RESEARCH PAPER

Lipid Profile And Its Association With Glycemic Status In Type 2 Diabetes Mellitus: A Cross-Sectional Retrospective Study From South India

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Abstract

Background: Diabetes mellitus (dm) is an endocrine disease defined by the body's inability to use glucose, which results from absolute or relative lack of insulin. It is a chronic metabolic disease with a complex interplay among genetic, environmental and lifestyle factors.

Objective: To evaluate the relation of lipid profile with glycated haemoglobin in type ii diabetes mellitus.

Methods: A total of 273 participants were classified into good glycemic control (hba1c ≤ 7%), and poor glycemic control (hba1c > 7%) groups. Lipid parameters and lipid ratios were analyzed, and correlation with hba1c was assessed. We performed receiver-operating characteristic (roc) analysis to test prediction accuracy of lipid ratios.

Results: Hdl-c level was higher in good control group, whereas the levels of total cholesterol, ldl-c, non-hdl cholesterol and triglyceride were not significantly different. Hba1c correlated positively with triglycerides ($r = 0.211$, $p < 0.001$) and the tg/hdl ratio ($r = 0.205$, $p < 0.001$). Further, lipid ratios had limited predictive value according to roc analysis, while tg/hdl cholesterol presented the highest auc (0.593) followed by tc/hdl, ldl/hdl and non-hdl cholesterol.

Conclusion: Hdl-c and triglyceride-related indices indicate the glycemic states; however, lipid ratios follow a weak predictive value for diagnosis and cannot substitute hba1c. They could be used as adjunctive markers for assessing cardiometabolic risk.

Keywords: Glycemic Control, Lipid Ratios, Triglycerides, Tg/Hdl Ratio, Diabetes Mellitus.

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INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a metabolic disorder that results in sustained hyperglycemia caused by insufficient insulin production and/or action. It has become a global epidemic and public health problem in the low- and middle-income countries with an increasing epidemic cluster over time.[1,2]

Hyperglycaemia in type 2 DM results in metabolic derangements that are related to a remarkably higher risk of CVD morbidity and mortality; therefore, early detection/management of these CVD risk factors is essential.[3,4]

One of the most common metabolic abnormalities in diabetic patients is dyslipidemia that is characterized by elevation of TG, decrease in HDL-C and presence of small dense LDL—so-called "diabetic dyslipidemia".[5,6] These are the lipid abnormalities that are central in atherosclerosis and CVD.[7] Meanwhile,

lipid abnormalities in diabetes are well known, and their interrelationship with the glycemic state remains a topic of substantial investigation.

Common lipid profiles, such as cholesterol, LDL-C, HDL-C, and triglyceride, are widely utilized to assess metabolic health. Nonetheless, increasing evidence suggests that lipid ratios (e.g., TG/HDL, TC/HDL, LDL/HDL, and non-HDL), which reflect the overall pathways of clinical development associated with underlying cardiometabolic risk and insulin resistance, could be an improved single index.[8-10] Of these, the TG/HDL ratio has been proposed as a surrogate marker of atherogenic dyslipidemia and insulin resistance, and it is associated with endothelial dysfunction and early vascular changes.[11,12]

Despite the increasing literature, the associations of these lipid ratios with direct measures of glycemia, especially HbA1c, remain ambiguous across different studies. Some studies have demonstrated good correlations between TG/HDL and poor glycemic status,[13,14] while others have shown that lipid ratios have limited diagnostic capability compared to direct markers of glycemia when assessed.[15,16] Nevertheless, this difference has implications in terms of clinical use of these assays as screening-tests or monitoring tests under routine conditions for glycemic control.

In addition, majority of the literature available is derived from Western populations with little evidence from South Asian or Indian populations who tend to manifest different metabolic phenotypes, such as greater visceral fat mass and more atherogenic lipidaemic profile.[17,18] Thus, it is of clinical interest to clarify whether the relationship between lipid ratios and glycemic control persists in these populations.

