Original Research Article

EVALUATION OF LIPID TETRAD INDEX FOR DETECTING CORONARY ARTERY DISEASE IN TYPE 2 DIABETIC PATIENTS – A PROSPECTIVE STUDY IN A TERTIARY CARE CENTRE

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ABSTRACT

Background: Type 2 Diabetes Mellitus (T2DM) is a significant metabolic illness closely linked to accelerated atherosclerosis and heightened risk of coronary artery disease (CAD). Traditional lipid metrics, including total cholesterol, low-density lipoprotein cholesterol (LDL-C), and triglycerides, typically fail to fully elucidate the risk profile in diabetic individuals, who commonly exhibit unusual lipid irregularities. The Lipid Tetrad Index (LTI) has been suggested as a more comprehensive indicator of atherogenic load. **Aim:** This study was conducted to evaluate the role of LTI as a marker for CAD in patients with Type 2 Diabetes Mellitus attending a tertiary care hospital.
Materials and Methods: This observational cross-sectional study was performed in the Department of General Medicine in the outpatient clinic of a tertiary care hospital. One hundred forty individuals with T2DM were enrolled throughout an eight-month period. Clinical history, demographic information, and risk factor profiles were documented. Patients were categorized into two groups: Group A (T2DM patients with angiographically or clinically confirmed CAD) and Group B (T2DM patients without CAD). Fasting blood specimens were collected to assess total cholesterol, triglycerides, HDL-C, and lipoprotein(a). The LTI was computed utilizing the conventional formula. Statistical analysis was conducted utilizing suitable methods, with $p < 0.05$ being significant.
Results: Among 140 individuals, 72 (51.4%) were male and 68 (48.6%) were female, with a mean age of 56.7 ± 8.9 years. Group A consisted of 70 patients with CAD, while Group B contained 70 patients without CAD. Mean LTI values were markedly elevated in Group A relative to Group B ($p < 0.001$). A positive association was noted between LTI and the number of coronary vessels affected, indicating that LTI increases with the severity of CAD. Lipid parameters (LDL-C, triglycerides) exhibited a diminished association with CAD in comparison to LTI. The receiver operating characteristic (ROC) curve study indicated that LTI exhibited enhanced sensitivity and specificity in predicting CAD in individuals with T2DM compared to individual lipid markers.
Conclusion: The LTI serves as a valuable and dependable indicator for evaluating the risk of CAD in individuals with T2DM. It has superior predictive value compared to traditional lipid markers and exhibits a significant association with the severity of CAD.
Keywords: Atherosclerosis, Cardiovascular Risk, Coronary Artery Disease, Dyslipidemia, Lipid Tetrad Index.

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a prevalent chronic metabolic condition, defined by insulin resistance, diminished insulin production, and sustained hyperglycemia.[1] It has attained epidemic levels worldwide, with India among the nations bearing the greatest burden of diabetes patients. A significant issue with T2DM is its robust correlation with premature atherosclerosis and cardiovascular consequences, especially coronary artery disease (CAD).[2] Cardiovascular morbidity and mortality constitute a substantial fraction of fatalities among diabetic individuals, with the risk of CAD being two to four times greater in patients with T2DM compared to the non-diabetic population.[3]

Dyslipidemia is crucial in the development of atherosclerosis and CAD in diabetes. Diabetic dyslipidemia is characterized by higher triglycerides, reduced high-density lipoprotein cholesterol (HDL-C), and a predominance of tiny dense low-density lipoprotein cholesterol (LDL-C) particles.[4] Conventional lipid profile tests, despite their widespread usage, frequently may not adequately reflect the full extent of atherogenic load in diabetic individuals. This constraint has stimulated the pursuit of novel, more extensive markers that can offer enhanced prediction value for CAD.

The Lipid Tetrad Index (LTI) is an emerging biomarker. The calculation is performed using the formula:

LTI = Total Cholesterol × Triglycerides × Lipoprotein(a) / HDL-C,[5]

This composite index amalgamates many lipid abnormalities into a singular measure. The LTI provides a comprehensive evaluation of the atherogenic environment in diabetic patients by include lipoprotein(a), an established independent risk factor for CAD, and considering the equilibrium between atherogenic lipids and protective HDL-C. Prior research indicates that LTI exhibits a stronger correlation with the existence and severity of CAD compared to conventional lipid markers.[6,7]

