e-ISSN: 2807-7970

AKSONA

Volume 3 Number 2, July 2023

HDL Cholesterol and Functional Scale Measured by the NIHSS in Acute Thrombotic Stroke Patients

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Article info

Article History:
Received Mar 29, 2023
Revised Jun 21, 2023
Accepted Jul 3, 2023
Published Jul 31, 2023

Keywords:
Acute thrombotic stroke
Cardiovascular disease
HDL
NIHSS

ABSTRACT

Introduction: Stroke is one of the world's leading causes of death and disability. Acute thrombotic stroke accounts for 87% of all stroke cases. The study of the correlation between high-density lipoprotein (HDL) cholesterol levels and acute thrombotic stroke is still limited, especially on the relationship between HDL levels and the degree of functional stroke. **Objective:** This study aimed to prove a correlation between HDL cholesterol and the functional scale measured by the NIHSS (National Institutes of Health Stroke Scale) in acute thrombotic stroke. **Methods:** The design study was cross-sectional, with sampling by consecutive admission based on inclusion and exclusion criteria in the neurological ward (Seruni A) at Dr.Soetomo General Academic Hospital, Surabaya. The NIHSS was used to determine the degree of functional scale, and HDL levels were measured by enzymatic endpoint methods. **Results:** From the 40 subjects studied, 16 (40%) had normal HDL levels of ≥ 40 mg/dL with an NIHSS score between 0–10, and 24 (60%) had lower HDL levels of ≤ 40 mg/dL with an NUHSS score between 0–20. There were significant results in this study ($r = 0.391$ and $p = 0.013$). **Conclusion:** There was a negative correlation between HDL cholesterol levels and the functional scale measured by the NIHSS in acute thrombotic stroke patients.

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INTRODUCTION

The World Health Organization (WHO) defines a stroke as a sudden brain attack caused by a blockage of blood vessels in a part of the brain. This blockage is due to fat deposits or artery rupture, causing the flow of blood supply to stop and symptoms of brain tissue death to appear.[1] In general, symptoms include half-body paralysis, impaired speech, visual disturbances, and decreased consciousness.[2]

Stroke is a major health problem and the third leading cause of death in developed countries after cardiovascular disease and cancer. Other than being a cause of death, stroke is also a major cause of disability.[3] A stroke affects almost 795,000 people worldwide each year. According to statistics, 610,000 patients had their first attack, while the rest had repeated attacks.[4] Thrombotic stroke accounts for approximately 87% of all strokes, while intracerebral hemorrhage accounts for 10% and subarachnoid hemorrhage accounts for 3%.[3]

The ASNA (ASEAN Neurological Association) conducted a fairly large-scale survey of 28 Indonesian hospitals. Dyslipidemia, or an imbalance in blood lipid profile levels, was found to be one of the high-risk factors for stroke. The impact of dyslipidemia on the enhancement of stroke risk factors correlates with the declining rate of high-density lipoprotein (HDL) cholesterol. A decline in HDL levels may increase the risk of plaque formation and atherosclerosis, resulting in ischemic stroke due to reduced blood supply to the brain.[5] Patricia *et al*. (2015) discovered that HDL cholesterol levels are declining in as many as 60% of 75 thrombotic patients at Prof. Dr. RD Kandou General Academic Hospital.[6]

A thrombotic stroke is a disease that can cause disability and even death. The patient's quality of life and psychology will suffer as a result of the disability. Stroke can be a serious problem for both patients and their families. A stroke survivor may be unable to return to work, communicate with others, or manage their daily living activities. Stroke can occur at any age, whether productive or elderly. Stroke has the potential to disrupt national health development efforts.[7]

Obesity, hypertension, diabetes mellitus, smoking, and dyslipidemia (lipid metabolism disorders) are all risk factors for stroke.[8,9] Dyslipidemia is a lipid disorder characterized by abnormalities (increases or decreases) in the lipid fraction in plasma. The liver produces a lipid substance called cholesterol, which is detected in the blood.[10]