Based on these limitations, the aim of this study was to evaluate the association between common lipid markers and their ratios with glycemic measures in adult patients with T2DM. Through considering the relationship with HbA1c and predictive ability of lipid ratios, we evaluate whether these novel lipids are candidate biomarkers for glycemic condition and cardiometabolic profile.

MATERIALS AND METHODS

Study Design and Setting

This was a cross-sectional study carried out at a tertiary care hospital in Chennai after obtaining the approval of the Institutional Human Ethics Committee [Ref: CSP/20/NOV/87/214]. All participants provided informed consent before enrollment. The study period is from August 2018 to June 2021.

Study Participants and Sample Collection

This study enrolled 273 participants. According to their glycemic control (HbA1c), patients were divided into 2 groups:

Group I (Favorable Glycaemic Control): Patients with HbA1c ≤ 7% (n=158).

Group II (Uncontrolled): Patients whose HbA1c was > 7% (n=115).

Three milliliters of venous blood were withdrawn from each patient with T2DM. 2 ml of blood was isolated by centrifuge from the whole sample volume and serum separated for biochemical estimation of lipids. 1 mL of whole blood was used for HbA1c analysis. All vacutainers were labelled with a particular sample number. Serum samples were stored frozen at –20°C until analyzed to prevent degradation.

Laboratory Analysis

The serum lipid profile, including total cholesterol, triglycerides, HDL-C, LDL-C, and non-HDL cholesterol, was estimated using an automated spectrophotometric analyzer (M/s Olympus 400 Autoanalyzer; Olympus Diagnostica GmbH, Kiel, Germany) based on standard enzymatic procedures. Glycated hemoglobin (HbA1c) was estimated using HPLC, a known gold standard method due to its specificity and reproducibility.

Statistical Analysis

Statistical analysis SPSS software (V.16.0 SPSS, Inc., Chicago, IL) was used for statistical analysis. Continuous variables with normal distribution are expressed as mean ± SD, and asymmetrically distributed continuous variables as median (IQR).

Since the data distribution was not normal, we used Mann–Whitney U test to compare good (HbA1c ≤ 7%) and poor control group (HbA1c > 7%). Pearson correlation was used to evaluate the correlation of HbA1c with lipids or lipid profile indices. Receiver operating characteristic (ROC) curve analysis was used to evaluate the discriminatory ability of lipid ratios for predicting poor glycemic control. ROC curves were generated to establish the cut-off values and sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), false-positive rate, and false-negative rate of the optimal cut-off point was obtained. In all tests, a difference with $p < 0.05$ was taken as significant.

RESULTS

A total of 273 subjects were included in the study, of whom 158 had good glycemic control (HbA1c ≤ 7%) and 115 had poor glycemic controls (HbA1c >7%). The two cohorts were similar and no significant difference was found regarding age distribution and sex composition (Table 1 & 2).

Table 1: Demographic Distribution of Study Participants by Glycemic Control Status (N=273)

Characteristics	Group I (Good Glycemic Control) (HbA1c ≤7%) (n=158)	Group II (Poor Glycemic Control) (HbA1c > 7%) (n=115)	Total
Gender	n (%)	n (%)	n (%)
Males	100 (63.3%)	74 (64.3%)	174 (63.7%)
Females	58 (36.7%)	41 (35.7%)	99 (36.3%)

Table 1 shows the categorization of all of our 273 patients included in the study into two groups, according to their glycemic control (Group I; Good Control HbA1c ≤7% and Group II; Poor Control HbA1c >7%).

Table 2: Demographics and Lipid Parameters of Two Study Groups

Variables	Group I (Good Glycemic Control) (n=158)	Group II (Poor Glycemic Control) (n=115)	p-value
Age (years) (mean ± SD)	54.13 ± 7.89	54.08 ± 8.4	0.961
Gender (M/F)	100 / 58	74 / 41	—
Total Cholesterol (mg/dL)	199.2 ± 55.4	191 ± 67.7	0.292
Triglycerides (mg/dL) median (IQR)	149 (107–208)	179 (114–245)	0.085
HDL-C (mg/dL)	**39.21 ± 11**	**36.56 ± 10**	**0.043***
LDL-C (mg/dL)	132.92 ± 41	124 ± 44	0.098
TC/HDL-C Ratio	5.27 ± 1.5	5.35 ± 1.6	0.689
TGL/HDL-C Ratio	5.2 ± 4.4	8.3 ± 19	0.094
LDL/HDL Ratio	3.6 ± 2	3.5 ± 1.1	0.451
Non-HDL (mg/dL)	160 ± 51	154 ± 62	0.449

