A COMPARISON OF LIPID PROFILE IN ISCHEMIC STROKE PATIENTS WITH DIABETES MELLITUS AND NON-DIABETES MELLITUS AT RSUD CIAMIS 2020

Niken Puspa Kuspriyanti[1*], Dina Nabila Lestari[2], Sofie Kaniawati[3]

[1]Departemen Biokimia, Fakultas Kedokteran, Universitas Pasundan, Indonesia
[2]Fakultas Kedokteran, Universitas Pasundan, Indonesia
[3]Departemen Neurologi, Fakultas Kedokteran, Universitas Pasundan, Indonesia

*Correspondence email: nikenpuspa@unpas.ac.id

ABSTRACT

Diabetes mellitus causes lipid profile abnormalities, resulting in dyslipidemia in diabetic patients leading to ischemic stroke. This research aims to contrast lipid profiles in ischemic stroke patients with type two diabetes mellitus (T2DM) and non-type two diabetes mellitus (non-T2DM) to prevent stroke recurrence, treat dyslipidemia in diabetes mellitus, and evaluate for treatment of T2DM and non-T2DM ischemic stroke patients. A cross-sectional design was conducted at RSUD Ciamis using secondary medical record data in 2020. The data was collected using a nonprobability sampling approach, with the sampling extent determined by inclusion and exclusion criteria. Univariate analysis was used to determine the quantity and calculation. Besides, an independent t-test and chi-square test was utilized to test two hypotheses in bivariate analysis. Multifaceted analysis in age, gender, hypertension, and coronary heart disease was incorporated to observe its influence on T2DM and non-T2DM ischemic stroke patients. By using four lipid profile indicators, the differences were only in the triglyceride. At the same time, the total cholesterol, low-density lipoprotein (LDL), and high-density lipoprotein (HDL) were insignificant. Meanwhile, hypertension and coronary heart disease (CHD) significantly affect the incidence of ischemic stroke.

Keywords: Ischemic stroke; Diabetes mellitus; Lipid profile; Dyslipidemia.

INTRODUCTION

The incidence of stroke is the main distress in grown and growing countries. Following coronary heart disease, stroke is ranked in third place. The incidence of stroke is 80% due to ischemic stroke and 10% due to hemorrhagic stroke.[1]

Increased total cholesterol, triglycerides, LDL, and a decreased HDL cause dyslipidemia. It results in abnormal serum lipid levels that lead to ischemic stroke by forming atherosclerotic plaque.[2–5]

Dyslipidemia in T2DM patients causes increased triglycerides, increased LDL, and decreased HDL, causing oxidative stress and an increase in fatty acids from adipose tissue that affects insulin and increases liver concentration, triggering the development of atherosclerosis. High serum lipids, including triglycerides, can be the main risk factor for stroke.[6–10]

Gender is a different factor that may cause an ischemic stroke, with women having a higher stroke incidence than men; the age of ≥ 45 years old may be the most critical stroke factor. Furthermore, patients with hypertension records have four instances of risk of stroke. Strokes are more than twice as standard in coronary heart disease patients.[11–14]

Based on research by Bruno Verges[8], 72-85% of type two diabetes mellitus have cholesterol abnormalities resulting in dyslipidemia.[8,15] According to research by Lik-Hui Lau, it is found that one in three stroke patients has diabetes mellitus.[16] This is because dyslipidemia in diabetes mellitus patients increases, causing blockages in blood vessels which can lead to stroke.[17,18] Research Woro Riyadina states that the ischemic stroke incidence will increase twice in patients who were previously diagnosed with coronary heart disease seen from the age factor above 45 years, which has a large stroke risk.[12] In terms of gender, stroke incidence arises a lot in women.[12–14]

Based on data from Riskesdas, about 4.5 times the risk of diabetes mellitus patients having a stroke, while in hypertension patients, it is four times.[12,19] In Ciamis, the incidence of stroke has increased, making it one of West Java's five most common stroke events. Stroke is the ten most common disease at RSUD Ciamis.[11,16,20]

Gender, age, hypertension, CHD, T2DM, and dyslipidemia can be risk factors in the incidence of ischemic stroke, so researchers are interested in assessing the comparison of lipid profiles in T2DM and non-diabetes mellitus ischemic stroke patients at the RSUD Ciamis in 2020. It aims to contrast lipid profiles in T2DM and non-T2DM ischemic stroke patients to prevent stroke recurrence, treat dyslipidemia in diabetes mellitus, and evaluate for treatment of T2DM and non-T2DM ischemic stroke patients.