CAD in diabetes frequently remains asymptomatic in the initial stages due to autonomic neuropathy and unusual manifestations, resulting in a postponed diagnosis. Thus, identifying a straightforward yet dependable marker that can facilitate early prediction and risk classification holds substantial therapeutic importance.[8] The LTI, a singular determined value from standard lipid assessments and lipoprotein(a), may effectively fulfill this role in clinical practice.[9]

Notwithstanding its potential, LTI has not been well examined in Indian populations, where diabetes and cardiovascular disease are significantly prevalent. South Asian communities exhibit an elevated susceptibility to insulin resistance, central obesity, and dyslipidemia, hence exacerbating the risk of CAD.[10]

Assessing the efficacy of LTI in this high-risk population may yield significant insights and enhance preventive and treatment approaches. This may facilitate the establishment of LTI as a pragmatic and dependable instrument in standard diabetes management for cardiovascular risk evaluation.

Aims and Objectives

- To evaluate the role of LTI as a marker for CAD in patients with Type 2 Diabetes Mellitus attending a tertiary care hospital.

MATERIALS AND METHODS

This observational cross-sectional study was conducted at the Department of General Medicine at Govt. Sivagangai Medical College, Sivagangai, over a duration of six months (December 2024 to May 2025). The research was carried out in the outpatient department over eight months, enrolling a total of 140 patients with T2DM according to established inclusion and exclusion criteria.

The study population comprised male and female patients aged 35 to 70 years with a verified diagnosis of T2DM according to American Diabetes Association (ADA) criteria. individuals were categorized into two groups: Group A included diabetes individuals with angiographically or clinically confirmed CAD, whereas Group B comprised diabetic patients without evidence of CAD.

CAD was identified using clinical criteria, including a history of myocardial infarction, angina, and ischemic alterations on electrocardiography, or through findings from coronary angiography, when accessible. The severity of CAD in Group A patients was evaluated by recording the number of affected vessels (single-vessel, double-vessel, or triple-vessel disease) as shown in angiographic examinations. Patients lacking clinical or angiographic indications of CAD were classified as Group B.

Individuals with Type 1 diabetes mellitus, severe systemic diseases, hypothyroidism, chronic renal disease, nephrotic syndrome, or those undergoing cholesterol-lowering treatment such as statins were excluded from the study.

All participants provided informed consent. A comprehensive clinical history was collected from all participants, encompassing demographic information, diabetes duration, related comorbidities including hypertension, smoking and alcohol consumption, family history of cardiovascular disease, and current medications. Every patient received a comprehensive physical examination, encompassing blood pressure measurement, body mass index (BMI) assessment, and cardiovascular evaluation.

Blood samples were obtained following a fasting period of 10 to 12 hours overnight. Venous blood was collected under aseptic conditions for the assessment of fasting blood glucose, glycated hemoglobin (HbA1c), and lipid profile. The lipid profile comprised the assessment of total cholesterol, triglycerides, high-density lipoprotein cholesterol

(HDL-C), and low-density lipoprotein cholesterol (LDL-C). Lipoprotein(a) [Lp(a)] was quantified utilizing immunoassay techniques available at the institution's biochemistry laboratory.

The LTI has been computed. All biochemical assessments were conducted at the central laboratory of Govt. Sivagangai Medical College. with standard automated analyzers, thereby ensuring rigorous internal and external quality control.

The collected data were organized and analyzed statistically. Continuous variables were represented as mean ± standard deviation, whereas categorical variables were represented as percentages. The Student's t-test was employed to compare continuous variables between the two groups, whereas the chi-square test was utilized for categorical data. The relationship between LTI and the severity of CAD was evaluated using Pearson's correlation coefficient. An examination of the receiver operating characteristic (ROC) curve was conducted to assess the diagnostic accuracy of LTI in relation to traditional lipid measurements. A p-value below 0.05 was deemed statistically significant.

RESULTS

A total of 140 patients with T2DM were included in the study, of which 70 had angiographically or clinically proven CAD (Group A) and 70 did not have CAD (Group B).

Patients with CAD were significantly older and more likely to be male compared to those without CAD ($p < 0.05$). The mean age of patients with CAD was significantly higher than those without CAD, suggesting that increasing age is a strong risk factor for coronary artery involvement in T2DM. Male patients were more commonly affected by CAD than females, reflecting the higher cardiovascular risk profile in men, possibly due to hormonal differences, lifestyle factors, and a higher prevalence of smoking and hypertension among them.