***Statistically Significant at p-value < 0.05**

Table 2 shows a comparison of mean lipid parameter levels and their ratios among the two groups of glycemic control. Comparison was performed using the independent-samples t-test or Mann–Whitney U-test. There were no differences between the means ($p > 0.05$) for HDL-C, which was significantly higher in the good glycemic control group. The poor control group had numerically higher triglyceride concentrations.

Biochemical Parameters and Correlation Analysis

There were no differences between most of the lipid parameters in both groups. HDL-C was significantly greater among the good glycemic control participants ($p = 0.043$). Total Cholesterol, LDL-C, Non-HDL Cholesterol and Triglycerides levels did not differ significantly between the groups (Table 2). Correlations were also found between HbA1c and Triglycerides ($r = 0.211$, $p < 0.001$), as well as the TGL/HDL ratio ($r = 0.205$, $p < 0.001$). HbA1c was weakly associated with other indices (TC, LDL-C, HDL-C and LDL/HDL) and no associations were significant (Table 3).

Table 3: Correlation of Lipid Parameters and Ratios with HbA1C Levels

Variables	Correlation Coefficient (r)	95% CI	p-value
Total Cholesterol	-0.063	(-0.16 to 0.04)	0.299
Triglycerides	**0.211**	**(0.10 to 0.31)**	**<0.001***
HDL-C	-0.095	(-0.20 to 0.01)	0.118
LDL-C	-0.116	(-0.22 to -0.01)	0.056
TC/HDL-C	0.18	(0.06 to 0.29)	0.765
TGL/HDL-C	**0.205**	**(0.10 to 0.31)**	**<0.001***
LDL/HDL-C	-0.064	(-0.18 to 0.05)	0.294

***Statistically Significant at p-value < 0.05**

Table 3 presents the correlation between lipid parameters and ratios with HbA1c levels using Pearson's r. 54 HbA1c was significantly associated with Triglyceride (r=0.211) and the Triglyceride-to-HDL-C ratio (r=0.205). Weak and insignificant associations of Total Cholesterol, HDL-C, LDL-C, and LDL-C/HDL-C were detected.

Diagnostic Performance

According to ROC analysis, the lipid ratios had overall poor discriminative performance for detecting PGCS (Table 4; Figure 1a–d). The AUC for TGL/HDL was most excellent (0.593), followed by TC/HDL (0.525), LDL/HDL (0.505), and Non-HDL-C (0.464). Comparative statistics at optimal cut-offs (Table 4) showed that, among the tested parameters, the TGL/HDL measurement was most promising, with moderate specificity (65.2%) but low sensitivity (49.4%) at its threshold level of 3.95.

Table 4. Diagnostic Performance of Lipid Ratios for Predicting Glycemic Control (PGCS)

Parameter	AUC	95% CI	Cut-off Value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
TC/HDL	0.525	0.45–0.59	5.25	52.5	53	60.6	44.9
TGL/HDL	**0.593**	**0.52–0.66**	**3.95**	**49.4**	**65.2**	**66.1**	**48.4**
LDL/HDL	0.505	0.43–0.57	3.51	51.3	53	60.1	44.1
Non-HDL	0.464	0.39–0.53	162	53.2	49.6	—	—

(HbA1c > 7%) *95% CI → "Confidence Interval*PPV → Positive Predictive Value, *NPV → Negative Predictive Value

