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Original Research Article

Association Between Glycated Hemoglobin (HbA1c) and the Lipid Profile in Patients with Type 2 Diabetes Mellitus at a Tertiary Care Hospital: A Retrospective Study

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Abstract

Background: HbA1C is not only a glycemic index but can also be used as a marker of dyslipidemia and thus can be used as a preventive measure for the development of CVD in patients with T2DM.

Methods: This retrospective cross-sectional study was conducted during the year 2012-13. Venous blood samples were collected from 300 type 2 diabetic patients. The sera were analyzed for HbA1c, fasting blood glucose (FBG) and lipid profile panel test. Dyslipidemia was defined as per the National Cholesterol Education Programme (NCEP) Adult Treatment Panel (ATP) III guidelines. Diabetes was defined as per American diabetes association criteria. The statistical analysis was done on Microsoft excel and Epi info-6 software.

Result: In our present study 95(81.89%) females out of 116 and 151 (82.06 %) males out of 184 were dyslipidemic. HbA1c demonstrated positive and significant correlations with total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), high density lipopro-tein cholesterol (HDL-C) and LDL-C. Patients with HbA1c value > 7.0% had significantly higher value of TC, Triacylglycerol (TAG), LDL-C, HDL-C as compared to the patients with HbA1c ≤ 7.0%. HbA1c can be used as a biomarker for predicting dyslipidemia in type 2 diabetic patients in addition to glycemic control.

Keywords: Diabetes mellitus, Dyslipidemia, Glycated hemoglobin, Lipid Profile panel, Biomarker

Introduction

Diabetes mellitus is the commonest metabolic disorder affecting the people all over the world. Globally, the number of diabetes patients has risen sharply. While in 2000, 171 million people had diabetes, the number rose to 285 million in 2010. However, by 2030, an estimated 435 million people are expected to suffer from this disease[1].

Diabetes is a group of metabolic disease characterized by high blood glucose in context of insulin resistance and relative insulin deficiency[2]. Diabetes Mellitus is a multifactorial disease characterized by hyperglycemia, lipoprotein abnormalities and altered intermediary metabolism of major food substrate. Diabetes causes about 5% of all deaths globally each year. The chronic hyperglycaemia of diabetes is associated with long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels.50% of people with diabetes die of cardiovascular disease (primarily heart disease and stroke)[3,4].

Dislipidemia, an abnormal amount of lipids in the blood, is a primary risk factor for cardiovascular deaths. Patients with type 2 diabetes often exhibit an atherogenic lipid profile and have 2-3 fold higher rate of coronary artery disease, a fourfold higher mortality rate during MI and 2 fold higher risk of post MI morbidity than non - diabetic patients[5]. An early intervention to normalize circulating lipids has been shown to reduce cardiovascular complications and mortality[6,7].

Glycated hemoglobin (HbA1c) is used as a marker for long-term glycemic control. Apart from it's function as an predictor for the mean blood glucose level, HbA1c predicts the risk for the development of diabetic complications in diabetes patients[4]. Along with dyslipidemia, elevated HbA1c has now been regarded as an independent risk factor for CVD in subjects with or without diabetes[8]. Positive relationship between HbA1c and CVD has been demonstrated in non-diabetic cases even within normal range of HbA1c[9-12]. The aim of our study is to find out association between HbA1c and serum lipid profile in type 2 diabetic patients.

Materials and Methods

A total of 300 type 2 diabetic patients (184 males and 116 females) visiting the OPD of GMC, Kota (Raj.) from 2012-13 were included in this study. Venous blood samples were collected from patients after at least 10 hours fasting. The Serum was analyzed for Fasting Blood Glucose (FBG), Lipid Profile i.e. Serum Total cholesterol (TC), HDL-cholesterol (HDL-C), Triacylglycerol (TAG) on EM - 360 and LDL cholesterol was calculated by Friedwald and Frederickson formula. HbA1c was estimated by using HPLC.

For serum lipid reference level, was taken from the National Cholesterol Education Programme (NCEP) Adult Treatment Panel III (ATP III) guideline. According to NCEP-ATPIII guideline, hypercholesterolemia is defined as TC>200 mg/dl, high LDL-C when value >100 mg/dl, hy-pertriglyceridemia as TAG >150 mg/dl and low HDL-C when value <40 mg/dl. Diabetes was defined as per American Diabetes Association (ADA) criteria. The data were evaluated by Epi info - 6 software. Independent samples t-test was used to compare means of different parameters. Value of HbA1c was given as percentage of total haemoglobin and values of all other parameters were given in mg/dl. All Values are expressed as mean ± standard error of mean. The results were considered significant if $P < 0.05$.

Results

Among total 300 type 2 diabetic individuals included in this study, 184 were male and 116 were female. The mean age ± SD of male and female subjects were 61.72±10.24 and 56.46 ± 11.98 years respectively. The mean value of HbA1c and FBG were slightly higher in females in comparison to male patients but the differences were not significant. Among the circulating lipids, TC and LDL-C were significantly higher ($P<0.05$) in females patients. Although the mean level of TAG was slightly lower and of HDL-C slightly higher in females than males, these

differences were statistically non- significant.

