Original Research Article

Association of HbA1c with Lipid profiles in patients with type 2 diabetes mellitus

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Abstract

Background: Patients with type 2 diabetes have an increased prevalence of dyslipidemia. A timely intervention to normalize circulating lipids could reduce the chances of cardiovascular diseases. Glycated hemoglobin (HbA1c) is the indicator of glycemic status over long term. This study was conducted to find the association between HbA1c and lipid profiles in patients with type 2 diabetes mellitus.

Methods: A confirmed 52 cases with type 2 diabetic mellitus were enrolled in the study. Fasting blood samples were collected and different lipid fractions along with fasting blood glucose were estimated by enzymatic method. LDL-C and VLDL-C were determined by Friedewald's formula Glycated hemoglobin (HbA1c) with radioimmunoassay.

Results: HbA1c has significant positive correlation (p<0.016-0.001) with FBG, TC, TG, LDL-C and LDL-C/HDL-C. Among the lipid components, TC has significant positive correlations (p<0.007-0.001) with TG, LDL-C, TC/HDL-C, TG/HDL-C and LDL-C/HDL-C, where as TG has significant positive correlations (p<0.001) with TC/HDL-C and TG/HDL-C.HDL-C has significant negative correlations (p<0.002-0.0001) with TC/HDL-C, TG/HDL-C and LDL-C/HDL-C whereas, LDL-C has significant positive correlations (p<0.001) with TC/HDL-C and LDL-C/HDL-C. VLDL-C has significant positive correlation (p<0.001) with HDL-C and significant negative correlation (p<0.002) with TG mg/dl. Lastly, TC/HDL has significant positive correlation (p<0.001) with TG/HDL-C and LDL-C/HDL-C.

Conclusion: Significant positive correlation of HbA1c with lipid profiles suggested that HbA1c can also be used as predictor of Dyslipidemia in addition to as a glycemic control parameter.

Keywords: Type 2 diabetes mellitus, HbA1c, Lipid profile, insulin resistance, dyslipidemia

1. Introduction

Diabetes mellitus is a chronic metabolic disease which is characterized by hyperglycemia and various lethal combinations. There are two major clinical classifications of diabetes type 1 and type 2. Type 1 is immune mediated and requires daily administration of insulin and type 2 is more prevalent and occurs either when the β-cells of pancreas do not produce enough insulin or when body cannot utilize insulin effectively. Type 2 diabetes mellitus often associated with both qualitative and quantitative abnormalities of lipoproteins which are responsible for increased incidence of micro vascular and macro vascular complications [1]. India, a developing country with fast industrialization and modern lifestyle is facing a grave problem having the largest number of patients with diabetes [2,3] which is estimated to reach 80 million by the end of 2030 [4,5]. It is because of this, India is close to becoming the diabetic capital of the world. Incidence of acute myocardial infarction is four-fold, post myocardial infarction is two-fold and risk of coronary heart disease is two

to three folds higher in diabetic patients as compare to non-diabetic. It is also a leading cause of blindness, limb amputation and kidney failure [6]. Lipoprotein abnormality present in type 2 diabetes mellitus includes abnormal high level of triglycerides (TG), high level of small dense lipoprotein (LDL-C), high level of very Low density lipoprotein (VLDL-C) and low level of high density lipoprotein (HDL-C) [7-9]. This lipid profile pattern in diabetic patients is known as diabetic dyslipedemia. Many factors are responsible for diabetic dyslipedemia, these are: effect of insulin on liver Apoprotein productions, regulation of lipoprotein lipase (LpL), actions of cholesteryl ester transfer protein, and action of insulin on adipose and muscle tissues [10,11]. Dyslipidemia (raised triglycerides, raised cholesterol, raised LDL-C, raised VLDL-C and low HDL-C) were common in type 2 diabetes mellitus, which is further associated with insulin resistance like hyperinsulinemia, hypertension with obesity collectively known as metabolic

