a relationship between LDL levels and stroke.

For respondents with ischemic stroke, 102 (100%) respondents had HDL levels \geq 30mg / dL and no respondents had HDL levels <30mg/dL. Whereas in hemorrhagic stroke, 11 (84,6%) respondents had HDL levels \geq 30mg/dL, and 2 (15,4%) respondents had HDL levels <30mg / dL. After being analyzed, the p value was 0.012 so that it is concluded there is a significant relationship between HDL levels and the incidence of stroke.

In respondents with ischemic stroke, 79 (77.5%) respondents had triglyceride levels <160 mg / dL, and triglyceride levels $\ge 160 \text{ mg} / dL$ were 23 (22.5%) respondents. Respondents with hemorrhagic stroke who had triglyceride levels <160 mg / dL were 6 (46.2%) respondents, and 7 (53.8%) respondents had triglyceride levels $\ge 160 \text{ mg} / dL$ were 6 (46.2%) respondents, and 7 (53.8%) respondents had triglyceride levels $\ge 160 \text{ mg} / dL$. After analyzing the test, p value<0.038 can be concluded that there is a relationship between triglyceride levels and stroke.

Table 2. Relationship between risk factors and stroke (N = 115)

		CT-Scan			
Variable		SI		SH	\mathbf{p}^{F}
	Ν	%	Ν	%	-
Sex					
Men	65	63,7	5	38,5	0,079
Women	37	36,3	8	61,5	
Age Classification					
12 – 16	1	1,0	0	0	<0,001 *
26 - 35	3	2,9	2	15,4	
36 - 45	7	6,9	6	46,2	
46 - 55	29	28,4	4	30,8	
56 - 65	37	26,3	1	7,7	
> 65	25	24,5	0	0	
History of Hypert	ension				
Yes	77	75,5	13	100,0	0,044*
No	25	24,5	0	0	
History of Diabete	s				
Yes	27	26,5	0	0	0,079
No	64	62,7	12	92,3	
Unknown	11	10,8	1	7,7	
Heart Disease					
Positive	64	62,7	12	92,3	0,034*
Negative	38	37,3	1	7,7	
Kidney Disorders		•			
Positive	9	8,8	0	0	0,595
Negative	93	91,2	13	100	
Total Cholesterol					
< 200	45	44,1	2	15,4	0,047*
≥ 200	57	55,9	11	84,6	
LDL					
< 160	68	66,7	11	84,6	<0,001 *
≥160	34	33,3	2	15,4	
HDL					
< 30	0	0	2	15,4	0,012*
≥ 30	10 2	100	11	84,6	
Triglycerides					
< 160	79	77,5	6	46,2	0,038*
≥160	23	22,5	7	53,8	

DISCUSSION

Basically, ischemic stroke can occur at a young age, but according to research results it tendsto show the incidence of ischemic stroke experienced in old age. This can be caused by diseases that occur due to disruption of blood flow. Blood vessels at an older age tend to change degeneratively and begin to seem the results from the process of atherosclerosis. Based on a meta-analysis, the average incidence of intracerebral hemorrhagic strokes is 25/100,000 and the highest incidence is in the elderly.⁶ In a study conducted by de Rooij et al, the average incidence of hemorrhagic subarachnoid strokes was 9/100,000 and the average age was 43 years in Japan, and in South and Central America vary between 25 to 35 years [7]. The results of the study are similar to the results of this study, that the incidence of hemorrhagic strokes is more commonly found at younger ages. Several risk factors that can cause hemorrhagic strokes at a genetic, hypertension, young age are smoking, excessive alcohol consumption, and drug abuse. These risk factors can cause weakness of the endothelial wall, rupture of brain blood vessels [7].