Table 1: Age and Sex Distribution of Study Population

Variable	Group A (n=70)	Group B (n=70)	Total (n=140)	p-value
Mean Age (years)	58.4 ± 7.6	55.1 ± 8.2	56.7 ± 8.9	0.018*
Male (%)	42 (60%)	30 (42.9%)	72 (51.4%)	0.041*
Female (%)	28 (40%)	40 (57.1%)	68 (48.6%)	

Longer duration of diabetes was significantly associated with CAD (p=0.006), with >10 years duration seen more frequently in Group A. [Table 2]

Hypertension, smoking, and family history of CAD were significantly more common in diabetic patients with CAD. [Table 3]

Table 2: Duration of Diabetes in Study Population

Duration of T2DM (years)	Group A (n=70)	Group B (n=70)	p-value
<5 years	12 (17.1%)	24 (34.3%)	0.006*
5–10 years	22 (31.4%)	28 (40.0%)	
>10 years	36 (51.4%)	18 (25.7%)	

Table 3: Baseline Risk Factors in Study Population

Risk Factor	Group A (n=70)	Group B (n=70)	p-value
Hypertension	44 (62.9%)	28 (40.0%)	0.007*
Smoking	30 (42.9%)	18 (25.7%)	0.038*
Family H/o CAD	20 (28.6%)	10 (14.3%)	0.049*

Diabetic patients with CAD demonstrated significantly elevated total cholesterol, triglycerides, LDL-C, and lipoprotein(a), along with reduced HDL-C levels compared to those without CAD. [Table 4]

Table 4: Lipid Profile Comparison Between Groups

Parameter (mg/dl)	Group A (With CAD)	Group B (Without CAD)	p-value
Total Cholesterol	212.3 ± 28.6	190.8 ± 26.2	0.001*
Triglycerides	182.4 ± 40.2	158.6 ± 35.7	0.002*
HDL-C	36.2 ± 6.4	42.5 ± 7.1	0.001*
LDL-C	128.7 ± 25.4	116.3 ± 22.8	0.010*
Lipoprotein(a)	32.6 ± 8.2	24.5 ± 6.8	<0.001*

The LTI was significantly higher in diabetic patients with CAD than those without CAD. Comparison between the group showed statistical significance. [Table 5]

Table 5: Mean Lipid Tetrad Index Between Groups

Group	Mean LTI Value (×10^5)	p-value
Group A	3.28 ± 0.76	<0.001*
Group B	2.10 ± 0.54	

Higher LTI values were associated with greater severity of CAD, showing a strong positive correlation. A clear stepwise rise in LTI values was noted from single-vessel disease to triple-vessel disease. This demonstrates a positive correlation between LTI and severity of CAD, suggesting that higher LTI values not only indicate presence of CAD but also predict the extent of vascular involvement.

Table 6: Correlation of LTI with Severity of CAD

Severity of CAD (by angiography)	Mean LTI Value (×10⁵)	p-value
Single Vessel Disease (n=24)	2.86 ± 0.64	0.001*
Double Vessel Disease (n=22)	3.32 ± 0.71	
Triple Vessel Disease (n=24)	3.74 ± 0.82	

LTI showed the highest diagnostic accuracy in predicting CAD compared to conventional lipid parameters. Receiver operating characteristic curve analysis revealed that LTI had the highest area under curve (AUC) compared to traditional lipid parameters. Its sensitivity (80%) and specificity (78%) were superior, establishing LTI as a better predictor of CAD in diabetic patients.

Table 7: ROC Curve Analysis of LTI vs Conventional Lipid Parameters in Predicting CAD

Parameter (mg/dl)	Group A (With CAD)	Group B (Without CAD)	p-value
Total Cholesterol	212.3 ± 28.6	190.8 ± 26.2	0.001*
Triglycerides	182.4 ± 40.2	158.6 ± 35.7	0.002*
HDL-C	36.2 ± 6.4	42.5 ± 7.1	0.001*
LDL-C	128.7 ± 25.4	116.3 ± 22.8	0.010*
Lipoprotein(a)	32.6 ± 8.2	24.5 ± 6.8	<0.001*
LTI	**0.85**	**80**	**78**

DISCUSSION

T2DM has been recognized as a significant independent risk factor for the onset of CAD. The aggregation of metabolic disorders, especially dyslipidemia, hastens atherosclerosis and substantially impacts cardiovascular morbidity and death.[11]

In this study, patients with CAD were considerably older than those without CAD, and males were more frequently affected than females. This observation corresponds with previous epidemiological evidence indicating that advancing age and male sex are significant non-modifiable risk factors for CAD. An extended duration of diabetes correlates with an increased prevalence of CAD, reinforcing the notion that prolonged hyperglycemia exacerbates vascular injury by mechanisms including advanced glycation end-products, oxidative stress, and endothelial dysfunction.

