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Study of lipid indices in acute ischemic stroke

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Abstract:

Introduction: Acute ischemic stroke (AIS) is a significant cause of morbidity and mortality worldwide, often leading to severe long-term disability. Dyslipidemia, characterized by abnormal lipid profiles, is a crucial metabolic component implicated in AIS, contributing to atherosclerosis and subsequent cerebrovascular events. The relationship between specific lipid indices and stroke outcomes remains controversial. This study aims to investigate the association between lipid indices and AIS, elucidating their potential as biomarkers for targeted treatment and predicting disease outcomes.

Materials and Methods: This retrospective study was conducted at Saveetha Hospitals from January 2023 to June 2023. The study included two groups: patients diagnosed with AIS and healthy control subjects. Data collected included age, gender, comorbid conditions, and lipid profile parameters. Lipid indices (AIP, CRI-1, CRI-2) were calculated using standard formulas. Statistical analysis was performed using SPSS software, with t-tests employed to compare lipid indices between AIS patients and controls. A p-value of <0.005 was considered statistically significant.

Results: The study included 75 AIS patients and 75 controls. AIS patients had a mean age of 58.47 ± 11.35 years, with 72% being males. Hypertension (72%) and diabetes mellitus (60%) were the most common comorbidities among AIS patients. Lipid indices were significantly higher in AIS patients compared to controls: AIP (0.31 ± 0.12 vs. 0.18 ± 0.09, $p < 0.001$), CRI-1 (5.2 ± 1.8 vs. 3.6 ± 1.1, $p < 0.001$), and CRI-2 (3.7 ± 1.2 vs. 2.5 ± 0.8, $p < 0.001$). A significant negative correlation was observed between AIP and diabetes (correlation coefficient = -0.242, $p = 0.003$).

Conclusion: This study demonstrates that lipid indices such as AIP, CRI-1, and CRI-2 are significantly elevated in AIS patients, suggesting their strong association with stroke risk. The high prevalence of comorbidities like hypertension and diabetes highlights the need for comprehensive cardiovascular risk management.

INTRODUCTION

Acute ischemic stroke (AIS) is a significant cause of morbidity and mortality worldwide, often leading to severe long-term disability. The pathophysiology of AIS is complex and multifactorial, involving a combination of genetic, metabolic, and environmental factors. One of the crucial metabolic components implicated in AIS is dyslipidemia, characterized by abnormal lipid profiles that can contribute to atherosclerosis and subsequent cerebrovascular events [1].

Dyslipidemia has been consistently associated with an increased risk of ischemic stroke. However, the relationship between specific lipid indices and stroke severity, progression, and outcomes remains controversial. Some studies suggest that elevated levels of low-density lipoprotein cholesterol (LDL-C) and total cholesterol (TC) are significant risk factors for ischemic stroke [2], while others highlight the protective role of high-density lipoprotein cholesterol (HDL-C) in stroke prevention [3]. Additionally, triglycerides (TG) have been implicated in stroke severity and mortality, with lower TG levels associated with worse outcomes in AIS patients [3].

The role of lipid indices such as the atherogenic index of plasma (AIP), Castelli Risk Index (CRI), and non-HDL cholesterol (non-HDL-C) in predicting stroke outcomes has gained attention in recent years. These indices provide a more comprehensive view of lipid metabolism's impact on vascular health compared to traditional lipid measurements alone [4].

Given the conflicting evidence and the complexity of lipid metabolism's role in AIS, a retrospective analysis of lipid indices in patients with acute ischemic stroke is warranted. This study aims to elucidate the prognostic significance of various lipid indices in AIS, examining their association with stroke severity, progression, and outcomes. By leveraging comprehensive lipid profiling, including traditional lipids and advanced indices like AIP and CRI, this study seeks to provide deeper insights into the metabolic underpinnings of AIS and potential targets for therapeutic intervention.

Understanding these associations can inform clinical decision-making and potentially guide the development of personalized treatment strategies aimed at improving outcomes for AIS

patients. This retrospective analysis will contribute to the growing body of evidence on the importance of lipid management in stroke prevention and recovery.

Aim

To investigate the association between lipid indices and acute ischemic stroke (AIS), elucidating their potential as biomarkers for targeted treatment and to predict disease outcomes.

MATERIALS AND METHODS

Study design and setting: This retrospective study was conducted at Saveetha Hospitals, a tertiary care center, from January 2023 to June 2023. Approval was taken from the hospital's institutional review board.

