

## RESEARCH ARTICLE

# Results Characteristics of Lipid Profile Examination of Acute Ischemia Stroke Patients at RSUP Dr. Soedono Madiun, East Java

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### ABSTRAK

**Pendahuluan:** Dislipidemia merupakan salah satu abnormalitas yang sering ditemukan pada penderita serangan stroke iskemik akut. Penelitian mengenai karakteristik profil lipid pada penderita stroke iskemik akut diharapkan mampu menjadi landasan perencanaan terapi dan pencegahan yang efektif terhadap penyakit tersebut. **Tujuan:** Mengetahui karakteristik profil lipid pada penderita stroke iskemik akut di RSUP Dr. Soedono Madiun, Jawa Timur.

**Metode:** Penelitian ini merupakan studi deskriptif dengan pendekatan cross-sectional menggunakan data sekunder yang diambil dari rekam medis dari 72 pasien stroke iskemik akut rawat inap secara random di Unit Stroke RSUP Dr. Soedono Madiun, Jawa Timur pada periode Januari-Desember 2015. Hasil pemeriksaan profil lipid yang meliputi kolesterol total, LDL, HDL, dan trigliserida dikategorikan sebagai tinggi, normal, dan rendah sesuai kadar dan nilai referensi masing-masing.

**Hasil:** Kadar kolesterol total ditemukan tinggi pada 52,78% subjek, normal pada 36,11% subjek, dan rendah pada 11,11% subjek. Kadar LDL ditemukan tinggi pada 54,17% subjek, normal pada 22,22% subjek, dan rendah pada 23,61% subjek. Kadar HDL ditemukan rendah pada 31,94% subjek, normal pada 50,00% subjek, dan tinggi pada 18,06% subjek. Kadar trigliserida ditemukan tinggi pada 26,39% subjek, normal pada 33,33% subjek, dan rendah pada 40,28% subjek.

**Kesimpulan:** Hasil pemeriksaan profil lipid menunjukkan kadar kolesterol total dan LDL secara umum tinggi, kadar HDL secara umum normal, serta kadar trigliserida secara umum rendah pada penderita stroke iskemik akut di RSUP Dr. Soedono Madiun, Jawa Timur.

**Kata Kunci:** Profil lipid, dislipidemia, stroke iskemik akut

### ABSTRACT

**Introduction:** Dyslipidemia is among the most common abnormalities in acute ischemic stroke patients. Studies assessing the characteristic of these findings for an effective plan of treatment and prevention to overcome the burden of the disease. **Objective:** To evaluate the lipid profile of acute ischemic stroke patients at Soedono General Hospital, Madiun, East Java.

**Methods:** This research is a descriptive study with a cross-sectional approach using data from the medical records of acute ischemic stroke inpatients admitted to the Stroke Unit of Dr. Soedono General Hospital, Madiun East Java in January-December 2015. Using simple random sampling, 72 cases were selected as subjects. Lipid profile examination consisted of total cholesterol, LDL, HDL, and triglycerides and was categorized as high, normal, and low based on their respective levels and reference values.

**Results:** Level of total cholesterol was high in 52.78%, normal in 36.11%, and low in 11.11% of the subjects. Level of LDL was high in 54.17%, normal in 22.22%, and low in 23.61% of the subjects. Level of HDL was low in 31.94%, normal in 50.00% and high in 18.06% of the subjects. Level of triglycerides was high in 26.39%, normal in 33.33%, and low in 40.28% of the subjects.

**Conclusion:** Total cholesterol and LDL are generally high, HDL is generally normal, while triglycerides are generally low among acute ischemic stroke patients in Dr. Soedono General Hospital, Madiun East Java.

