

## "Dyslipidemia and its Correlation with Glycated Hemoglobin Levels in Type 2 Diabetes Mellitus: Unraveling the Intricate Relationship for Comprehensive Patient Management"

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### Abstract

**Background:** Diabetes Mellitus features chronic hyperglycemia from insulin secretion or action defects, often leading to dyslipidemia. Type 2 diabetes sufferers are prone to dyslipidemia, a key cardiovascular risk. Glycated hemoglobin reflects glycemic control, disease progression, and complications in diabetes patients. **Aim of the study:** To evaluate the level of HbA1c and lipid profile in type 2 diabetes patients & find out the correlation between HbA1c and lipid profile parameters in type 2 diabetic patients. **Material & Methods:** In a correlational cross-sectional study, 150 type 2 diabetic patients at tertiary care hospital assessed between April and August 2022. HbA1c, fasting blood glucose, and lipid profiles were measured after overnight fasting. Pearson's correlation tested HbA1c's link to lipid profile components. **Results:** Mean levels of fasting blood glucose, glycated hemoglobin, triglycerides, high-density lipoprotein-cholesterol, and very low-density lipoprotein-cholesterol were similar in males and females. However, females exhibited significantly higher TC ( $p=0.031$ ) and LDL-C ( $p=0.018$ ) than males among type 2 diabetes patients. HbA1c strongly correlated with FBG ( $r=0.684$ ), and glycated hemoglobin displayed a notable positive correlation with total cholesterol ( $r=0.174$ ). **Conclusion:** Notably, HbA1c's positive correlation with lipid profiles, particularly TC, implies its potential as a predictor for dyslipidemia alongside glycemic control.

**Keywords:** Diabetes mellitus, Dyslipidemia, Glycated hemoglobin, Lipid profile

### List of Abbreviations

**T2DM-** Type 2 Diabetes Mellitus, **T1DM-** Type 1 Diabetes Mellitus, **DM-** Diabetes Mellitus, **HbA1c-** Hemoglobin A1C, **FBG-** Fasting Blood Glucose, **BMI-** Body Mass Index, **TG-** Triglyceride, **TC-** Total Cholesterol, **LDL-C-** Low Density Lipoprotein- Cholesterol, **HDL-C-** High Density Lipoprotein- Cholesterol, **VLDL-C-** Very Low Density Lipoprotein- Cholesterol, **NCEP-** National Cholesterol Education Programme, **ATP III-** Adult Treatment Panel III, **IDF-** International Diabetic Federation, **ADA-** American Diabetes Association, **WHO-** World Health Organization, **CVD-** Cardiovascular Disease

## Introduction

DM is defined as a group of metabolic diseases manifest by hyperglycemia which results from defects in insulin production and/or insulin action. Untreated chronic hyperglycemia can lead to long-term complications including microvascular and macrovascular problems that cause disturbances of carbohydrate, fat, and protein metabolism[1-3].

DM is a global endemic with rapidly increasing prevalence in both developing and developed countries[4]. Among individuals diagnosed with diabetes, the majority (90–95%) will have T2DM while 5–10% of this population will have T1DM. T1DM is diagnosed at birth or at a very early age whereas T2DM is typically diagnosed later in life, however, an increasing number of younger people are being diagnosed with T2DM[5]. Insulin is the principal hormone that regulates the uptake of glucose from the blood into most cells of the body, especially liver, adipose tissue and muscle. Therefore, deficiency of insulin or the insensitivity of its receptors plays a central role for DM[6].

In diabetes, the cells don't receive glucose and most of it is accumulated in the blood. The chronic hyperglycemia of diabetes is associated with long term damage, dysfunction and failure of various organs, especially the eyes, kidney, nerves, heart and blood vessels[7,8]. DM lead to hyperglycemia, excessive urine production, compensatory thirst, increased fluid intake, blurred vision, unexplained weight loss, etc[9]. T2DM is caused by the failure of insulin secretion or action. The impairment of insulin actions is known as insulin resistance, presented as a suppression or retard in metabolic responses of the muscle, liver and adipose tissue to insulin action. This failure is located at the signaling pathways held after insulin binding to its specific receptor. Chronic insulin resistance leads to hyperglycemia which mainly is involved in the etiology of development of diabetic complications[10]. Diabetes cause about 5% of all deaths globally each year[11].

