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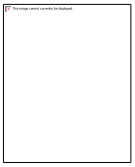

HIGH LEVEL OF INDIVIDUAL LIPID PROFILE AND LIPID RATIO AS A PREDICTIVE MARKER OF POOR GLYCEMIC CONTROL IN TYPE 2 DIABETES MELLITUS

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Abstract:***Background:***Dyslipidemia is a major contributor to cardiovascular risk among individuals with Type 2 diabetes mellitus (T2DM). This study aimed to characterize lipid profiles in this population and to determine whether lipid abnormalities varied across demographic or clinical subgroups encountered in routine clinical practice.***Study Design:*** Cross-sectional study.Place and Duration of Study: Department of Medicine, Aga Khan University Hospital, Karachi, Pakistan, from April to October 2025.***Methods:*** A cross-sectional study was conducted among 171 adults with T2DM attending a tertiary care facility. Demographic and clinical data were collected for each participant. Fasting lipid profiles were measured, lipid ratios were calculated, and glycemic control was assessed using glycated hemoglobin (HbA1c). Clinical characteristics were compared between participants with and without dyslipidemia, and lipid parameters were summarized for the entire cohort.***Results:*** The majority of participants were middle-aged with an established duration of diabetes. Poor glycemic control was prevalent; however, dyslipidemia was observed across all subgroups and showed no statistically significant variation by age, sex, treatment modality, obesity status, or disease duration. The overall lipid pattern was distinctly atherogenic, characterized by elevated triglycerides, reduced HDL cholesterol, and unfavorable lipid ratios — particularly TG/HDL-C and LDL/HDL-C.***Conclusion***: Atherogenic dyslipidemia is highly prevalent among adults with long-standing T2DM, independent of demographic and clinical profiles. Routine incorporation of lipid ratios into clinical assessments may enhance identification of patients at elevated cardiometabolic risk and facilitate more targeted therapeutic interventions

Keywords: Diabetes mellitus, type 2; dyslipidemias; lipoproteins; cholesterol; triglycerides; lipid metabolism; hemoglobin A, glycosylated; cardiovascular diseases/prevention & control; cross-sectional studies.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance, progressive beta-cell dysfunction, and chronic

hyperglycemia. It is one of the fastest-growing public health challenges globally, with its prevalence rising sharply in both developed and developing nations due to urbanization, sedentary lifestyles, and increasing rates of obesity. [1] Beyond its direct glycemic consequences, T2DM is frequently accompanied by a constellation of lipid abnormalities that substantially amplify the risk of cardiovascular disease (CVD). These disturbances typically include moderate hypertriglyceridemia, reduced high-density lipoprotein cholesterol (HDL-C), and variably elevated low-density lipoprotein cholesterol (LDL-C), collectively constituting what is recognized as diabetic dyslipidemia.

Cardiovascular disease remains the leading cause of morbidity and mortality among individuals with T2DM, accounting for a disproportionate share of diabetes-related deaths worldwide. [3] The interplay between metabolic dysregulation and lipid abnormalities creates a milieu highly conducive to atherosclerosis and its clinical sequelae, including coronary artery disease, cerebrovascular accidents, and peripheral arterial disease. The global burden of CVD is further compounded by the rising prevalence of obesity, driven by sedentary behaviors and energy-dense dietary patterns, which independently promotes dyslipidemia through multiple metabolic pathways. [3]

The pathophysiology of dyslipidemia in T2DM is deeply rooted in insulin resistance and relative insulin deficiency. Under normal physiological conditions, insulin suppresses hepatic very-low-density lipoprotein (VLDL) synthesis and promotes lipoprotein lipase activity, facilitating triglyceride clearance. In the setting of insulin resistance, these regulatory mechanisms are disrupted, resulting in excess hepatic triglyceride production, impaired peripheral lipolysis, and accelerated HDL catabolism. [4] Concurrently, elevated free fatty acid flux from visceral adipose tissue further amplifies hepatic VLDL secretion. The net result is a dyslipidemic state marked by high triglycerides, low HDL-C, elevated LDL-C, and an increased proportion of small dense LDL particles, a particularly atherogenic lipoprotein subclass with enhanced capacity to penetrate the arterial wall and trigger oxidative and inflammatory cascades.[5]

Glycemic control, as assessed by glycated hemoglobin (HbA1c), has emerged as an important determinant of lipid profile severity in T2DM. Recent studies have consistently demonstrated a significant association between poor glycemic control (HbA1c ≥ 7%) and worsening lipid parameters, including elevated total cholesterol, triglycerides, and LDL-C, alongside reduced HDL-C levels.[6–7] Chronic hyperglycemia promotes non-enzymatic glycation of lipoproteins, alters their receptor-mediated clearance, and enhances oxidative modification, collectively intensifying the atherogenic burden.[8–9] These findings underscore glycemic optimization not merely as a strategy for microvascular protection but also as a critical lever for cardiovascular risk reduction.