syndrome or Reaves's syndrome; strongly correlated with atherosclerosis. Atherogenic indices i.e. TC/HDL-C ratio (<5) and LDL-C/HDL-C (<3.5) is the main indicator of cardiovascular disease (CVD). TG/HDL-C which is considered as reliable as fasting serum insulin levels and is determined to assess insulin resistance status in type 2 diabetes [12]. Dyslipidemia, especially high LDL-C, is common in diabetes mellitus and strongly associated with poor glycemic control. Glycated hemoglobin (HbA1c) is main routinely used tool for measuring long term glycemic control [13]. HbA1c is a main indicator for mean blood glucose level; HbA1c predicts the risk of diabetic complications in diabetic patients. Thus, in the present study an attempt has been made to find any correlation of HbA1c with lipid profile in patients with type 2 diabetes mellitus.

2. Material and Method

2.1 Study participants

A total of 52 confirmed cases of type 2 diabetes mellitus were obtained from Dr. Puneet Arora Diabetic and Research Centre, Green Avenue, Amritsar, Punjab. The samples comprised both males and females. All diabetic patients were aged 40 and above. The informed consent form was voluntarily taken from each diabetic patient who participated in the study. This study was approved by institutional ethical committee.

2.2 Measurement of Biochemical Parameters

After an overnight fasting, approximately 5 ml venous blood was collected with the help of disposable syringe. The serum was separated immediately after collecting the blood sample via centrifugation at 3000 rpm for 10 minutes. Fasting blood glucose concentrations were measured within 30 minutes to 1 hour of sample collection. Lipid profile (total cholesterol, triglycerides, high density lipoprotein) was measured using automatic blood analyzer cobas c 111(according to the manufacturer's instructions). Low density lipoprotein and very low density lipoproteins were measured using the Friedewald's formula (given below)

Low density lipoprotein = Total Cholesterol – (High density lipoprotein – Triglycerides/5)
VLDL= Triglycerides/5

The Glycated hemoglobin (HbAIc) were measured with a radioimmunoassay (HbA1c LD-500 Analyzer)

2.3 Statistical Analysis

Standard descriptive statistics (mean ± standard deviation) were determined for directly measured variable. Pearson's correlation coefficients were applied to establish the correlations of anthropometric variables, FBG, Hba1c, Lipid profiles, atherogenic indices were measured. Data were analyses using SPSS (Statistical Package for Social Science) version 20.0. A 5% level of probability was used to indicate statistical significance.

3. Results

Table 1: Mean±SD of anthropometric variables, FBG, Hba1c of type 2 diabetes mellitus with reference range

Variables	Mean	Standard Deviation	Reference range
Age (Years)	54.40	9.84	
Height(cm)	167.54	9.14	
Weight(kg)	77.43	13.03	
Body mass index (BMI) kg/m^2	27.54	4.17	18.3 - 25
Fasting blood glucose(FBG)	206.42	48.24	120
HbA1c (%)	8.59	1.70	4-6

Table 1 shows mean value of age, height, weight, BMI, FBG and HbA1c were observed to be 54.40±9.84 years, 167.54±9.14 cm, 77.43±13.03 kg, 27.54±4.17 kg/m^2, 206±48.24 and 8.59±1.70 respectively. Results of the BMI in the present study indicate that subjects were not obese but their mean fasting blood sugar and HbA1c were more than the normal value.