Excessive cholesterol in the body can cause problems, especially in the heart's and brain's blood vessels. Two types of cholesterol, LDL (low-density lipoprotein) and HDL (high-density lipoprotein), have an important role in the lipid metabolism associated with stroke disorders.[11] When LDL concentrations in the blood are excessive, LDL will precipitate and form clots that clog blood vessels. HDL cholesterol functions to clean up LDL cholesterol that sticks to blood vessels.[12]

According to the Framingham research, HDL cholesterol levels have more potential as a risk predictor of cardiovascular disease and stroke compared to LDL levels, but it cannot be explained with certainty whether low HDL levels are a significant cause of stroke.[11]

Currently, there are still a few studies related to HDL cholesterol levels in acute thrombotic stroke patients with the functional degree of the NIHSS, in which theoretically there is a correlation between HDL cholesterol levels as a predictor of the formation of atherosclerosis of blood vessels in acute thrombotic stroke, which can affect the functional degree in thrombotic stroke sufferers.[13]

OBJECTIVE

This study examined and evaluated the correlation between HDL cholesterol levels and the measured functional degree on the NIHSS (National Institutes of Health Stroke Scale) in patients with acute thrombotic stroke.

METHODS

This study has passed ethical clearance and received a certificate from the research ethics committee of Dr. Soetomo General Academic Hospital, Surabaya. This study used a cross-sectional design with a consecutive sampling method with acute thrombotic stroke patients in the neurological ward (Seruni A) at Dr. Soetomo General Academic Hospital, Surabaya, who met the inclusion and exclusion criteria during the period from August to October 2016. The inclusion criteria were patients with acute thrombotic stroke with an onset of less than 5 days, first attack stroke, Glasgow Coma Scale (GCS) 456, and willingness to participate in the study. Exclusion criteria were recurrent thrombotic stroke, patients with sepsis, and impaired cognition.

HDL cholesterol levels were obtained through blood tests using the enzymatic endpoint method (colorimetric) with a normal reference value of ≥ 40 mg/dL.[12] The nurse took 3 ml of venous blood and then calculated the HDL level in the clinical pathology laboratory at Dr. Soetomo General Academic Hospital, Surabaya. Assessment of the functional degree of stroke with the NIHSS scale was carried out on the 5th day of the onset of thrombotic stroke. Mild clinical severity (score < 5), moderate clinical severity (score 5–15), and severe clinical severity (score > 15).[14]

Hypertension if systolic blood pressure is ≥ 140 mmHg and/or diastolic pressure is ≥ 90 mmHg and/or there is a history of using antihypertensive drugs.[15] The condition of fasting blood glucose is high when it is ≥ 110 mg/dL.[16]

Statistical analysis was performed using the SPSS 17.0 program. The data that has been collected is tested for normality using the Shapiro-Wilk test. In the Shapiro-Wilk test, the data were normally distributed, and then a parametric test was performed using Pearson's correlation.[17]

RESULTS

The total number of subjects was 40, consisting of 22 men (52.5%) and 18 women (47.5%), of whom 11 were smokers (27.5%) and 29 were non-smokers (72.5%). The mean age of the subjects was 58.13 ± 10.41 years. The average systolic blood pressure was 157.75 ± 24.75 mmHg, and the average diastolic blood pressure was 88.50 ± 11.88 mmHg. There is an average fasting blood glucose level of 141.08 ± 65.11 mg/dl. The average HDL cholesterol level was 38.02 ± 7.69 mg/dl. The lowest HDL level is 13 mg/dL, and the highest HDL level is 52 mg/dL. There were 8 male patients (20%) with normal HDL levels of ≥ 40 mg/dL and 14 male patients (35%) with HDL levels of ≤ 40 mg/dL. There was a woman (2.5%) with normal HDL levels, namely ≥ 50 mg/dL, and the remaining 17 women (42.5%) had HDL levels ≤ 50 mg/dL. The results of the NIHSS examination on the subjects of this study showed that the mean NIHSS score was 5.92 ± 4.88. There were 17 patients (42.5%) with NIHSS <5 (minor stroke), of whom 10 were male and 7 were female. There were 21 patients (52.5%) with NIHSS values between 5–15 (moderate stroke), consisting of 10 male patients and 11 female patients. Patients with NIHSS values > 15 (severe stroke) were 2 patients (5%) consisting of 1 male and 1 female. The characteristics of the research subject data can be seen in Table 1.