The results show the incidence of stroke was more common in men than women, but there is no significant relationship found between sex and stroke. Research Roy et al. reports that the incidence of stroke in men will have a greater tendency to stroke compared to premenopausal women, but with age, postmenopausal women have a greater risk of stroke [8]. In a study conducted by Kabi, it also points out that there were 55% male and 45% female of 60 patients who were getting treatment for stroke ischemic in Neurology inpatient at Prof. Dr. D. Kandou, Manado.

However, the different results obtained in hemorrhagic stroke that the ratio between men and women are not significant. In the study of Justin et al, states that men are more susceptible to intracerebral hemorrhagic strokes than women of all ages besides those over 80 years. However, the existence of differences in gender prevalence can be

influenced by several risk factors that can be modified or cannot be modified as well as comorbid by the patient itself [10].

The results of this research show that the average level of education of stroke respondents tend to be low. In a study conducted by Kabi et al, the results also showed a higher proportion of strokes in the non-school and non-primary school group than in the primary school group and above [9]. Prospective cohort studies conducted by Caroline et al in Australia also revealed that low education had a relationship with an increased risk of stroke in men and women [11].

Even though the average level of is low, from education the onset classification an average of <24 hours is obtained. These results can be categorized quite well. Based on the instructions for the management of ischemic stroke, the onset of the arrival of the patient to the hospital is also important in the decision making of the therapy that will be given to the patient and can affect the clinical outcome of the patient after hospitalization. From research conducted by Amit R et al on the effect of hospital admission time and therapy with patient clinical outcomes revealed, patients who received therapy <24 hours had better clinical outcomes after 12 and 18 months later [12]. According to information from the patient's family, there are many reasons for delay in coming to the hospital and the most reason is waiting for family, transportation problems, and ignorance of the patient and family.

Based on hypertension risk factors, a history of uncontrolled hypertension has the greatest frequency in this study. The study conducted by Usrin et al states, 194 people suffering from hypertension, 137 people (70.6%) had an ischemic stroke, and of 50 people who did not, 9 people (18.0%) had an ischemic stroke [13]. Studies that conducted by INTERSTROKE state that respondents with hypertension (either history or blood pressure> 160 / 90mmHg) have a risk of stroke 2.8 times greater than respondents without hypertension.¹⁴ Hyper-tension can cause strokes through many mechanisms. High intraluminal pressure will cause extensive changes in the endothelium and smooth muscle function in the intracerebral arteries. Increased stress in the endothelium can increase permeability to the blood-brain barrier and local or multifocal brain edema. Endothelial damage and altered bloodendothelium cell interactions can cause local thrombus formation and ischemic lesions. Fibrinoid necrosis can cause lacunar infarction through focal stenosis and occlusion. Degenerative changes in smooth muscle cells and endothelium predispose to intracerebral hemorrhage. In addition. hypertension speeds up the arteriosclerotic process, thereby increasing the possibility of cerebral lesions associated with stenosis and emboli originating from extracranial large blood vessels, aortic arches and from the heart. Adaptive structural changes in resistant blood vessels can disrupt collateral circulation and increase the risk of ischemic events associated with episodes of hypertension [15].

In this study, it is found that hypertension was significantly related to the incidence of stroke. These results are in line with the theory and some of the research previously discussed. In a study conducted by Taufik, it was found that there was no significant relationship between ACE gene variants in the development of ischemic stroke in patients with a history of hypertension in a population in Palembang. Several recent studies have shown that there are different genetic control patterns in ACE compared to previous studies that have been carried out in Caucasian races, which suggest that there is an association between ACE gene variants and ischemic stroke. Angiotensin-Converting Enzyme (ACE) gene variants are known to play a role in the pathogenesis from primary hypertension, atherosclerosis and remodeling and the occurrence of left ventricular hypertrophy.

