



Association between Glycated haemoglobin and Serum Lipid Profile in Type 2 Diabetic Patients in Kumaun Region, Uttarakhand

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Abstract

Type 2 diabetes is known to have increased prevalence of lipid abnormalities leading to high risk of cardiovascular diseases (CVD). Diabetic patients are at more risk for altered lipid profile than normoglycemic persons. Glycated hemoglobin (HbA1c) is a routinely used marker for long-term glycemic control and as a screening tool for the diagnosis of diabetes. A value over 6% gives an indication of altered glucose control. Also, HbA1c nowadays is considered an independent risk factor for CVD. In this study association between Glycated haemoglobin (HbA1c) and diabetic dyslipidemia was found. Venous blood samples were collected from 113 type 2 diabetic patients. The whole blood and serum were analyzed for HbA1c, fasting blood sugar (FBS) and lipid profile using cobas c 501 system. The statistical analysis was done by SPSS statistical package version 21. HbA1c showed significant correlations with total cholesterol (TC), triglycerides (TG), low density lipoprotein cholesterol (LDL-C) and TC/HDL-C ratio. Patients with HbA1c value > 7.0% had significantly higher value of TC, Triacylglycerol (TG), VLDL-C, LDL-C and TC/HDL-C ratio as compared to the patients with HbA1c ≤ 7.0%. However, there was no significant difference in value of HDL-C between two groups. Thus, HbA1c can be used as a potential biomarker for predicting dyslipidemia in type 2 diabetic patients.

Keywords: Diabetes mellitus, Dyslipidemia, Glycated hemoglobin, Lipid Profile.

Introduction

Diabetes mellitus is one of the major public health problems in world today. Initially more in developed nation now it has become an epidemic in developing nation like India also. It is characterized by hyperglycemia due to lack of insulin or defects in its receptor. The major cause

of its morbidity is due to its chronic complications like nephropathy, neuropathy and retinopathy^[1] Diabetic patients are also accompanied by dyslipidemia which is the leading cause of cardiovascular deaths. Diabetic patients are at more risk for altered lipid profile than normoglycemic persons. Dyslipidemia in diabetes

is characterized by high plasma triglyceride concentration, reduced high density lipoprotein cholesterol (HDL-C) concentration, and increased concentration of small dense LDL particles, so early detection and treatment of dyslipidemia can markedly help in prevention of cardiovascular morbidity and mortality in persons suffering from diabetes mellitus.^[2]

Glycated hemoglobin (HbA1c) is a routinely used marker for long-term glycemic control for the preceding 6 to 8 weeks. HbA1c is formed by non-enzymatic addition of glucose to globin part of hemoglobin. A value of less than 7% is ideal. A value above 7 shows some degree of uncontrolled blood glucose levels for past 3 months and HbA1c predicts the risk for the development of diabetic complications in diabetes patients.^{[3][4]}

HbA1c is also used as a screening tool for the diagnosis of diabetes. A value over 6% gives an indication of perturbed glucose metabolism.^[5]

HbA1c nowadays is considered an independent risk factor for CVD in subjects with or without diabetes apart from classical risk factors like dyslipidemia. Positive relationship between HbA1c and CVD has been demonstrated in non-diabetic cases even within normal range.^{[6][7]}

The aim of this study was to find out association between HbA1c (as a marker of glucose control) and serum lipid profile in type 2 diabetic patients of kumaun region of uttarakhand state, India.

Materials and methods

A total of 114 type 2 diabetic patients (74 males and 39 females) visiting the medicine OPD of sushila tiwari Hospital, haldwani, Uttarakhand from October 2014 to august 2015 were included in this study. Venous blood samples were collected from all the subjects after at least 8 hours fasting. The Serum was used for analyzing Fasting Blood sugar (FBS), Serum total cholesterol (TC), HDL-cholesterol(HDL-C), total triacylglycerol (TG), TC/HDL-C ratio by using cobas c501 (Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim) and Indirect LDL-cholesterol and VLDL-C was calculated by

Friedwald formula^{[8][9][10]}. HbA1c was estimated by turbidimetric inhibition immunoassay (TINIA) for hemolyzed whole blood by using cobas c501 (Roche Diagnostics GmbH). Value of HbA1c was given as percentage of total haemoglobin and values of all other parameters were given in mg/dl^[11].

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 when one or more than one abnormal serum lipid concentration was found^[12]. Diabetes was defined as per American Diabetes Association (ADA) criteria^[13].

The data were evaluated by SPSS statistical package version 21. Independent samples t-test (2-tailed) was used to compare means of different parameters. All Values are expressed as mean \pm standard error of mean. The results were considered non-significant when $P > 0.05$.

