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Does the Glycated Hemoglobin have an Impact on Atherogenic Cholesterol in Type 2 Diabetes Patients?

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ABSTRACT

Diabetes mellitus is a group of metabolic disease characterized by hyperglycemia resulting from defective insulin secretion, insulin action or both. Studies on chronic complications of diabetes established the role of glycosylated hemoglobin (HbA_{1c}) as a marker of evaluation of long term glycemic control and risk for chronic complications. This is a cross sectional study carried out on 40 diabetic patients and 50 normal individuals, between the age group of 40- 60 years attending medicine OPD were included as study subjects. Diabetes was diagonsed based on laboratory and clinincal co-relation. 5ml of fasting venous sample was taken from study sujects and following parameters were estimated LDL, FPG and glycatedhemoglobin.The values of HbA_{1c} and FPG were statistically significant in diabetic subjects when compared to controls ($p< 0.001$). The levels of LDL-C were increased in diabetic subjects but were not statistically significant. In conclusion, significant co-relation between HbA_{1c} and LDL-C levels can be used as a potential biomarker for predicting dyslipidemia in type 2 diabetic patients in addition to long term glycemic control.

Keywords: Diabetes, glycated hemoglobin, FPG.

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INTRODUCTION

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Diabetes mellitus is a group of metabolic disease characterized by hyperglycemia resulting from defective insulin secretion, insulin action or both.The long term complication of uncontrolled diabetes are manily, dysfunctionor failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels.Most common caues of death in diabetic patients were either cardiovascular or renal complications [1,2]. Studies on chronic complications of diabetes established the role of glycosylated hemoglobin (HbA_{1c}) as a marker of evaluation of long term glycemic control and risk for chronic complications [3]. The Diabetes Control and Complication Trial (DCCT) study, has demonstrated that 10% stable reduction in HbA_{1c} determines a 35% risk reduction for retinopathy and a 25- 44% risk reduction for nephropathy [4].Glycated hemoglobin (HbA_{1c}) predicts the risk for the development of diabetic complications in diabetes patients [2]. Apart from classical risk factors like dyslipidemia, elevated HbA_{1c} has now been regarded as an independent risk factor for cardiovasculr disease (CVD) in subjects with or without diabetes. Estimated risk of CVD has shown to be increased by 18% for each 1% increase in absolute HbA_{1c} value in diabetic population [5]. Positive relationship between HbA_{1c} and CVD has been demonstrated in non-diabetic cases even within normal range of HbA_{1c}[6, 7, 8, 9]. It is a routinely used marker for long-term glycemic control. The most common type of lipid abnormalities encountered in a subject with diabetes mellitusare elevated plasma levels of triglycerides, very low density lipoprotein cholesterol (VLDL-C), low density lipoprotein cholesterol (LDL-C) and lower level of high density lipoprotein cholesterol (HDL-C) [10]. The stabilization of lipoprotein level decreases the incidence of atherosclerotic cardiac heart diseases.Lipid profile, which greatly increases the risk of CVD compared with people without diabetes. An early intervention to normalize circulating lipids has been shown to reduce cardiovascular complications and mortality [11, 12].

Diabetes therapy is mainly about restoring glycemic control to avoid long-term consequences such as impaired vision, kidney failure or angiopathy. Ways to prevent these vascular diseases include dietary measures, oral drugs or insulin substitution. The aim of this study was to find out association between long term glycemic control in the form of HbA_{1c} and LDL-C levels in type 2 diabetic patients.

METHODS AND MATERIALS

This is across sectional study carried out on 40 diabetic patients and 50 normal individuals, between the age group of 40- 60 years attending medicine OPD were included as study subjects. Diabetes was diagonsed based on laboratory and clinincal co-relation. Patients with dehydration,muscle dystrophy, glomerulonephritis, pyelonephritis, hypertension and congestive cardiac failure were excluded from the study. After obtaining informed consent from the study group, 5 ml of fasting venous blood sample was collected.Plasma glucose was estimated by GOD – PAP method [13]. After estimating lipid profile, LDL-C was calculated by Friedwald and Frederickson formula [14].Glycated hemoglobin estimated by auto analyzer using Cobas commercial kit [15].

Statstical Analysis

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The data were evaluated by SPSS statistical package version 13.0. Pear-son's co-relation test was performed to examine various co-relations. Independent sample t-test (2-tailed) was used to compare means of different parameters. Value of HbA_{1c} was given as percentage of total haemoglobin and values of all other parameters were given in mg/dl. All values were expressed as mean ± standard deviation. The results were considered significant when $P < 0.05$.