In parallel, lipid ratios — including TG/HDL-C, LDL-C/HDL-C, and TC/HDL-C — have gained considerable attention as practical, cost-effective surrogates of atherogenic risk and insulin resistance. Unlike individual lipid parameters, these ratios capture the balance between pro-atherogenic and anti-atherogenic fractions, offering potentially superior predictive value for cardiovascular outcomes and metabolic derangement.[10] Their utility is particularly relevant in resource-constrained settings where advanced lipoprotein subfractionation is not routinely available.

Despite the well-established relationship between T2DM, dyslipidemia, and cardiovascular risk, data from our local clinical setting remain limited regarding the correlation between individual lipid components, lipid ratios, and glycemic control status. A clearer understanding of these relationships could inform more targeted screening and management strategies in this high-risk population. Therefore, this study aims to evaluate the predictive value of individual lipid parameters and lipid ratios in identifying poor glycemic control among patients with T2DM attending a tertiary care facility

METHODS

This descriptive cross-sectional study was conducted in the Department of Medicine at Aga Khan University Hospital (AKUH), Karachi, Pakistan, over four months following CPSP synopsis approval. The sample size of 171 participants was calculated using the WHO formula, based on a previously reported dyslipidaemia prevalence of 68.1%, absolute precision of 7%, and 95% confidence interval. Consecutive non-probability sampling was employed.

Patients aged 30–60 years of either sex with confirmed T2DM for at least two years were included. Those on lipid-lowering therapy or with conditions known to alter lipid metabolism — hypothyroidism, nephrotic syndrome, or hepatobiliary disease — were excluded.

Following Ethics Review Committee approval, demographic and clinical data including age, sex, BMI, diabetes duration, and treatment regimen were recorded on a structured proforma. Obesity was defined as BMI ≥ 30 kg/m². Fasting lipid profiles and HbA1c were retrieved from existing records or obtained from freshly collected fasting venous samples processed at a single institutional laboratory. Lipid ratios — TC/HDL-C, TG/HDL-C, and LDL-C/HDL-C — were calculated from results. Glycaemic control was classified as controlled

(HbA1c < 7%) or uncontrolled (HbA1c ≥ 7%).

Data were analysed using SPSS version 23. Continuous variables were tested for normality via the Shapiro–Wilk test and expressed as mean ± SD or median (IQR). Categorical variables were reported as frequencies and percentages. Independent t-test or Mann–Whitney U test was used for quantitative comparisons, and chi-square test for categorical variables. A p-value < 0.05 was considered statistically significant. Patient confidentiality was maintained through serial-number coding, and informed consent was waived given the retrospective nature of data retrieval

RESULTS

A total of 171 adults with T2DM were enrolled. The majority were older adults aged 46–60 years (86.5%), with a slight male predominance (56.1%). Nearly all participants (93.6%) had diabetes duration exceeding five years. Combination therapy (insulin plus oral hypoglycemics) was the most common treatment regimen (42.1%), followed by oral hypoglycemics alone (40.4%). Poor glycemic control (HbA1c ≥ 7%) was prevalent in 71.9% of participants, while obesity was present in 16.4%. Dyslipidemia was identified in 46.8% of the cohort (Table 1).

Table 1: Distribution of baseline characteristics among study participants (n = 171)

Table 1: Baseline Characteristics of Study Participants (n = 171)	
Variables	**Mean (SD) / n (%)**
Age	
30–45 years	23 (13.5)
46–60 years	148 (86.5)
Gender	
Male	96 (56.1)
Female	75 (43.9)
Duration of T2DM	
≤ 5 years	11 (6.4)
> 5 years	160 (93.6)
Type of Treatment	
Insulin	30 (17.5)
Oral hypoglycemics	69 (40.4)
Combined therapy	72 (42.1)
Glycemic Control	
Controlled (HbA1c < 7%)	48 (28.1)
Uncontrolled (HbA1c ≥ 7%)	123 (71.9)
Obesity Status	
Yes	28 (16.4)
No	143 (83.6)
Dyslipidemia	
Yes	80 (46.8)
No	91 (53.2)
Total	171 (100)

When clinical and demographic characteristics were stratified by dyslipidemia status, no statistically significant differences were observed across any subgroup (Table 2). Dyslipidemia was present in 52.2% of younger participants versus 45.9% of the older group (p = 0.57), and in 50.0% of males versus 42.7% of females (p = 0.34). Disease duration, treatment regimen, glycemic control, and obesity status similarly showed no significant association with dyslipidemia (all p > 0.05). Notably, dyslipidemia was marginally more frequent among those on insulin alone (50.0%) or combination therapy (52.8%) compared with oral hypoglycemics alone (39.1%), though this trend did not reach significance (p = 0.24).