**Keywords:** Lipid profile, dyslipidemia, acute ischemic stroke

### INTRODUCTION

Along with the aging of the global population, the health burden caused by stroke continues to increase, especially in developing countries. As the second leading cause of death in the world, the disease is reported to have 5.7 million deaths during 2005 with 87% were subjected in middle and low income countries. The figure grew to 6.2 million in 2008 and without

proper intervention, it is predicted to increase to 7.8 million by year 2030 (Strong, Mathers and Bonita, 2007; Mendis, Puska and Norrving, 2011; Feigin, V., Krishnamurthi, R., Parmar, P., Norrving, B., Mensah, G., 2015). Furthermore, at least 40% of stroke survivors may experience functional disorders, generally in the form of paralysis and dementia. This poses a risk of positioning them in dependency, creating a problem

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for the families and the caregivers (Young and Forster, 2007; Di Carlo, 2009).

Similar trends also occur in Indonesia. The prevalence of stroke of 8.3 per 1,000 people in 2007 were increased to 12.1 per 1,000 people in 2013 (Badan Penelitian dan Pengembangan Kesehatan Departemen Kesehatan Republik Indonesia, 2008, 2013). Total expenditure of Indonesian households due to this disease reached 0.29 billion dollars in 2010 and is expected to grow to 0.45 billion dollars by 2020 (Finkelstein, Chay and Bajpai, 2014). In East Java alone, the prevalence of stroke at 7.7 per 1,000 population in 2007 was still below national prevalence. Nevertheless, by 2013 the figure has reportedly more than doubled to 16.0 per 1000 population and placed the province at the fourth highest in prevalence of stroke in Indonesia (Badan Penelitian dan Pengembangan Kesehatan Departemen Kesehatan Republik Indonesia, 2008, 2013).

To mitigate the problem, an adequate understanding of the pathophysiology and factors affecting the incidence of stroke is required to develop an efficient preventive and curative strategy. One of the most common abnormalities in patients with acute ischemic stroke is dyslipidemia. This condition is characterized by high total cholesterol, triglyceride, and low-density lipoprotein cholesterol (LDL-C) and low level of high-density lipoprotein cholesterol (HDL-C). This disorder will lead to atherosclerosis, the main pathogenesis mechanism of acute ischemic stroke, especially in the elderly (Koba and Hirano, 2011; Bharosay et al., 2013; Bradac, 2014; Sharmin, N., Sultana, N., Mazumder, P., and Rahman, 2015).

This study aims to determine the characteristics of lipid profile examination results in patients with acute ischemic stroke in RSUP Dr. Soedono Madiun, East Java. The results of this study are expected to be the baseline of therapy planning and the effective prevention of the disease, especially in the Madiun

District, East Java.

## METHODS

This research is a descriptive study with cross-sectional approach using secondary data taken from 72 medical records of acute ischemic stroke patients in Stroke Unit of Dr. Soedono Madiun, East Java from January to December 2015 were randomly selected.

## RESEARCH SUBJECT

The total of 72 medical records were selected by random (figure 1) according to inclusion and exclusion criteria as shown in Table 1.

The variables investigated consisted of demographic data and lipid profile examination results. The demographic data such as age and gender, while the results of the lipid profile includes total cholesterol, low-density lipoproteins (LDL), high-density lipoproteins (HDL), and triglycerides.

## DIAGNOSIS CRITERIA OF ISCHEMIC STROKE

The acute ischemic stroke in this study was defined as an episode of neurological dysfunction:

1. Caused by a focal infarction of the brain, spine, or retina
2. Diagnosed based on evidence of clinical symptoms persisting  $\geq 24$  hours or until resulting death, pathological examination, imaging (CT-scan or MRI), as well as other objective evidence by excluding etiologic possibilities beyond ischemic injuries
3. Takes place at 6-72 hours after symptom onset.

