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Research Article

ASSOCIATION BETWEEN GLYCEMIC CONTROL AND SERUM LIPID PROFILE IN TYPE 2 DIABETIC PATIENTS

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ABSTRACT

Background: Diabetic patients are known to have increased prevalence of lipid abnormalities, contributing to their high risk of cardiovascular diseases (CVD). An early intervention to normalize circulating lipids has been shown to reduce cardiovascular complications and mortality. Glycosylated hemoglobin is a routinely used marker for long-term glycemic control.
Objective: Association between glycemic control and serum lipid profile in type 2 diabetic patients.
Materials and methods: The study subjects included 100 type 2 diabetic patients and 100 healthy controls, in whom fasting serum glucose (FSG), glycosylated hemoglobin (HbA1c), serum total cholesterol (TC), triacylglycerol (TAG), Low density lipoprotein-cholesterol (LDL-C) and High density lipoprotein -cholesterol (HDL-C) levels were measured.
Results: According to the levels of HbA1c, the patients were classified into two groups; patients with HbA1c <8% as Group I [60 patients] and those with HbA1c > 8% [40 patients] classified as Group II. The levels of FSG, TC, TAG, LDL-C and HDL-C in two Groups were compared with controls. It was found that the levels of FSG, TC, TAG and LDL-C were increased significantly in Group I &II patients as compared to the controls ($p< 0.05$). They were increased significantly in group II when compared with Group I ($p<0.05$), whereas the HDL-C levels were significantly low in group I & II patients as compared with controls ($p< 0.05$) and were significantly low in group II when compared with Group I ($p< 0.05$). HbA1c is positively correlated with FSG, TC, TAG, LDL-C and negatively correlated with HDL-C.
Conclusion: These findings clearly suggest that HbA1c can provide valuable supplementary information about the extent of circulating lipids besides its primary role in monitoring long-term glycemic control.
Keywords: Diabetes mellitus, glycosylated hemoglobin, Total cholesterol, triacylglycerol, Low density lipoprotein cholesterol and high density lipoprotein cholesterol.

INTRODUCTION

Diabetes mellitus is a complex and multifactorial disease. It is characterized by absolute or relative deficiencies in insulin secretion and/or insulin action associated with chronic hyperglycemia and disturbances of carbohydrate, lipid and protein metabolism[1].

In India, diabetes is not an epidemic anymore but has turned into a pandemic, according to the International Journal of Diabetes in developing Countries which labeled India the diabetes capital of the world, mainly because India now has the highest number of diabetic patients in the world. The International Diabetes Federation estimates that the number of diabetic patients in India more than doubled from 19 million in 1995 to 40.9 million in 2007. It is projected to increase to 69.9 million by 2025. Currently, up to 11 per cent of India's urban population and 3 per cent of rural population above the age of 15 has diabetes. The most prevalent is Type 2 diabetes, which constitutes 95 per cent of the diabetic population in the country. Indian population faces higher risk for diabetes and its complications[2].

Hyperglycemia is the apparent feature of diabetes due to diagnostic dependency of patients on blood glucose measurements. However, most of the individuals may also carry unnoticed dyslipidemia, characterized by increased levels of total cholesterol, triacylglycerol and LDL-C and decreased HDL-C. Individuals with coexisting diabetes and metabolic syndrome (Dyslipidemia + Hyperglycemia +

Hypertension) have the highest prevalence of CVD[3]. It is also observed that there is a significantly higher level of hypercholesterolemia and hyperlipidemia in type 2 diabetic patients with CVD as compared to diabetic patients without CVD[4]. Early therapeutic interventions, aiming to reduce triacylglycerol and LDL-C and to increased HDL-C, significantly reduce cardiovascular events and mortality in patients with type 2 diabetes[5, 6].