RESULTS

The mean age of the study subjects was 52.53 ± 9.82 and 58.47± 10.04 years respectively in controls and cases. The values of HbA_{1c} and FPG were statistically significant in diabetic subjects when compared to controls ($p< 0.001$). The levels of LDL-C were increased in diabetic subjects but were not statistically significant as shown in Table 1.

Between the cases HbA_{1c} and LDL-C are highly significantly co-related ($p<0.001, r = 0.763$). Where as between the cases and control group FPG were significantly co-related with HbA_{1c}($p<0.001$, $r=0.807$) as shown in Figure 1.

Table 1: LDL-C, $HbA_{1c}$and fasting plasma glucose levels in patients with diabetic patients compared to healthy controls. (Values are expressed in mean ± SD)

	Controls (n=50) Mean± SD	Cases (n=40) Mean± SD
Age (Years)	52.53±9.82	58.47±10.04
FPG (mg/dl)	86.37±11.88	158.47±74.21***
HbA1c%	5.24±1.01	8.52±2.48***
LDL-C (mg/dl)	99.11±20.14	105.16±34.81

P<0.001=***

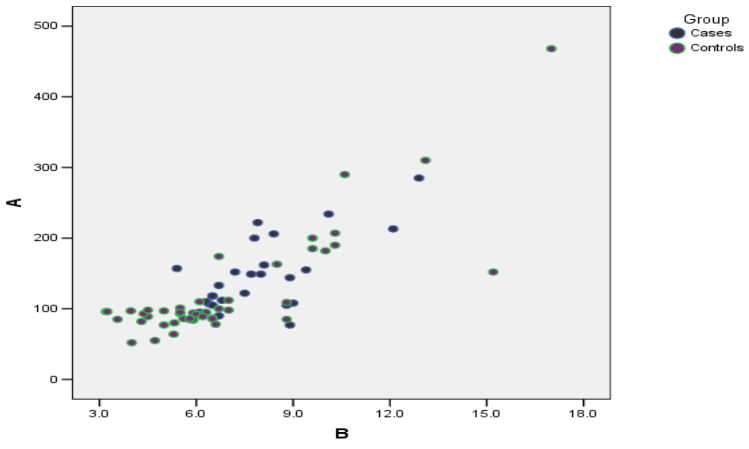

Figure 1

A= Fasting Plasma Glucose (FPG)
B= HbA_{1c}

DISCUSSION

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Glycated hemoglobin is the product of non-enzymatic reaction between glucose and free amino groups ofhemoglobin. This reaction, called glycosylation, involves lots of other proteins too and it is theprincipal mechanism through which glucotoxicity is formed.In the present study, we have evaluated the LDL-Cholesterol levels in diabetic subjects and compared with HbA_{1c}.

HbA_{1c} is a marker of long term glycemic control,increase in HbA_{1c} increases the relative risk for CVD events. Atherosclerosis in diabetes mellitus is more progressive in diabetic children than non diabetic controls. Both type-1 and type-2 diabetes are associated with abnormalities of lipid metabolism. Several researchers reported abnormal lipid metabolism in uncontrolled diabetic patients [16].

In our study we found asignificantly increased level of glycated hemoglobin in diabetic patients along with increased levels of LDL-C.The increased LDL-C get oxidised to form oxidized LDL (OxLDL), which commonly involved in atherogenesis by inducing smooth muscle cell proliferation and generation of foam cells in smooth muscle [17]. The results of the study suggested that elevated LDL- C levels in diabetic patients may get oxidised due to increased oxidative stress and led to structural changes of the arteries in asymptomatic person [18] in future. In the study of Sehran et al in Pakistan, 54% diabetic individuals had elevated LDL-C and > 50% individuals had increased TG. These findings are similar to our study.

We also found a statstically significant co-relation between $HbA_{1c}$and LDL-C levels in diabetic subjects, which is related to long term glycemic status.Studies of Kilpatrick et al [19] in diabetic patients showed significant +ve co-relationbetween HbA_{1c}& age as well as duration of diabetes. In contrast Kabadiet al [20] found nosignificant relation between age, duration of diabetes, fasting glucose &HbA_{1c}. In contrast our study found a significant co-relation between FPG and HbA_{1c} and is similar with various previous studies [21-23].

In conclusion, the diabetic complications and control trial (DCCT) established,HbA_{1c} as the gold standard of glycemic control. The level of HbA_{1c} value ≤7.0% was said to be appropriate for reducing the risk of cardiovascular complications [24]. Significant co-relation between $HbA_{1c}$and LDL-C levelscanbe used as a potential biomarker for predicting dyslipidemia in type 2 diabetic patients in addition to long term glycemic control.

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