

Original Research Article

## Association of HbA1c with Dyslipidemia in Diabetes Mellitus

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**Abstract:** Type-2 Diabetes Mellitus (T2DM) is a rising pandemic with the number of patients expanding rapidly in both developed and developing countries around the world. Diabetic patients with associated dyslipidemia are easy targets for cardiovascular diseases (CVD). This study was an attempt to determine lipid abnormalities associated with Type-2 Diabetes Mellitus and association between glycosylated hemoglobin (HbA1c) levels and serum lipid profile to assess the importance of HbA1c as an indicator of dyslipidemia and future risk of cardiovascular disease in our local population of Jodhpur city which is situated in the north west of India. In this cross-sectional study, 140 known patients of Type-2 Diabetes Mellitus within 40-70 years of age were randomly selected. They were investigated for HbA1c and lipid profile. The data obtained were analyzed by appropriate statistical methods. Amongst the experimental group, 64.3% patients showed poor glycemic control and the rest 35.7% with good glycemic control, acted as the control subjects. In the present study, dyslipidemia was observed in 70.16% patients of Type-2 Diabetes Mellitus. Of these, 16.8% had single abnormal lipid parameter while 53.36% had associated dyslipidemia. There was exceptionally critical relationship between HbA1c and total cholesterol (TC), HbA1c and low density lipoprotein cholesterol (LDL-C), HbA1c and triglycerides (TG), HbA1c and Tc/HDL proportion and HbA1c and non HDL-cholesterol. Likewise, exceedingly huge reverse connection between HbA1C and HDL cholesterol was established. Apart from dependable glycemic control, HbA1c can likewise be utilized as an indicator of dyslipidemia and in this way early diagnosis of dyslipidemia can be utilized as a preventive measure for the improvement of CVD in patients with T2DM.

**Keywords:** Diabetes Mellitus, cardiovascular disease, dyslipidemia, glycosylated hemoglobin, lipid profile.

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### INTRODUCTION

Diabetes Mellitus, the most common endocrine disease, is characterized by metabolic abnormalities and by long-term complications involving the eyes, kidneys, nerves and blood vessels. The ailment is quickly expanding all inclusive particularly in developing nations like India. Numerous epidemiological researches have exhibited that diabetes is outstanding danger calculate for creating cardiovascular, cerebrovascular illness as a rule populace. Diabetes causes about 5% of all deaths globally each year [1]. T2DM is a quickly developing general medical issue around the world, with significant effect on wellbeing, personal satisfaction and the healthcare systems of the nations. As per current measurements from the International Diabetes Federation (IDF), 415 million grown-ups have

DM around the world; this figure was relied upon to achieve the 642 million check by 2040, which implies every eleventh individual will be analyzed as having T2DM [2]. The extent of individuals with T2DM is expanding in many nations. Keeping in perspective of the disturbing increment in the frequency and prevalence of diabetics in India, WHO has declared the developing nation, India as the – Diabetic Capital of the World [3].

Glycosylated hemoglobin (HbA1c) is routinely utilized as an indicative device for measuring long haul glycemic control. As per its capacity as a pointer for the mean blood glucose level, HbA1c predicts the hazard for the improvement of diabetic inconvenience in diabetes patients. In several studies it is seen that in

patients with type-2 diabetes, the danger of diabetic entanglements were emphatically related with past hyperglycemia. Glycemic control with diminished level of HbA1c is probably going to lessen the danger of complications [4]. Patients with T2DM have increased risk of cardiovascular disease associated with atherogenic dyslipidemia. Coronary artery disease, especially myocardial infarction is the leading cause of morbidity and mortality worldwide [5]. Hyperglycemia and atherosclerosis are related in type-2 diabetes. Control of hyperglycemia with diminished level of HbA1c is probably going to decrease the danger of extreme complexities [6]. Thus, the aim of this study was to assess the relationship between glycemic control (assessed by measuring HbA1c levels) and serum lipid profile as well as to evaluate the importance of HbA1c as an indicator of dyslipidemia in patients with T2DM in local population of Jodhpur region.

