

Association of Atherogenic Index of Plasma with Stroke Subtypes: A Hospital-Based Study

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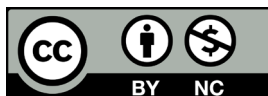
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ABSTRACT

Introduction: Stroke is the second leading cause of death worldwide, affects about 15 million people annually. While secondary prevention of atherosclerotic stroke (AS) mainly focuses on lowering LDL-C with statins, the roles of triglycerides (TG) and HDL-C remain unclear. The atherogenic index of plasma (AIP) may help explain this relationship. This study aimed to assess the association between AIP and stroke.

Methods: A hospital-based retrospective study was conducted at Bir Hospital from May to December 2019 using consecutive non-probability sampling. Sixty adult stroke patients were classified as cerebral infarction, lacunar infarction, or intracerebral hemorrhage based on non-contrast CT findings. Lipid profile (TC, TG, HDL-C) was measured using an automated photometric analyzer, and LDL-C was calculated using the Friedewald formula. Measurements were obtained within 24 hours of stroke onset or after 12 weeks. AIP was calculated as $\log_{10}(\text{TG}/\text{HDL-C})$. Ethical approval was obtained from the Institutional Review Board of National Academy of Medical Sciences, and data were analyzed using SPSS version 22.0 with Chi-square and Fisher's exact tests.

Results: Higher AIP levels were more associated with lacunar infarction than other stroke types and correlated with LDL-C in these patients. Hypertension was associated with higher AIP in lacunar infarction, while no association was observed between AIP and BMI. The mean patient age was 61.6 ± 16.5 years (range 26–99), with a higher incidence of stroke in males than females.

Conclusions : Lacunar infarction showed a stronger association with the atherogenic index of plasma (AIP). AIP demonstrated a significant negative correlation with LDL-C in patients with lacunar infarction. High-risk AIP levels were observed in a minority of patients with smoking history and hypertension.

Keywords: Atherogenic Index ; Plasma; Stroke

INTRODUCTION

Stroke is the second most common cause of mortality worldwide.¹ It is broadly classified into five subtypes.² Atherosclerosis is formed by lipoprotein constituents which includes VLDL, IDL, LDL, HDL and triglyceride.³ Several lipoprotein ratios or “atherogenic indices” have been defined to predict the effects of lipid profile in the atherosclerotic process.⁴ Atherogenic Index of Plasma (AIP), defined as $\log(\text{TG}/\text{HDL-c})$, has recently been proposed as a marker of plasma atherogenicity and reflects the balance between risk and protective lipoprotein forces thus showing the strong association

with coronary atherosclerosis and its complications.^{5,6} In atherosclerotic stroke (AS), the emphasis has been given to lower the LDLc. However, treatment strategies for triglycerides (TG) and high density lipoprotein cholesterol (HDL-C) have not yet been clearly defined for secondary prevention of stroke. In order to explain it, the association between TG, HDL-C, and AS should be searched, especially in patients who have already had low LDL-C levels. It is therefore essential to find AIP in such cases.⁷ This study was aimed to find out the association of atherogenic index of plasma (AIP) with stroke.

METHODS

This is hospital based observational study where consecutive non-probability sampling technique was used. It was conducted from May 2019 to December 2019. A total of 60 consecutive adult patients admitted in Bir Hospital with stroke were assessed and categorized as cerebral infarction, lacunar infarction and intracerebral hemorrhage through neuroimaging with non-contrast CT of the head. Patients with clinically diagnosed stroke, presenting within 48 hours of onset of symptoms, with CT or MRI findings were included in the study. Also, patients with cardioembolic stroke as evident by history or previous documents or ECG features suggestive of arrhythmia or echocardiographic evidence of thrombus either in the left atrium, atrial appendage or in the left ventricle as well as with prior use of hypolipidemic agents recently within last 180 days and with a history of liver disease, renal failure, and thyroid disease were excluded. Following the ethical clearance from the Institutional Review Board (IRB) of the National Academy of Medical Sciences (NAMS), patients were explained about the purpose of the study and methods to be used.

All of the patients included were cooperative and responded properly. All the participants underwent detail clinical examination and neuroimaging with non-contrast CT of the head. Cerebral infarction was diagnosed if neurological deficits were accompanied by a hypo dense lesion >15 mm in diameter in an appropriate area on a cranial CT scan. Lacunar infarction was diagnosed if the patient presented with a pure motor stroke, a pure sensory stroke, ataxic hemiparesis, or a sensorimotor stroke in the absence of a visual field defect and evidence of higher cerebral dysfunction and a hypo dense lesion of <-15 mm in diameter or normal CT scan. Neurological deficits if accompanied by having hyperdense lesion were diagnosed as a hemorrhagic stroke.