This study is expected to provide information concerning laboratory tests, that is, lipid profiles in ischemic stroke patients with T2DM and non-T2DM at RSUD Ciamis. This information is expected to prevent the incidence of stroke and appropriate management from preventing the recurrence of stroke in patients with T2DM and non-T2DM so that it can be an evaluation for treating ischemic stroke patients. Finally, the results of this study can be used as information regarding the relationship between diabetes mellitus and the incidence of stroke.

MATERIAL AND METHODS

Secondary medical record data of a cross-sectional analysis was conducted at RSUD Ciamis. A total of 146 medical record data samples were collected. This study applied all inclusion criteria and registered patients with an ischemic stroke as evidenced by a CT scan with an attachment of a lipid profile laboratory result and was registered and hospitalized at RSUD Ciamis in 2020. However, patients with hemorrhagic stroke, recurrent stroke, T2DM, kidney failure, liver failure, smoking and alcohol consumption record, obesity, gout arthritis, and hematological disorders were excluded.

One hundred forty-six medical record data samples from 95 T2DM ischemic stroke patients and 51 non-T2DM ischemic patients were employed. The ethic of this research has been approved by Universitas Padjadjaran Ethical Commission with protocol No. 594/UN6.KEP/EC/2022.

SPSS 26.0 was used to analyze the data. It implied relevance if the p-value <0.05 and irrelevant if it>0.05. To determine the frequency distribution presented in the form of numbers and percentages, a univariate analysis was performed. An Independent t-test was incorporated for bivariate analysis. Besides, when the data were homogenous or not normally distributed for the two hypotheses, an assessment of Mann-Whitney was applied. Investigating confounding factors impact such as gender; age <45 or ≥45-year-old; hypertension, and coronary heart disease, a chi-square test were incorporated. Multifaceted analysis with binary logistic regression was used to measure the lipid profile influence on overall cholesterol, triglycerides, LDL, and HDL, as well as confounding factors on T2DM and non-T2DM.

RESULT

A total of 146 medical records were collected with 95 T2DM ischemic stroke patients and 51 non-T2DM ischemic stroke patients. According to table 1, the mean total cholesterol for stroke ischemic with T2DM was 195.7, and for ischemic stroke without T2DM was 185.3, total cholesterol in the T2DM ischemic stroke patients was greater than in non-T2DM ischemic stroke patients. According to table 2, the T2DM ischemic stroke patients' triglycerides mean were higher than those in ischemic non-T2DM. According to table 3, the T2DM stroke patients' LDL mean was increased by contrast to non-T2DM ischemic stroke patients. According to table 4, the T2DM ischemic stroke patients' HDL mean, was greater than in non-T2DM ischemic stroke patients. Meanwhile, the table shows the number and percentage of confounding variables in the study based on gender; women dominated the incidence. Furthermore, ≥ 45-year-olds were more susceptible than <45-year-old. The characteristic of hypertension accompanied by T2DM dominated patients non-T2DM. Besides, the coronary heart disease incidence was low.

Based on the bivariate analysis in tables 6-7, the p-value was not <0.05; thus, the data were naturally distributed, which can be tested by an independent t-test consisting of HDL and LDL. Meanwhile, data that were not normally distributed were tested for total cholesterol and triglyceride levels using the Mann-Whitney test. Table 8 shows the lipid profile with a probability p-value <0.05 was triglyceride. At the same time, the other three lipid profiles, total cholesterol, LDL, and HDL, had a probability p-value >0.05. Table 9 used the chi-square test to examine the effect of the gender variables on T2DM and non-T2DM ischemic stroke patients. It is insignificant because it had a probability p-value >0.05, and then hypertension and coronary heart disease had a p-value <0.05; thus, both had significance. Triglycerides, hypertension, and coronary heart disease were found to have a significant impact on T2DM and non-T2DM ischemic stroke occurrence. Binary logistic lapse and altogether variables had >0.05 p-value, as shown in Table 10. All of the above variables had an insignificant effect on T2DM and non-T2DM ischemic stroke patients.