IDF in 2015 reported that 415 million people have diabetes in the world and 78 million people in the South-East Asia Region. It is estimated that 642 million people may develop diabetes by the year 2040[12,13].

T2DM is associated with a two to fourfold excess risk of coronary heart disease.[14,15] Dyslipidemia encompasses changes in HDL-C, the size and density of LDL-C, VLDL-C and TG level.[16,17] For serum lipid reference level NCEP ATP III guideline was referred. According to NCEP ATP III guideline hypercholesterolemia defined as TC > 200 mg/dl, high LDL-C when value > 100mg/dl, hypertriglyceridemia > 150 mg/dl and low HDL-C when value < 40 mg/dl. Dyslipidemia defined by presence of one or more than one abnormal serum lipid concentration. The term diabetic dyslipidemia comprises a triad of raised triglycerides, reduced HDL-C and excess of small, dense LDL particles. The lipid abnormalities are prevalent in DM because insulin resistance or deficiency affects key enzymes and pathways in lipid metabolism[18, 19].

Glycated hemoglobin is routinely measured to check the glycemic control over a preceding 8-12 weeks of time[20]. It is used as an indicator for the state of glycemic control, progression of the disease and development of complications in diabetic patients[21, 22]. HbA1c is the most commonly measured method of assessing

chronic glycaemia in clinical practice[23].IDF has designated HbA1c level of <7% as a goal of optimal blood glucose control and the American Association of Clinical Endocrinologist has further recommended HbA1c level of <6.5% as target of glycemic control[24,25] . The risk for cardiovascular disease is higher in diabetic subjects than non-diabetic subjects [26]. The causal association between atherosclerosis and dyslipidemia is well established. In diabetes the associated hyperglycemia, obesity and insulin changes highly accelerate the progression to atherosclerosis[27, 28].

The aim of present study is check glycated hemoglobin and lipid profile in diabetic patients attending in a tertiary care hospital and find prevalence of dyslipidemia in T2DMpatients with comparative study of diabetic dyslipidemia in male versus female. Others objective to find the correlation between HBA1c and lipid profile.

## Materials and Methods

### Ethical Approval

The correlation cross-sectional study was carried out in the department of clinical Biochemistry of Aarogyam Medical college & hospital, Roorkee, Uttarakhand. Patients with proper prior consentfrom OPD of tertiary care teaching hospital diabetes mellitus patients were included.Ethical approval was taken from AMCH-IEC(Institutional Ethical committee) with Ref. no. ofAMCH-IEC/22-103.The samples were collected from April to August 2022. Data were collected from medical records. Laboratory test results and physical examination was observed. These were verified by first checking from their medical records and with a questionnaire. Samples were run in fully automated analyzer. After consent, fasting plasma glucose levels and glycated hemoglobin level were determined by venous blood samples. Plasma sample run in AU480 fully automated analyzer. Plasma samples were estimated using hexokinase-method. Glycosylated hemoglobin (HbA1C) tests were determination by Tosoh HLC-723X Automated Glycohemoglobin Analyzer with HPLC method. The sample size included in this study was 150 diabetic patients between 30-75 years age group. Sample size calculated by Population:  $N = z_{\alpha/2} \times P(1 - P)/E^2$  where  $z_{\alpha/2} = 1.96$ ,  $P = 95\%$  and  $E = 0.05$ ,  $N$  is the population size.

### Selection criteria

**Inclusion criteria:** Clinically diagnosed cases of T2DM with the age group 30-75 years were included in the study group. Diabetes should diagnosed as per ADA and WHO criteria. For serum lipid reference level, NCEPATP III guideline must be followed.

**Exclusion criteria:** The patients with type 1 diabetes mellitus, Gestational diabetes mellitus and type 2 diabetic patients with the age group below 30 years or above 75 years were excluded and patients with systemic infectious diseases or malignancy.

### Statistical data analysis

Collected data were reviewed, check and rechecked for its completeness, consistency and accuracy of information. Data was edited, classified, coded and transcribed into SPSS version 20 software for analysis. The findings wererepresented on the relevant tables. Data were summarized as frequency and percentages. Data were expressed as mean  $\pm$  SD for quantitative variables.Pearson's correlation test was applied to evaluate the correlation between HbA1c and components of lipid profile. P value less than 0.05 was considered statistically significant.