HbA_{1c} is a routinely used marker for long-term glycemic control. The Diabetes Complications and Control Trial (DCCT) established HbA1c as the gold standard of glycemic control[7]. In accordance with its function as an indicator for the mean blood glucose level, HbA1c predicts the risk for the development of diabetic complications in diabetes patients[8]. Apart from classical risk factors like dyslipidemia, elevated HbA1c has now been regarded as an independent risk factor for CVD in subjects with or without diabetes. Estimated risk of CVD has shown to be increased by 18% for each 1% increase in absolute HbA1c value in diabetic population[9]. Positive relationship between HbA1c and CVD has been demonstrated in non-diabetic cases even within normal range of HbA1c[10-13]. The aim of this study was to find out association between glycemic control (HbA1c as a marker) and serum lipid profile in type 2 diabetic patients.

MATERIALS AND METHODS

A case control study was carried out in Al Ameen Medical College and Hospital. The study comprises of 200 subjects which includes 100 type 2 diabetic patients attending to outpatient and inpatient departments and 100 controls. All the patients in the diabetic group were confirmed diabetics who previously had fasting serum glucose levels >126 mg/dl on more than two occasions based on the American diabetes association (ADA) 2010 criteria for diagnosis of DM[14] and who were receiving treatment such as insulin, glybenicide, glucophage, or physical exercise therapy for diabetes mellitus. General health characteristics such as age, sex, smoking status, menopausal status, alcohol consumption, and dietary habits (particularly as related to preference) were investigated by a self-administered questionnaire. All subjects were informed about the objectives of the study and what roles they were expected to play. Age and sex-matched healthy volunteers without a history of diabetes and with normal blood sugar were considered to be control subjects.

Biochemical investigations: Under all aseptic precautions, using a sterile disposable syringe about 5 ml of venous blood is drawn from subjects after overnight fasting. 3 ml of blood is taken into plain vacutainer and is subjected for centrifugation, serum is separated which is used for estimation of fasting serum glucose and lipid profile (Total cholesterol, triacylglycerol, HDL- C). 2 ml blood is taken into EDTA containing vacutainer and is used for estimation of HbA_{1c}.

Glycosylated hemoglobin is estimated By Cation-Exchange resin method in Semi autoanylyser ERBA Chemtouch.[15] Fasting Serum glucose was measured by Glucose oxidase (GOD-POD) method[16]. Serum total cholesterol by enzymatic cholesterol oxidase – phenol aminoantipyrine method (CHOD-PAP). Serum triacylglycerol by enzymatic glycerol phosphate oxidase – phenol aminoantipyrine method (GPO-PAP method). Estimation of serum HDL cholesterol by phosphotungstic acid and enzymatic cholesterol oxidase-phenol aminoantipyrine (CHOD-PAP) method. The serum LDL cholesterol was determined using Friedwald's formula[17]. All the investigation were carried out in fully automated analyzer ERBA MANNHEIM EM 200.

For 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 when value >100 mg/dl, hypertriglyceridemia as TAG >150 mg/dl and low HDL-C when value <40 mg/dl. Dyslipidemia was defined by presence of one or more than one abnormal serum lipid concentration[8].

STATISTICAL ANALYSIS

Results are expressed as Mean ± SD, and range values for continuous data, number and percentage for discrete data. The data were evaluated by SPSS statistical package version 13.0. Pearson's correlation test was performed to examine various correlations. Unpaired t-test was used for two group comparison. For all the tests p value of < 0.05 was considered for statistical significance.

RESULTS

Among the 100 type 2 diabetic patients studied, 47 were males and 53 were females with mean age of 55.5 ± 6.2 years. Among the 100 healthy controls studied, 49 were males and 51 were females with mean age of 55.8 ± 6.5years. Both male and female diabetic patients exhibited similar patterns of glycemic control depending on cutoff values of HbA1c. Among 100 diabetic patients, 60 patients are found to have HbA1c value <8.0% and are classified as group I, 40 patients are found to have HbA1c value > 8.0% and are classified as group II.

As shown in Table 1, the levels of FSG, TC, TAG and LDL-C were increased significantly in Group I & II patients as compared to the controls ($p< 0.05$). Whereas the HDL-C levels were significantly low in group I & II patients as compared with controls ($p< 0.05$).