Results

Among total 113 type 2 diabetic individuals included in this study, 74 were male and 39 were female. The mean age \pm SEM of male and female subjects were 55.8 ± 9 and 50.4 ± 1.04 years respectively.

HbA1c was significantly correlated with FBS, TC, VLDL, LDL and risk ratio (TC/HDL) with the respective pearson coefficient given in Table 1 and scatter plot in figure 1.

The mean value of HbA1c was almost equal in females and male patients and the difference was not significant. Among the circulating lipids, TC and LDL-C and TC/HDL ratio (risk ratio) were significantly higher ($P < 0.05$) in female's patients. The level of TAG and HDL-C were statistically non-significant (Table 2).

Hypercholesterolemia was found in 8.9% individuals. Similarly, decreased HDL-C was

found in 38.03% individuals and increased LDL-C was found in 66.37% individuals.

Diabetic patients were classified into 2 groups as per their glycemic index; first group consists of patients with HbA1c value $\leq 7.0\%$ and second group consists of patients with HbA1c value $>7.0\%$ (Table 3). This was done to see any association of HbA1c value on the lipid profile of the patients. Although there

was no significant difference in the values of high density lipoproteins (HDL-C), there was a significant difference in the values of fasting blood sugar (FBS), total cholesterol (TC), triglyceride levels(TG), very low density lipoprotein(VLDL), low density lipoprotein (LDL) and risk ratio (TC/ HDL-C) between the two groups.

Table 1 Correlations

	GHb	FBS	TC	HDL	TG	VLDL	LDL	RATIO
Pearson Correlation	1	.876**	.520**	-.045	.772**	.772**	.349**	.268**
GHb Sig. (2-tailed)		.000	.000	.636	.000	.000	.000	.004
N	113	113	113	113	113	113	113	113

** . Correlation is significant at the 0.01 level (2-tailed)

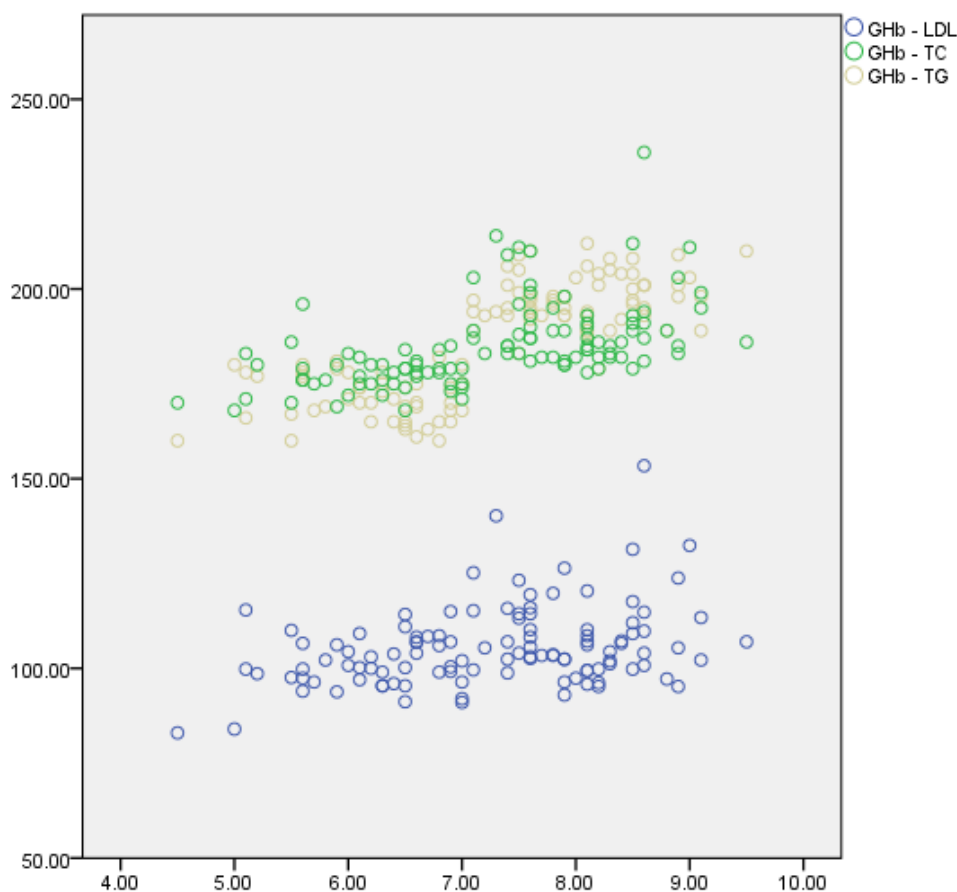


Figure 1 Scatter plot

Table 2. Values of various parameters in males and females patients expressed in mean \pm standard error of mean (SEM)