Table 4 shows diagnostic test comparisons between the two study groups. The performance characteristics of lipid ratio and non-HDL cholesterol for detecting poor glycemic control (HbA1c > 7%) among Type 2DM patients are presented. The TGL/HDL ratio had the highest discriminatory power among the markers, with an AUC of 0.593 and a specificity of 65.2% at a cut-off level of 3.95, indicating better predictive ability among these parameters. Conversely, the AUC values of TC/HDL, LDL/HDL, and n-HDL cholesterol were very close to 0.5, indicating that these parameters have a poor diagnostic value. The corresponding sensitivities, specificities, PPVs, and NPVs for each lipid parameter are also displayed in the table, enabling a head-to-head comparison of their predictive value for glycemic status**.**

DISCUSSION

This study investigated the association between lipid parameters and ratios and glycemic status in 273 adults with type 2 diabetes mellitus (T2DM). The two study groups were similar in age and sex (Table 1), thereby avoiding possible confounding factors that could affect lipid metabolism. Main finding: HDL-C and triglyceride-related variables demonstrate substantial heterogeneity by glycemic categories; most other lipid variables do not differ materially.

Lipid Profile Across Glycemic Groups

We found that high HDL-C levels were increased among adults well controlled with their diabetes (p = 0.043), as indicated in Table 2. This is in line with the well-known observation that chronic hyperglycemia suppresses HDL synthesis, impairs HDL maturation, and attenuates its antioxidant and anti-inflammatory activity.[19,20] Better glycemic control is thus related to improved HDL metabolism and maintenance of the cardioprotective lipid profile. In contrast, total cholesterol, LDL-C, non-HDL cholesterol, and triglycerides did not exhibit significant differences across glycemic levels categories. Similar to our results, others have reported elsewhere that glutathione is not a predictor of CVD disease,[21] suggesting that LDL concentration alone might be insufficient to reflect metabolic disturbances in diabetes, and known qualitative changes such as the increased small dense LDL particles are recognized among patients with diabetes irrespective of their cholesterol levels.[22,23] These findings further support the notion that traditional lipid parameters may have low sensitivity to changes in glycemic state.

Relationship Between HbA1c and Lipid Levels

In the correlation analysis (Table 3), significant positive correlations were observed with HbA1c for triglycerides (r = 0.211) and the TG/HDL ratio (r = 0.205). This suggests that triglycerides rise and the

TG/HDL ratio deteriorates with worsening glycemic control. These observations are consistent with reports that hypertriglyceridemia is a feature of insulin resistance and defective hepatic lipid metabolism in diabetes.[24,25] Increased TG/HDL ratios have also been linked to endothelial dysfunction, vascular inflammation, and early atherosclerotic changes in diabetes.[26,27] The correlation between HbA1c and TC, LDL-C, HDL-C, and LDL/HDL ratio was weak, but non-significant. This finding is consistent with previous studies that have found glycemic exposure impacts the composition, oxidation, and density of lipid particles to a greater extent than absolute lipid quantity.[28,29]

Lipid ratios in predicting glycemic status

ROC curve analysis (Table 4; Figures 1: a-d) showed that lipid ratios have a poor discriminative capacity in distinguishing between good and poor glycemic control. The AUC was highest for TG/HDL ratio (0.593), followed by TC/HDL (0.525), LDL/HDL (0,505), and non-HDL cholesterol (0.464). These numbers suggested poor overall predictive ability. Likewise, other studies have confirmed that lipid ratios reflect atherogenic risk but do not correlate well with glycemic control compared to HbA1c.[30,31] The results of diagnostic performance analysis in Table 4 showed that the motif TGL/HDL-C ratio had the best discriminatory power in predicting poor glycemic control among the lipid ratios examined (AUC = 0.593). The AUC value is not high in its diagnostic strength, but it is significantly higher than that for TC/HDL-C and LDL/HDL-C and non-HDL cholesterol, which have AUC as well as near 0.5 (indicative of low predicting ability to glycemic challenges). The relatively higher performance of TGL/HDL may be due to the well-established link between hypertriglyceridemia, insulin resistance and deteriorated glycemic control as documented in other studies that show a robust association of triglyceride-rich lipoproteins and triglyceride-based ratios with metabolic dysfunction and high levels of HbA1c.[32]

Moreover, the TGL/HDL-C ratio (65.2%) seems to be better in terms of negative predictive value when excluding good glycemic control patients, so it could play a complementary role in clinical screenings. But the low sensitivity means it must be combined with existing biomarkers for context, rather than a test in its own right.

