Original Research Article

Association of HbA1c with Dyslipidemia in type 2 diabetic patients

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Abstract

Background: Dyslipidemia is a very common finding in patients with type 2 Diabetes Mellitus (DM) which strongly increases risk for the development of cardiovascular diseases. The aim of this study was to determine the pattern of dyslipidemia and to establish the correlation between glycated haemoglobin (HbA1c) and lipid profile in type 2 DM. **Methods:** The sera of 162 patients (100 males and 62 females) with type 2 DM were analyzed for HbA1c, fasting blood sugar (FBS), postprandial blood sugar (PPBS), total cholesterol (TC), triglycerides (TGs), high-density lipoprotein (HDL) and low-density lipoprotein (LDL) levels. We divided the subjects based on their glycemic index into three groups; HbA1c< 6% (good), HbA1c 6%-9% (poor) and HbA1c>9% as worse glycemic control. A correlation between the variables was done by pearson's correlation analysis. **Results:** A significant positive correlation was found between HbA1c with FBS (r=0.504), PPBS (r=0.628), TC (r=0.557), TGs (r=0.517), LDL (r=0.592) and significant negative correlation with HDL (r=-0.449). The low mean values of HbA1c, FBS, PPBS, TC, TGs and LDL and high mean values of HDL were observed in patients with good glycemic control than those with poor and worse glycemic control. Our study shows very little variations of HbA1c, FBS, PPBS and lipid profile parameters in male and female diabetic patients. **Conclusion:** Our study shows that HbA1c can be utilized as a potential biomarker for predicting dyslipidemia in type 2 diabetic patients in addition to glycemic control.

Key Words: Diabetes Mellitus, Cardiovascular disease, Dyslipidemia, Glycated hemoglobin, Lipid profile.

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INTRODUCTION

Type 2 Diabetes mellitus (DM) is a common metabolic disorder which is characterized by impaired pancreatic β-cell function leading to insulin resistance, increased production and decreased utilization of glucose[1]. DM is expeditious growing health problem in the world wide with the development of cardio vascular disease (CVD) associated with atherogenic dyslipidemia and other chronic complications leading to significant morbidity and mortality [2]. Dyslipidemia in type 2 DM patients is characterized by elevated triglycerides (TGs), low density lipoproteins (LDL) and reduced high-density lipoprotein (HDL) and increased circulating insulin concentration[3]. The higher prevalence of lipid abnormalities in DM has been attributed to insulin resistance or deficiency that affects key enzymes and pathways in lipid metabolism. The conditions like hyperglycemia, dyslipidemia and CVD are inter-related well with each other in type 2 DM [4] and recently, elevated glycated haemoglobin (HbA1c) has been regarded as an independent risk factor for CVD and stroke in patients with or without DM. HbA1c is routinely utilized as standard biomarker for measuring glycemic control. In accordance with its function as an indicator for the mean blood glucose level, HbA1c predicts the risk of diabetic

complications and also as valuable biomarker for prognosticating serum lipid status in DM.[5] Very few investigators have reported the significant correlations between HbA1c and lipid profile [6, 7 and 8] and suggested the importance of HbA1c in predicting the dyslipidemia in DM. Thus, we aimed to study and assess the relationship between HbA1c levels and serum lipid profile as well as to evaluate the importance of HbA1c as an indicator of dyslipidemia in patients with Type 2 DM. Hence, the present study was undertaken to observe the correlation of HbA1c with lipid profile for the early determination of dyslipidemia in type 2 DM patients.

MATERIALS AND METHODS

This study was a cross sectional study conducted in the Department of Biochemistry at Mahavir Institute of Medical Sciences (MIMS), Vikarabad, Telangana. A total of 162 (100 males, 62 females) consecutive patients attending General Medicine OPD either diagnosed as type 2 diabetic as per American Diabetes Association guidelines 2013 [9] or already taking treatment for type 2 diabetes from October 2019 to January 2020 were enrolled in the study. The type 2 DM patients with irrespective duration of disease, with good treatment, in regular follow-up and those willing to participate were included in this study. An exclusion criterion was patients taking statins for dyslipidemia, with gestational diabetes and diabetic pregnant women. The study was approved by the institutional ethical committee and informed consent was taken from all the patients. Venous blood samples were collected from all the patients after 8hrs of fasting and serum was separated by centrifugation at 3000rpm for 15min. The serum was used for analyzing fasting blood sugar (FBS), Post prandial blood sugar (PPBS), total cholesterol (TC), triglycerides (TGs) and high-density lipoprotein cholesterol (HDL) using the semi automated clinical chemistry analyzer (ERBA EM-200 analyzer, Germany). The level of LDL cholesterol was determined using the Friedewald formula: LDL = (cholesterol-TG)/ (2.2 HDL) [10]. For a serum lipid reference level, National Cholesterol Education Programme (NCEP) Adult Treatment Panel III (ATP III) guideline was referred. According to NCEP-ATPIII guideline, hypercholesterolemia is defined as TC>200 mg/dl, high LDL-C>100 mg/dl, hypertriglyceridemia as TAG >150 mg/dl and low HDL-C<40 mg/dl. Dyslipidemia was defined by presence of one or more than one abnormal serum lipid concentration [11]. All the patients were investigated for HbA1c using an Hb Vario analyzer (Transasia Biomedicals Pvt Ltd, USA). The impact of glycemic control on various parameters was evaluated into 3 categories on the basis of HbA1c levels: HbA1c<6% (good glycemic control), HbA1c 6-9% (poor glycemic control) and HbA1c >9 % (worse glycemic control). The selection of these cut-off values of HbA1c was based on earlier studies [12]. The data was evaluated by SPSS version 11.0. Independent sample t-test (2-tailed) was used to compare means of different parameters. Pearson correlation analysis was performed to examine the correlations between HbA1c, FBS, PPBS and lipid profile parameters. All values are expressed as mean± standard deviation (SD) and P-value<0.05 was considered as statistically significant. The estimation of HbA1c was given as percentage of total haemoglobin and values of all other parameters were given in mg/dL.