Table 1. Total serum cholesterol data ischemic stroke patients with T2DM and non-T2DM.

Ischemic Stroke	Median (Min-Max)	Mean	S.D
T2DM (+)	192.0 (91.0-371.0)	195.7	53.8
T2DM (-)	185.0 (115.0-287.0)	185.3	41.5
Total	191.0 (91.0-371.0)	192.1	50.0

Table 2. Data on serum triglycerides in ischemic stroke patients with T2DM and non-T2DM.

Ischemic Stroke	Median (Min-Max)	Mean	S.D
T2DM (+)	136.0 (35.0-679.0)	157.0	94.7
T2DM (-)	122.0 (10.0-329.0)	128.3	60.5
Total	132.0 (10.0-679.0)	147.7	85.4

Table 3. Data on serum LDL in ischemic stroke patients with T2DM and non-T2DM.

Ischemic Stroke	Median (Min-Max)	Mean	S.D
T2DM (+)	119.0 (24.0-247.0)	123,7	36.8
T2DM (-)	117.5 (61.0-219.0)	121.6	24.0
Total	119.0 (24.0–247.0)	123.0	41.3

Table 4. Data on serum HDL in T2DM and non-T2DM ischemic stroke patients.

Ischemic Stroke	Median (Min-Max)	Mean	S.D
T2DM (+)	39.0 (10.0-80.0)	41.3	11.3
T2DM (-)	39.5 (16.0-80.0)	40.1	11.5
Total	39.0 (10.0-80.0)	40.9	41.3

Table 5. Characteristic data of T2DM and non-T2DM ischemic stroke patients.

Patient Characteristics	n	(%)
Gender		
Man	72	49.3%
Woman	74	50.7%
Age		
<45-year-old	18	12.3%
≥45-year-old	128	87.7%
Hypertension		
Yes	45	30.8%
No	101	69.2%
Coronary Heart Disease (CHD)		
Yes	2	1.4%
No	144	98.6%
Total	146	100.0%

Table 6. Data of normality test results.

Lipid Profile	Group	Normality test[a]	
		P	Conclusion
Total Cholesterol	T2DM	0.024	Abnormal
	Non-T2DM	0.200	Normal
Triglycerides	T2DM	0.001	Abnormal
	Non-T2DM	0.047	Abnormal
HDL	T2DM	0.060	Normal
	Non-T2DM	0.200	Normal
LDL	T2DM	0.183	Normal
	Non-T2DM	0.200	Normal

a superscript = kolmogorov smirnov

Table 7. Data of homogeneity test results.

Lipid Profile	Group	Homogeneity Test	
		P	Conclusion
Total Cholesterol	T2DM	0.182	Homogeneous
	Non-T2DM		
Triglycerides	T2DM	0.152	Homogeneous
	Non-T2DM		
HDL	T2DM	0.972	Homogeneous
	Non-T2DM		
LDL	T2DM	0.366	Homogeneous
	Non-T2DM		

b superscript = Levene's test

Table 8. Comparative data on lipid profile in ischemic stroke T2DM and non-T2DM.

Lipid Profile	Ischemic Stroke				P
	T2DM (+)		Non-T2DM (-)		
	Mean	S.D	Mean	S.D	
Total cholesterol	195.7	53.8	185.3	41.5	0.309b
Triglycerides	157.0	94.7	128.3	60.5	0.039b
LDL	123,7	36.8	121.6	24.0	0.773a
HDL	41.3	11.3	40.1	11.5	0.576a

Table 9. Comparative data on confounding variables in ischemic stroke patients with T2DM and non-T2DM.