Table 2: Mean±SD of lipid profiles of patients with type 2 diabetes mellitus

Variables	Mean	Standard Deviation	Reference range
Total cholesterol (TC) mg/dl	178.61	46.99	<200
Triglycerides (TG) mg/dl	210.61	133.69	<150
High density lipoprotein (HDL) mg/dl	41.92	10.72	>40
Low density lipoprotein (LDL) mg/dl	96.17	33.72	<100
Very low density lipoproteins (VLDL)	42.12	26.74	<30

Table 2 shows the quantitative analysis of lipid profiles of type 2 diabetes mellitus and found that the mean total cholesterol (178.61±46.99), triglycerides (210.61±133.69), HDL (41.92±10.72), LDL(96.17±33.72), VLDL(42.12±26.74). According to NCEP-ATP III guidelines, hypercholesterolemia is defined as TC>200 mg/dl, high LDL-C when value >100 mg/dl, hyperglyceridemia as TG>150 mg/dl and low HDL-C when value <40 mg/dl. Dyslipidemia was defined by presence of one or more than one abnormal lipid concentration

Table 3: Mean±SD of atherogenic indices in patients with type 2 diabetes mellitus

Variables	Mean	Standard Deviation	Reference range
Total cholesterol/ high density lipoprotein (TC/HDL)	4.47	1.51	<5
Low density lipoprotein/ high density lipoprotein (LDL/HDL)	2.42	1.04	<3.5
Triglycerides/High Density Lipoprotein (TG/HDL)	5.54	4.27	nd

nd=not determined

Table 3 Mean of Atherogenic indices were 4.47± 1.51, 5.54±4.27, 2.42±1.04. Atherogenic indices i.e. TC/HDL-C ratio (<5) and LDL-C/HDL-C (<3.5) is the main indicator of cardiovascular disease (CVD). TG/HDL-C which is considered as reliable as fasting serum insulin levels and is determined to assess insulin resistance status in type 2 diabetes mellitus

Table 4: Correlation matrix of demographic and lipid profiles in patients with type-2 diabetes mellitus

Variables	Age (years)	Height (cm)	Weight (kg)	BMI (kg/m²)	FBG	HbA1c (%)	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	VLDL-C mg/dl	TC/HDL-C	TG/HDL-C	LDL-C/HDL-C
Age (years)	1	0.085 0.55	0.86 0.55	-0.118 0.404	-0.167 0.238	-0.165 0.243	-0.238 0.090	-0.034 0.810	-0.035 0.803	-0.278 0.046	0.097 0.622	-0.160 0.258	-0.025 0.862	-0.188 0.182
Height (cm)		1	1.000 0.000	-0.178 0.207	0.125 0.376	0.127 0.369	-0.061 0.665	-0.043 0.763	-0.067 0.637	-0.021 0.884	-0.114 0.565	0.013 0.929	-0.001 0.993	0.028 0.844
Weight (kg)			1	-0.178 0.207	0.126 0.375	0.127 0.368	-0.061 0.665	-0.042 0.767	-0.067 0.636	-0.021 0.882	-0.243 0.212	0.013 0.928	-0.001 0.997	0.028 0.845
BMI (kg/m²)				1	0.087 0.542	0.022 0.875	0.160 0.256	0.260 0.063	-0.209 0.137	0.103 0.469	-0.201 0.305	0.330 0.017	0.323 0.020	0.233 0.096
FBG					1	0.881 0.000	0.407 0.003	0.245 0.080	0.031 0.827	0.376 0.006	-0.190 0.333	0.223 0.111	0.103 0.468	0.238 0.089
HbA1c (%)						1	0.537 0.000	0.332 0.016	0.057 0.686	0.496 0.000	-0.196 0.318	0.331 0.16	0.178 0.206	0.347 0.012
TC mg/dl							1	0.562 0.000	0.257 0.066	0.802 0.000	-0.246 0.207	0.592 0.000	0.367 0.007	0.478 0.000
TG mg/dl								1	-0.140 0.321	0.071 0.618	-0.395 0.037	0.564 0.000	0.895 0.000	0.101 0.477
HDL-C mg/dl									1	0.128 0.367	0.415 0.028	-0.569 0.000	-0.426 0.002	-0.504 0.000
LDL-C mg/dl										1	-0.112 0.570	0.517 0.000	-0.029 0.837	0.738 0.000
VLDL-C mg/dl											1	-0.408 0.031	-0.353 0.066	-0.302 0.119
TC/HDL-C												1	0.695 0.000	0.828 0.000
TG/HDL-C													1	0.222 0.115
LDL-C/HDL-C														1