Table 2: Distribution of Patient Characteristics by Dyslipidemia Status

Variables	Dyslipidemia Yes n (%)	Dyslipidemia No n (%)	p-value
Age			0.57
30–45 years	12 (52.2)	11 (47.8)	
46–60 years	68 (45.9)	80 (54.1)	
Gender			0.34
Male	48 (50.0)	48 (50.0)	
Female	32 (42.7)	43 (57.3)	
Duration of T2DM			0.47
≤ 5 years	04 (36.4)	07 (63.6)	
> 5 years	76 (47.5)	84 (52.5)	
Type of Treatment			0.24
Insulin	15 (50.0)	15 (50.0)	
Oral hypoglycemics	27 (39.1)	42 (60.9)	
Combined therapy	38 (52.8)	34 (47.2)	
Glycemic Control			0.38
Controlled (HbA1c < 7%)	25 (52.1)	23 (47.9)	
Uncontrolled (HbA1c ≥ 7%)	55 (44.7)	68 (55.3)	
Obesity Status			0.7
Yes	14 (50.0)	14 (50.0)	
No	66 (46.2)	77 (53.8)	

The overall lipid profile revealed a distinctly atherogenic pattern (Table 3). Mean triglyceride levels were markedly elevated at 232.5 ± 110.38 mg/dL, while HDL cholesterol was low at 40.7 ± 11.46 mg/dL. Total cholesterol averaged 156.8 ± 44.36 mg/dL and LDL cholesterol 85.1 ± 36.55 mg/dL. Lipid ratios further reflected significant cardiometabolic risk; the TG/HDL-C ratio (7.27 ± 2.83) and TC/HDL-C ratio (14.4 ± 8.33) were notably elevated, with the LDL/HDL-C ratio averaging 2.24 ± 1.26.

Table 3: Lipid profile and lipid ratios of the study cohort

Parameter	Mean ± SD
Total Cholesterol (mg/dL)	156.8 ± 44.36
Triglycerides (mg/dL)	232.5 ± 110.38
LDL Cholesterol (mg/dL)	85.1 ± 36.55
HDL Cholesterol (mg/dL)	40.7 ± 11.46
TC/HDL-C Ratio	14.4 ± 8.33
TG/HDL-C Ratio	7.27 ± 2.83
LDL/HDL-C Ratio	2.24 ± 1.26

DISCUSSION

Dyslipidemia appeared widely across the data set, affecting nearly half the participants. Yet it did not concentrate within any specific subgroup. Age, sex, duration of diabetes, obesity, and treatment type showed no clear relationship with lipid status. This broad distribution echoes observations from South

Asian settings.10 Where dyslipidemia often emerges independently of anthropometric measures and may reflect underlying metabolic vulnerability rather than demographic characteristics alone. 10

The lack of association between dyslipidemia and patient characteristics also aligns with reports showing that lipid abnormalities develop early in the course of glucose dysregulation and may precede substantial rises in HbA1c. 11 Given that most participants in this study had lived with diabetes for more than five years, dyslipidemia may have already become entrenched across individuals regardless of variations in their clinical profiles. Klisic et al. similarly noted that disturbances in lipid handling, chronic low-grade inflammation, and hepatic metabolic stress can shape lipid patterns in ways that are not always captured by conventional clinical indicators. 12

Despite the absence of differences between groups, the lipid profile of the sample data revealed a clear atherogenic pattern. Triglyceride levels were notably high, HDL-C remained low, and the lipid ratios—particularly TG/HDL-C, LDL/HDL-C, and TC/HDL-C, all were markedly elevated. These features mirror findings from Artha et al., who reported substantially higher triglycerides and unfavorable lipid ratios among individuals with poor glycemic control. 13 Panjeta et al. also described strong correlations between HbA1c and both triglycerides and TG/HDL-C, highlighting how triglyceride-rich dyslipidemia intensifies with deteriorating metabolic control. 14

The elevated lipid ratios observed here deserve particular attention. Ratios such as TG/HDL-C and LDL/HDL-C often reflect deeper disruptions in insulin action and lipoprotein remodeling. Evidence from Babic et al. showed that TG/HDL-C and the TyG index tracked closely with glycemic control and were able to distinguish individuals with higher metabolic risk. 15 Panjeta et al. linked high TG/HDL-C ratios to the predominance of small, dense LDL particles, which are highly atherogenic and commonly seen in insulin-resistant states. 14 These findings support the view that lipid ratios may capture cardiometabolic strain more effectively than individual lipid values alone.