Confounding Variable	Ischemic Stroke		P
	T2DM (+)	Non-T2DM (-)	
Gender			
Man	48 (66.7%)	24 (33.3%)	0.819
Woman	48 (64.9%)	26 (35.1%)	
Age			
<45-year-old	13 (72.2%)	5 (27.8%)	0.537
≥45-year-old	83 (63.8%)	45 (35.2%)	
Hypertension			
Yes	1 (2.2%)	44 (97.8%)	0.001
No	95 (94.1%)	6 (5.9%)	
Coronary Heart Disease (CHD)			
Yes	0 (0.0%)	2 (100.0%)	0.048
No	96 (66.7%)	48 (33.3%)	

*Chi-square Test Analysis, CI95%

Table 10. Data on lipid profile and confounding variables affect ischemic stroke with T2DM and non-T2DM.

Variables	B	P
Gender	0.376	0.710
Age	-0.940	0.561
Hypertension	-7.012	0.001
Coronary Heart Disease	-24.122	0.999
Total cholesterol	-0.001	0.951
Trigyceride	0.003	0.721
LDL	-0.002	0.922
HDL	0.005	0.923
Constant	3.737	0.222

*Logistic Regression Analysis, CI95%

DISCUSSION

Dyslipidemia increases the risk of stroke due to atherosclerosis in the cerebral arteries, both extracranial and intracranial. Furthermore, dyslipidemia in T2DM is marked by increased serum triglyceride, VLDL, and LDL levels, plus a fall in HDL.[2,21,22]

In this research, the increase in serum cholesterol in T2DM and non-T2DM ischemic stroke patients was insignificant. This result, however, was similar ($p>0.05$) to Jeetendrakumar et al.'s research.[23] This study found statically increased triglycerides in T2DM and non-T2DM ischemic stroke patients ($p<0.05$).[23] In contrast, the increase in triglycerides in T2DM and non-T2DM ischemic stroke patients was insignificant, as researched by Marques et al. Furthermore, based on Yuan et al.'s research, increased triglyceride levels in stroke patients ($p<0,05$) were linked with acute ischemic stroke, small vessel stroke, and large artery ischemic stroke.[24] Triglycerides-rich lipoprotein overproduction and altered clearance, with decreased lipoprotein lipase causing hypertriglyceridemia, are common in Diabetes.[10]

Atherosclerosis and vascular thrombosis form heterogeneous pathological conditions in ischemic stroke patients.[25] Increased cholesterol in residual lipoproteins, considered atherogenic similar to LDL cholesterol accumulating in artery walls and raised triglycerides.[26] Dyslipidemia is significant in the incidence of ischemic stroke because triglycerides can be a risk factor for the formation of carotid intima coagulating and cerebral atherosclerosis.[27,28] Recently, disagreements about triglycerides have arisen among some researchers. They believe that there is a major or irrelevant association between triglycerides and ischemic stroke incidence.[29–35]

These data are appropriate with Bezafibrate Infarction Prevention (BIP); they discovered prodigious triglycerides as a stand-alone ischemic stroke risk factor at > 60 years old.[36–38] Even though an increase in triglycerides does not escalate ischemic stroke incidence, as stated by some researchers.[25,38,39]

Based on the experience of the researchers during the research process, several limitations and other factors are involved. Some of these limitations include incomplete data on medical record data, limited research time, and limitations on research objects that focus on several risk factors for ischemic stroke with T2DM and non-T2DM only.

Thus, future research may pay attention to the shortcomings that exist in this study. In particular, classifying the effect of triglycerides and its causal relationship on ischemic stroke patients' lipid profile with T2DM and non-T2DM.

CONCLUSION

A comparison of lipid profiles in T2DM and non-T2DM ischemic stroke is not statistically significant. Triglycerides vary primarily due to statistical calculation of the lipid profile. In both T2DM and non-T2DM ischemic stroke patients, total cholesterol, LDL, and HDL levels were insignificant. Meanwhile, the confounding variables of hypertension and coronary heart disease were significant outcomes that can be high risk in ischemic patients.

Based on the results of this study, triglycerides have an insignificant value which can be a major influence on ischemic stroke risk factors in T2DM and non-T2DM patients. Not only that, a record of diseases such as diabetes mellitus, dyslipidemia, hypertension, and coronary heart disease can be a risk factor for ischemic stroke in T2DM and non-T2DM patients.

This, the researcher suggests that further research should use a larger sample, a longer research period, and additional primary data to make the information obtained more comprehensive and reliable.

