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Original Research Article

Gender-based evaluation of atherogenic indices in ischemic stroke: a retrospective study in a neuropsychiatric facility

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ABSTRACT

Background: An ischemic stroke is a condition that causes permanent damage to brain tissues and neurological disorders when blood flow to the brain is blocked. The lipid profiles can provide the baseline data, but more precise predictions of patient recovery can be affected by researchers studying some ratios between the lipoproteins called atherogenic indices. The research will help evaluate and determine the dependence of atherogenic indices of lipids on predictive value on ischemic stroke and to investigate potentially existing gender differences in the predictive value.
Methods: This was a retrospective cohort study conducted from June 2025 to January 2026 in one of the tertiary Neuropsychiatric centers in Northern India and followed up on 80 cases of ischemic stroke patients (20-90) in 6 months. The research participants were divided into two groups (with and without stroke), and those who had hemiplegia caused by a stroke. Lipid profile data was used to calculate atherogenic indices: Atherogenic index of plasma (AIP=log[TG/HDLc]), Castelli risk indices I and II (CRI-I=TC/HDLc and CRI-II=LDLc/HDLc), and atherogenic coefficient (AC=[TC–HDLc]/HDLc). Indices were evaluated separately for males and females.
Results: Males were reportedly seen to associate significantly with stroke and hemiplegia ($p=0.027$). There were more males affected by hypertension ($p=0.046$), but no significant gender difference in diabetes. A statistically significant difference found between genders in AIP ($p=0.032$). In males, CRI-II was the highest-predicting variable (AUC=0.503; CI=0.373-0.632), but it was not significant.
Conclusions: AIP and CRI-II could be useful as gender-sensitive predictors of ischemic stroke, as they provide cost-effective tools in clinical risk assessment.

Keywords: Atherogenic index, Cholesterol, Ischemic stroke, Lipid profile, Lipid ratios

INTRODUCTION

Ischemic stroke has the highest cause of mortality and the inability to fully recover neurological impairment globally of approximately 62% of all strokes. Despite the gains in acute management, secondary prevention is yet to become the most appropriate one because the risk stratification remains not complete, as well as the modifiable vascular risk factors remain still or partially available.[1] One among them, dyslipidemia is foundational to an atherosclerosis-mediated cerebrovascular disease and is always related to the incidence of stroke, the recurrence rate, and the unfavorable recovery.[2]

Traditional risk factors, including hypertension or diabetes mellitus, smoking, and dyslipidemia have a significant role in the pathogenesis of stroke, and this has provided relevance to identifying consistent biomarkers that can be used to stratify risk factors and as the main preventive method.

The prevalence of stroke in India rises proportionally with age: a recent nationally representative survey of adults (age ≥45 years) found a self-reported approximately overall stroke prevalence of 1.71% with the prevalence rate accelerating with increasing age; in adults aged 45-54 years the prevalence rate is approximately 0.80% but in adults aged 55-69 years is 1.97% with a prevalence rate of 3.10 in adults aged ≥70 years. These results underscore the increasing burden of stroke with age among Indians.[3]

The traditional lipid measures, such as total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and the high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG), are well-tested in clinical practice, but not likely to be indicative of the complex atherogenic milieu leading to ischemic stroke. The composite lipid indices that can also be called the atherogenic index of plasma (AIP), Castelli risk indices I and II (CRI-I and CRI-II), atherogenic coefficient (AC) and non-high-density lipoprotein cholesterol (NHC) have become more effective predictors of vascular risk. Recent reports have indicated strong links between high atherogenic indices and the occurrence of ischemic stroke, early neurological impairments and deteriorations, and poor functional outcomes.[4,5]

Two significant indicators are used in determining the AIP, which are TG and HDLc. It is a ratio with a combination of TG and HDLc and the interaction of the compounds in the various lipoprotein metabolism pathways, and it can be an effective marker of plasma-atherogenicity. It was estimated using the following equation: AIP=Log (TG/serum HDLc).[6] CRI-I and CRI-II are the two vascular risk predictors, the predictive value of which is better than the one of the corresponding lipid parameters and is calculated in the following way: CRI-I=Serum (TC/HDL-C), CRI-II=Serum (Low-density lipoprotein (LDL)/HDL-C).[7] NHC is the cholesterol content of the aggregate atherogenic lipoproteins. It represents the calculation of a difference between TC and high-density cholesterol (serum TC- HDLc). Atherogenic coefficient was calculated as ratio of serum (TC-HDLc)/HDLc (Table 1).[8]

Morbidity and disability caused by stroke is huge and poses a big burden to the healthcare system in countries with poor resources or insufficient infrastructure.[9] Intake of prevention measures is of immense importance. Lipid profiles may be obtained with the healthcare center on a regular basis at comparatively low prices, and lipid ratios obtained based on the results may contribute to the value of prevention of stroke. However, limited study has been done to demonstrate the correlation between atherogenic indices and stroke patients.