Diabetes mellitus is a disease that occurs due to two things, that is, insufficient insulin production, or the body is unable to use insulin effectively, so there is excess sugar in the blood [17]. History of diabetes mellitus is only a little obtained in this study. The data obtained in this study show that stroke patients in Prof. dr. H. Aloei Saboe Gorontalo Hospital, the majority do not have a history of diabetes mellitus, so after analyzing there is no relationship between diabetes mellitus and the incidence of stroke. The results of this study are contradicted to the study of Mallmann study for patients at the Hospital of Sao Vicente de Paulo, South Brazil, which have a significant relationship bet-ween diabetes mellitus and stroke with an OR of 2.4 (95% CI: 1.4 - 4,0), which means that diabetes mellitus is a risk factor for stroke with a 2.4 times greater risk than non-diabetes mellitus patients [18]. High levels of blood sugar in the body pathologically play a role in increasing the concentration of glycoprotein, which is a trigger to some vascular diseases. High blood glucose levels during a stroke will increase the possibility of expanding infarction areas due to the formation of lactic acid due to anaerobic glucose metabolism that damages brain tissue, but it does not cause stroke directly at a young age [19]. However, this study has the same results as research performed on 60 ischemic stroke patients in the Neurology inpatient at Prof. Dr. RD Kandou Manado, which only 26.6% of respondents with a history of diabetes mellitus [9]. It shows that the proportion of people affected by ischemic stroke due to diabetes is rare, this means that most patients get first ischemic stroke are not because they have diabetes mellitus.

In this study the risk of stroke was found respondents with cardiac more in abnormalities, which consists of several disorders such as arrhythmia, coronary heart disease and the presence of cardiomegaly. After analyzing this study, a significant relationship was found between heart and stroke abnormalities. The incidence of atrial fibrillation increased with age. The Framingham study shows the percentage of strokes due to atrial fibrillation increases gradually from 1.5% at age 50-59 years, to 23.5% at age 80-89 years.²⁰ Patients with

atrial fibrillation face a very high risk of stroke that is about 3 to 5 times higher after adjusting for risk factors. Atrial fibrillation is consistently associated with stroke in different groups. Uncoordinated myocyte activity will cause disruption of atrial contraction in atrial fibrillation. So. according to the Virchow trials, the resulting stasis increases the risk blood of thromboembolism [21]. About 10% of patients with lacunar strokes have atrial fibrillation and atherosclerosis in large arteries twice more common in patients with atrial fibrillation compared to those without [22]. Research conducted by Khaira-tunnisa, et al. also found a higher propor-tion of strokes in coronary heart disease than those without coronary heart disease [23]. Amarenco, et al in a review article stated that a quarter of stroke patients had a history of coronary symptoms recurrent [24]. Myocardial infarction is a major risk factor for ischemic stroke. That is because in myocardial infarction there is damage from the endocardial surface of the heart and local stasis due to dysfunction of the heart muscle (akinetik segment) which results in the formation of thrombus in the heart and if the embolism is lodged in the cerebral arteries, occlusion will cause a decrease in oxygen supply resulting in hypoxia neurons that are blooded or ischemic [24]. If there is no collateral blood supply and this decreases in blood flow cannot be fulfilled will cause brain tissue to die or on the other word it is called infarction.

Research on the relationship between dyslipidemia and stroke shows very mixed results. Research conducted at Prof. RSUP Dr. R.D. Kandou Manado shows the highest levels of total cholesterol in ischemic stroke and hemorrhagic stroke at optimal values [25]. A study by Jusuf using the case-control method in Indonesia reveals that a history of dyslipidemia could be a predictor of ischemic stroke [26]. Different in research conducted at the RSUP dr. Kariadi Semarang that there is a significant relationship between total cholesterol and the incidence of stroke [27]. Prospective studies conducted

in Asia Pacific in Asian and non-Asian populations show a strong relationship between total cholesterol and ischemic stroke that every 1 mmol / 1 increase in total blood cholesterol or about 38.7 mg / dl will increase 25% the incidence of stroke. But unlike non hemorrhagic stroke, each increase of 1 mmol / 1 total blood cholesterol or about 38.7 mg / dl there is a 20% reduction in risk of hemorrhagic stroke [28]. Research in Taiwan reveals the same thing, that total cholesterol <160mg / dL more often occurs in acute intracerebral hemorrhagic stroke patients and has a relationship with the risk of suffering from more severe neurological abnormalities in clinical outcomes in the first 3 months [29]. However, there is a difference in a study conducted in Turkey which stated total cholesterol ≥200mg / dL was a risk factor for hemorrhagic stroke [30].