### Outcome measures

Samples collected were in sodium fluoride for sugar estimation and plain red top vial (serum) for TC, TG, HDL-C, LDL-C, VLDL-C. Lipid profiles were measured after overnight fasting. Samples were run in AU480 fully spectrophotometric based automated analyzer.[45] Glycosylated hemoglobin (HbA1C) tests were determined by Tosoh HLC-723X Automated Glycohemoglobin Analyzer with HPLC method.[46]

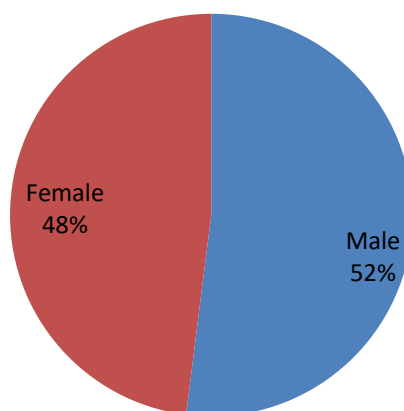
## Results

### Gender wise distribution of T2DM patients

A total of 150 patients (T2DM) were enrolled in the study. Among them

78 (52%) patients were males and 72 (48%) were females.

**Figure 1: Gender wise distribution**



### Gender wise BMI of study patients

In this study, the mean BMI is  $26.97 \pm 4.55$ . The mean BMI of male is  $25.57 \pm 4.25$  and that of female is  $28.58 \pm 4.40$  and p-value is 0.004. Females had significantly higher BMI in comparison with males ( $p < 0.01$ ).

**Table 1: Categories of BMI of enrolled cases**

Categories	BMI range (kg/m <sup>2</sup> )	Percent
Underweight	<18.5	2.7
Normal weight	18.5-24.9	30.7
Overweight	25-29.9	42.6
Obese	>30	24.0

Table 1 Shows that percentage of categories of BMI of enrolled cases was higher.

### Prevalence of dyslipidemia in T2DM

Study shows that 82% of type II diabetes mellitus patients were dyslipidemia whereas 18% of enrolled cases were normolipidemic.

### Gender wise distribution of blood glucose, HbA1c and lipid profile

The mean fasting blood glucose, glycated hemoglobin, TC, TG, HDL, LDL and VLDL were 175.47±63.27, 9.30±2.38, 186.07±48.52, 183.49±82.59, 42.43±6.88, 105.29±38.5 and 36.65±16.45. The levels of HbA1c and FBG did not differ significantly between male and female. TC (p=0.031) and LDL-C (p=0.018) was significantly higher in female as compared to male type 2 diabetic patients. Although there was no significant difference in TG, HDL-C and VLDL-C levels between male and female.

**Table 2: Gender wise distribution of blood glucose, HbA1c and lipid profile**

Parameters	Total	Male	Female	P-value
FBG	175.47±63.27	175.79±61.92	175.13±65.12	0.949
HbA1c	9.30±2.38	9.49±2.39	9.10±2.37	0.316
TC	186.07±48.52	177.88±46.97	194.93±48.92	0.031*
TG	183.49±82.59	183.38±90.85	183.61±73.23	0.987
HDL-C	42.43±6.88	42.29±7.02	42.58±6.77	0.799
LDL-C	105.29±38.5	98.17±34.44	113.01±41.34	0.018*
VLDL-C	36.65±16.45	36.53±18.04	36.79±14.67	0.921

\* (P<0.05) statistically significant

### Age group distribution of worse glycemic control with dyslipidemia among the enrolled cases

The worse glycemic control with dyslipidemia was seen maximum in the individual of the age group 46-60 years which was shown in table 3 and figure 3.

**Table 3: Age group distribution of worse glycemic control with dyslipidemia among the enrolled cases**

Age groups	Percent
30-45	33.3
46-60	46.7
61-75	20.0

**Correlation between HbA1c and lipid profile**

A highly significant correlation between HbA1c and FBG was noted in this study ( $r=0.684$ ). Significant correlation between glycated hemoglobin and total cholesterol ( $r=0.174$ ) was observed from this study. Table 4 shows correlation between HbA1c and lipid profile reflected by Pearson correlation.

