Glycaemic control and its impact on lipid profile and renal function in type II diabetes mellitus: a comparative analysis by disease duration.

ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is associated with a cluster of metabolic derangements including dyslipidaemia and progressive renal dysfunction. Hyperglycaemia is the central driver of both lipid abnormalities and diabetic kidney disease (DKD). However, the interplay between glycaemic control as measured by HbA1c, lipid parameters, and kidney function tests (KFT) across different disease durations remains insufficiently studied in the Indian clinical setting.

Objectives: To compare lipid profiles and kidney function parameters between T2DM patients with disease duration <5 years and >5 years, and to assess their correlation with HbA1c within each subgroup.

Methods: A hospital-based cross-sectional study was conducted on 121 T2DM patients (59 with disease duration <5 years and 62 with >5 years). Fasting lipid profile (total cholesterol, HDL, LDL, TG, VLDL, TC:HDL ratio), serum electrolytes (Na, K), and kidney function tests (serum urea and creatinine) were measured. Pearson's correlation and independent t-test were used for statistical analysis (SPSS v23; $p<0.05$ significant).

Results: Patients with disease duration >5 years showed significantly higher VLDL (32.6 vs 27.8 mg/dL, $p=0.042$) and TC:HDL ratio (6.18 vs 5.42, $p=0.028$) compared to the <5 years group. Serum urea (38.6 vs 24.8 mg/dL, $p<0.0001$) and serum creatinine (0.94 vs 0.68 mg/dL, $p=0.005$) were significantly elevated in the longer-duration group. HbA1c showed significant positive correlations with total cholesterol, LDL, TG, serum urea, and serum creatinine, and a significant negative correlation with HDL in the >5 years group, while these correlations were non-significant in the <5 years group. Dyslipidaemia prevalence rose from 26.7% in well-controlled patients (HbA1c <6.5%) to 83.8% in severely uncontrolled patients (HbA1c >10%).

Conclusion: Prolonged poor glycaemic control in T2DM is associated with progressive atherogenic dyslipidaemia and worsening renal function. The relationship between HbA1c and these cardiorenal risk markers is significantly amplified by disease duration, reinforcing the need for comprehensive metabolic management from the earliest stages of T2DM.

Keywords: *Type 2 diabetes mellitus; HbA1c; dyslipidaemia; lipid profile; kidney function tests; serum creatinine; diabetic kidney disease; disease duration; cardiovascular risk*

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a multisystem metabolic disorder characterised not only by chronic hyperglycaemia but also by a constellation of associated metabolic derangements

that collectively drive macrovascular and microvascular complications [1]. Among these, dyslipidaemia and chronic kidney disease (CKD) are two of the most clinically significant comorbidities, each independently and synergistically increasing the risk of cardiovascular morbidity and mortality [2,3].

Diabetic dyslipidaemia is characterised by elevated triglycerides, reduced high-density lipoprotein cholesterol (HDL-C), increased small dense low-density lipoprotein (sdLDL), and elevated very low-density lipoprotein (VLDL), constituting an atherogenic lipid triad that substantially elevates cardiovascular risk in T2DM [4]. Hyperglycaemia promotes this dyslipidaemia through multiple mechanisms: increased free fatty acid flux from insulin-resistant adipose tissue, hepatic overproduction of VLDL, impaired lipoprotein lipase activity, glycation of apolipoproteins, and enhanced cholesteryl ester transfer protein (CETP) activity [5].

Concurrently, diabetic kidney disease (DKD) represents the most common cause of end-stage renal disease worldwide, with glomerular hyperfiltration, podocyte injury, and tubulointerstitial fibrosis developing insidiously over years of sustained hyperglycaemia [6]. Early markers of DKD include rising serum creatinine and urea, often preceding overt proteinuria. The intersection of dyslipidaemia and DKD creates a vicious cycle: dyslipidaemia accelerates glomerular injury through lipid deposition and foam cell formation, while impaired renal clearance worsens the lipid profile through reduced lipoprotein lipase activity and altered apolipoprotein metabolism [7].

Glycated haemoglobin (HbA1c) serves as the biomarker integrating both glycaemic exposure and its downstream metabolic consequences. As disease duration increases, the cumulative glycaemic burden drives progressive lipid abnormalities and renal injury. Yet, systematic characterisation of how disease duration modulates the relationship between HbA1c and these cardiorenal risk markers is limited, particularly from the Indian subcontinent where T2DM tends to present at a younger age and with more rapid progression.