Group II Patients with HbA1c value >8.0% had significantly higher values of FSG ($P<0.05$), TC ($P<0.05$), TAG ($P<0.05$), LDL-C ($P<0.05$) and significantly lower values of HDL-C ($P<0.05$) as compared to the group I patients with HbA1c value ≤ 8.0%.

As shown in figure 1, highly significant correlation was observed between FSG and HbA1c ($p <0.001$). Figure 2, 3, 4 and 5 show that HbA1c demonstrated direct and significant positive correlations with TC, TAG, and LDL-C while HDL-C was found to have significant negative correlation with HbA1c ($p<0.05$).

DISCUSSION

This study reveals high prevalence of hypercholesterolemia, hypertriglyceridemia, high LDL-C and low HDL-C which are well known risk factors for cardiovascular diseases. Several factors are likely to be responsible for diabetic dyslipidemia: insulin effects on liver apoprotein production, regulation of

lipoprotein lipase (LpL), actions of cholesteryl ester transfer protein (CETP), and peripheral actions of insulin on adipose and muscle[18].

In our study, we found that Patients with HbA1c value >8.0% had significantly higher value of FSG, TC, TAG, LDL-C, and significantly lower values of HDL-C as compared to the patients with HbA1c value ≤ 8.0%. This suggests that dyslipidemia worsens when glycemic control is disturbed in diabetic patients. Our results are in accordance with these studies[7,8,19,20]. HbA1c demonstrated positive and significant correlations with TC, TAG and LDL-C and negative correlation with HDL-C. Severity of dyslipidemia increases in patients with higher HbA1c value.

As elevated HbA1c and dyslipidemia are independent risk factors of CVD, diabetic patients with elevated HbA1c and dyslipidemia can be considered as a very high risk group for CVD. Improving glycemic control can substantially reduce the risk of cardiovascular events in diabetics[21]. It has been estimated that reducing the HbA1c level by 0.2% could lower the mortality by 10%[22].

Table 1: Comparison of parameters among study groups

Parameters		Healthy controls	Group I (HbA1c <8%)	Group II (HbA1c >8%)	p value
FSG (mg/dl)	Mean ± SD	85.46 ± 6.59	145.25 ± 9.57	176.45 ± 28.32	<0.05
TC (mg/dl)	Mean ± SD	174.01± 21.21	218.06± 25.95	247.92 ± 42.70	<0.05
TAG (mg/dl)	Mean ± SD	115.05 ± 25.91	189.55± 39.27	208.97± 55.13	<0.05
LDL-C (mg/dl)	Mean ± SD	96.54 ± 22.49	140.63± 30.59	172.97± 42.91	<0.05
HDL-C (mg/dl)	Mean ± SD	55.02 ± 8.99	39.50± 7.64	34.56± 6.82	<0.05