**Table 4: Correlation between HbA1c and lipid profile**

Variables	FBG	TC	TG	HDL	LDL	VLDL
HbA1c	0.684**	0.174*	0.155	0.152	0.056	0.156
TC			0.482**	0.340**	0.895**	0.483**
TG				0.227**	0.144	0.995**
HDL					0.200**	0.236**
LDL						0.144

\*\* ( $p<0.01$ ) statistically significant

\* ( $p<0.05$ ) statistically significant

Figure 2: Relationship between HbA1c and FBG

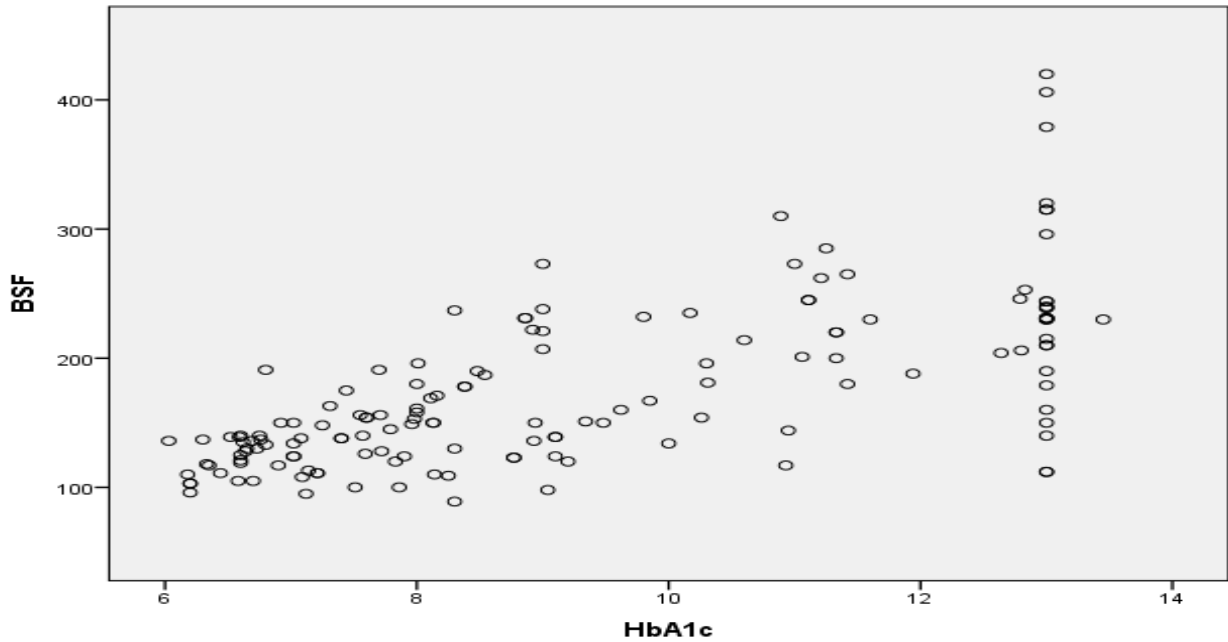


Figure 2 shows that there was positive significant relationship between HbA1c and FBG ( $r=0.684$ ).