The present study therefore aimed to (1) compare lipid profiles and kidney function tests between T2DM patients stratified by disease duration (<5 years vs >5 years), (2) examine the correlation between HbA1c and these metabolic parameters in each subgroup, and (3) determine the prevalence of dyslipidaemia and renal impairment across HbA1c categories.

MATERIAL AND METHODS

Study Design and Ethics

A cross-sectional observational study was conducted in the Department of Medicine at a tertiary care teaching hospital, Aurangabad, Maharashtra. Institutional Ethics Committee approval and written informed consent from all participants were obtained prior to the study.

Study Participants

One hundred and twenty-one confirmed T2DM patients were enrolled and categorised as Group A (disease duration <5 years, n=59) and Group B (>5 years, n=62). Inclusion criteria were:

age 18-65 years; T2DM diagnosed per ADA 2023 criteria [8]; stable clinical condition. Patients with known primary hyperlipidaemia, chronic kidney disease not attributable to diabetes, active urinary tract infection, haemoglobinopathies, use of lipid-lowering drugs within 4 weeks, acute febrile illness, or pregnancy were excluded.

Laboratory Investigations

After a 10-12 hour overnight fast, venous blood was collected for: (i) HbA1c (HPLC method), (ii) fasting lipid profile by direct enzymatic method — total cholesterol (TC), triglycerides (TG), HDL-C, calculated LDL-C using Friedewald equation [LDL = TC - HDL - TG/5], VLDL [TG/5], and TC:HDL ratio, (iii) kidney function tests — serum urea (urease-GLDH method) and serum creatinine (modified Jaffe method), and (iv) serum electrolytes (Na, K) by ion-selective electrode method. Dyslipidaemia was defined as TC >200, LDL >100, TG >150, HDL <40 (males) or <50 (females) mg/dL per ATP-III/AHA guidelines [9]. Elevated serum creatinine was defined as >1.2 mg/dL (males) or >1.0 mg/dL (females).

Statistical Analysis

All data were analysed using SPSS version 23. Continuous variables are expressed as mean ± standard deviation. Between-group comparisons used the independent samples t-test. Pearson's correlation coefficient (r) assessed associations between HbA1c and lipid/KFT parameters. Chi-square test examined categorical associations. $p<0.05$ was considered statistically significant.

RESULTS AND OBSERVATIONS

Baseline Characteristics

The study cohort comprised 121 T2DM patients: 59 in Group A (<5 years) and 62 in Group B (>5 years). Overall mean age was 48.1 ± 8.0 years (range 28-60). The cohort included 59 males and 62 females. Mean HbA1c was significantly higher in Group B (10.26 ± 1.70%) than Group A (6.82 ± 0.80%; $p<0.0001$). Groups were comparable in age, sex, urban-rural distribution, and smoking status (all $p>0.05$).

Lipid Profile Comparison

While total cholesterol, LDL, and TG showed a non-significant trend towards higher values in the >5 years group, VLDL (32.6 vs 27.8 mg/dL, p=0.042) and TC:HDL ratio (6.18 vs 5.42, p=0.028) were significantly elevated (Table 1). HDL cholesterol showed a trend towards reduction in the longer-duration group (30.6 vs 33.2 mg/dL), though not reaching statistical significance (p=0.225).

Table 1: Comparison of Fasting Lipid Profile between Groups

Lipid Parameter (mg/dL)	<5 Years (n=59)	>5 Years (n=62)	t-value	p-value
Total Cholesterol	174.5 ± 38.2	181.3 ± 42.6	-1.04	0.301 (NS)

HDL Cholesterol	33.2 ± 11.8	30.6 ± 12.4	1.22	0.225 (NS)
Triglycerides	142.3 ± 71.2	161.8 ± 68.9	-1.64	0.103 (NS)
LDL Cholesterol	106.4 ± 33.8	112.6 ± 37.2	-1.02	0.309 (NS)
VLDL	27.8 ± 13.4	32.6 ± 14.2	-2.06	0.042*
TC : HDL Ratio	5.42 ± 1.82	6.18 ± 2.14	-2.23	0.028*

Statistically significant (p<0.05). NS = Not Significant. Values expressed as Mean ± SD.

Kidney Function Test Comparison

Serum urea was significantly elevated in the >5 years group (38.6 ± 22.4 vs 24.8 ± 16.3 mg/dL, p<0.0001) and serum creatinine was significantly higher (0.94 ± 0.62 vs 0.68 ± 0.42 mg/dL, p=0.005). Serum sodium was marginally but significantly lower in the longer-duration group (133.6 vs 136.8 mEq/L, p=0.002), while serum potassium did not differ significantly (Table 2).