Data analysis revealed a weak negative correlation between HDL cholesterol levels and the NIHSS score, with a correlation coefficient (r) of 0.391 and a p-value of 0.013. There were 8 male patients (20%) who had normal HDL levels of ≥ 40 mg/dL with an NIHSS score between 0-10 and 14 male patients (35%) who had HDL levels of ≤ 40 mg/dL with an NIHSS score between 0-16. There was a female (2.5%) with normal HDL levels of ≥ 50 mg/dL with an NIHSS score of 2, and the remaining 17 females (42.5%) had HDL levels of ≤ 50 mg/dL with an NIHSS between 0–20. The results of the analysis can be seen in Table 2.

DISCUSSION

Based on the 40 research subjects, 22 men (52.5%) and 18 women (47.5%) were present. This finding is consistent with stroke epidemiology data that suggests men suffer more strokes than women.[18] Stroke increases with age. Stroke incidence increased from 22% (age 45–55 years) to 32% (age 55–64 years) and 83% (age 65–74 years).[19] Our study complements the findings of Boehme *et al.* who discovered that men have a higher risk than women, particularly those over the age of 65.[20]

Based on smoking record data from 40 subjects, 11 (27.5%) of them were smokers, and 29 (72.5%) were non-smokers. This study matches a previous study that found smoking behavior to be uncorrelated with the functional degree of stroke.[21] However, some epidemiological data state that smoking has a significant impact on the increased risk of stroke and atherosclerosis.[22,23]

Hypertension is a major risk factor for stroke. Based on clinical data, the mean systolic blood pressure was 157.75 ± 24.75 mmHg, and the mean diastolic blood pressure was 88.50 ± 11.88 mmHg. From the results of the data analysis, a weak positive correlation was obtained between systolic blood pressure and the NIHSS values. From the 40 research subjects, 11 subjects (27.5%) had prehypertension (systolic pressure 120–139 mmHg) and 7 subjects (17.5%) had stage 1 hypertension (systolic pressure 140–159 mmHg). While the remaining 22 subjects (55%) had stage 2 hypertension (systolic pressure ≥ 160 mmHg). Based on these data, it can be assumed that hypertension is a significant risk factor for the incidence of stroke. Several related studies suggest that the contingency of blood vessels caused by the accumulation of atherosclerotic plaque on the endothelial walls of blood vessels might encourage high blood pressure and worsen stroke results.[24] Hartono *et al.* supported other related studies by examining that blood pressure was controlled in the acute phase (the first to seventh day), and as many as 63.3% experienced clinical improvements as assessed by the NIHSS scale.[5]

Hyperglycemia is common during an acute thrombotic stroke. There were 18 subjects (45%) with normal fasting blood glucose levels, and the remaining 22 subjects (55%) had high blood glucose levels. The subjects' average fasting blood glucose was 141.08 ± 65.11 mg/dl. The data analysis revealed a very weak positive correlation between fasting blood glucose levels and the NIHSS values. This study corresponds with a study by Chen *et al.* which stated that high fasting blood glucose levels can cause brain blood vessel stiffness and cell death if acidosis occurs as a result of diabetes mellitus.[25] Observational studies

showed that patients with hyperglycemia on admission had a worse clinical outcome than patients without hyperglycemia.[26]

Based on the results of HDL cholesterol levels on 40 subjects, it was found that the mean HDL cholesterol level was 38.02 ± 7.69 mg/dl, with the lowest HDL level being 13 mg/dL and the highest HDL level being 52 mg/dL. There were 8 male patients (20%) who had normal HDL levels of ≥ 40 mg/dL and 14 male patients (35%) who had HDL levels of ≤ 40 mg/dL. There was a female (2.5%) with a normal HDL level ≥ 50 mg/dL, and the remaining 17 females (42.5%) had HDL levels ≤ 50 mg/dL.