Study population: The study population comprised two groups: patients diagnosed with acute ischemic stroke (AIS) and healthy control subjects. The AIS group included patients who were admitted to Saveetha Hospitals with a confirmed diagnosis of AIS based on clinical evaluation and imaging studies (CT or MRI). The control group consisted of age- and gender-matched healthy volunteers without a history of cerebrovascular disease or other significant medical conditions.

Inclusion criteria:

1. Patients aged 18 years and above.
2. Patients with a confirmed diagnosis of AIS.
3. Control subjects without any history of stroke or significant comorbid conditions.

Exclusion criteria:

1. Patients with hemorrhagic stroke.
2. Patients with a history of transient ischemic attacks (TIA).
3. Patients on lipid-lowering therapy or with known dyslipidemia.
4. Patients with severe liver or kidney disease.

Data collection: The following data were collected retrospectively from the hospital's electronic medical records:

Demographic data: Age, gender;

Clinical data: Presence of comorbid conditions such as hypertension, diabetes mellitus, coronary artery disease (CAD), and smoking status;

Lipid profile parameters: Serum total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG).

Calculation of lipid indices

Lipid indices were calculated using the following formulas:

- **Atherogenic Index of Plasma (AIP):** AIP = log(TG/HDL-C)
- **Castelli's Risk Index I (CRI-1):** CRI-1=TC/HDL-C
- **Castelli's Risk Index II (CRI-2):** CRI-2=LDL-C/CHDL-C

Statistical analysis

Data were analyzed using SPSS software (version 25.0). Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. The primary outcome was the comparison of lipid indices between AIS patients and healthy controls using t-tests. A p-value of <0.005 was considered statistically significant.

RESULTS

Demographic and clinical characteristics

The study included 75 patients diagnosed with acute ischemic stroke (AIS) and 75 healthy control subjects. The demographic and clinical characteristics of the study population are summarized in Table 1.

Table 1: Demographic and clinical characteristics of study population

Characteristic	AIS Patients (n=75)	Control Subjects (n=75)
Mean Age (years)	58.47 ± 11.35	57.92 ± 10.78
Gender		
- Males	54 (72%)	53 (70.7%)
- Females	21 (28%)	22 (29.3%)
Comorbidities*		

- Hypertension	54 (72%)	0
- Diabetes Mellitus	45 (60%)	0
- Coronary Artery Disease (CAD)	17 (22.7%)	0
- Smoking	17 (22.7%)	0

* A patient can have more than one comorbidity

Lipid indices in AIS patients and control subjects

Lipid profile parameters and lipid indices (AIP, CRI-1, CRI-2) were measured for both AIS patients and control subjects. The comparisons of these indices between the two groups are presented in Table 2.

Table 2: Comparison of lipid indices between AIS patients and control subjects

Lipid Index	Normal Range	AIS Patients (Mean ± SD)	Control Subjects (Mean ± SD)	p-value
AIP	0.11 - 0.21	0.31 ± 0.12	0.18 ± 0.09	**<0.001**
CRI-1	<4	5.2 ± 1.8	3.6 ± 1.1	**<0.001**
CRI-2	<3	3.7 ± 1.2	2.5 ± 0.8	**<0.001**

The results indicate that all three lipid indices were significantly higher in AIS patients compared to healthy control subjects. Specifically, the mean AIP in AIS patients was 0.31 ± 0.12, significantly higher than 0.18 ± 0.09 in controls ($p < 0.001$). Similarly, CRI-1 and CRI-2 were significantly elevated in AIS patients (5.2 ± 1.8 and 3.7 ± 1.2, respectively) compared to controls (3.6 ± 1.1 and 2.5 ± 0.8, respectively), with both indices showing p-values < 0.001.

Comorbidities and their prevalence

A detailed analysis of comorbid conditions among AIS patients revealed the prevalence of hypertension, diabetes mellitus, CAD, and smoking. Hypertension was the most common comorbidity, present in (54) 72% of the AIS patients, followed by diabetes mellitus in (45) 60%, CAD in (17) 22.7%, and smoking in (17) 22.7%.

Correlation analysis

Correlation analysis was conducted to evaluate the relationships between individual lipid profile components and lipid indices.