Table 2: Comparison of Kidney Function Tests and Electrolytes between Groups

KFT Parameter	<5 Years (n=59)	>5 Years (n=62)	t-value	p-value
Serum Urea (mg/dL)	24.8 ± 16.3	38.6 ± 22.4	-4.13	<0.0001*
Serum Creatinine (mg/dL)	0.68 ± 0.42	0.94 ± 0.62	-2.88	0.0047*
Serum Sodium (mEq/L)	136.8 ± 5.2	133.6 ± 6.8	3.11	0.0023*
Serum Potassium (mEq/L)	4.31 ± 0.48	4.28 ± 0.72	0.29	0.772 (NS)

Statistically significant (p<0.05). NS = Not Significant. Values expressed as Mean ± SD.

Correlation of HbA1c with Lipid and Renal Parameters

In Group B (>5 years), HbA1c showed significant positive correlations with total cholesterol (r=0.318, p=0.012), LDL (r=0.296, p=0.019), TG (r=0.352, p=0.005), serum urea (r=0.401, p=0.001), and serum creatinine (r=0.374, p=0.003), and a significant negative correlation with HDL (r=-0.281, p=0.027). In Group A (<5 years), none of these correlations achieved statistical significance, though the trend was consistent. Overall correlations were significant for all parameters (Table 3).

Table 3: Pearson Correlation of HbA1c with Lipid and Renal Parameters by Disease Duration

Parameter	r (<5yr)	p (<5yr)	r (>5yr)	p (>5yr)	Overall p
Total Cholesterol	0.182	0.168 NS	0.318	0.012*	0.018*
LDL Cholesterol	0.164	0.212 NS	0.296	0.019*	0.024*
Triglycerides	0.201	0.129 NS	0.352	0.005*	0.009*

HDL Cholesterol	-0.145	0.274 NS	-0.281	0.027*	0.031*
Serum Urea	0.224	0.089 NS	0.401	0.001*	0.002*
Serum Creatinine	0.196	0.138 NS	0.374	0.003*	0.004*

**Statistically significant (p<0.05). NS = Not Significant. r = Pearson correlation coefficient.*

HbA1c Category and Cardiorenal Risk

Stratification by HbA1c category revealed a progressive rise in dyslipidaemia prevalence (from 26.7% at HbA1c <6.5% to 83.8% at HbA1c >10%), elevated serum urea (6.7% to 56.8%), and elevated serum creatinine (3.3% to 37.8%) with worsening glycaemic control (Table 4). This dose-response pattern underscores the cumulative metabolic impact of chronic hyperglycaemia on both lipid and renal parameters.

Table 4: Prevalence of Dyslipidaemia and Renal Impairment by HbA1c Category

HbA1c Category	n	Dyslipidaemia n (%)	Elevated Sr. Urea n (%)	Elevated Sr. Creat n (%)
<6.5% (Controlled)	30	8 (26.7%)	2 (6.7%)	1 (3.3%)
6.5-8% (Moderate)	31	14 (45.2%)	6 (19.4%)	4 (12.9%)
8-10% (Uncontrolled)	23	17 (73.9%)	11 (47.8%)	8 (34.8%)
>10% (Severely Uncontrolled)	37	31 (83.8%)	21 (56.8%)	14 (37.8%)

Dyslipidaemia defined as any abnormality in TC, LDL, TG, or HDL per ATP-III guidelines. Elevated serum creatinine: >1.2 mg/dL (males), >1.0 mg/dL (females). Elevated serum urea: >40 mg/dL.

DISCUSSION

The central findings of this study are that (1) disease duration >5 years in T2DM is associated with significantly worse atherogenic dyslipidaemia and impaired renal function compared to shorter disease duration, and (2) HbA1c correlates significantly with lipid and renal parameters only in the longer-duration group, suggesting that the cardiorenal metabolic impact of hyperglycaemia accumulates over time.

The observation of significantly elevated VLDL and TC:HDL ratio in the >5 years group is consistent with the pathophysiology of insulin resistance and progressive beta-cell failure. In T2DM, insulin resistance in adipose tissue increases non-esterified fatty acid (NEFA) flux to the liver, driving hepatic VLDL overproduction. Concurrently, reduced lipoprotein lipase (LPL) activity, which is normally insulin-dependent, impairs TG hydrolysis, further elevating circulating VLDL and TG [10]. The TC:HDL ratio, a validated surrogate of cardiovascular risk, was significantly higher in the >5 years group, indicating greater atherogenic burden with disease chronicity.