## STATISTICAL ANALYSIS

The data obtained were descriptively analyzed to know the description of distribution of each variable. Reference categorization of the results of each variable

Table 1. Inclusion and Exclusion Criteria of the research

Inclusion Criteria	Exclusion Criteria
1. Patients with acute ischemic stroke hospitalized in Stroke Unit of Dr. Soedono General Hospital, Madiun, East Java from January to December 2015	1. There is evidence of bleeding strokes on CT-scan results and/or MRI
2. The diagnosis of acute ischemic stroke is based on clinical symptoms and CT-scan results and/or MRI	2. There is an infection or malignancy of the central nervous system that can affect the results of CT-scan and/or MRI examinations
3. Lipid profile examination in patients with acute ischemic stroke was performed at Dr. Soedono General Hospital, Madiun, East Java at 6-72 hours after onset	3. The medical record is incomplete, including if the time of symptom onset is not documented
4. Age ( $\geq 18$ years old)	*) The comorbidities of diabetes mellitus and hypertension were not considered as exclusion criteria

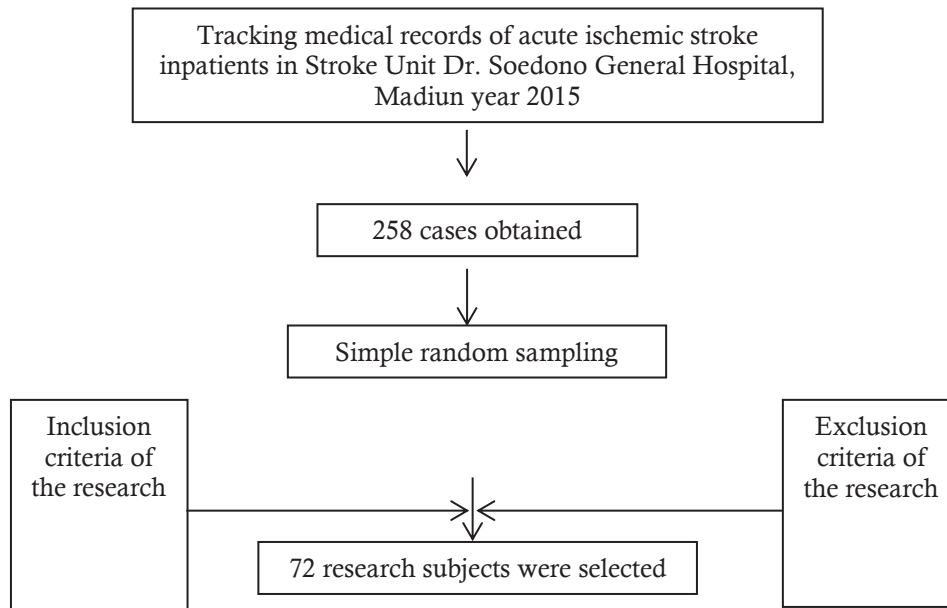


Figure 1. Research sampling process scheme

Table 2. References of Research Variables Categorization

Variables	Subvariables	Measurement results
Demographics	Gender	1. Male 2. Female
	Age	1. <20 years 2. 20-29 years old 3. 30-39 years old 4. 40-49 years 5. 50-59 years 6. ≥60 years
Lipid profile	Total cholesterol	1. Low: <150 mg/dl 2. Normal: 150-200 mg/dl 3. Height: >200 mg/dl (Rakhman & Khodijah, 2014)
	<i>Low-density lipoproteins</i> (LDL)	1. Low: <100 mg/dl 2. Normal: 100-130 mg/dl 3. Height: >130 mg/dl (Fydryszewski & Keohane, 2014)
	<i>High-density lipoproteins</i> (HDL)	1. Low: <35 mg/dl for men or <45 mg/dl for women 2. Normal: 35-55 mg/dl for men or 45-65 mg/dl for women 3. Height: >55 mg/dl for men or >65 mg/dl for women (Rakhman & Khodijah, 2014)
	Triglycerides	1. Low: <120 mg/dl 2. Normal: 120-190 mg/dl 3. Height: >190 mg/dl (Rakhman & Khodijah, 2014)

which can be seen in Table 2.