Table 3: Correlation Matrix

Summary of correlation coefficients for AIP

Variable	**Correlation**	**p-value**
CRI-1	0.149	0.070
CRI-2	0.043	0.614
Age	0.067	0.424
Gender	0.085	0.311
Hypertension	0.026	0.762
Diabetes	-0.242	**0.003**
Smoking	0.026	0.765

Significant Correlation: Among the variables analyzed, only diabetes showed a statistically significant correlation with AIP (p-value = 0.003). This moderate negative correlation suggests that as AIP increases, the likelihood of having diabetes decreases, or vice versa. Non-Significant Correlations: The correlations between AIP and CRI-1, CRI-2, age, gender, hypertension, and smoking were not statistically significant.

DISCUSSION

Demographic and clinical characteristics

The demographic and clinical characteristics of the study population revealed a slightly higher prevalence of acute ischemic stroke (AIS) among males (72%) compared to females (28%). This gender distribution aligns with existing literature indicating a higher incidence of stroke in males. The mean age of AIS patients (58.47 ± 11.35 years) was similar to that of the control group (57.92 ± 10.78 years), indicating that age was well-matched between the two groups.

Comorbidities were prevalent among AIS patients, with hypertension (72%) and diabetes mellitus (60%) being the most common. These findings are consistent with established risk factors for stroke. The absence of these comorbidities in the control group highlights the significant difference in baseline health status between the two populations. Coronary artery disease (CAD) and smoking were present in 22.7% of AIS patients, underscoring the role of cardiovascular risk factors in stroke etiology.

Lipid indices in AIS patients and control subjects

The analysis of lipid indices demonstrated significantly higher levels of Atherogenic Index of Plasma (AIP), Castelli's Risk Index I (CRI-1), and Castelli's Risk Index II (CRI-2) in AIS patients compared to controls. Specifically, AIP, CRI-1, and CRI-2 were elevated in AIS patients, with mean values of 0.31 ± 0.12, 5.2 ± 1.8, and 3.7 ± 1.2, respectively, compared to 0.18 ± 0.09, 3.6 ± 1.1, and 2.5 ± 0.8 in controls. These differences were highly significant ($p < 0.001$).

The elevated lipid indices in AIS patients suggest a stronger atherogenic lipid profile, which may contribute to the pathogenesis of ischemic stroke. These indices provide a more comprehensive assessment of lipid metabolism and cardiovascular risk compared to traditional lipid measures alone.

In this study, Atherogenic Index of Plasma (AIP), Castelli's Risk Index I (CRI-1), and Castelli's Risk Index II (CRI-2) were significantly higher in AIS patients compared to controls. These results are consistent with the findings of Bhardwaj et al. (2013) [5], who reported that higher values of AIP, CRI-1, and CRI-2 were associated with an increased risk of cardiovascular events, including stroke. Their study emphasized the predictive value of these indices for cardiovascular risk assessment. Togha et al. (2011) [6] reported that stroke patients generally exhibit dyslipidemia characterized by elevated total cholesterol, LDL-C, and triglycerides, which contribute to the pathogenesis of stroke. The elevated AIP, CRI-1, and CRI-2 values reflect this dyslipidemic profile.

Comorbidities and their prevalence

The high prevalence of hypertension (72%) and diabetes mellitus (60%) among AIS patients highlights the critical role of these conditions as risk factors for stroke. Hypertension is well-known to cause endothelial damage and promote atherosclerosis, thereby increasing the risk of ischemic events. Similarly, diabetes mellitus is associated with dyslipidemia and increased atherosclerotic burden, contributing to stroke risk.

Coronary artery disease (CAD) and smoking were each present in 22.7% of AIS patients, reinforcing the multifactorial nature of stroke risk. The coexistence of these comorbidities underscores the importance of comprehensive cardiovascular risk management in stroke prevention.

Shahar et al. (2003) [7] found that hypertension and diabetes were significant risk factors for stroke in the Atherosclerosis Risk in Communities (ARIC) study. Their research indicated that these comorbidities are closely linked to an increased incidence of ischemic stroke due to their roles in promoting atherosclerosis and endothelial dysfunction.

Correlation analysis

The correlation analysis between AIP and other variables revealed a statistically significant moderate negative correlation with diabetes (correlation coefficient = -0.242, p-value = 0.003). This suggests that as AIP increases, the likelihood of having diabetes decreases, or vice versa. This finding is intriguing and may warrant further investigation to understand the underlying mechanisms.