The aim of this study was to evaluate the effectiveness of specific ratios based on conventional lipid profile parameters to determine individuals who risk a stroke.

METHODS

This was a retrospective cohort study that was conducted by the Neurology and the Neurochemistry units of a IHBAS Hospital, neuropsychiatric center, Delhi, India from June 2025 to January 2026. The study included 110 patients aged 20-90 years who had a stroke hospitalization within the last 6 months, and 66 of them were determined fit to take part in the study based on the inclusion and exclusion criteria. The study population consisted of patients who had all the clinical symptom data and the biochemical tests, and no previous coronary artery diseases or stroke, no alcohol intake (Daily drinking habit) or smoking (average >5 cigarettes/day). To continue the analysis, the data were compared between males and females who had a stroke episode.

Comprehensive data on demographics, clinical history, and examinations were obtained from medical records. Data on essential biochemical parameters, such as TC, HDLc, LDLc, and TG, were also recorded. All participants of the study were not smokers and alcohol drinkers, and had no family history of coronary artery disease (CAD) based on the records. A blood pressure of 140/90 mmHg or higher was used to define hypertension.

Statistical analysis

Baseline characteristics were analyzed using descriptive statistics. We evaluated continuous variables through Student's t-tests or Mann-Whitney U-tests, while categorical variables were assessed using chi-square or Fisher's exact tests. The accuracy, specificity, sensitivity and area under the curve (AUC) were used to evaluate model performance. We performed all statistical calculations in SPSS software.

RESULTS

The study population comprised 66 individuals (Table 2). Stroke has become the most important risk factor which is hypertension and diabetes mellitus. The majority of the females were already postmenopausal, with a mean age of 59.44±16.27 years. The difference in age between the genders was not statistically significant (p=0.689). Among the participants, 75% (n=36) were male, and 93.75% (n=30) were female. Of the males, 25% (n=12) were hemiplegic, while 6.25% (n=2) of the females had hemiplegia. Hypertension was observed in 61.1% (n=49) of the males, and diabetes mellitus in 58.3% of the males (n=47), whilst hypertension was observed in 38.9% (n=31) of the females and diabetes mellitus in 41.7% of the females (n=33).

The lipid profiles and lipid ratio results are presented in (Table 3). Average AIP was calculated as 0.48±0.21 for males and 0.48±0.22 for females, and was found to be statistically significant (p=0.032). However, there were no other statistically significant variations in lipid profiles or atherogenic indices between the stroke with/without hemiplegia. The reason could be the smaller sample size of stroke patients with hemiplegia.

The relative risk for stroke in females is higher than that for men in our study group (Table 4). The odds ratio was significant in both women (pOR=0.0045), as well as, in the relative risk (pRR=0.0188), thus, suggesting that there was a significant relationship between sex and stroke.

The AUC analysis is depicted in (Table 5) shows that among all lipid ratios, CRI-II demonstrated the highest predictive capability for stroke risk in males (p=0.06), although this was not statistically significant when compared to females (p=0.96). The values of the AUC of all tests were relatively close to 0.5, indicating that such tests do not provide strong discriminatory ability to prove that the results are associated with gender.

Table 1: The atherogenic ratios were calculated as follows.

Variables	Ratios
Atherogenic index of plasma	log T.G./HDLc[5]
Castelli's risk index (CRI-I)	T.C./HDLc[6]
Castelli's risk index (CRI-II)	LDLc/HDLc[6]
Atherogenic coefficient	(T.C.-HDLc)/HDLc[7]
NHC (Non HDLc)	(T.Chol-HDLc)[7]

Table 2: Characteristics of the study populations.