Figure 3: Relationship between HbA1c and TC

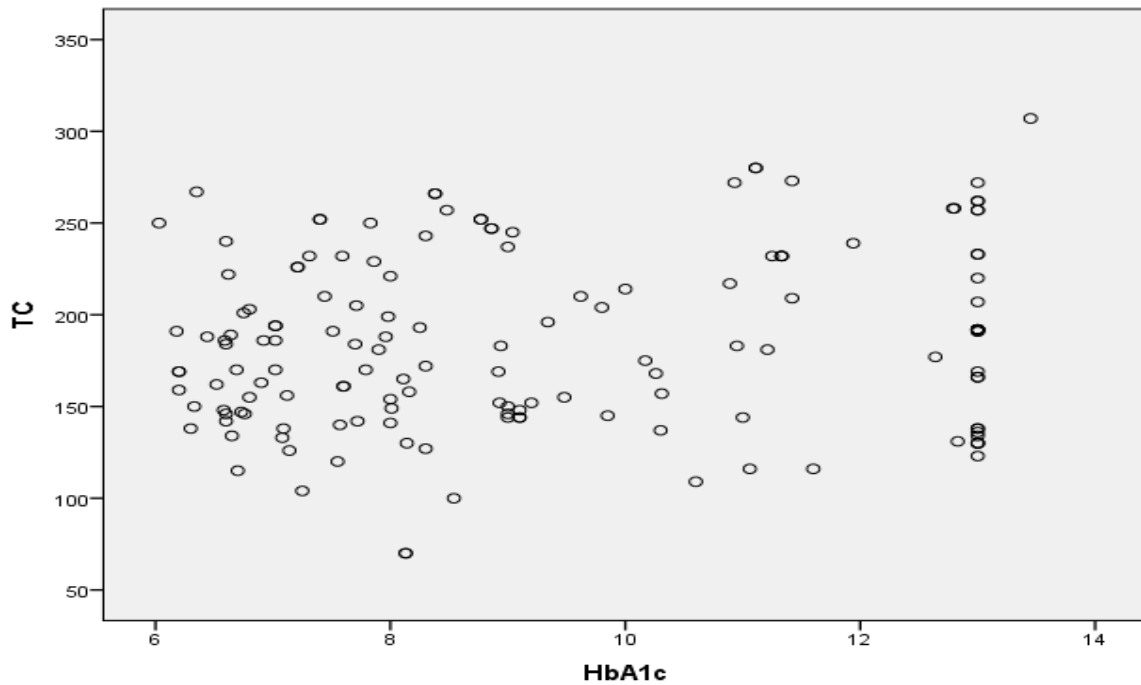


Figure 3 shows that there was positive significant relationship between HbA1c and TC ( $r=0.174$ ).

Figure 4: Relationship between HbA1c and TG

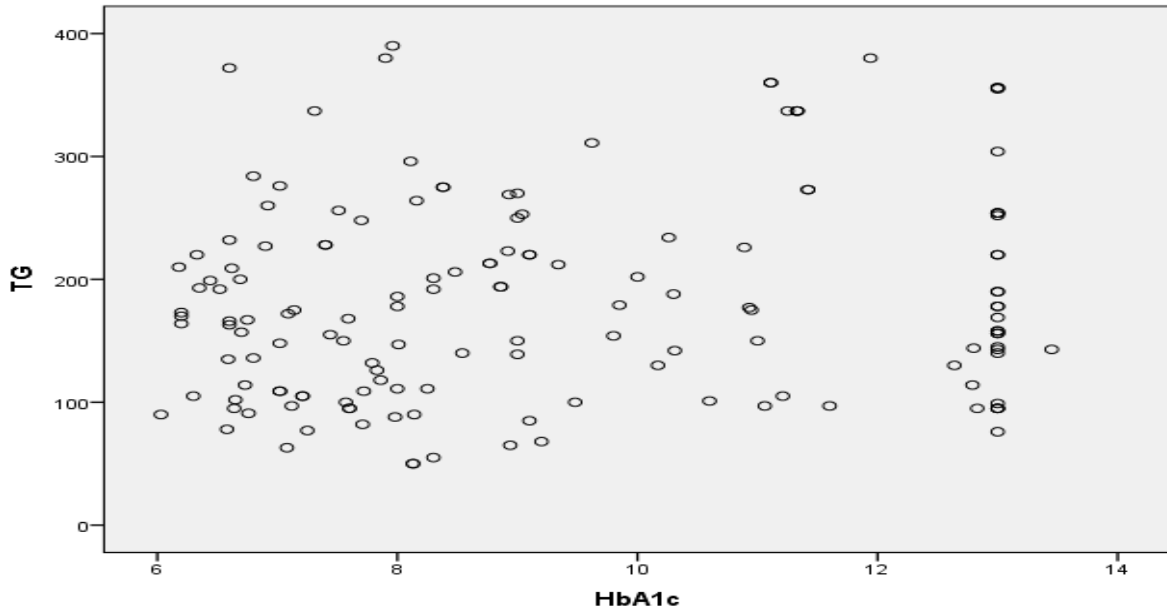


Figure 4 shows that there was no significant relationship between HbA1c and TG ( $r=0.155$ )