#### MATERIALS AND METHODS

A cross-sectional study was conducted on the patients previously diagnosed with T2DM (confirmation of diagnosis sought from physician, confirmed by analyzing the prescription and by asking questions related to the patient's history of taking antidiabetic medicines) who visited the SRL Diagnostics, Centre for Blood Test, Jodhpur, Rajasthan, India for investigations. Patients were asked to fill a written consent form before enrolling them in the study. The study was conducted as part of a summer training programme in this leading diagnostic centre. SRL has over 3500 tests in its repertoire which is the largest menu of tests in India. In the initial phase of the study a total of 157 patients were included but in due course of time, some of the samples have to be excluded because of low sample volume, grossly hemolyzed / lipemic samples, patient was not in a fasting condition, etc. Among the finally selected patients to be included in the study, 90 patients showed poor glycemic control and 50 patients had good glycemic control as observed by the HbA1c results. These 50 patients with good glycemic control acted as control. All subjects included in the study fulfilled following inclusion and exclusion criteria:

#### Inclusion criteria

- Patients included in the study must be continuously residing in Jodhpur region for a minimum period of 10 years or more.
- Patients of T2DM who were suffering with the disease for a minimum of 1 year.

#### Exclusion criteria

- Any patient suffering from any other metabolic disease or disorder other than Type-2 Diabetes Mellitus was excluded from the study.
- Patients suffering from CRF (chronic renal failure) or liver function impairment or any other grave disease were excluded from the study.

Data about subject's age, sex, way of life, family history of diabetes and other constant sicknesses/issue were composed in pre configuration design. Venous blood samples were collected from a total of 157 patients with T2DM. Serum was separated by centrifuging blood at 3000 rpm for 10 min. All the patients were investigated for HbA1c using an ARCHITECT c4000 analyzer (Abbott Diagnostics, USA). The serum was used for analyzing fasting blood sugar (FBS), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), triglycerides (TGs), and low-density lipoprotein cholesterol (LDL-C) using the fully automated clinical chemistry analyzer (Roche/Hitachi 912/Modular Analyzers: CAN 435, Germany). For the serum lipid reference level, the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) rule was eluded. As per the guidelines, hypercholesterolemia is defined as TC greater than 200 mg/dl, high LDL-C when the value is over 100 mg/dl, hypertriglyceridemia when TG is greater than 150 mg/dl and low HDL-C as a value less than 40 mg/dl. Dyslipidemia was defined as the presence of one or more abnormal serum lipid concentrations [7]. Erclays *et al* also presented positive correlation of HbA1C level with Total Cholesterol and Triglycerides level in Diabetic people [8]. Diabetes Mellitus was characterized according to American Diabetes Association criteria [9]. All patients were classified into two groups as Group A and Group B indicated by their HbA1c levels. Group A consisted of patients with HbA1c values < 7% and Group B consisted of patients with HbA1c values ≥ 7%. The information was assessed by means of the SPSS statistical package version 24.0. Pearson's correlation test was performed to look at different correlation. Independent sample Student's t test (two tailed) was utilized to think about methods for various parameters. All p values under 0.05 were considered factually critical. The estimation of HbA1c was given as the percentage of the aggregate hemoglobin and estimations of every single other parameter were given in mg/dl. All parameters were communicated as mean ± standard deviation (SD).

**RESULTS**

A total of 140 patients with T2DM were included as indicated by the inclusion and exclusion criteria in this study. Patients were separated into two groups according to their glycemic index (HbA1c); the primary group i.e. Group A comprised of patients with HbA1c values < 7.0% and the second group i.e. Group B comprised of patients with HbA1c values  $\geq$  7.0%. For Group A, mean  $\pm$  SD for age was 54.19 $\pm$ 15.18 years while for Group B it was 58.65 $\pm$  12.15 years (Table 1). Similarly, different parameters were calculated in Table 1 for both groups. For Group A (HbA1c<7% ), the mean  $\pm$  SD of BMI, TC, TG, HDL-C, LDL-C, TC/HDL ratio and non-HDLc were (30.48 $\pm$ 1.15), (199.01 $\pm$ 16.15), (150.96 $\pm$ 20.14), (42.32 $\pm$ 13.05), (105.32 $\pm$ 18.19), (4.32 $\pm$ 2.05), (136.69 $\pm$ 31.02) respectively. In addition the mean  $\pm$  SD for Group B (HbA1c  $\geq$  7%) of BMI, TC, TG, HDL-C, LDL-C, TC/HDL ratio and non-HDLc were (31.63 $\pm$ 1.04), (210.62 $\pm$ 12.10), (178.21 $\pm$ 23.12), (39.24 $\pm$ 10.15), (126.38 $\pm$ 16.37), (5.78 $\pm$ 3.12), (168.38 $\pm$ 40.80) respectively. As stated by NCEP-ATPIII guideline, hypercholesterolemia is defined as TC>200 mg/dl, high LDL-C when value >100 mg/dl, hypertriglyceridemia as TG >150 mg/dl and low HDL-C when value <40