Other variables, including CRI-1, CRI-2, age, gender, hypertension, and smoking, did not show statistically significant correlations with AIP. This indicates that these variables do not have a meaningful linear relationship with AIP in this dataset. The weak correlations and high p-values suggest that AIP may be independently associated with stroke risk, without significant influence from these demographic and clinical factors.

Park et al. (2014) [8] found that nontraditional serum lipid variables, including AIP, were positively associated with recurrent stroke risk in diabetic patients. This discrepancy may be due to differences in study populations and methodologies, warranting further investigation.

Bang et al. (2008) [9] found that elevated levels of serum triglycerides and non-HDL cholesterol, but not LDL cholesterol, were associated with large artery atherosclerotic stroke. This aligns with our findings where AIP, CRI-1, and CRI-2 were significantly elevated in AIS patients, indicating a stronger atherogenic lipid profile.

Park et al. (2015) [10] analyzed the effects of non-traditional serum lipid indices on recurrent stroke risk. They found that the triglycerides/HDL ratio was a significant predictor of recurrent stroke, similar to our study's finding that elevated lipid indices are associated with AIS.

Sujatha and Kavitha (2017) [11] reported that lipid indices such as CRI-I, atherogenic coefficient, and non-HDL cholesterol were significantly higher in stroke patients compared to controls. This supports our findings of elevated AIP, CRI-1, and CRI-2 in AIS patients.

Zhang et al. (2022) [12] found that higher levels of lipid accumulation product (LAP) were associated with an increased risk of stroke. This study's finding of significant elevations in AIP, CRI-1, and CRI-2 in AIS patients adds to the evidence that various lipid indices are predictive of stroke risk.

Liu et al. (2018) [13] reported that higher TC/HDL-C ratios were associated with an increased risk of ischemic stroke, which is consistent with our findings that CRI-1 and CRI-2 were significantly elevated in AIS patients.

Tziomalos et al. (2017) [3] found that lower triglyceride and HDL-C levels were associated with more severe stroke and higher in-hospital mortality, which contrasts with our finding of elevated lipid indices in AIS patients. This discrepancy may be due to differences in study populations or methodologies.

Denti et al. (2003) [14] found that low HDL-C levels and high LDL-C/HDL-C ratios were independent risk factors for stroke in the elderly, similar to our findings of elevated CRI-1 and CRI-2 in AIS patients.

This study has several limitations that must be acknowledged. Its retrospective design precludes establishing causality between elevated lipid indices and acute ischemic stroke (AIS). The sample size of 75 AIS patients and 75 controls limits generalizability, and the single-center nature of the study may not reflect different geographical or healthcare settings. Additionally, the lack of longitudinal data restricts insights into long-term outcomes, and potential confounders not accounted for in the analysis may influence the observed associations. Furthermore, the study did not consider genetic predispositions or lifestyle factors such as diet and physical activity, which are significant determinants of lipid levels and stroke risk.

Future research should focus on prospective cohort studies with larger and more diverse populations to confirm these findings and establish causality. Interventional studies assessing the impact of lipid-lowering therapies on lipid indices and stroke risk are also needed. Longitudinal follow-up studies would help evaluate the prognostic value of lipid indices over time. Additionally, integrating genetic and lifestyle factors into future research could provide

a more comprehensive understanding of stroke etiology. Mechanistic studies exploring the biological pathways linking lipid indices to stroke risk could identify new therapeutic targets. Conducting multi-center and international studies would enhance the generalizability of findings and contribute to global stroke prevention efforts.

CONCLUSION

This study aimed to investigate the association between lipid indices and acute ischemic stroke (AIS), elucidating their potential as biomarkers for targeted treatment and predicting disease outcomes. The findings demonstrated that lipid indices such as Atherogenic Index of Plasma (AIP), Castelli's Risk Index I (CRI-1), and Castelli's Risk Index II (CRI-2) were significantly elevated in AIS patients compared to healthy controls, suggesting their strong association with stroke risk. Additionally, the high prevalence of comorbidities like hypertension and diabetes among AIS patients underscores the importance of comprehensive cardiovascular risk management. The significant negative correlation between AIP and diabetes further highlights the complex interplay between lipid metabolism and stroke risk. Despite the study's limitations, these results underscore the potential of lipid indices as valuable biomarkers for assessing stroke risk and guiding therapeutic interventions. Future research should focus on prospective, longitudinal, and interventional studies to establish causality, improve generalizability, and develop effective prevention and treatment strategies for stroke.

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