The pattern detected in the present study suggests that lipid ratios, particularly TG/HDL ratio, may reflect underlying metabolic disturbances associated with poor glycemic regulation. But these ratios in isolation are not robust enough to be utilized as independent indicators of glycemic status. This is consistent with previous research to suggest blood glucose, rather than CRP or possibly inflammation, adversly effect lipid profiles but also that the measure of HbA1c remains better in measuring long-term glycemic exposure and provides further information over fasting plasma glucose alone.[33,34]

In the LRS, where HbA1c may not be routinely assessed, TG/HDL ratio could potentially emerge as an additional marker for assessing the risk of cardio metabolism [35]. The high triglycerides and TG/HDL ratio found in subjects with elevated HbA1c, as described by these previously established metabolic pathways, suggest a more atherogenic lipid profile with the worsening glycemic control.

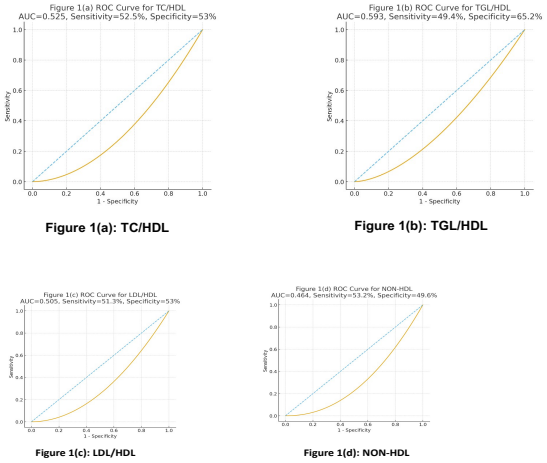

Figure 1 (a-d): ROC curves compared the diagnostic performance of four lipid-based markers in predicting poor glycemic control (HbA1C>7%) (a-d). The predictive power of the TGL/HDL ratio was higher, although marginal (AUC 0.593). The remaining ratios (TC/HDL, LDL/HDL, and Non-HDL) had low discriminatory properties; their AUCs were near 0.5. Consequently, the TGL/HDL ratio appeared to be the most favorable lipid-derived index for discriminating poor glycemic control in this population.

***ROC=Receiver Operating Characteristic, * AUC=Area Under the Curve**

STUDY LIMITATIONS

The present study has a number of weaknesses that must be considered when interpreting its findings. Its cross-sectional design makes that we can't infer causality between glycemic control and lipid abnormalities. Limitations This was a single-center study and thus observations may not apply to larger or different populations. In addition, life style (e.g., diet, physical activity and adherence to the medication's regimen for lipid control) were not covered in our

examination. Moreover, advanced lipid markers such as apolipoproteins and LDL particle size were not measured that might have provided additional information.

CONCLUSION

This research reveals that the lipid-related indices, in particular TG/HDL ratio, are more associated with poor glycemic control among type 2 DM patients than other lipid values. Despite the relatively better performance comparison to other lipid ratios, TG/HDL ratio has a limited capacity to identify high HbA1c and may not replace testing of HbA1c.

Thus, HbA1c continues to be the best marker for measuring longer-term control of blood sugar. But the TG/HDL ratio could be used as a further measure particularly where HbA1c testing cannot be readily assessed. It might be useful to track triglyceride-based markers to find people who are developing deteriorations in metabolic health, so we can intervene with lifestyle or other adjustments sooner." On the whole, the study concludes in support of employing triglyceride related ratios as useful adjuncts but not replacements for known glycemic indices.

FUTURE DIRECTIONS

Further longitudinal research is necessary to understand temporal variations of lipid ratios in association with glycemic status. Larger sample size, comprehensive measures of lifestyle and advanced lipid profiling should be considered to improve sensitivity or specificity of predictions by lipid ratios. Furthermore, evaluation of these markers in other ethnic groups would increase their clinical relevance

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