Table 1: Lipid Profile parameters result of Male and Female Type 2 Diabetic Patients

Parameters	Male(n=184)	Female (n=116)	P value
FBG	148.96±5.86	159.21±7.24	>0.05
TC	176.08 ± 4.05	195.98±4.34	<0.05
TAG	192.39 ± 7.96	182.54±9.31	>0.05
LDL-C	92.78± 4.01	120.24±5.56	<0.05
HDL-C	46.10±0.77	46.54±.89	>0.05
HbA1C	7.18±0.12	7.68±0.19	>0.05

Hypercholesterolemia was found in 85(28.33%) individuals. Similarly, hypertriglyceridemia was found in 198(66%) individuals, decreased HDL-C was found in 47(15.66%) individuals and increased LDL-C was found in 141(47%) individuals. Among the diabetic individuals, 111(37%) individuals had only one abnormal lipid profile parameter, 88(29.93) had two abnormal lipid parameter and 70(23.33%) individuals had more than 2 abnormal lipid profile parameters. According to NCEP-ATPIII guideline, 95(81.89%) females out of 116 and 151 (82.06 %) males out of 184 were dyslipidemic.

Diabetic patients were classified into 2 groups as per their glycemic index; first group consists of patients with HbA1c value ≤7.0 % and second group consists of patients with HbA1c value >7.0%. Patients with HbA1c value >7.0% had significantly higher value of TC (<0.05), TAG (P<0.05), LDL-C (P<0.05), and HDL -C had significant lower value (<-0.05) as compared to the patients with HbA1c value ≤ 7.0%

Table 2: Biochemical Parameters categorized by patient's glycemic control (HbA1c)

Parameter	Glycated Hemoglobin (HbA1C) ≤7.0(n=41)	Glycated Hemoglobin (HbA1C) >7.0(59)	P- value
TC	172.82 ± 5.34	181.59 ± 5.21	<0.05
TAG	168.76 ± 6.28	198.78. ± 8.28	<0.05
HDL-C	49.35 ± 0.96	46.21 ± 0.72	<- 0.05
LDL-C	92.66 ± 4.27	108.79 ± 4.72	<0.05
FBG	124.32 ± 3.13	177.11 ± 5.01	<0.05

Discussion

In the present study, we analyze the lipid profile of diabetic subjects and its association with HbA1c. There are no significant differences in levels of HbA1c and FBG between male and female. Although the levels TAG and HDL-C had no significant difference between male and female, the levels of TC and LDL-C were significantly higher in female as compared to male type 2 diabetic patients. The above finding is similar to the previous studies[13-17]. Hyperlipidemia in females may be due to the effects of sex hormones especially estrogen on body fat distribution, which leads to altered lipoproteins[18].

This study reveals high prevalence of hypercholesterolemia,
hypertriglyceridemia, high LDL-C and low HDL-C levels which are well known risk factors for cardiovascular diseases. Insulin affects 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 Diabetes mellitus[19]. Moreover, insulin deficiency

reduces the activity of hepatic lipase and several steps in the production of biologically active LpL may be altered in DM[20]. The main disorder in lipid metabolism was hypertriglyceridemia in our study. This finding is in concord with our previous study. It is suggested that insulin resistance has a central role in the development of diabetic dyslipidemia. One of the causes is increased free fatty acid release from insulin-resistant fat cells. If the glycogen stores are adequate, these free fatty acids promote TG production which further stimulates Apolipoprotein (Apo-B) and very low density lipoprotein[21].

A highly significant correlation between HbA1c and FBG in our study is similar with various previous studies. We observed that the association between HbA1c and HDL-C was negative, however there was a positive, significant correlation between HbA1c and TC, LDL-C, and TGs. Various studies have described this before[22-24]. A rather interesting finding was that HbA1c was found to be a predictor of hypercholesterolemia by linear regression analysis.In one Pakistani study by Firdous and colleagues, 38% of people with DM were found to have high TG levels. In our study, women with DM were found to have slightly higher LDL levels compared with men, which is consistent with previous studies[25]. Total number of apo-B containing particles and small LDL-C Particles are increased in diabetes Significant association of HbA1c with various lipid parameters, Non-HDL-C, in present study suggests the importance of glycemic control in order to control dyslipidemia.

The Diabetes complications and control trial (DCCT) established HbA1c as the gold standard of glycemic control. The level of HbA1c value ≤7.0% was said to be appropriate for reducing the risk of cardiovascular complications[26]. In the present study, we divided diabetic patients into 2 groups as per the HbA1c cutoff of 7.0%. The diabetic patients with HbA1c > 7.0% showed a significant increase in TC, LDL-C, TAG, HDL-C in comparison to patients with HbA1c value ≤7.0%. Khan HA et al.[27] showed the impact of glycemic control on various lipid parameters in which the diabetic patients were categorized into 3 groups according to their HbA1c levels: group 1, good glycemic control (HbA1c<6%); group 2, poor glycemic control (HbA1c >6%–9%) and group 3, worst glycemic control (HbA1c>9%). Though there were no significant differences in LDL–C in 3 groups with regard to glycemic control, alterations in other lipid parameters were statistically significant in three different groups.

Our study showed, severity of dyslipidemia increases in patients with higher HbA1c value. High HbA1c and dyslipidemia are two important and independent risk factors of CVD, combined effect of diabetic patients with elevated HbA1c and dyslipidemia can be considered as a very high risk for CVD. Improving glycemic control can substantially reduce the risk of cardiovascular events in diabetics[28]. Calculated risk shows that reducing the HbA1c level by 0.2% could lower the mortality by 10%[29].

Conclusion

In our study we have seen a significant association between HbA1c and various circulating lipid parameters. We noted a significant difference in lipid parameters in two groups (⩽7.0% and >7.0%) of HBA1c. This may indicate that HbA1c can be used as a biomarker for dyslipidemia in patients with T2DM in addition to glycemic control. Hence, HbA1C can be used for early diagnosis and in screening of high-risk patients with DM for timely intervention with lipid-lowering drugs.

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