REFERENCES

1. World Health Organisation (WHO) . WHO definition of palliative care 2016 ; Available from: http//www.who.int/cancer/palliative/definition/en.
2. Aman AM, Soewondo P, Soelistijo AS, Arsana MP, Wismandari, Zufry H, et al. Pedoman Pengelolaan Dislipidemia di Indonesia. 2019. 5–7 p.
3. Jameson JL, Fauci A, Kasper D, Hauser S, Longo D, Loscalzo J. Harrison's Principles of Internal Medicine. 20th ed. McGraw-Hill; 2018. 2892 p.
4. Jameson JL. Harrison's Endocrinology. 4th ed. McGraw-Hill; 2016. 608–609 p.
5. Chaudhury D, Ankita A. Diabetic dyslipidemia: Current concepts in pathophysiology and management. J Clin Diagnostic Res. 2018;12(1).
6. Haffner SM. Cardiovascular risk factors in confirmed prediabetic individuals. Does the clock for coronary heart disease start ticking before the onset of clinical Diabetes? JAMA J Am Med Assoc. 1990;263(21):2893–8.
7. Dean D, Durrington P. Treatment of dyslipoproteinaemia in diabetes mellitus. Diabet Med A J Br Diabet Assoc. 1996;13(4):297–312.
8. Verges B. Pathophysiology of diabetic dyslipidaemia: Where are we? Diabetologia. 2015;58(5):886–899.
9. Schofield J, Liu Y, Rao-Balakrishna P, Malik R, Soran H. Diabetes dyslipidemia. Diabetes Ther Res Treat Educ Diabetes Relat Disord. 2016;7(2):203–219.
10. Galicia-Garcia C, Benito-Vicente U, Jebari A, Larrea-Sebal S, Siddiqi A, Uribe H, et al. Pathophysiology of type 2 diabetes mellitus. Int J Mol Sci. 2020;21(17):6275.
11. Badan Penelitian dan Pengembangan Kesehatan Kementrian Kesehatan RI. Laporan Nasional Riskesdas. 2018.
12. Riyadina W, Ekowati R. Determinan penyakit stroke. Kesmas Natl Public Heal J. 2013;7(7):324.
13. Saputra M, Muhith A, Fardiansyah A. Analisis sistem informasi faktor resiko hipertensi berbasis posbindu di dinas keseharan kabupaten sidoarjo. Pros Semin Nas Seri Ke-1. 2017;7(17).
14. Feske S. Ischemic stroke. Am J Med. 2021;
15. Doucet J, Le-Floch JP, Bauduceau B, Verny C, Intergroup S. GERODIAB: Glycaemic control and 5-year morbidity/mortality of type 2 diabetic patients aged 70 years and older: 1. Description of the population at inclusion. Diabetes Metab [Internet]. 2012;38(6):523–30. Available from: https://pubmed.ncbi.nlm.nih.gov/23062595/
16. Lik-Hui L, Jeremy L, Karen B, Vincent T, Elif E. The prevalence of Diabetes and its effects on Stroke Outcomes; a meta - analysis and literature review. J Diabetes Investig. 2018;10(3):780–92.
17. American Diabetes Association. Diagnosis and classification of Diabetes mellitus. Am Diabetes Assoc. 2013;36(Supplement_1):67–74.
18. Taskinen MR. Diabetic dyslipidaemia: From basic research to clinical practice. Diabetologia [Internet]. 2003;46:733–749. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4392164/#CR6
19. RI BP dan PKKK. Laporan hasil riset kesehatan dasar (RISKESDAS) Provinsi Jawa Barat tahun 2007. Kementrian Kesehat. 2007;
20. Chen W, Pan Y, Jing J, Zhao X, Liu L, Meng X, et al. Recurrent stroke in minor ischemic stroke or transient ischemic attack with metabolic syndrome and/or siabetes mellitus. J Am Heart Assoc. 2017;6(6).
21. Seung-Hoon L. Stroke Revisited: Pathophysiology of Stroke: From Bench to Bedside. 1st ed. Spinger; 2020. 288–304