## RESULTS

Based on data from the Medical Record Division of Dr. Soedono General Hospital Madiun, from January to December 2015 there were 258 cases of

acute ischemic stroke hospitalized in the Stroke Unit. Using simple random sampling, 72 cases were selected as subjects. Based on sex, there are 43 male subjects and 29 female subjects. The youngest subject was 29 years old while the oldest was 87 years old. The mean age of the subjects was 61.64 years (SD 11.46). The age

**Table 3. Characteristics of demographic data of research subjects**

Characteristics	Frequency	Percentage
<b>Gender</b>		
Male	43	59,72%
Female	29	40.28%
<b>Age</b>		
<b>(mean 61.64 years (SD±11.46))</b>		
20-29 years old	1	1.39%
30-39 years old	1	1.39%
40-49 years	9	12.50%
50-59 years	18	25.00%
≥60 years	43	59,72%

**Table 4. Characteristics of lipid profile examination results of the subjects**

Characteristics	Frequency	%
<b>Total cholesterol</b>		
<b>(mean 214,60 mg/dl (SD±56,05))</b>		
Low (<150 mg/dl)	8	11.11%
Normal (150-200 mg/dl)	26	36.11%
High (> 200 mg/dl)	38	52.78%
<b>LDL</b>		
<b>(mean 135.70 mg/dl (SD±46.75))</b>		
Low (<100 mg/dl)	17	23.61%
Normal (100-130 mg/dl)	16	22.22%
High (> 130 mg/dl)	39	54.17%
<b>HDL</b>		
<b>(mean 46.60 mg/dl (SD±15.09))</b>		
Low (<35 mg / dl for male or <45 mg/dl for female)	23	31.94%
Normal (35-55 mg/dl for male or 45-65 mg/dl for female)	36	50.00%
High (>55 mg/dl for male or > 65 mg/dl for female)	13	18.06%
<b>Triglycerides</b>		
<b>(mean 173,32 mg/dl (SD±115,01))</b>		
Low (<120 mg/dl)	29	40.28%
Normal (120-190 mg/dl)	24	33.33%
High (>190 mg/dl)	19	26.39%

group with the highest frequency is the group of ≥60 years, which consist of 43 subjects (59.72 %). The age group of 20-29 years and 30-39 years has the lowest frequency, consisting of only 1 subject (1.39 %) each (Table 3).

The results on the levels of total cholesterol, LDL, HDL, and triglycerides among acute ischemic stroke patients in the Stroke Unit of Dr. Soedono General Hospital Madiun is presented in Table 4.

Mean total cholesterol level was 214.60 mg/dl (SD±56.05). The highest total cholesterol level was 321 mg/dL while the lowest were 72 mg/dl. From these data, there were 8 study subjects (11.11 %) with low cholesterol (<150 mg/dl), 26 subjects (36.11%) with normal cholesterol levels (150-200 mg/dl), and 38 subjects (52.78%) with high cholesterol (>200 mg/

dl).

Mean LDL concentration of the subjects were 135.70 mg/dL (SD±46.75). The highest LDL level was 242.89 mg/dl while the lowest was 19.09 mg/dl. From these data, there were 17 subjects (23.61 %) with low LDL (<100 mg/dl), 16 subjects (22.22%) with normal LDL levels (100-130 mg/dl), and 39 subjects (54.17%) with high LDL (> 130 mg/dl).

Mean HDL level of the study subjects was 46.60 mg/dl (SD±15.09). The highest HDL level was 93.2 mg/dl while at the lowest was 2.8 mg/dl. From these data, there were 23 subjects (31.94 %) with low HDL (<35 mg/dL for male or <45 mg/dL for female), 36 subjects (50.00%) with normal HDL (35-55 mg/dL for male or 45-65 mg/dL for female), and 13 subjects (18.06%) with high HDL (>55 mg/dl for male or >65

mg/dl for female).

Mean triglyceride level was 173.32 mg/dl (SD  $\pm$ 115.01). The highest triglyceride level was 691 mg/dl while the lowest was 57 mg/dl. From these data, there were 29 subjects (40.28 %) with low triglyceride levels (<120 mg/dl), 24 subjects (33.33%) with normal triglyceride levels (120-190 mg/dl), and 19 subjects (26.39%) with high triglyceride levels (> 190 mg/dl).