In contrast to the measurement of TC and LDLc which ideally were measured either within 24 hours or after 12 weeks following the stroke⁹, so blood sample for estimation of these parameters were taken up to within 48 hours of onset of symptoms. Prior initiation of statin therapy, blood specimen were obtained by venipuncture in tubes containing EDTA in fasting state, preferably in 12 hour fasting period. In the laboratory, fully automatic biochemistry analyzer (Erba EM 360, Mannheim®, Germany) based on the principle of photometry was used to carry out the lipid analysis for TC, TG and HDLc, while LDLc was estimated by using the Friedewald formula (FF), which is; $LDLc(mg/dl) = \text{Non-HDLc} - TG/5$. Non-HDLc was turn be estimated by the formula as; $\text{Non-HDLc} = TC - HDLc$

Once all the components of the lipid profile were available, the atherogenic index of plasma was calculated using the calculator using the formula $\log_{10}(TG/HDL-C)$, with the values converting from mg/dl into equivalent molar concentration. The collected data was stored and analyzed with statistical software (SPSS version 22.0 for windows) to get final interpretation. Results were analyzed using appropriate statistical methods. All the meaningful statistics was worked out. Chi-square test, Fisher test were used when appropriate. P-value was calculated under the predetermined level of significance (0.05) and confidence interval of 95% was constructed. The strength of association between the two quantitative, continuous variables was measured using Pearson's correlation and accordingly the coefficient (r) was calculated. Results were expressed as percentages, mean +/- standard deviation and median for variables. Appropriate tables and figures were made during the data analysis.

RESULT

The total number of patients included in the study was 60. Out of these, 61.7% had cerebral infarction, 20% presented with intracerebral hemorrhage and 18.3% had lacunar infarction. Minimum age of patient in the study was 26 years and maximum age was 99 years. The mean age of presentation of cerebral infarction in the study was 61 years, while that of both lacunar infarction and intracerebral hemorrhage was 63 and 64 respectively. In the study, regardless of the types of stroke, 63.3% of affected individuals were male, and 36.67% were female. 54.1% of those with cerebral infarction were male, remaining were female. Similarly in those with lacunar infarction, 81.8% were male and only 18.2% were female. While 75% of those with intracerebral hemorrhage were male and remaining were female.

This study shows 97.3% of those with cerebral infarction and all those with lacunar infarction and intracerebral hemorrhage had total cholesterol in the desirable level ie <200mg/dl. (Table 1) Almost 90% of the cases with lacunar infarction and those with intracerebral hemorrhage and 81% cases of cerebral infarction had their LDLc levels in the optimal range ie, <100, while non-had high level of LDLc. (Table 2)

Here 43.2% of those with cerebral infarction, 54.5% of lacunar stroke and 33.3% had low level of HDLc ie. <40 mg/dl (Table 3)

Table 1: Details on the demographic and clinical characteristics.

Total cholesterol category	Cerebral infarction	Percent	Lacunar infarction	Percent	Intracerebral hemorrhage	Percent	P
<200; Desirable	36	97.3	11	100.0	12	100.0	1.0
200-239; Border-line High	1	2.7	0		0		

Table 2. LDLc levels in stroke subtypes

	Cerebral infarction	Percent	Lacunar infarction	Percent	Intracerebral hemorrhage	Percent	P
<100; Optimal	30	81.1	10	90.9	11	91.7	0.92
100-129; Near Optimal	6	16.2	1	9.1	1	8.3	
130-159; Border-line High	1	2.7	0		0		
Total	37	100.0	11	100.0	12	100.0	

Table 3. HDLc Levels in stroke subtype

HDLc Category	Cerebral infarction	Percent	Lacunar infarction	Percent	Intracerebral hemorrhage	Percent	P
<40; Low	16	43.2	6	54.5	4	33.3	0.42
40-59; Desirable	21	56.8	5	45.5	7	58.3	
More than or equal to 60; High	0		0		1	8.3	

TRIGLYCERIDE LEVELS

Also 31.4% of those with cerebral infarction, 18.2% of those with lacunar stroke had their triglyceride level above the normal, while all the case of hemorrhagic stroke had their TG level within normal range as shown in table 4.