RESULTS

Table 1: Baseline characteristics of the patients

Parameter	Mean± SD
Age (years)	49.16±13.48
HbA1c (%)	8.37±2.61
FBG (mg/dl)	119.83±20.36
PPBS (mg/dl)	165.24±31.38
TC (mg/dl)	180.25±53.45
TGs (mg/dl)	198.0± 90.50
HDL (mg/dl)	29.53 ±7.72
LDL (mg/dl)	150.72 ± 55.71
VLDL (mg/dl)	39.61 ± 18.10

HbA1c: Hemoglobin A1c, TC: Total cholesterol, TGs: Triglycerides, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low-density lipoprotein, FBS: Fasting blood sugar, PPBS: Post-prandial blood suga, SD: Standard deviation

Table 2: HbA1c and Lipid Profile parameters of Male and Female Type 2 Diabetic patients

Parameter	Male (n=100)	Female (n=62)
Age (years)	49.88 ±12.72	47.93±14.49
HbA1c (%)	8.34 ± 2.49	8.48 ±2.81
FBG (mg/dl)	120.74±19.23	118.55±22.1

PPBS (mg/dl)	165.88±29.0	165.2±35.5
TC(mg/dl)	176.27±47.8	186.3 ± 61.8
TGs (mg/dl)	195.01 ±89.02	204.02 ± 93.6
HDL(mg/dl)	29.50±7.62	29.06 ±7.46
LDL(mg/dl)	146.76 ±50.70	157.24±40.8
VLDL(mg/dl)	39.0 ±17.80	40.80±18.73

HbA1c: Hemoglobin A1c, TC: Total cholesterol, TGs: Triglycerides, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low-density lipoprotein, FBS: Fasting blood sugar, PPBS: Post-prandial blood sugar

Table 3. Lipid Profile parameters categorized by Glycemic control

Parameter	HbA1c		
	<6% (n=32) Good control	6-9% (n=70) Poor control	> 9% (n=60) Worse control
HbA1c (%)	5.54±0.28	7.21 ±1.01	11.32±1.65
FBG(mg/dl)	93.03±8.15	123.17±15.16	130.79±17.68
PPBS (mg/dl)	124.62±20.67	166.4 ±18.91	187.05±26.1
TC(mg/dl)	150.59± 25.92	163.75±31.62	216.76±64.38
TGs(mg/dl)	143.21±49.67	175.39±64.29	257.10±102.24
HDL(mg/dl)	34.53±8.39	30.06±6.97	25.85±6.44
LDL(mg/dl)	116.05±23.10	133.7±33.58	190.91±65.25
VLDL(mg/dl)	28.64±9.93	35.1±12.9	51.42±20.44

HbA1c:HemoglobinA1c, TC: Total cholesterol, TGs: Triglycerides, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low-density lipoprotein, FBS: Fasting blood sugar, PPBS: Post-prandial blood sugar

Table 4: Correlation between HbA1c, FBS and Lipid profile

		TC	TGs	HDL	LDL	VLDL
HbA1c	Pearson Correlation	0.557***	0.517	-0.449***	0.592***	-0.012
FBS	Pearson Correlation	0.276***	0.478	-0.222***	0.296***	0.478***

***P<0.001.HbA1c: HemoglobinA1c, TC: Total cholesterol, TGs: Triglycerides, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low-density lipoprotein, FBS: Fasting blood sugar.

The baseline and biochemical parameters of the total study subjects were shown in **Table 1**. **Table 2** shows gender-wise distribution of the study subjects, out of the total 162 subjects, 100 were male and 62 were females. The mean age ±SD of males and females was 49.88±12.72 years (range: 37-63years) and 47.93±14.49 (range: 33-63years), respectively. Our study results showed very little variations in levels of HbA1c, FBS, PPBS and HDL in male and female diabetic patients. The levels of TC, TGs, LDL and VLDL were slightly higher in females than males that were not statistically significant. Therefore, no significant difference was observed in the present study in HbA1c and lipid profile parameters for gender categorization. To study the utility of HbA1c as a marker of dyslipidemia, we divided subjects into three groups depending upon the levels of HbA1c i.e. good (<6%), poor (6-9%) and worse (>9%) glycemic control groups **(Table 3)**. The mean±SD levels of FBS, PPBS and glycemic index HbA1c was found to be increased in poor control (123.1±15.1;166.4±18.9 and7.21±1.01 respectively) and more in worse control (130.7±17.6;187.0±26.1and11.32±1.65 respectively) compared to good control (93.03±8.15;124.6±20.6 and 5.54±0.28) patients. Similarly the mean value of TC, TGs, LDL and VLDL was found to be lower in patients with good glycemic control than those with poor and worse glycemic control patients. However, the higher mean value of HDL was found in patients with good glycemic control than those with poor and worse glycemic control.