## DISCUSSION

The characteristics of the baseline data obtained in this study are similar with the previous studies. Based on sex, the number of male subjects in this study were higher than the number of female subjects with a percentage of 59.72 % versus 40.28%, respectively. This finding is not very different from the results of research by (Yao et al., 2012) on 1,027 acute ischemic stroke patients in China that was dominated by male subjects with a percentage of 60.5%. A study conducted by (Caso et al., 2010) on 1,136 ischemic stroke patients in Italy also had male subjects of 642 patients (56.51%), higher than the number of female subjects of 494 patients (43.49%). Meanwhile, based on age, the  $\geq$ 60 years group had the highest percentage in this study, with a percentage of 59.72 %. Similar results were shown by (Gezmu et al., 2014) who studied lipid profiles and the risk of ischemic stroke in different ethnic groups. Data from the South Asian group in their study showed that the mean age of patients diagnosed with acute ischemic stroke was 64.5 years (SD 13.8) for male and 66.0 years (SD $\pm$ 15.6) for female. This finding is also in line with a study for WHO conducted by (Mackay et al., 2004) who mentioned a doubled risk of stroke every 10 years after the age of 55 years old.

The results of this study indicated that the mean total cholesterol of ischemic stroke patients was above the normal value, which is 214.60 mg/dl (SD $\pm$ 56.05). In terms of mode, groups with high total cholesterol levels also had the largest percentage, of 52.78 %. Cholesterol accumulation in the subendothelial spatium is a process underlying the formation of atherosclerotic plaque as a major pathogenesis mechanism of ischemic stroke (Bradac, 2014). The results obtained in the Multiple Risk Factor Intervention Trial (MR FIT) with a large sample size indicate an increased risk of ischemic stroke in total cholesterol level above 200 mg/dl. If the level exceeds 280 mg/dl, the risk of ischemic stroke will be twice higher (Iso et al., 1989). However, inconsistencies regarding the relationship between total cholesterol level and the incidence of ischemic stroke are still common. Several previous studies have shown no significant correlation between hypercholesterolaemia

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and ischemic stroke events (Fahimfar et al., 2012; Saeed et al., 2015). Meanwhile, a study by (Mirghani and Zein, 2009) found that hypercholesterolaemia is not an independent risk factor in cases of ischemic stroke, but it may interact with other atherosclerotic factors in increasing the risk of ischemic stroke. Further studies are still needed to provide a proper profile of the effect of total cholesterol on the risk of ischemic stroke.

Similarly, the mean LDL concentration of the subjects in this study was also above the normal limit of 135.70 mg/dl (SD $\pm$ 46.75). The highest percentage of 52.78 % was indicated by the group with LDL levels exceeding 130 mg/dl. Based on the results of the study by (Biswas, N. and Sangma, 2017), the risk of ischemic stroke may increase up to fifteen-fold in subjects with high blood LDL level. This is because the accumulated and oxidized LDL in the tunica intima is a major initiator in the forming of atherosclerotic plaque. Furthermore, LDL will stimulate an inflammatory process that helps the growth of plaque through the formation of foam cells until it is large enough to clog the blood vessels of the brain. This inflammatory process itself may begin in adolescence and last for more than 40 years to form thin-cap atheroma. Due to its fragile nature, this structure is at risk of ruptures, leading to thromboembolism which is also an underlying pathogenesis of ischemic stroke (Insull, 2009; Libby, 2009; Bentzon et al., 2014). LDL is known to significantly increase the risk of cardiovascular disease at a level above 190 mg/dl. More specifically, level of LDL correlated with an increased risk of ischemic stroke, is above 130 mg/dl (Joshua Z. Willey, MD et al., 2009; Hao and Friedman, 2014).