There is a difference between normal HDL cholesterol levels in males and females. The presence of the female hormone estrogen causes the difference in HDL levels between male and female subjects. According to research by Gao *et al*. based on several samples analyzed in six countries, women's HDL levels tend to be higher than men's in the presence of estrogen. Women with high levels of HDL have a lower risk of cardiovascular disease and stroke than men.[27]

Several studies state that HDL levels affect the functional degree of stroke, but these results are still debatable because there are different research results. According to Yeh *et al*. patients with low HDL levels (≤ 40mg/dl) had poor clinical results.[28] Other research suggests that patients with low HDL levels have good clinical results.[29] Necrosis from membrane-cell blood vessel medial arteries may occur in patients with low HDL cholesterol levels. The endothelium is disrupted as a result of the necrosis that ensues. Disrupted endothelium induces swelling and blood vessel blockage, resulting in an acute to external thrombotic stroke effect, as measured clinically with the NIHSS scale.

The mean NIHSS score was 5.92 ± 4.88. There were 17 patients (42.5%) with NIHSS <5 (minor stroke), with 10 males and 7 females. There were 21 patients (52.5%) with NIHSS scores between 5 to 15 (moderate stroke), consisting of 10 males and 11 females. Patients with NIHSS scores > 15 (severe stroke) were 2 patients (5%) consisting of 1 male and 1 female. Based on this study, the mean research subjects suffered a moderate to severe stroke. The NIHSS can be used for acute stroke management, screening, and assessment for monitoring. The NIHSS has demonstrated validity and reliability for assessing long-term results.[30]

The Pearson correlation test revealed a weak negative correlation between HDL cholesterol levels and the NIHSS functional degree, with a correlation coefficient (r) of 0.391 and statistical significance with p = 0.013. This demonstrates that the higher the level of HDL cholesterol, the lower the NIHSS score, and vice versa. This can be interpreted as meaning that the higher the level of HDL cholesterol in the blood of patients with acute thrombotic stroke, the less severe the stroke, and vice versa. Several related studies have validated the hypothesis that low serum HDL levels are closely related to stroke severity.[28] Aside from the study by Yeh PS *et al*. another report by Putaala *et al*. found that low HDL levels were correlated with high NIHSS scores.[31] Tanimoto *et al*. found that plasma HDL levels did not correlate with the general degree of stroke severity; however, high HDL levels may lessen the risk of stroke severity in subjects under the age of 50.[32]

The advantage of our study is that there are few publications regarding the correlation between HDL cholesterol levels and the functional degree of NIHSS in patients with thrombotic stroke, so this research will contribute to strengthening the related research hypothesis. The limitation of this research is the existence of a correlation between two variables in the form of a correlation, which has a weakness due to other factors such as the patient's education level, which might influence the results of the research. The sample is too small and not evenly distributed. This research is based on data collected in the hospital, so the conclusions cannot be drawn absolutely.

CONCLUSION

There was a negative correlation between plasma HDL cholesterol level and the measured functional degree on the NIHSS scale in patients with acute thrombotic stroke. The lower level of plasma HDL cholesterol is related to the higher NIHSS score or the heavier level of stroke severity.

Acknowledgment
We would like to thank the staff of Medical Records Installation and the Department of Neurology at Dr. Soetomo General Academic Hospital Surabaya for helping with the data collection process.

Conflict of Interest
The authors have no conflicts of interest.

Funding
This research was fully funded by the authors without receiving grants from any institution.

Author Contribution
The first author conceived and designed the analysis, collected data, conducted data analysis, and wrote the paper. The second author helped organize and design the analysis and collect data. The third author helped collect data and revise the paper.