Figure 5: Relationship between HbA1c and HDL-C

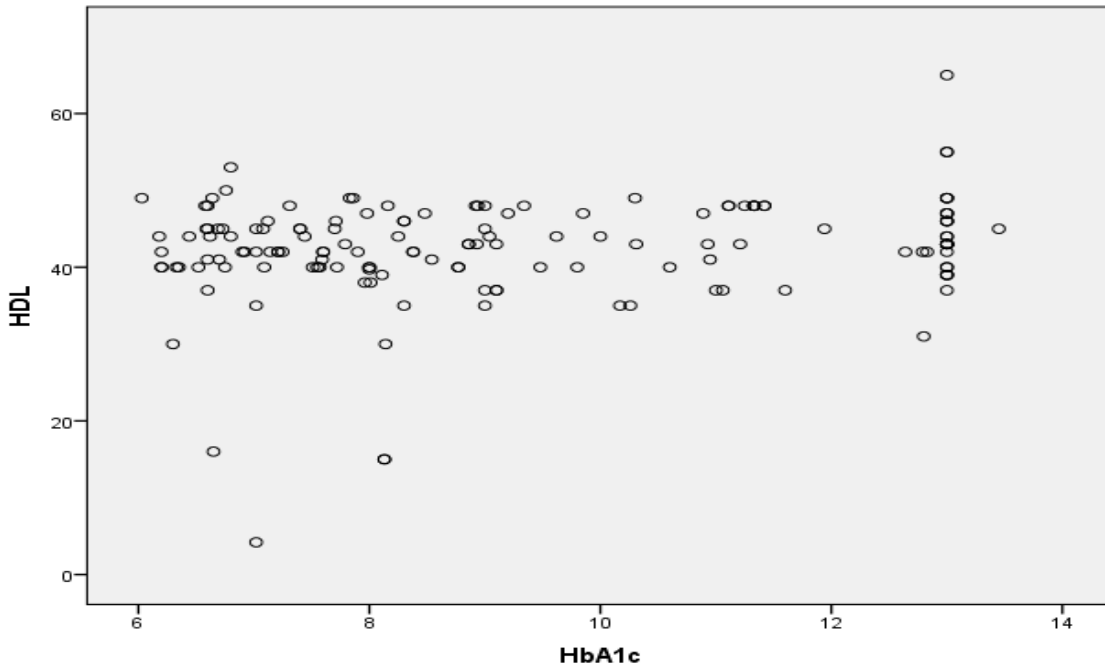


Figure 5 shows that there was no significant relationship between HbA1c and HDL ( $r=0.152$ )



Figure 6: Relationship between HbA1c and LDL-C

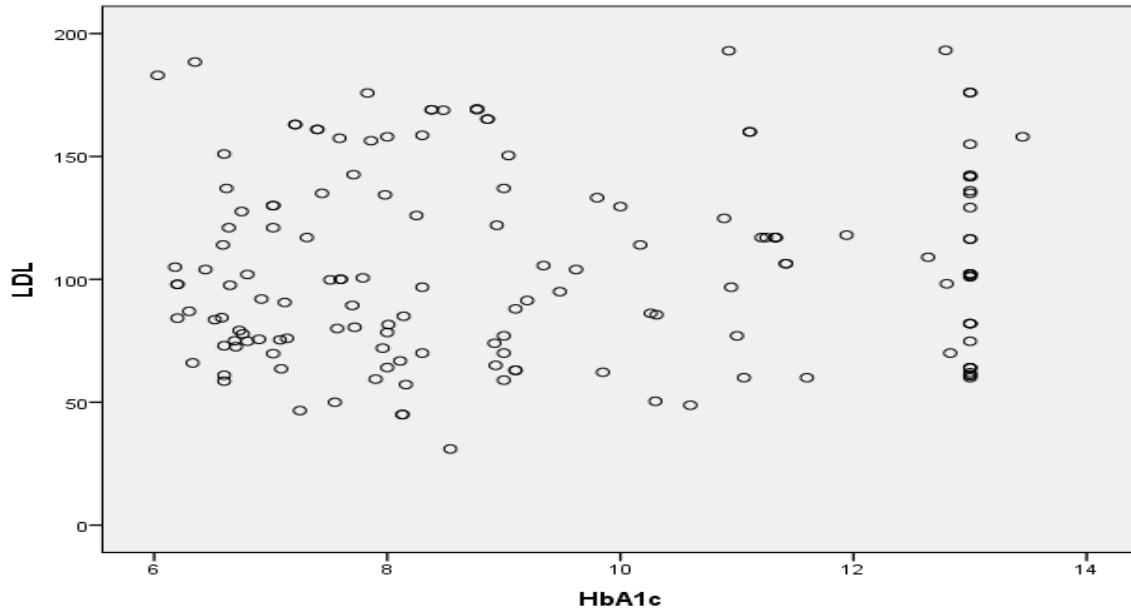


Figure 6 shows that there was no significant relationship between HbA1c and LDL ( $r=0.056$ )