High total cholesterol is often associated with the formation of atherosclerosis so that it can cause the risk of ischemic stroke. Conversely, low cholesterol is often associated as a risk factor for hemorrhagic stroke due to smooth muscle walls of arteries that are prone to necrosis. Disturbances in the endothelial wall have a tendency to occur with microaneurysmswhich are the main pathological findings in hemorrhagic strokes [31].

This research is in line with research at RSUP dr. Kariadi Semarang that there is a significant relationship between LDL levels and the incidence of stroke.²⁷ Tsuyoshi et al in his study also stated that elevated LDL levels were significantly related to the development of atherothrombotic infarction [32]. However, these results are not in line with research at Dr. dr. Moewardi Surakarta who stated that there is no significant relationship between LDL levels and the incidence of stroke. Meanwhile in hemorrhagic stroke, a systematic review study and meta-analysis reveals a decrease in total cholesterol and LDL levels can be a risk factor for hemorrhagic stroke, especially intracerebral hemorrhagic stroke [33].

Research on the relationship of HDL with stroke also found mixed results.

Research conducted at RSUP dr. Kariadi Semarang reveals a significant relationship between HDL and the incidence of stroke [26]. A prospective study reveals an inverse relationship between HDL and the risk of ischemic stroke in men and women [34]. In contrast to studies conducted in Europe (EUROSTROKE) that found an increase in HDL levels was associated with increased risk of cerebral infarction in women [35]. Whereas in the Asia Pacific cohort study found no association between HDL levels and the risk of ischemic stroke [36]. In hemorrhagic strokes, HDL levels increase the risk of intracerebral hemorrhagic stroke significantly for an increase per 1 mmol / L [33].

The results in this study are in line with research conducted at Sukoharjo Hospital that statistically there is a relationship between triglyceride levels and the incidence of ischemic stroke (OR = 2,800, 95% CI = 1,070-7,328)[36]. In a prospective study reveals that there was a 15% increase in risk ischemic stroke for each increase of 89mg / dL of non-fasting triglycerides [38]. In contrast to studies in RSUD dr. Kariadi Semarang, who said there was no significant relationship between triglyceride levels and stroke events [27]. homas's research also revealed the same thing that found no significant relationship between triglycerides strokes and ischemic in 296 male respondents [39]. In hemorrhagic strokes, a cohort study prospectively states that low triglyceride levels are associated with an increased risk of hemorrhagic stroke. As with total cholesterol, low levels of triglycerides are also associated with blood vessel endothelial cells undergoing arterionecrosis so that cerebral blood vessels become fragile [40].

The data obtained in this study show that stroke patients in Prof. dr. H. Aloei Saboe Gorontalo Hospital, the majority do not have a history of kidney disorders, so after analyzing, there is no relationship between kidney disorders and events. These results are contradicted to the study conducted by Lee, patients with GFR <60 mL / min can increase the incidence of stroke by 43%. Proteinuria that occurs in patients with kidney disorders can also worsen the clinical outcome of stroke and post stroke, thereby increasing mortality [41].

In this study there are several limitations, so that it can affect the results of the study. There is no analysis of other risk factors such as heredity, body mass index, history of drug consumption; anticoagulants, antithrombotics, statins which can affect the state of the lipid profile or be an independent risk factor for stroke itself.