REFERENCES

1. Coupland AP, Thapar A, Qureshi MI, Jenkins H, Davies AH. The definition of stroke. *J R Soc Med*. 2017;110(1):9–12.
2. Thomalla G, Gerloff C. Treatment concepts for wake-up stroke and stroke with unknown time of symptom onset. *Stroke*. 2015;46(9):2707–13.
3. Viswanathan R, Arafath MM. Study of clinical profile of stroke in a tertiary care centre - A retrospective study. *Int J Sicentific Study*. 2021;8(10):182–5.
4. Le Danseur M. Stroke rehabilitation. *Crit Care Nurs Clin North Am* . 2020 ;32(1):97–108.
5. Hartono E, Puspitasari M, Adam O. Gambaran tekanan darah pada pasien stroke hemoragik dengan diabetes melitus dan non diabetes melitus di bagian saraf rumkital Dr. Ramelan Surabaya. *J Sinaps*. 2019;2(1):1–8.
6. Patricia H, Kembuan MAHN, Tumboimbel MJ. Karakteristik penderita stroke iskemik yang di rawat inap di RSUP Prof. Dr. R. D. Kandao Manado tahun 2012-2013. e-*CliniC*. 2015;3(1):445–51.
7. Crichton SL, Bray BD, McKevitt C, Rudd AG, Wolfe CDA. Patient outcomes up to 15 years after stroke: Survival, disability, quality of life, cognition and mental health. *J Neurol Neurosurg Psychiatry*. 2016;87(10):1091–8.
8. Putaala J. Ischemic stroke in the young: Current perspectives on incidence, risk factors, and cardiovascular prognosis. *Eur Stroke J*. 2016;1(1):28–40.
9. Boehme AK, Esenwa C, Elkind MSV. Stroke risk factors, genetics, and prevention. *Circ Res*. 2017;120(3):472–95.
10. Opoku S, Gan Y, Fu W, Chen D, Addo-Yobo E, Trofimovitch D, et al. Prevalence and risk factors for dyslipidemia among adults in rural and urban China: Findings from the China National Stroke Screening and prevention project (CNSSPP). *BMC Public Health*. 2019;19(1500):1–15.
11. Sniderman AD, Islam S, McQueen M, Pencina M, Furberg CD, Thanassoulis G, et al. Age and cardiovascular risk attributable to apolipoprotein B, low-density lipoprotein cholesterol or non-high-density lipoprotein cholesterol. *J Am Heart Assoc*. 2016 ;5(10):e003665.
12. Brites F, Martin M, Guillas I, Kontush A. Antioxidative activity of high-density lipoprotein (HDL): Mechanistic insights into potential clinical benefit. *BBA Clin*. 2017;8:66–77.
13. Papagiannis A, Gkolfinopoulou C, Tziomalos K, Dedemadi A-G, Polychronopoulos G, Milonas D, et al. HDL cholesterol efflux capacity and phospholipid content are associated with the severity of acute ischemic stroke and predict its outcome. *Clin Chim Acta*. 2023 ;540:117229.
14. Asadollahi M, Nikdokht P, Hatef B, Sadr SS, Sahraei H, Assarzadegan F, et al. Protective properties of the aqueous extract of saffron (Crocus sativus L.) in ischemic stroke, randomized clinical trial. *J Ethnopharmacol*. 2019 ;238:111833.
15. Flack JM, Adekola B. Blood pressure and the new ACC/AHA hypertension guidelines. *Trends Cardiovasc Med*. 2020 ;30(3):160–4.
16. Park C, Guallar E, Linton JA, Lee D-C, Jang Y, Son DK, et al. Fasting glucose level and the risk of incident atherosclerotic cardiovascular diseases. *Diabetes Care* . 2013 ;36(7):1988–93.
17. Dahlan MS. Statistik untuk kedokteran dan kesehatan. 5th ed. Jakarta: Salemba Medika; 2016.
18. Peters SAE, Huxley RR, Woodward M. Diabetes as a risk factor for stroke in women compared with men: A systematic review and meta-analysis of 64 cohorts, including 775 385 individuals and 12 539 strokes. *Lancet*. 2014 Jun;383(9933):1973–80.