Characteristics		Males	Females	Statistical test	P value*
Age (in years)$^{+}$		56.33±13.57	59.44±16.27	t (78)=0.40§	0.689
Diagnosis¶	Stroke	36 (75%)	30 (93.75%)	χ^2 (1, n=80)=4.89$^{\parallel}$	0.027
	Stroke with hemiplegia	12 (25%)	2 (6.25%)		
Risk factors¶	Hypertension	49 (61.1%)	31(38.9%)	χ^2 (1, n=80)=4.00$^{\parallel}$	0.046
	DM	47 (58.3%)	33 (41.7%)	χ^2 (1, n=80)=2.56$^{\parallel}$	0.110

*P≤0.05 is considered statistically significant; $^{+}$Values are expressed as Mean±S.D. (Standard deviation); §t-test: Independent samples t-test used to compare mean ages between males and females; $^{\parallel}\chi^2$-test: Chi-square test of independence used to assess the association between gender and categorical variables (Diagnosis, risk factors); ¶Values are expressed as N (%).

Table 3: Lipid profile and ratios among cases.

Variables	Males^{+} (n=36), (Mean±SD)	Females^{+} (n=30), (Mean±SD)	Statistical test**	P value*
Lipid profile (mg/dl)				
TC	149±52.37	161.34±44.32	t (64)=1.18	0.278
TG	130.67±54.52	139±64.94	t (64)=0.62	0.537
HDLc	41.29±10.97	43.34±9.58	t (64)=0.84	0.392
LDLc	88.81±47.38	91.44±36.20	t (64)=0.24	0.791
Lipid ratios				
§AIP	0.48±0.21	0.48±0.22	t (64)=0.00	0.032*
$^{\parallel}$CRI I	3.73±1.22	3.83±1.20	t (64)=0.23	0.214
$^{\parallel}$CRI II	2.24±1.29	2.18±0.99	t (64)=0.15	0.412
¶AC	2.73±1.22	2.83±1.20	t (64)=0.23	0.214

*P≤0.05 is considered statistically significant; $^{+}$Values are expressed as Mean±S.D. (Standard deviation); §AIP: Atherogenic index of plasma; $^{\parallel}$CRI: Castelli's risk index; ¶AC: Atherogenic coefficient; **t-test: Independent samples t-test used to compare mean values of lipid profiles between males and females.

Table 4: Area under curve of lipid ratios.

Tests	Males AUC (CI)	Test statistic (Z)	P value*	Females AUC (CI)	Test statistic (Z)	P value*
CRI-I	0.474 (0.345-0.603)	Z=0.35	0.698	0.526(0.397-0.655)	Z=0.38	0.698
CRI-II	0.503(0.373-0.632)	Z=0.35	0.066	0.497(0.368-0.627)	Z=0.05	0.969
AIP	0.496(0.364-0.627)	Z=0.01	0.949	0.504(0.373-0.636)	Z=0.01	0.949
AC	0.474(0.345-0.603)	Z=0.35	0.698	0.526(0.397-0.656)	Z=0.38	0.698

*P<0.05, considered statistically significant, and p<0.001 was considered highly significant; test statistic (Z): Z-test statistic used to compare the AUC values; P value: P value corresponding to the Z-test for comparing AUCs; AUC: Area under the curve, calculated using ROC analysis.

DISCUSSION

The purpose of this study was to assess the usefulness of the selected ratios using the parameters of the routine lipid profiles in determining people at high risk of stroke. These affordable indicators are specifically relevant to those healthcare institutions that have scarce resources or restricted healthcare systems. Our evidence provided great correlation between some atherogenic indices and stroke occurrence.[10]

Among the stroke cohort, a greater proportion of females, especially those who are likely to be post-menopausal, was observed, which has also been observed in other large population-based studies, indicating the possible effects that changes in hormones have on cerebrovascular burden.[11] Irrespective of this observation, there was no significant age difference observed between male and female patients meaning that there is no difference in the situations when stroke occurs in male and female patients. Male patients on the other hand showed a higher rate of hemiplegia and a higher burden of any established cardiovascular risks including hypertension and diabetes, a pattern which is comparable to previous population-based studies that have shown a more severe clinical manifestation and greater cardiometabolic risk concentration in male patients.[12]

In respect of lipid parameters, females had comparatively higher mean lipid levels and lipid-derived indexes as compared to males but these differences were not statistically significant. These trends have been common within large epidemiological cohorts where females-especially during the postmenopausal period-have already been observed to be less favorable lipid phenotypers, although without any consistent sex-based statistical differences across all lipid measures.[13] These findings reinforced the argument that lipid atherogenic risk is perhaps equally distributed between sexes in stroke-affected populations, and that composite indexes and not on single lipid parameters can be the most discriminatory of all.