mg/dl. Dyslipidemia was characterized by presence of at least one unusual serum lipid concentration. As shown in [Table-1] when t-test was applied to the HDL-C and age of the patients for Group A and Group B, t value was 1.55, 1.9 respectively and p value was 0.12, 0.06 respectively, which was statistically insignificant. As shown in [Table-1], the data of the Group A and Group B regarding Body Mass Index (BMI), Total cholesterol, Triglycerides, LDL cholesterol showed statistically significant difference in research of the 't' test and p value. Further, it was found that glycated hemoglobin (HbA1c) was positively and significantly direct correlation with total cholesterol (correlation coefficient 0.5825, P< 0.0001), triglycerides (correlation coefficient 0.5413, P< 0.0001) and very low density lipoproteins (correlation coefficient 0.6182, P< 0.0001), TC/HDL ratio (correlation coefficient 0.6914, P<0.0001) and non-HDL (correlation coefficient 0.6351, P<0.0001) as shown in [Table 2]. However, HDL-C was significantly inversely correlated with HbA1c (correlation coefficient -0.5157, P<0.0001). Results show that dyslipidemia was observed in 70.16% patients of T2DM. Of these, 16.8% had single abnormal lipid parameter while 53.36% had associated dyslipidemia.

**Table-1: Statistical analysis of various parameters between the two study groups**

Parameter	Group A (n=50)	Group B (n=90)	t value	p value
	Control Subjects			
	HbA1c < 7%	HbA1c $\geq$ 7%		
	Mean $\pm$ SD	Mean $\pm$ SD		
Age (yrs)	54.19 $\pm$ 15.18	58.65 $\pm$ 12.15	1.9	0.06*
Body mass index(kg/m <sup>2</sup> )	30.48 $\pm$ 1.15	31.63 $\pm$ 1.04	6.0	0.0001***
Total cholesterol(mg/dl)	199.01 $\pm$ 16.15	210.62 $\pm$ 12.10	4.8	0.0001***
HDL cholesterol(mg/dl)	42.32 $\pm$ 13.05	39.24 $\pm$ 10.15	1.55	0.12*
LDL cholesterol(mg/dl)	105.32 $\pm$ 18.19	126.38 $\pm$ 16.37	7.0	0.0001***
Triglycerides(mg/dl)	150.96 $\pm$ 20.14	178.21 $\pm$ 23.12	6.99	0.0001***
Tc/HDL ratio	4.32 $\pm$ 2.05	5.78 $\pm$ 3.12	2.97	0.0035**
Non HDL cholesterol (mg/dl)	136.69 $\pm$ 31.02	168.38 $\pm$ 40.80	4.78	0.0001***

\*  $\rightarrow$  Not Significant, \*\*  $\rightarrow$  Highly Significant, \*\*\*  $\rightarrow$  Extremely Significant

**Table-2: Correlation among HbA1c and lipid profile of type 2 diabetic patients**

Parameter	Correlation coefficient	P value	Correlation
Total cholesterol	0.5825	< 0.0001	Direct
HDL cholesterol	-0.5157	< 0.0001	Inverse
LDL cholesterol	0.6182	< 0.0001	Direct
Triglycerides	0.5413	< 0.0001	Direct
Tc/HDL ratio	0.6914	< 0.0001	Direct
Non HDL cholesterol	0.6351	< 0.0001	Direct