CONCLUSION

Stroke is one of the main causes of the emergency patients coming to department at the hospital, causing morbidity and mortality rates to increase. Generally, in this study stroke patients were found to be at the age criteria of 55-65 years old, male gender, level of education with elementary school certificate, and had less than 24 hours of onset. The most common risk factors found are patients who had a history of high blood pressure who are not controlled, present with grade 2 hypertension, total cholesterol levels that exceed >200mg / dL, and cardiomegaly as the most common heart abnornalities. Based on the significant relationship between risk factors and the incidence of stroke in the Gorontalo are age, history of hypertension, heart disease, total cholesterol, LDL, HDL and triglycerides. Meanwhile diabetes mellitus, and kidney disorders did not have a significant relationship.

REFERENCES

- [1] American Heart Association. Heart disease and stroke statistics. Circulation; 2012. Available from: URL : HIPERLINK http://circ.ahajournals.org/content/125/1/e2.full.pdf+html downloaded on Tuesday, 12 Feb 2019 at 20.48 eastern Indonesia time (GMT +9)
- [2] Amarenco, et al. Prevalence of Coronary Atherosclerosis in Patients With Cerebral Infarction. Stroke. 2011;42:22-

29.

doi.10.1161/STROKEAHA.110.584086

- [3] Arifnaldi MS. (2014) Hubungan Kadar Trigliserida Dengan Kejadian Stroke Iskemik di RSUD Sukoharjo. Fakultas Kedokteran. Universitas Muhammadiyah Surakarta
- [4] Balitbang Kemenkes RI. Hasil utama RISKESDAS 2018. Jakarta: Balitbang Kemenkes RI; 2018
- [5] Bonaventure A, Kurth T, Pico F, Barberger-Gateau P, Ritchie K, Stapf C, et al.. Triglycerides and risk of hemorrhagic stroke vs. ischemic vascular events: The Three-City Study. Atherosclerosis. 2010; 210:243– 248.doi:10.1016/j.atherosclerosis.2009.1 0.04
- [6] Bots ML, Elwood PC, Nikitin Y, Salonen JT, Freire de Concalves A, Inzitari D, et al. Total and HDL cholesterol and risk of stroke. Eurostroke: a collaborative study among research centres in Europe. J Epidemiol Community Health. 2002;56(suppl 1):i19–i24
- [7] Bowman T.S, Sesso H.D, Ma J, et al. Cholesterol and Risk of Ischemic Stroke. Stroke.2003;34:2930– 2934.<u>https://doi.org/10.1161/01.STR.00</u> 00102171.91292.DC
- [8] Bozluolcay, M. et al. 2013. Hypercholesterolemia As One of The Risk Factors of Intracerebral Hemorrhage. <u>Acta Neurol Belg.</u> 2013 Dec;113(4):459-62. doi: 10.1007/s13760-013-0222-6. Epub 2013 Jun 26
- [9] Chen Y-W, Li C-H, Yang C-D, et al. (2017) Low cholesterol level associated with severity and outcome of spontaneous intracerebral hemorrhage: Results from Taiwan Stroke Registry. PLoS ONE 12(4): e0171379. https://doi.org/10.1371/journal.pone.017 1379
- [10] Cipolla, M.J., Huang, Q., Sweet, J.G.,
 2011. Inhibition of Protein Kinase Cβ
 Reverses Increased Blood–Brain Barrier
 Permeability During Hyperglycemic

Stroke and Prevents Edema Formation In Vivo. Journal of The American Heart Association. 42:3252-7 Available from: http://stroke.ahajournals.org/content/42/ 11/3252.full?sid=e7f3b82b-3e63- 46c8a92b-291cb6992cdd