Parameter	Females(n=39)	Males(n=74)	P-value
Age	50.4 \pm 1.04	55.8 \pm 8.3	0.001*
FBS	152.3 \pm 4.9	156.3 \pm 3.7	0.52
GHb	7.2 \pm 0.2	7.2 \pm 0.1	0.79
TC	191.7 \pm 2.3	181.2 \pm 0.64	0.0001*
HDL-C	42 \pm 1.09	42 \pm 0.45	0.96
TG	187 \pm 2.4	185 \pm 1.67	0.54
VLDL-C	37.4 \pm 0.48	37.1 \pm 0.33	0.54
LDL-C	112 \pm 2.2	102.1 \pm 0.61	0.0001*
TC/HDL-C	4.6 \pm 0.12	4.3 \pm 0.04	0.004*

*indicates significant p values (<0.05)

Table 3 Biochemical Parameters categorized by patients' glycemic control (HbA1c)

Glycated Hemoglobin (HbA1c)			
Parameter	≤ 7.0 (n=48)	>7.0 (n=65)	P-value
Age	53.3 \pm 1.2	54.4 \pm 0.9	0.5
FBS	121.1 \pm 1.3	179 \pm 1.7	0.0001*
TC	177 \pm 0.75	190.5 \pm 1.3	0.0001*
HDL-C	41.9 \pm 0.72	42 \pm 0.6	0.9
TG	171.1 \pm 0.9	197.5 \pm 0.8	0.0001*
VLDL	34.2 \pm 0.18	39.5 \pm 0.16	0.0001*
LDL	101 \pm 1.03	108.9 \pm 1.41	0.0001*
TC/HDL-C	4.2 \pm 0.07	4.5 \pm 0.07	0.005*

*indicates significant p values (<0.05)

Discussion

In the present study the pattern of lipid profile parameters in diabetic subjects and its correlation with HbA1c was investigated. The levels of HbA1c and FBS did not differ significantly between male and female. This shows that FBS and HbA1c have no sex predilection. There was no significant difference in TAG and HDL-C and VLDL-C levels between male and female but the levels of TC and LDL-C and risk ratio (TC/HDL-C) were significantly higher in female as compared to male type 2 diabetic patients. This finding has also been reported in previous studies [14][15][16]. Hyperlipidemia in females may be due to the effects of sex hormones on body fat distribution, which leads to differences in lipoproteins levels [17].

HbA1c was significantly correlated with FBS, TC, VLDL, LDL and risk ratio (TC/HDL) as described in table 1. This study reveals high prevalence of hypercholesterolemia, hypertriglyceridemia, high LDL-C and low HDL-C levels present in the studied population. These are the known risk factors for development of

cardiovascular disease. Insulin which is deficient in diabetes, affects the liver apolipoprotein production. It regulates the enzymatic activity of lipoprotein lipase (LpL) and Cholesterol ester transport protein. A decrease in insulin causes inactivation of LpL leading to hypertriglyceridemia and subsequently hypercholesterolemia. These factors cause dyslipidemia in Diabetes mellitus [18]. Moreover, insulin deficiency reduces the activity of hepatic lipase and several steps in the production of biologically active LpL may be altered in DM. In our study the main disorder in lipid metabolism was hypertriglyceridemia and hypercholesterolemia.

A highly significant difference was found between HbA1c and FBG in our study which was similar to many other previous studies [19][20]. Also, significant difference between two groups divided by the levels of HbA1c (<7% and >7%) was found with respect to the level of TC, TG, VLDL, LDL and risk ratio for CAD (TC/HDL-C). The Diabetes complications and control trial (DCCT) established HbA1c as the gold standard of glycemic control [21]. The level of HbA1c value

$\leq 7.0\%$ was said to be appropriate for reducing the risk of cardiovascular complications. Hence the logic of dividing groups with HbA1c cutoff of 7.0% . The diabetic patients with HbA1c value $> 7.0\%$ exhibited a significant increase in TC, LDL-C, TG, TC/HDL-C ratio, without any significant alteration in HDL-C in comparison to other group. Severity of dyslipidemia increased in patients with increasing HbA1c value. So HbA1c can act as a marker of dyslipidemia. Elevated HbA1c is an independent risk factor of CVD other than dyslipidemia, so that diabetic patients with elevated HbA1c and dyslipidemia can be considered as a very high-risk group for CVD. Improving glycaemic control can substantially reduce the risk of cardiovascular events in diabetics hence the need of glycated haemoglobin measurement.

Conclusion

Significant difference of lipid parameters in two groups ($\leq 7.0\%$ and $> 7.0\%$) of glycated hemoglobin indicates that HbA1c can be used as a marker for predicting dyslipidemia in type 2 diabetic patients.

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