Although relatively few studies have focused specifically on dyslipidemia in stroke populations, there is growing positive evidence of the clinical utility of lipid ratios and atherogenic indices as predictors of risk of stroke, despite inconsistent relationships by conventional individual lipid markers. As an example, extensive prospective studies reveal that high TG/HDL-C, TC/HDL-C, and LDL/HDL-C ratios, are positively linked with stroke incidence and better discrimination of high-risk persons but have dose-response relationships in pooled cohorts with hundreds of thousands of subjects.[14] Moreover, other research in ischemic stroke cohorts has reported that increased non-traditional lipid ratios, such as AIP are strongly related to poor prognosis, and are perhaps more predictive of risk as compared to independent lipids.[15] These results support the hypothesis that composite lipid indices are effective predictors of stroke risk when individual lipid parameters are not statistically significant, as observed in our study. Previous studies have linked lipid indices/ratios to increased cardiovascular risk.[16-18] In our study, AIP demonstrated a significant increase in females compared to males.

Associative atherogenic indices such as AIP, CRI-I of Castelli, independent variable AC indicate the role of non- traditional lipid ratios as stroke risk factor. Higher CRI-I reflects an imbalance between atherogenic and protective lipoproteins, and increased CRI-I, CRI-II, and AC are linked to atherosclerotic alterations pertinent to ischemic stroke and carotid atherosclerosis in both large clinical cohorts.[19] Increasing AC values were signs of an increasing vascular risk in our article and are consistent with reports that the ratios predict progressively over and above traditional lipids.[14] Moreover, greater AIP levels, which were measured as a continuous variable, were linked to greater stroke risk, which supports its usefulness as an atherogenic dyslipidemia sensitive marker and was found in large longitudinal cohorts.[20] High levels of TG indicate increased load of triglyceride-enriched remnant lipoproteins, which lead to a deposition of cholesterol in the intima of arteries, giving rise to atherosclerosis and ischemic stroke.[21]

The recent studies have reported that the AIP is a good predictor of stroke outcomes. Jiang et al found AIP to be the most significant and influential independent risk factor of stroke which was ischemic in patients with metabolic illnesses, out-of-pocket, compared with the conventional markers.[22] Similarly, another recent study has found that, although CRI-II monitors carotid plaque neovascularization, AIP is a better indicator of small, dense LDL-driven recurrence.[23] Moreover, a 2022 national prospective cohort study of the relationship between AIP and obese-related risk of incident stroke was conducted and found that high risk levels of AIP levels were significantly associated with a higher incidence of stroke, particularly in obese individuals.[24]

Our analysis using the AUC showed that CRI-I and AC had better predictive capacity for stroke risk in females than other lipid metrics. A retrospective observational cohort study found that the recurrence of brain ischemia increased with increasing levels of CRI-I and CRI-II in embolic stroke patients.[25]

The atherogenic indices assessed in the study can provide a more convenient way to identify preventive measures for stroke. These results may have an impact on clinical practice, especially in resource-limited institutions where highly sensitive diagnostic equipment is not readily accessible and also in risk stratification for identifying individuals at higher risk to initiate timely interventions.

Limitations

Our study was done on the retrospective data collected in a hospital and over a short span of time. However, large scale prospective studies can be conducted across various regions and cultural differences to establish a causal relationship.

CONCLUSION

This retrospective cohort study demonstrates clinical appropriateness of atherogenic indices, more specifically the AIP and CRI-II developed by Castelli, as possible risk factors of ischemic stroke. The results highlight the existence of notable sex-based discrepancies. AIP is of more significance in risk assessment in females whereas, CRI-II demonstrated higher predictive value among males. The results allow one to suggest the hypothesis that the lipid-derived ratios could be more diagnostic indicators of the stroke risk, particularly in case the single lipid parameters are in the reference range or slightly higher.

Another key issue that the study highlights is that sex-specific risk profiles should be put into consideration as post-menopausal changes predispose women to higher risk of stroke due to hormonal changes. Since the lipid profiling is relatively cheap and available across all the healthcare facilities, the application of the indices may be a viable solution in terms of early detection of at-risk patients in healthcare providers with limited resources.

Future prospective data, using increased sample sizes and more subject populations, is justified to further confirm these findings and understand a role of atherogenic indices in the stroke risk assessment models.

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