p.
22. Corbett D, Carmichael S, Murphy T, Jones T, Schwab M, Jolkkonen J, et al. Enhancing the alignment of the preclinical and clinical stroke recovery research pipeline: Consensus-based core recommendations from the stroke recovery and rehabilitation roundtable translational working group. nternational J Stroke. 2017;12(5):462–71.
23. Jeetendrakumar J, Ashoka A, Chethan C, Shivraj S, Umesh U. A comparative study of lipid profile in ischemic stroke between diabetic and non diabetic patients at tertiary care center. J Evol Med Dent Sci. 2015;4(29):2278–4748.
24. Holanda MDA, Filizola R, Costa DCC, De Andrade R, Gonçalves DS. Plasma lipoprotein(A) levels: A comparison between diabetic and non-diabetic patients with acute ischemic stroke. Arq Neuropsiquiatr. 2004;62(2A):233–6.
25. Shahar E, Chambless L, Rosamond W. Plasma lipid profile and incident ischemic stroke: the Atherosclerosis Risk in Communities (ARIC) study. Stroke. 2003;34(3):623–31.
26. Kim S, Park Y, Kim J. Plasma fasting and nonfasting triglycerides and high density lipoprotein cholesterol in atherosclerotic stroke: Different profiles according to low-density lipoprotein cholesterol. Atherosclerosis. 2012;223(2):463–467.
27. Meschia J, Bushnell C, Boden-Albala B. Guidelines for the primary prevention of stroke: A statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014;45(12):3754–832.
28. Wein T, Lindsay M, Côté R. Canadian stroke best practice recommendations: Secondary prevention of stroke, sixth edition practice guidelines, update 2017. Int J Stroke. 2018;13(4):420–43.
29. Iso H, Imano H, Yamagishi K. Fasting and non-fasting triglycerides and risk of ischemic cardiovascular disease in Japanese men and women: The Circulatory Risk in Communities Study (CIRCS). Atherosclerosis. 2014;237(1):361–8.
30. Tanne D, Koren-Morag N, Graff E. Blood lipids and first-ever ischemic stroke/transient ischemic attack in the Bezafibrate Infarction Prevention (BIP) Registry: High triglycerides constitute an independent risk factor. Circulation. 2001;104(24):2892–7.
31. Lindenstrom E, Boysen G, Nyboe J. Influence of total cholesterol, high density lipoprotein cholesterol, and triglycerides on risk of cerebrovascular disease: The Copenhagen City Heart Study. BMJ. 1994;309(6946):11–15.
32. Håheim L, Holme I, Hjermann I. Risk factors of stroke incidence and mortality: A 12-year follow-up of the Oslo Study. Stroke. 1993;24(10):1484–9.
33. Simons L, McCallum J, Friedlander Y. Risk factors for ischemic stroke: Dubbo Study of the elderl. Stroke. 1998;29(7):1341–6.
34. Simons L, Simons J, Friedlander Y. A comparison of risk factors for coronary heart disease and ischaemic stroke: The Dubbo study of Australian elderly. Hear Lung Circ. 2009;18(15):330–3.
35. Wannamethee S, Shaper A, Ebrahim S. HDL-Cholesterol, total cholesterol, and the risk of stroke in middle-aged British men. Stroke. 2000;31(8):1882–8.
36. Shahar E et al. Plasma lipid profile and incident ischemic stroke: the Atherosclerosis Risk in Communities (ARIC) study. 2003;34(3):623–31.
37. TG and HDL Working Group of the Exome Sequencing Project, National Heart, Lung, and Blood Institute, Crosby J, Peloso GM, Auer PL, Crosslin DR, Stitziel NO, Lange LA, Lu Y, Tang ZZ, Zhang H, Hindy G, Masca N, Stirrups K, Kanoni S, Do R, Jun G, Hu Y, Kang KS. Loss-of-function mutations in APOC3, triglycerides, and coronary disease. 2014;371(1):22–31.
38. Bowman TS. Cholesterol and the risk of ischemic stroke. 2003;34(12):2930–4.
39. Crosby J, Peloso G, Auer P, Crosslin D, Stitziel N, Lange L. Loss-of-function mutations in APOC3, triglycerides, and

coronary disease. N Engl J Med. 2014;371(1):22–31.