## DISCUSSION

In this study, T2DM patients visiting the SRL DIAGNOSTICS S.S. WELLNESS CENTRE, Jodhpur were randomly selected. The participants were already diagnosed patients of T2DM and were under intervention at the diabetic clinic. The subjects included were residing in Jodhpur region for a minimum period of 10 years or more and were suffering from this disease from a minimum of 1 year. Early detection and treatment of dyslipidemia related with DM may be one step in decreasing the CVD risk [10]. It was for the most part induced from the investigation that protein glycation happens more higher among subjects with T2DM. From this present examination, it was observed that the diabetic subjects were moderately older. This display T2DM begins typically in middle life or later, the prevalence increases with age. This likewise suggests effect of age as a hazard element of diabetes can't be overemphasized as this pattern has been exhibited in most examination populaces around the globe. It has been anticipated that abatement in the HbA1c esteem by 0.2% could bring down the mortality by 10% [11]. It was ascertained that duration of T2DM had an affirmative correlation with glycated hemoglobin. This is on the grounds that the body turns out to be more impervious to insulin with expanding term of diabetes. In a study, it was observed commonness of dyslipidemia to be 90.7% [12]. Different investigations demonstrate that the measure of carbohydrate appended to the HbA1c rises with expanding tenure of the disease [13, 14]. In contrast Kabadi *et al* (1998) found no significant relation between age, duration of diabetes, fasting glucose and HbA1c [15]. Abdominal obesity is progressively being perceived as a noteworthy hazard calculates for cardiovascular ailment. The cardiovascular and metabolic dangers related with stomach corpulence are ascribed in close proximity to instinctive fat tissue (VAT), which advances insulin resistance, dyslipidemia, and hypertension. Subjects with higher HbA1C levels likewise had altogether significantly higher measurements in BMI, BAI and waist circumference as contrasted with those of alluring HbA1C levels. In this analysis, the example of lipid profile parameters in diabetic subjects and its relationship with HbA1c was assessed. Our investigation is as per the examination directed by Khan *et al.* They have demonstrated that there is an immediate relationship amongst HbA1c with TC, TG and LDL and inverse correlation with HDL [16]. This study reveals high prevalence of high LDL-C and low

HDL-C levels among subjects with high HbA1C levels which are well known risk factors for cardiovascular diseases. Insulin has impact on the liver apolipoprotein production. It regulates the enzymatic activity of lipoprotein lipase (LpL) and Cholesterol ester transport protein. All these factors are likely cause of dyslipidemia in T2DM [17]. In addition, insulin lack decreases the action of hepatic lipase and a few stages in the creation of naturally dynamic LpL might be adjusted in T2DM [18]. Moreover, NCEP ATPIII has recommended using Non-HDL cholesterol in assessing CVD risk in patients with diabetes. Significant association of HbA1c with various lipid parameters, Non-HDL-C, LDL-C/ HDL-C ratio and TC/HDL-C ratio in this study suggests the importance of glycemic control in order to control dyslipidemia. The Diabetes complications and control trial (DCCT) established HbA1c as the best level of glycemic control. The level of HbA1c value <7.0% was said to be apt for reducing the risk of cardiovascular complications [19]. In the immediate study, diabetic patients were bifurcated into 2 groups as per the HbA1c cutoff of 7.0%. The diabetic patients with HbA1c value  $\geq 7.0\%$  exhibited a significant increase in TC, LDL-C, TG, LDL-C/HDL-C ratio, Non-HDL-C without any significant alteration in HDL-C in comparison to patients with HbA1c value <7.0%. In similar findings as in Khan *et al* (2007) the impact of glycaemic control on various lipid parameters in which the diabetic patients were categorized into 3 groups according to their HbA1c levels: group 1, good glycaemic control (HbA1c<6%); group 2, poor glycaemic control (HbA1c >6%–9%) and group 3, worst glycaemic control (HbA1c>9%) [20]. Though there was no significant differences in LDL-C in 3 groups with regard to glycaemic control, alterations in other lipid parameters were statistically significant in three different groups. Severity of dyslipidemia rises in diabetic patients with higher HbA1c levels. As hoisted HbA1c and dyslipidemia are autonomous hazard elements of CVD, diabetic patients with lifted HbA1c and dyslipidemia can be considered as a high hazard assemble for CVD. Significant correlations between HbA1c and the lipid parameters and a linear relationship between HbA1c and dyslipidemia point towards the usefulness of HbA1c for screening high-risk diabetic patients. Furthermore, there were no significant interactions between sex and HbA1c with respect to lipid profile suggesting the validity of HbA1c for predicting dyslipidemia irrespective of patient's gender.

## CONCLUSION

The results drawn from the study which include HbA1C displayed affirmative correlations with TC, TG, LDL-C and negative correlations were observed between HbA1c and HDL-C levels. It was concluded from the results of this study that HbA1c can be utilized as an indicator of dyslipidemia in T2DM and could be additionally used as glycaemic control parameter. Hence, early diagnosis of dyslipidemia can be used as a pre-emptive measure for the development of cardiovascular disease (CVD) in T2DM.

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