Table 4 shows Correlation matrix of demographic and lipid profiles of patients with type-2 diabetes mellitus was given in table 2. HbA1c has significant positive correlations ($p<0.016-0.001$) with FBG, TC, TG, LDL-C and LDL-C/HDL-C. Among the lipid components, TC has significant positive correlations ($p<0.007-0.001$) with TG, LDL-C,TC/HDL-C,TG/HDL-C and LDL-C/HDL-C, where as TG has significant positive correlations ($p<0.001$) with TC/HDL-C and TG/HDL-C.HDL-C has significant negative correlations ($p<0.002-0.0001$) with TC/HDL-C, TG/HDL-C and LDL-C/HDL-C whereas, LDL-C has significant positive correlations ($p<0.001$) with TC/HDL-C and LDL-C/HDL-C.VLDL-C has significant positive correlation ($p<0.001$) with HDL-C and significant negative correlation ($p<0.002$) with TG mg/dl. Lastly, TC/HDL has significant positive correlation ($p<0.001$) with TG/HDL-C and LDL-C/HDL-C.

4. Discussion

Lipid abnormalities are common in diabetic patients and frequently seen in patients with type-2 diabetic mellitus. The abnormal lipid profile observed in type 2 Diabetes mellitus is said to be related to insulin resistance as reported in previous studies, which leads to increased release of free fatty acids from fatty tissue, impaired insulin dependent muscle uptake of free fatty acids and increase fatty acid release to the hepatic tissue [14] which has been closely associated with diabetic dyslipedema, hypertension [15] and enormous risk to cardiovascular diseases. Chronic hyperglycemia causes glycation of apolipoproteins and interferes with the normal pathways of lipoprotein metabolism [16]. Diabetic patients have much complication which includes elevated levels of LDL-C and triacylglycerol and low level of HDL-C. In the present study, the results showed that the lipid profile were higher in diabetic patients and that they were in agreement with the finding of Wexler *et al.*, 2005[17]. The study revealed that dyslipedemia was observed in the diabetic population, but that HDL-C and LDL-C were not significantly decrease or increase respectively. Lipoprotein lipase an insulin dependent enzyme which together with insulin resistance leads to increase in TG levels, results in type-2 diabetes having high levels of TG, HDL-C levels may be further reduced in DM due to elevated hepatic lipase activity that catalyzes HDL-C [18]. In the present study there is highly positive significant correction were observed between HbA1c and Lipid profiles (TC, TG and LDL-C) Erciyas *et al*, (2004) [19] also reported the positive correlation between HbA1c and TC, TG; in patients with type-2 diabetes .The Diabetic complication and control trial (DCCT) established HbA1c as the gold standard of Glycemic control. The HbA1c value $<7.0\%$ reduced the risk of cardiovascular diseases and value $>7.0\%$ leads to dyslipedemia to the patients. [20]. Controlling the glycemic levels may significantly decrease the risk of cardiovascular diseases in diabetes. Khaw *et al* [21] has reported that reducing the HbA1c level by 0.2% could lower the mortality

by 10% thus the present study suggests the importance of glycemic control in prevention of cardiovascular diseases in type2 diabetes.

5. Conclusion

It was concluded from the results of this study that type 2 diabetic patients are more prone to dyslipidaemia. HbA1c is significantly correlated with lipid profiles. HbA1c can be used as indicator of dyslipidaemia in type 2 diabetes in addition to as glycemic control biomarker. Atherogenic indices also associated with cardiovascular diseases and insulin resistance. Thus early diagnosis of dyslipidaemia can be used as a preventive measure for development of cardiovascular disease (CVD) in patients with type 2 diabetes mellitus.

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