Table 4: Triglyceride Levels in stroke subtypes

Triglyceride Category	Cerebral infarction	Percent	Lacunar infarction	Percent	Intracerebral hemorrhage	Percent	P
<150; Normal	25	67.6	9	81.8	12	100.0	0.42
150-199; Border-line High	8	21.6	2	18.2	0		
200-499; High	4	10.8	0		0		
Total	37	100.0	11	100.0	12	100.0	

AIP LEVELS

Below mentioned table shows, 21.6% of those with cerebral infarction, 27.3% of those with lacunar stroke and 8.3% of those with hemorrhagic stroke had AIP level more than 0.312 which is considered as high risk.

Table 5. AIP categorization with stroke subtypes

AIPCAT	Cerebral infarction	Percent	Lacunar infarction	Percent	Intracerebral hemorrhage	Percent	P
Less than or equal to 0.312; Low risk	29	78.4	8	72.7	11	91.7	0.48
>0.312	8	21.6	3	27.3	1	8.3	
Total	37	100.0	11	100.0	12	100.0	
Total	37	100.0	11	100.0	12	100.0	

MEAN VALUES OF LIPID PROFILE AND AIP IN STROKE SUBTYPES

The mean values of total cholesterol, LDLc, triglycerides as well as AIP level were found to be within optimal level in all three types of stroke, while that of HDLc was low in both cerebral infarction and lacunar stroke category as shown in table 6.

Table 6. Mean values of lipid profile and AIP in stroke

	Cerebral infarction	Lacunar infarction	Intracerebral hemorrhage	Percent	Intracerebral hemorrhage	Percent	P
	Mean	SD	Mean	SD	Mean	SD	0.48
Total Cholesterol	139.7	35.2	131.6	30.5	131.2	23.1	
HDL	39.9	9.9	38.5	9.7	45.2	10.2	
Triglyceride	130.3	55.9	114.6	32.2	91.4	30.5	
LDL	74.0	25.1	70.3	27.1	67.8	20.5	
AIP	0.2	0.2	0.2	0.1	0.0	0.2	

CORRELATION OF LDLc WITH AIP WITH STROKE SUBTYPES

There is significant negative correlation between LDLc and AIP values only in those with lacunar infarction, $r(9)=-0.618$, $p=0.043$ as shown in the table 7.

Table 7 Correlation between LDLc and AI

	Cerebral infarction	Lacunar infarction	Intracerebral hemorrhage
Pearson Correlation	-0.127	-0.618	0.081
P	0.452	0.043	0.802

COMPARISON OF MODIFIABLE RISK FACTOR WITH AIP VALUES

It is seen that that in those with cerebral infarction, only 20.7% smoker had AIP value more than 0.312, while 37.5% of those who smoke had AIP >0.312 in case of lacunar stroke and incase of hemorrhagic stroke, none of the smoker had AIP more than 0.312.

Table 8.:Correlation of Smoking habit with AIP value in stroke subtypes

	Smoking status	AIP		Total	P	
		<0.312	>0.312			
		Percent	Percent			
Cerebral infarction	Non -Smoker	6	75.0	2	25.0	0.793
	Smoker	23	79.3	6	20.7	
	Total	29	78.4	8	21.6	
Lacunar infarction	Non –Smoker	3	100.0	0		0.491
	Smoker	5	62.5	3	37.5	
	Total	8	72.7	3	27.3	
Intracerebral hemorrhage	Non –Smoker	4	80.0	1	20.0	0.417
	Smoker	7	100.0	0		
	Total	11	91.7	1	8.3	

On looking at the correlation of HTN with AIP values, 27.8 % of those with HTN had AIP>0.312 in case of cerebral infarction, while it was much higher in those with lacunar stroke(33.3%) and in hemorrhagic stroke, HTN didn't correlate with increased AIP level as shown in the Table 9.

Table 9 :Correlation of HTN with AIP values in stroke subtypes

	Hypertension	AIP		Total	P	
		<0.312	>0.312			
		Percent	Percent			
Cerebral infarction	Non hypertensive	16	84.2	3	15.8	0.627
	Hypertensive	13	72.2	5	27.8	
	Total	29	78.4	8	21.6	
Lacunar infarction	Non hypertensive	4	80.0	1	20.0	1
	Hypertensive	4	66.7	2	33.3	
	Total	8	72.7	3	27.3	
Intracerebral hemorrhage	Non hypertensive	5	83.3	1	16.7	1
	Hypertensive	6	100.0	0		
	Total	11	91.7	1	8.3	

DISCUSSION

Stroke accounts for a large proportion of inpatient admissions and is defined as the rapid onset of focal or global cerebral dysfunction lasting more than 24 hours or resulting in death, with a vascular cause. In this study, ischemic stroke (including cerebral and lacunar infarction) constituted 80% of cases, while hemorrhagic stroke accounted for 20%. This finding is consistent with reports from South Asian countries where 68–80% of strokes are ischemic and 20–32% are hemorrhagic.¹¹ The higher prevalence of ischemic stroke may be related to the high burden of small vessel disease, largely attributable to undiagnosed or poorly controlled hypertension.¹² However, the same review noted a relatively higher proportion of intracerebral hemorrhage (32–43%) among younger patients (15–45 years) in South Asia.