Figure 7: Relationship between HbA1c and VLDL-C

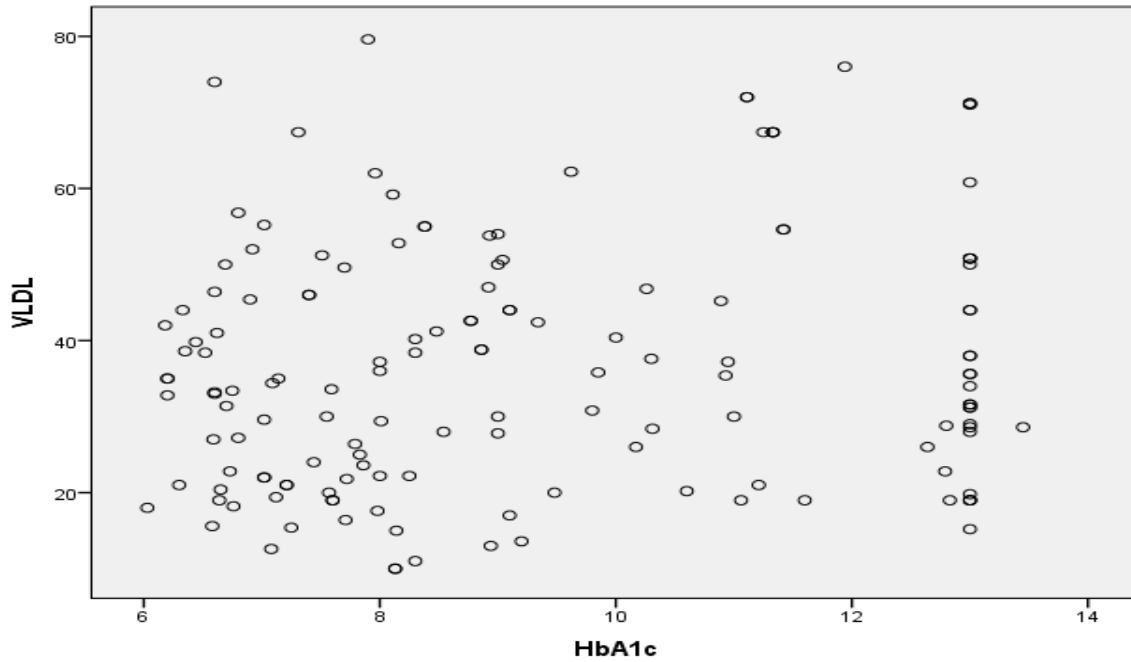


Figure 7 shows that no significant relationship between HbA1c and VLDL ( $r=0.156$ )

## Discussion

In this study, 150 T2DM patients attending the OPD at department of clinical Biochemistry were selected for the study. The participants were already diagnosed as having T2DM by observation of medical records. The subjects included 78 (52%) males and 72 (48%) females. In the first half of the last century the prevalence of T2DM was higher among women than among men, but this trend has shifted, so more men than women are now diagnosed with T2DM. [29]

The prevalence of dyslipidemia in diabetes patients was found to be 82%, which was similar to a previous study that found the prevalence of dyslipidemia to be 81.8%. [30] In a previous study, they found the prevalence of dyslipidemia among type 2 diabetic patients was 80.0% in females and 83.33% in males [31]. In another study, they found prevalence of dyslipidemia to be 90.7%. [32] Similar study was done, they found the prevalence of dyslipidemia to be 89% [33]. In another study, they found 89% patient with dyslipidemia [34].

In present study, it was noted that females ( $28.58 \pm 4.40$ ) had significantly higher BMI than in comparison with males ( $25.57 \pm 4.25$ ). In earlier study, females ( $27.8 \pm 0.5$ ) had significantly higher BMI than in comparison with males ( $24.9 \pm 0.40$ ) [35]. The relative difference in frequency between both sexes is probably related to the presence of underlying factors, such as pregnancy and obesity, rather than to a sex-specific genetic tendency [36].