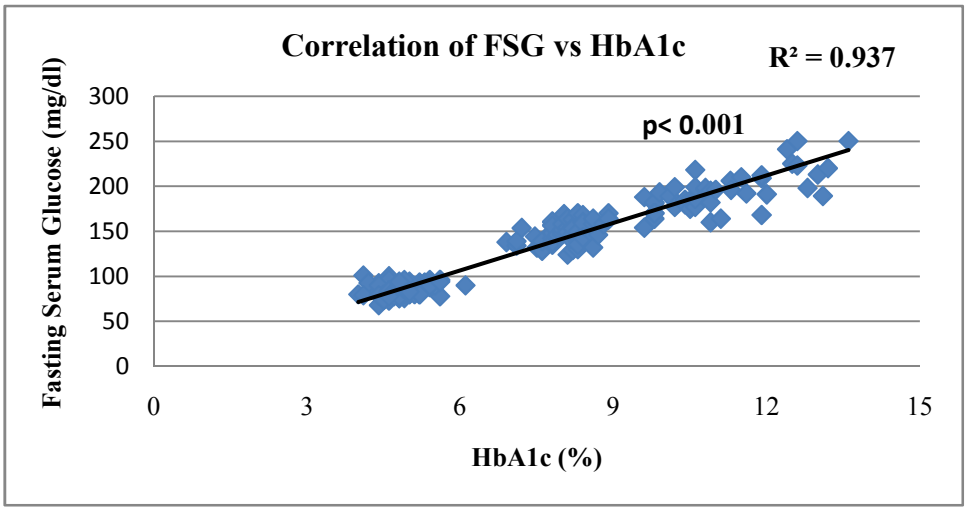

Figure 1: Correlation between Fasting serum glucose and HbA1c.

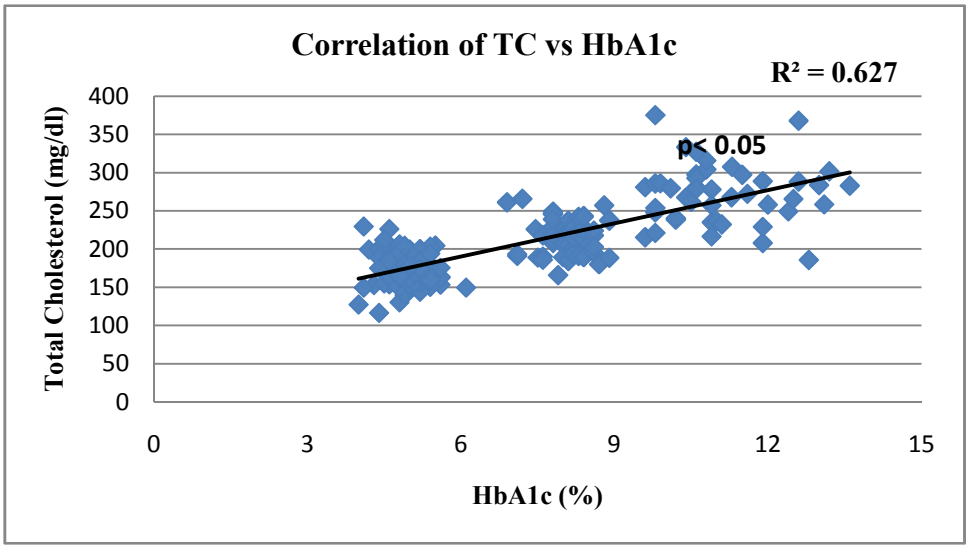

Figure 2: Correlation between Total cholesterol and HbA1c.