19. Hamdan M, Susilo H, Sugianto P, Sani AF, Ardhi MS, Setyowatie S. Comparison of clinical severity improvement degree between acute thrombotic stroke patients with low and high matrix Metalloproteinase-9 Levels. *Indian J Forensic Med Toxicol*. 2020;14(2):2385–90.
20. Boehme AK, Siegler JE, Mullen MT, Albright KC, Lyerly MJ, Monlezun DJ, et al. Racial and gender differences in stroke severity, outcomes, and treatment in patients with acute ischemic stroke. *J Stroke Cerebrovasc Dis*. 2014 ;23(4):e255–61.
21. Lennon O, Galvin R, Smith K, Doody C, Blake C. Lifestyle interventions for secondary disease prevention in stroke and transient ischaemic attack: A systematic review. *Eur J Prev Cardiol*. 2014 ;21(8):1026–39.
22. Herrington W, Lacey B, Sherliker P, Armitage J, Lewington S. Epidemiology of atherosclerosis and the potential to reduce the global burden of atherothrombotic disease. *Circ Res*. 2016;118(4):535–46.
23. Béjot Y, Daubail B, Giroud M. Epidemiology of stroke and transient ischemic attacks: Current knowledge and perspectives. Rev Neurol (Paris). 2016;172(1):59–68.
24. Liu Y, Luo X, Jia H, Yu B. The effect of blood pressure variability on coronary atherosclerosis plaques. *Front Cardiovasc Med*. 2022;9:803810.
25. Chen R, Ovbiagele B, Feng W. Diabetes and stroke: Epidemiology, pathophysiology, pharmaceuticals and outcomes. *Am J Med Sci*. 2016;351(4):380–6.
26. Pasquel FJ, Tsegka K, Wang H, Cardona S, Galindo RJ, Fayfman M, et al. Clinical outcomes in patients with isolated or combined diabetic ketoacidosis and hyperosmolar hyperglycemic state: A retrospective, hospital-based cohort study. *Diabetes Care*. 2020 ;43(2):349–57.
27. Gao Z, Chen Z, Sun A, Deng X. Gender differences in cardiovascular disease. *Med Nov Technol Devices*. 2019;4:100025.
28. Yeh P-S, Yang C-M, Lin S-H, Wang W-M, Chen P-S, Chao T-H, et al. Low levels of high-density lipoprotein cholesterol in patients with atherosclerotic stroke: A prospective cohort study. *Atherosclerosis*. 2013;228(2):472–7.
29. Markaki I, Nilsson U, Kostulas K, Sjöstrand C. High cholesterol levels are associated with improved long-term survival after acute ischemic stroke. *J Stroke Cerebrovasc Dis*. 2014;23(1):e47–53.
30. Grönberg A, Henriksson I, Lindgren A. Accuracy of NIH stroke scale for diagnosing aphasia. *Acta Neurol Scand*. 2021 ;143(4):375–82.
31. Putaala J, Strbian D, Mustanoja S, Haapaniemi E, Kaste M, Tatlisumak T. Functional outcome in young adult ischemic stroke: Impact of lipoproteins. *Acta Neurol Scand*. 2013 ;127(1):61–9.
32. Tanimoto A, Mehndiratta P, Koo BB. Characteristics of Wake-up stroke. *J Stroke Cerebrovasc Dis*. 2014 ;23(6):1296–9

TABLES AND FIGURES

Table 1. Basic characteristics of research subjects

Variable	Score	Range
Age	58.13 ± 10.41	40-81
Gender Male (percentage)	52.5	-
Gender of women (percentage)	47.5	-
Hypertension (percentage)	72.5	140-200
Systolic Blood Pressure (mmHg)	157.75 ± 24.75	120-200
Diastolic Blood Pressure (mmHg)	88.50 ± 11.88	70-110
Fasting Blood Glucose (percentage)	141.08 ± 65.11	64-325
Smoking (percentage)	27.5	-
Non Smoking (percentage)	72.5	-
HDL values mg/dL	38.02 ± 7.69	13-52
NIHSS score	5.92 ± 4.88	0-20

Table 2 HDL level with NIHSS Score

Gender	Total Respondent	HDL Level	NIHSS Score
Male	8	≥ 40	0-10
Male	14	≤ 40	0-16
Female	1	≥ 40	2
Female	17	≤ 40	0-20