The mean age of stroke onset in our study was approximately 62 years, with comparable mean ages across the three stroke subtypes. This finding is similar to a hospital-based study from South Korea involving 12,370 patients (64% ischemic and 36% hemorrhagic stroke), where the mean age of overall stroke was 63.9 ± 13 years. This trend may reflect demographic changes and the increasing prevalence of hypertension among younger populations.¹³ In this study, most stroke patients were male (63.3%) compared to females (36.7%). A similar male predominance has been reported in the Indian subcontinent, where among 392 patients with ischemic stroke, 72% were male. This disparity may partly reflect sociocultural factors, as women with stroke or cardiac arrest in this region are less likely to be brought to hospitals than men.¹⁴ In this study, all stroke types were more frequent among patients with a history of smoking. A study assessing stroke incidence, types, risk factors, and outcomes among 741,000 urban and 185,000 rural inhabitants in Kerala reported a smoking history in 46% of urban males and 24% of rural males. The contribution of smoking may have been underestimated as the study considered only current smoking.¹⁵

50 % of the stroke cases in our study had history of HTN. Our result is similar to that observed in the study done to evaluate the burden of stroke in Nepal, where 42% of the studied population reported to have been afflicted with HTN.⁸ In contrast to these, in a study carried out in Kerala, HTN was the most common risk factors amongst 83.2% stroke cases, which is much higher as compared to ours.¹⁵ Only 13 % of the total stroke cases in our study had history of diabetes. This is almost similar to that shown in the study by Oli et al. in which 10.8% of the total 683 stroke patients were found to have non specified

diabetes.¹⁶ In contrast to these, in the study in Kerala, where around 50% of the stroke cases had diabetes.¹⁵

In our study, 43% of cases had low HDLc levels (<40), 23% had triglyceride levels above the normal range (>150), and only 2% had borderline high LDLc levels. Similar findings were reported in another study of 281 admitted stroke patients, where 45% had HDLc <40 and 31% had elevated triglycerides.¹⁷ However, a study from Northern India reported elevated LDLc in 35% of stroke cases, including 30% of ischemic and 5% of hemorrhagic strokes.¹⁸ The mean value of AIP in our study was 0.1 with SD of 0.2. The value of AIP was more than 0.312 in 21.6% of those with cerebral infarction and 27.3% of those with lacunar infarction and only in 85 of those with intracerebral hemorrhage. This is much lower in contrast to the similar study done in Sri Lanka, where the mean AIP was 0.379 with SD of 0.205.⁹

The mean value of total cholesterol of ischemic stroke this case was 135.6mg/dl, that of HDLc was 39.2, that of TG was 122.45 and LDLc was 72.15. This is in contrast to the study done in India, where the mean value of TC was 189mg/dl, that of HDLc was 44.1, TG being 126.5 and LDLc being 119 mg/dl. Similarly in our study of those with hemorrhagic stroke the mean value of TC, HDLc, TG and LDLc were 131.2, 45.2, 91.4 and 67.8 respectively. However, in the same study, the mean values for the above-mentioned parameters were 188, 49.4, 116 and 114 mg/dl respectively. Thus is seen that the lipid parameters in those with ischemic stroke in both the studies are comparable while in those with hemorrhagic stroke, the difference is much higher.¹⁹

CONCLUSION

Most stroke patients had optimal total cholesterol, LDLc, and triglyceride levels, but a considerable proportion had low HDLc, indicating increased atherosclerotic risk. Atherogenic Index of Plasma (AIP) showed a stronger association with lacunar infarction than with other stroke types and was negatively correlated with LDLc in lacunar stroke. Hypertension was also associated with higher AIP levels in lacunar infarction, while no association was found with BMI. Overall, most patients across stroke subtypes had AIP values below 0.312, with only a small proportion of smokers and hypertensive patients showing high-risk AIP levels.

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