- [11] De Rooij, dkk. Incidence of subarachnoid haemorrhage: a systematic review with emphasis on region, age, gender and time trends J Neurol Neurosurg Psychiatry 2007;78:1365– 1372. doi: 10.1136/jnnp.2007.117655
- [12] Freiberg JJ, Tybjaerg-Hansen A, Jensen JS, Nordestgaard BG.Nonfasting triglycerides and risk of ischemic stroke in the general population. JAMA. 2008; 300:2142–2152. doi: 10.1001/jama.2008.621
- [13] Go AS, Mozaffarian D, Roger VL, et al. Heart Disease and Stroke Statistic-2013 update : A Report from American Heart Association, *Circulation*. 2013;127 (1)
- [14]Goldstein L.B., Bushnell C.D., Adams R.J., Appel L.J., Braun L.T., Chaturvedi S., Creager M.A., Culebras A., Eckel R.H., Hart R.G., Hinchey J.A., Howard V.J., Jauch E.C., Levine S.R., Meschia J.F., Moore W.S., Nixon J.V., Pearson T.A., 2011. Guidelines for the Primary Prevention of Stroke : A Guideline for Healthcare Professionals from the American Heart Association/American Stroke Association. Stroke AHA. 42:517-84
- [15] Goldstein LB, Adams R, Becker K, et al. Primary Prevention of Ischemic Stroke : A Statement for Healthcare Professionals From the Stroke Council of the American Heart Association. Circulation. 2006;113:873-923
- [16] Hakim, Reza. 2013. Hubungan Antara Dislipidemia Dengan Kejadian Stroke di Bangsal Rawat Inap IRNA B 1 Bagian Neurologi RSUP Dr. Kariadi Semarang. Fakultas Kedokteran. Universitas Muhammadiyah Semarang. Semarang
- [17] Hsieh JT, Ang BT, Ng YP, Allen JC, King NKK (2016) Comparison of Gender Differences in Intracerebral Hemorrhage in a Multi-Ethnic Asian

ISSN: 2654-8690, Vol. 2, Desember 2019

Population. PLoS ONE 11(4): e0152945. doi:10.1371/ journal.pone.0152945

- [18] Imamura, T., Yasufumi D., Hisatomi A., Koji Y., Jun H., et al. LDL cholesterol and the development of stroke subtype and coronary heart disease in general Japanese population. American Heart Association and American Stroke Association Journals. 2009; 40: 382-388.
- [19] Indrajaya, Taufik. The Role og ACE Gene Polymorphism on pathogenesis of Ischemic Stroke. Original Article Vol 3, Number 3. July 2011
- [20] Jackson CA, Sudlow CLM, Mishra GD.
 Education, sex and risk of stroke: a prospective cohort study in New South Wales, Australia. BMJ
 Open. 2018;8:e024070. doi: 10.1136/bmjopen-2018-024070
- [21] Johansson BB. Hypertension mechanisms causing stroke. <u>Clin Exp</u> <u>Pharmacol Physiol.</u> 1999 Jul;26(7):563-5
- [22] Jusuf MI, Machfoed MH, Keman S. Infarction Stroke Risk Prediction Model for Indonesian Population: A Case-Control Study. Bangladesh Journal of Medical Science Vol. 15 No. 2016.: 269-274
- [23] Kabi GYC, R Tumewa , Mieke AHN. Gambaran Faktor Risiko Pada Penderita Stroke Iskemik Yang Dirawat Inap Neurologi Rsup Prof. Dr. R. D. Kandou Manado Periode Juli 2012 - Juni 2013. Jurnal e-Clinic (eCl), Volume 3, Nomor 1, Januari-April 2015.
- [24] Kamel H, Okin PM, Elkind SVM. Atrial Fibrillation and Mechanism of Stroke. Stroke. 2016; 47:895–900
- [25] Khairatunnisa, Dian Maya Sari. Faktor Risiko Yang Berhubungan Dengan Kejadian Stroke Pada Pasien Di RSU H. Sahudin Kutacane Kabupaten Aceh Tenggara. Jurnal JUMANTIK Volume 2 nomor 1, Mei 2017
- [26] Konishi M, Iso H, Komachi Y, Iida M, Shimamoto T, Jacobs DR Jr, et al. Associations of serum total cholesterol,

different types of stroke, and stenosis distribution of cerebral arteries. The Akita Pathology Study. Stroke. 1993;24:954–964