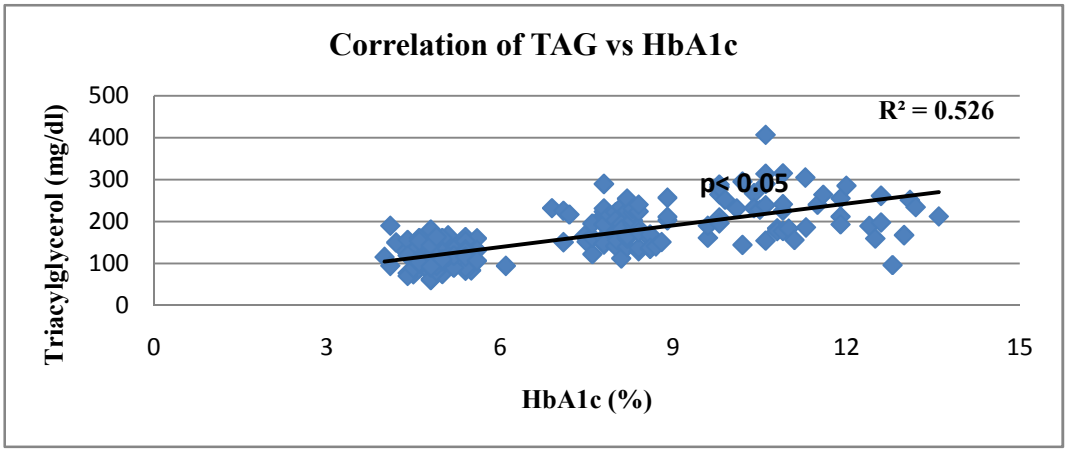

Figure 3: Correlation between Triacylglycerol and HbA1c

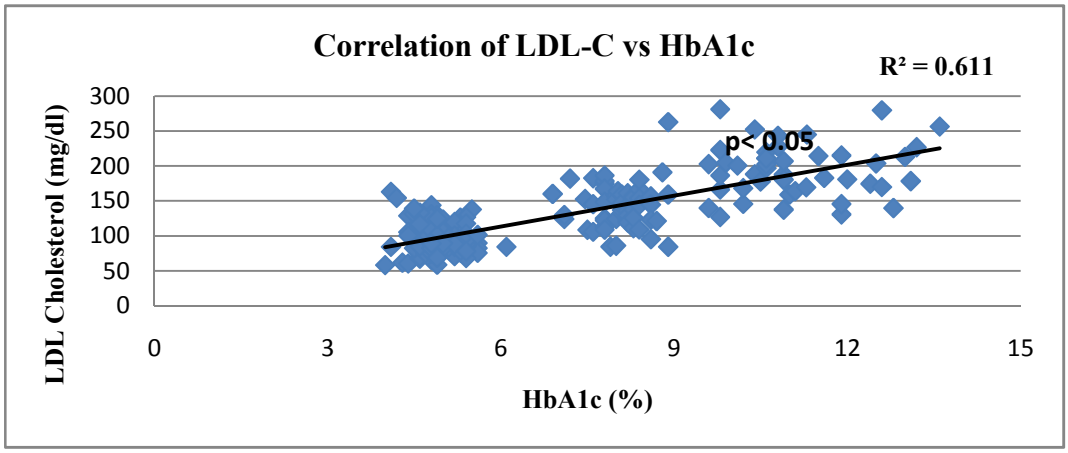

Figure 4: Correlation between LDL -C and HbA1c.

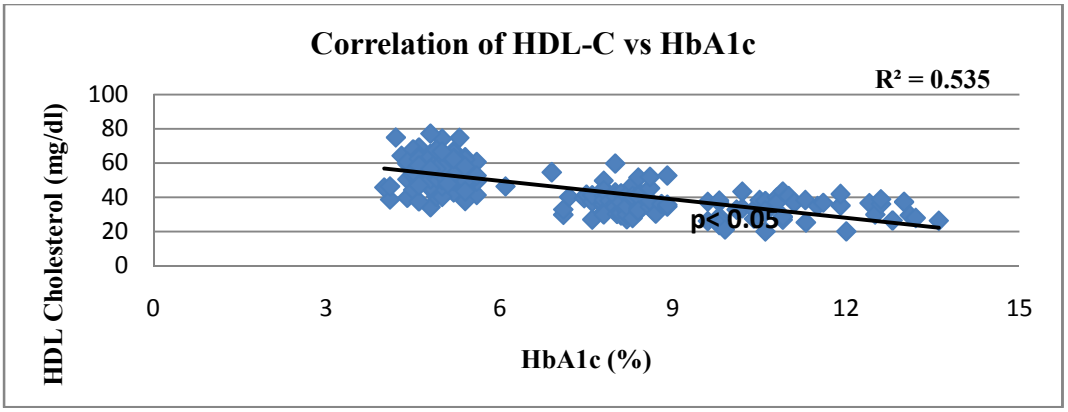

Figure 5: Correlation between HDL-C and HbA1c

CONCLUSION

This study reveals significant linear correlations between HbA1c and all these lipid parameters. The findings of this study clearly suggest that HbA1c endures the ability of predicting serum lipid profile in both male and female diabetic patients. Thus, dual biomarker capacity of HbA1c (glycemic control as well as lipid profile indicator) may be utilized for screening high risk diabetic patients for timely intervention with lipid lowering drugs.

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