Correlation between HbA1c and FBS, PPBS, TC, TGs, HDL, LDL and VLDL:

Pearson correlation coefficient (r) was calculated to find out the correlation between the FBS, PPBS and HbA1c and various lipid profile parameters. Highly significant correlation was observed between HbA1c, FBS (r=0.504; P<0.0001) and PPBS (r=0.628; p<0.0001) and also demonstrated direct and significant correlations with TC (r=0.557; p<0.0001), LDL (r=0.592; p<0.001 respectively). A positive correlation was found between HbA1c and TGs (r=0.517) with no statistical significance. However, a negative correlation was seen between HbA1c and HDL (r=-0.449; p<0.001) and mild negative correlation was observed between HbA1c and VLDL (r=-0.012) which is not statistically significant (Table 4). Along with HbA1c we also performed correlation between FBS and all lipid parameters. We found a significant positive correlation with PPBS (r=-0.728; p<0.001) TC

(r=0.276; p<0.001), LDL (r=-0.296; p<0.001) and VLDL (r=-0.478; p<0.001) and significant negative correlation with (r=-0.222; p<0.001). A positive correlation was found between FBS and TGs (r=0.478) with no statistical significance (**Table 4**).

DISCUSSION

The present study aimed to define the correlation between HbA1c and lipid profile and also to determine the pattern of dyslipidemia in type 2 DM patients. The glycemic parameters (FBS, PPBS and HbA1c) did not differ significantly in type 2 diabetic male and female subjects, where as the slight rise in TC, TGs, LDL and VLDL was found in female diabetic patients in the present study **(Table 2**). These findings suggest that the pattern of dyslipidemia could vary in male and female diabetic subjects. In both males and females, diabetes shows a markedly increase risk of events, however the diabetic woman is more susceptible to increased cardio vascular mortality. Our finding is in agreement with the previous studies [5, 13,14]. Hyperlipidemia in females may be attributed to the effects of sex hormones on body fat distribution, which leads to differences in altered lipoproteins. The Diabetes complications and control trial (DCCT) established HbA1c as the best level of glycemic control [15]. To see the impact of glycemic control on various lipid parameters the diabetic patients are categorized into 3 groups based on the HbA1c levels i.e. good glycemic control (HbA1c<6%); poor glycemic control (HbA1c 6%-9%) and worst glycemic control (HbA1c>9%) [6 and12]. We found a linear and increase in HbA1c, FBS, PPBS, TC, TGs, LDL, VLDL and decreased HDL in the patients with poor and worse glycemic control than in good glycemic control. Thus, HbA1c provides a reliable measure of chronic glycemia and correlates well with the risk of long-term diabetes complications, so that it is currently considered as gold standard test for the assessment and chronic management of diabetes mellitus [7].In the present study, we observed that HbA1c has direct and significant correlations with FBS, PPBS, TC, TGs and LDL and inverse correlation with HDL and VLDL. Our findings are concomitant with previous studies [6, 16, 17,18] who also reported a direct and significant correlation between HbA1c with TC, TG and LDL and reverse correlation with HDL. The cause of dyslipidemia in type 2 DM may be due to impaired liver apolipoprotein production which in turn regulates the enzymatic activity of lipoprotein lipase (LPL) and cholesterol ester transport protein [19, 20]. Dyslipidemia as a metabolic abnormality is strongly linked with type 2 DM and its prevalence vary, depending on the type and severity of diabetes, glycemic control, nutritional status, age and other factors [21]. In our study, the significant correlations were found between HbA1c, FBS, PPBS and all the lipid profile parameters finds a linear relationship between HbA1c and dislipidemia which points towards the usefulness of HbA1c for screening the high risk diabetic patients. This finding supports HbA1c is better predictor and can be used as a potential biomarker for predicting dyslipidemia in type 2 diabetic patients.

CONCLUSION

The findings of the present study showed a significant positive correlation between HbA1c with FBS, PPBS, TC, TGs, LDL and negative correlation with HDL and VLDL. In the present study, the levels of HbA1c, FBS, PPBS, TGs, LDL, VLDL, and HDL did not differ significantly between male and female diabetic patients. Thus, HbA1c endures the ability of predicting serum lipid profile in both male and female diabetic patients. To conclude, the findings of our study clearly show that HbA1c which is gold standard in the assessment of glycemic control together with its strong correlation with the lipid profile which makes an ideal marker for predicting dyslipidemia in type 2 DM.

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