The levels of HbA1c and FBG did not differ significantly between male & female. Although there were no significant difference in TG ( $p=0.987$ ), HDL-C ( $p=0.799$ ) and VLDL-C ( $p=0.921$ ) levels between male & female. TC ( $p=0.031$ ) and LDL-C ( $p=0.018$ ) was significantly higher in female as compared to male type 2 diabetic patients. Findings from were reported in which there was significantly higher TC ( $p=0.011$ ) and LDL-C ( $p=0.002$ ) in female as compared to male type 2 diabetes mellitus patients. [34] Hyperlipidemia in females may be attributed to the effects of sex hormones on body fat distribution, which leads to differences in altered lipoproteins [37].

Worse glycemic control with dyslipidemia was seen maximum in the individual of the age group 46-60 years, and found high prevalence of dyslipidemia in age group 45-60 years. [30] In another study found worse glycemic control with dyslipidemia was seen maximum in the individual of the age group 51-60 years [38]. A highly significant correlation between HbA1c and FBG was noted similar to earlier studies [38,39,40]. A significant correlation between HbA1c and TC was also observed. Similarly, significant correlations between HbA1c and TC were observed in a prospective cohort which included 418 T2DM patients with follow-up until the appearance of cardiovascular disorders [41]. HbA1c demonstrated positive and significant correlations with TC and LDL-C [42]. Positive correlation of HbA1c level with TC and TG in diabetic patients [43]. The cause of dyslipidemia in T2DM may be that insulin is not working properly which affects the liver apolipoprotein production. The apolipoprotein regulates the enzymatic activity of LPL and Cholesterol ester transport protein [44].

Correlation between DM and CVD is widely established, and it has been extensively addressed over the last few decades [47]. Lipid profile and diabetes mellitus are both found to be significant predictors of metabolic abnormalities, such as dyslipidemia, hypertension, cardiovascular disease, and hyperinsulinemia [17]. T2DM patients have a greater rate of cardiovascular morbidity and death. When compared to participants who did not have diabetes, they were disproportionately afflicted by CVD. Early diagnosis and treatment of dyslipidemia correlated with diabetes may be one step towards lowering CVD risk [48].

In this study, we looked at the correlation between HbA1c and lipid profile in T2DM. According to the NCEP ATP III guideline, dyslipidemia was diagnosed in 52.0 % of women and 48.0 % of men in present study. These

findings are in line with certain earlier studies.[49,50,51]Sex hormones have an impact on how body fat is distributed in women, which results in changed lipoproteins and hyperlipidemia.[52]

We observed that the correlation between HbA1c and HDL-C weak positive, however there was a positive significant correlation between HbA1c and TC. This has already been covered in several studies[53,54,55]. Linear regression and correlational analysis revealed that HbA1c was a predictor of hypercholesterolemia. It is suggested that a key factor in the development of diabetic dyslipidemia is insulin resistance. The release of free fatty acids from insulin-resistant fat cells has increased, which is one of the reasons[56]. These free fatty acids encourage the formation of TG, which further promotes Apolipoprotein (Apo-B) and very low density lipoprotein if the glycogen reserves are sufficient[57].

### Limitation

The current study has some limitations, first that it is a single-center study which only involved T2DM patients. Due to the limited time frame and duration of the investigation, in addition with small sample size. The study's sample size may not accurately reflect the characteristic population. It is challenging to infer a casual association between the variable. Further strong protocol based RCT's are required to investigate on large population samples.

### Future Recommendations

Effective national-level programmes should be launched and promoted for routine screening of diabetic patients in those at high risk, as well as screening for complications in diabetic patients who have already been diagnosed with T2DM. Large multicenter studies are required to be conducted in future to represent the wider aspects of population. Thorough and transparent researches are required in stated with clearer aims, methodology, findings, managing missing values, and giving extensive descriptive statistics.

### Conclusion

A significant positive correlation exists between HbA1c and lipid profile especially total cholesterol (TC) ( $r=0.174$ ). It was concluded from the results of this study that HbA1c can be used as a predictor of dyslipidemia in T2DM in addition to as glycemic control parameter. Achieving the target in HbA1c will contribute in improving the lipid state, and hence may lessen the diabetic complications in T2DM patients.

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