Low HDL-C, which was evident across the cohort, has consistently emerged as a sensitive indicator of metabolic imbalance. Hussain et al. reported an inverse relationship between BMI and HDL-C in a South Asian diabetic population, suggesting that HDL reductions may occur irrespective of adiposity. 10 Alam et al. similarly found that lower HDL-C correlated closely with higher HbA1c, reinforcing the link between chronic hyperglycemia and deteriorating lipid quality. 16 The persistence of low HDL-C in our sample, even in the absence of strong associations with other clinical variables, underscores its relevance as an early and sustained marker of metabolic stress.

Interestingly, dyslipidemia did not differ between participants with controlled and uncontrolled diabetes. This contrasts with work by Artha et al. and Alam et al., who both described more pronounced lipid abnormalities among individuals with higher HbA1c levels. 13.16 Several explanations may account for this discrepancy. The long duration of diabetes among our participants may have resulted in cumulative metabolic alterations that no longer track closely with recent glycemic trends. In addition, South Asian populations often exhibit dyslipidemic patterns that persist even when glycemic control improves, possibly due to genetic predisposition, dietary factors, or early onset of insulin resistance. 10 The high overall prevalence of dyslipidemia in our cohort may also have reduced the contrast between glycemic groups.

The elevated lipid ratios strengthen the argument for their routine use in clinical practice. Klisic et al. demonstrated that LDL-C, triglycerides, and total cholesterol independently predicted poor glycemic control, while HDL-C served as a protective factor. 12 Panjeta et al. highlighted the value of TC/HDL-C and LDL/HDL-C in identifying patients at heightened cardiovascular risk. 14 Babic et al. and Artha et al. further demonstrated the predictive utility of TG/HDL-C and TyG index across different populations. 13. 15 The consistency of these findings underscores the practicality of incorporating lipid ratios into routine monitoring, particularly in resource-constrained settings where they offer a low-cost means of identifying individuals at elevated metabolic risk.

Taken together, the results of this study reinforce the view that atherogenic dyslipidemia remains a persistent feature of Type 2 diabetes, even in individuals who are not obese and across varying levels of glycemic control. Elevated triglycerides, low HDL-C, and unfavorable lipid ratios reflect underlying disturbances in insulin function and hepatic lipid metabolism. These abnormalities may remain hidden if clinicians rely solely on traditional risk markers. As earlier work has shown, dyslipidemia contributes substantially to the burden of cardiovascular disease in diabetes, and its presence, even in those with moderate glycemic control, calls for systematic screening and timely intervention. 17 Future research may examine whether sustained improvements in glycemic control translate into meaningful shifts in lipid ratios and whether targeted lifestyle and pharmacologic strategies can modify these markers over time.

This study carries several limitations that warrant

attention. Because we used a cross-sectional design, we could not determine whether abnormal lipid ratios precede or follow changes in glycemic control. Our findings also reflect the characteristics of patients attending a single health facility. This may limit how far they can be generalized to other settings. We measured lipid and glycemic indices only once. Therefore could not account for day-to-day or seasonal variation in these parameters. We did not collect detailed information on diet, physical activity, or medication adherence, all of which could influence metabolic outcomes. In addition, unmeasured factors such as genetic predisposition, socioeconomic conditions, or underlying inflammation may have shaped the associations we observed.

CONCLUSION

Our findings indicate that unfavorable lipid patterns and elevated lipid ratios are widespread among individuals living with Type 2 diabetes in this setting. These observations underscore the importance of incorporating routine lipid ratio assessment into diabetes management to help identify patients who may carry a higher cardiometabolic risk.

ETHICAL APPROVAL:
The study was reviewed and approved for exemption by the Ethical Review Committee of AGA Khan University Hospital, Karachi, Pakistan (Reference No: 2025-11129-35591). The study was conducted in accordance with institutional standards and ethical guidelines.

PATIENTS CONSENT:
No patient physician interaction in this study, all data obtained from patients' files and medical records, no need of informed consent.

COMPETING INTEREST:
The author declared no conflict of interest.
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