The examination of baseline risk factors indicated that hypertension, smoking, and a familial history of CAD were more common in diabetic patients with CAD. These conventional risk factors interact with diabetes to accelerate the advancement of atherosclerosis. The simultaneous presence of hypertension and diabetes significantly increases the risk of cardiovascular events, whereas smoking causes direct endothelial damage and promotes thrombosis. This underscores the significance of proactive risk factor reduction in diabetes individuals.

The study by Dabla PK et al,[12] reported 135 instances of acute myocardial infarction, with a mean age of 36 ± 4.5 years. The majority (84%) of participants were aged between 31 and 45 years. The mean BMI was 25.7 ± 4.31 kg/m², with 15.5% of individuals exhibiting a BMI exceeding 30 kg/m². The average systolic and diastolic blood pressure was 118.4 ± 15.5/75.6 ± 9.61 mmHg, respectively. 9.63% of the patients studied were diabetic, 8.8% were hypertensive, and 8.9% had a history of dyslipidemia. 70.4% of patients were active smokers, 66.7% had a history of tobacco use, and 30.4% were drinkers.

Traditional lipid metrics were markedly abnormal in patients with CAD. The normal pattern of diabetic dyslipidemia is characterized by elevated total cholesterol, triglycerides, and LDL-C, alongside reduced HDL-C. Lipoprotein(a) levels were significantly elevated in CAD-positive patients, underscoring its status as an independent genetic risk factor. Lipoprotein(a) is recognized for facilitating atherogenesis by disrupting fibrinolysis and augmenting LDL oxidation. Nonetheless, despite their therapeutic relevance, traditional lipid markers frequently do not adequately represent the total atherogenic load in diabetes patients, as each statistic only reflects a singular facet of lipid metabolism.

The LTI mitigates this constraint by consolidating total cholesterol, triglycerides, and lipoprotein(a), normalized against HDL-C, into a singular composite metric. In the current study, LTI levels were markedly elevated in CAD-positive diabetics relative to those without CAD, and a progressive increase in LTI was noted with escalating degree of coronary involvement. This indicates that LTI not only recognizes high-risk people but also elucidates the degree of vascular injury.

Dabla PK et al,[12] observed that LTI was markedly elevated in acute MI cases relative to controls. A substantial positive association was identified between lipid parameters—total cholesterol, triglycerides, LDL-C, Lp(a), and ApoB/ApoA1—and LTI, with the exception of HDL-C, which exhibited a negative correlation with LTI. Chaturvedi M et al,[13] and Patil R et al,[14] also noted in their research that the LPI value was considerably elevated in cases relative to controls among the lipid indices. Holy B et al,[15] found that the mean levels of Apo A, Apo B, and lipoprotein a were elevated in diabetes participants relative to control subjects ($p < 0.05$). Tetrad had a sensitivity of 81.05%, specificity of 100%, and an accuracy of 90.5%, while the TC/HDL ratio demonstrated a lower accuracy of 75.76%.

The study conducted by Kalaivani R et al,[16] indicated that LTI exhibited the highest Positive Predictive Value (PPV) at 77.8% and Negative Predictive Value (NPV) at 72.7%; AIP had a PPV of 65.3% and an NPV of 66.2%. The study determined that LTI are the most appropriate for evaluating atherogenicity.

The diagnostic efficacy of LTI was further validated using ROC curve analysis, which revealed enhanced sensitivity and specificity of LTI in comparison to traditional lipid markers. This suggests that LTI may function as a more dependable predictor of CAD in diabetic individuals, facilitating earlier risk categorization and preventive measures.

CONCLUSION

The study indicates that the LTI serves as a dependable and effective biomarker for identifying CAD in individuals with T2DM. LTI exhibits a robust correlation with both the existence and severity of CAD, surpassing traditional lipid metrics. Regular assessment of LTI in diabetic patients can improve early risk classification and inform preventative measures, hence aiding in the reduction of cardiovascular morbidity and mortality in this high-risk group.

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