- [27] Laulo A, Tumboimbela M, Mahama C. (2016). Gambaran profil lipid pada pasien stroke iskemik dan stroke hemoragik yang di rawat inap di Irina F RSUP Prof. Dr. R. D. Kandou Manado periode Juli 2015-Juni 2016. Jurnal e-Clinic (eCl), Volume 4, Nomor 2, Juli-Desember 2016
- [28] Lee M., Saver J.L., Chang K.H., Liao H.W., Chang S.C., Ovbiagele B. Low glomerular filtration rate and risk of stroke: metaanalysis. BMJ. 2010;341:c4249.
- [29] Lodder J, Bamford JM, Sandercock PA, Jones LN, Warlow CP. Are hypertension or cardiac embolism likely causes of lacunar infarction? Stroke. 1990;21:375–381
- [30] Mallmann, A. B., Sandra Costa Fuchs, Miguel Gus, Flavio Danni Fuchs & Leila Beltrami Moreira, 2012, Population-Attributable Risks for Ischemic Stroke in a Community in South Brazil: A Case-Control Study, Plos One, Volume: 7, Issue: 4.
- [31] Mozzafarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al., on behalf of the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2016 update: a report from the American Heart

Association. *Circulation* 2016;133(4): e38–360.

- [32] Nayak, Amit et al. (2015). Impact of Admission Time on Treatment and Outcome of Stroke in Patients Admitted to Tertiary Care Hospital. doi: 10.7860/JCDR/2015/12000.6106
- [33] O'Donnell MJ, Xavier D, Liu L, et al. Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case-control study. Lancet. 2010;376(9735):112–123

- [34] Roy AM.dkk. Sex Differences in Stroke. Journal of Cerebral Blood Flow & Metabolism (2012) 32, 2100–2107.
- [35] Sustrani, Lanny. DIABETES. PT. Gramedia Pustaka Utama, Jakarta,2004.
- [36] Usrin I, Erna Mutiara, Yusniwarti Yusad. Pengaruh Hipertensi Terhadap Kejadian Stroke Iskemik Dan Stroke Hemoragik Di Ruang Neurologi Di Rumah Sakit Stroke Nasional (Rssn) Bukittinggi Tahun 2011. FKM USU
- [37] Van Asch CJ, Luitse MJ, Rinkel GJ, et al. Incidence, case fatality, and functional outcome of intracerebral hemorrhage over time, according to age, sex, and ethnic origin: a systematic review and meta-analysis. Lancet Neurol 2010; 9: 167–176.
- [38] Wang X, Dong Y, Qi X, Huang C, Hou L.(2013). Cholesterol Levels and Risk of Hemorrhagic Stroke.Jul;44(7):1833-9.

doi:10.1161/STROKEAHA.113.001326. Epub 2013 May 23.

- [39] Woodward M, Barzi F, Feigin V, Gu D, Huxley R, Nakamura K, et al. Associations between high-density lipoprotein cholesterol and both stroke and coronary heart disease in the Asia Pacific region. Eur Heart J. 2007; 28:2653–2660
- [40] Zhang X, Patel A, Horibe H, Wu Z, Barzi F, Rodgers A, et al.; Asia Pacific Cohor tStudies Collaboration. Cholesterol, coronary heart disease, and stroke in the Asia Pacific region. Int J Epidemiol. 2003; 32:563–572
- [41]Zhang Y, Tuomilehto J, Jousilahti P, et al. 2011. Total and High-Density Lipoprotein Cholestrol and Stroke Risk. <u>https://doi.org/10.1161/STROKEAHA.1</u> <u>11.646778Stroke. 2012</u>; 43:1768–1774