Although total cholesterol and LDL did not reach statistical significance individually between groups, the pattern of increasing TC:HDL ratio and VLDL with disease duration indicates a shift toward a more atherogenic lipoprotein phenotype over time. This is consistent with findings from the UKPDS lipid sub-study, which demonstrated progressive lipid deterioration with longer T2DM duration [11]. Interestingly, HDL cholesterol showed a non-significant downward trend in the longer-duration group. HDL reduction in T2DM is partly mediated by increased CETP-mediated exchange of cholesteryl esters for TG from VLDL, generating TG-enriched, rapidly catabolised HDL particles [5].

The significantly elevated serum urea and creatinine in the >5 years group reflect progressive glomerular injury accumulating over years of hyperglycaemic and haemodynamic insult. These findings are earlier than would be expected from overt nephropathy, suggesting subclinical but measurable glomerular dysfunction. Hyperglycaemia activates the renin-angiotensin-aldosterone system (RAAS), producing intraglomerular hypertension, mesangial matrix expansion, and podocyte apoptosis, collectively reducing glomerular filtration rate [6,12].

The emergence of significant correlations between HbA1c and lipid/renal parameters exclusively in the >5 years group, contrasted with non-significant trends in the <5 years group, is a novel contribution of this study. This finding suggests a threshold effect: below 5 years of diabetes duration, metabolic derangements may be sufficiently mild and heterogeneous to preclude significant correlation, whereas beyond 5 years, cumulative glycaemic toxicity produces metabolic changes of sufficient magnitude and consistency to generate significant correlations. This parallels the DCCT/EDIC observation that the magnitude of glycaemic exposure effects on complications escalates non-linearly with diabetes duration [13].

The dose-response relationship between HbA1c categories and the prevalence of both dyslipidaemia and renal impairment further reinforces this interpretation. At HbA1c <6.5%, dyslipidaemia was present in only 26.7% of patients; this rose sharply to 83.8% at HbA1c >10%. Similarly, elevated serum creatinine was found in only 3.3% of well-controlled patients but in 37.8% of severely uncontrolled patients. These data argue strongly that achieving HbA1c targets is not merely a glycaemic goal but a cardiorenal protection strategy.

Comparable findings have been reported by Chaudhary et al. [14], who documented higher TG and lower HDL with worsening HbA1c in T2DM, and by Srivastava et al. [15], who reported progressive renal function decline with increasing HbA1c quartiles. The present study extends these observations by stratifying the analysis by disease duration, demonstrating that duration is a key effect modifier.

The study has several limitations. The cross-sectional design precludes causal inference. The modest sample size may have underpowered detection of significant differences in some lipid subfractions in the <5 years group. Antihypertensive and lipid-lowering medication histories were not systematically controlled, which may have influenced lipid and renal measurements. eGFR was not calculated from creatinine values, limiting CKD staging.

CONCLUSION

Prolonged disease duration in T2DM is associated with progressive atherogenic dyslipidaemia and worsening renal function, and the correlation between HbA1c and these cardiorenal risk parameters strengthens significantly with disease chronicity. The dose-response relationship between HbA1c and prevalence of dyslipidaemia and renal impairment underscores the imperative of maintaining tight glycaemic control from the time of diabetes diagnosis. Clinicians should routinely assess fasting lipid profiles and kidney function tests at every HbA1c review, with more frequent monitoring as disease duration extends beyond five years. Integration of SGLT-2 inhibitors and GLP-1 receptor agonists, which offer simultaneous glycaemic, lipid, and renal benefits, should be considered early in the treatment algorithm.

LIMITATIONS

The cross-sectional design is unable to establish temporal causality between glycaemic control and lipid/renal outcomes.Antihypertensive and lipid-lowering drug usage was not systematically captured; these may have confounded lipid and KFT measurements.eGFR was not calculated; serum creatinine alone underestimates early CKD, particularly in the lower-muscle-mass diabetic population.Dietary assessment and exercise history were not recorded, limiting control of lifestyle confounders.The single-centre design and hospital recruitment may introduce referral bias, limiting generalisability to community-level T2DM populations.

FUTURE DIRECTIONS

Prospective longitudinal studies with annual lipid profile, eGFR, and HbA1c measurements to model the rate of cardiorenal risk accumulation with disease duration.Assessment of lipoprotein subfractions (sdLDL, large VLDL particles) and apolipoproteins (ApoB, ApoA1) to more precisely characterise atherogenic burden across HbA1c strata.

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