In this study, the average HDL level was 46.60 mg/dl (SD $\pm$ 15.09), meaning that it is still within normal limits for both male and female. Group of subjects with normal HDL levels also had the highest percentage of 50.00 %. HDL cholesterol has a protective effect against diseases arising from the process of atherosclerosis. This can be achieved primarily through the reverse transport mechanism of free cholesterol originally deposited by macrophages within the wall of the vein back into the liver for excretion. HDL cholesterol also acts as an antioxidant that can control oxidized lipid species in LDL particles to suppress its atherogenic effects (McGrowder et al., 2011). High level of HDL in the blood reduces the risk of ischemic stroke, while HDL level of less than 40 mg/dL can increase the risk of the disease up to threefold (Antonios and Silliman, 2009; Hao and Friedman, 2014).

The mean triglyceride level in the study was 173.32 mg/dL (SD $\pm$ 115.01), which means that it is still within normal limits. In terms of mode, the

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subject group with low triglyceride levels has the highest frequency with 29 subjects (40.28 %). Based on a prospective 31-year cohort study conducted by (Freiberg et al., 2009) among the general population in Denmark, high level of non-fasting triglycerides along with elevated LDL level are predictors of ischemic stroke. (Karim et al., 2016) in a study at Dhaka Medical College Hospital also confirmed the correlation between hypertriglycerides and the risk of ischemic stroke. There are several mechanisms that are thought to be contributing triglyceride pathways to the occurrence of ischemic stroke, among others through correlation with elevated levels C-reactive protein, its involvement in the process of atherosclerosis and thrombogenesis, as well as its ability to cause thrombogenic changes in the coagulation system and increase plasma viscosity (Antonios, Angiolillo and Silliman, 2008). However, inconsistencies in the data are still frequently found, as concluded by (Leonards et al., 2010) in a systematic review of the role of fasting and non-fasting triglycerides in ischemic stroke. Therefore, further research on the association between hypertriglycerides and the risk of ischemic stroke should be continued and developed.

Although elevated levels of total cholesterol, triglycerides, and LDL along with decreased level of HDL are associated with an increased risk of ischemic stroke, too low LDL and triglyceride levels can also lead to cerebrovascular accident through its correlation with increased risk of hemorrhagic stroke (Valappil et al., 2012; Bharosay et al., 2013). Ischemic stroke can also occur in patients with a normal lipid profile because dyslipidemia is not the only risk factor for the disease. One mechanism that is also often responsible for the incidence of ischemic stroke is cardioembolism, blockade in brain blood vessels by thrombus formation due to abnormalities in the heart. This may arise as a result of blood stasis, leading to the formation of thrombus in left ventricular space that has been enlarged (or affected by other structural changes of the heart), the release of material from the impaired heart valve, as well as the abnormal passage of the venous circulation into the arterial circulation (Arboix and Alioc, 2010). Cardiac anomalies at risk of cardioembolism can be divided into three main groups, namely abnormalities of the walls and chambers of the heart, heart valve abnormalities, and arrhythmias. Cardioembolism is known to contribute approximately 20% of ischemic stroke cases (Leary and Caplan, 2008).

This study has some limitations, mainly because we used secondary data from medical records so that sometimes we encountered incompleteness that may affect the accuracy of the data. Secondary data

also did not allow us to ensure that all lipid profile examination procedures are carried out in uniform operational standards. In terms of analysis, this study has not studied the correlation between the variables studied and has not considered the patients' lipid profile prior to the occurrence of stroke. Therefore, further investigations to study the role of the characteristic of the lipid profile test result as a predictor of the incidence and the output of ischemic stroke are needed. Moreover, further researches are required to assess the correlation between the characteristic of lipid profile test results with other factors that can affect the disease. Cohort study design with the use of primary data can be chosen to obtain more complete and accurate results.

## CONCLUSION

Lipid profile test results showed levels of total and LDL cholesterol are generally high, level of HDL cholesterol is generally normal, and level of triglyceride is generally low in acute ischemic stroke patients at Dr. Soedono General Hospital Madiun, East Java.

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