Association between level of HbA1c and lipid profile in T2DM patients attending diabetic OPD at BPKIHS

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Abstract

Hyperglycemia, dyslipidemia and coronary artery disease relate well with each other in type 2 diabetes and it has been proposed that higher prevalence of cardiovascular disease in type 2 diabetes is due to chronic uncontrolled hyperglycemia. Our study aimed to find utility of Hba1c as indicator of dyslipidemia in patients with type 2 diabetes mellitus. We enrolled 168 T2DM patients in our study and collected venous blood samples in both plain and EDTA vials after a fast of minimum 8 hours. Biochemical analysis was done in fully automated analyzer cobas c311. HbA1c was found to have significant positive correlation with total cholesterol, LDL-C, and triglyceride and significant negative correlation with HDL-C and HDL/LDL ratio. The mean value of TC, LDL-C and TG was found to be lower in patients with good glycemic control than those with poor glycemic control. But, mean value of HDL and HDL/LDL ratios were found to be higher in patients with good glycemic control than those with poor glycemic control. These differences were significant at the level of $p < 0.05$. Our study suggests additional use of HbA1c as indicator of dyslipidemia.

Key words: T2DM, HbA1c, Lipid profile, Nepal.

Introduction

Type 2 diabetes mellitus is a complex condition, combination of resistance to the actions of insulin in liver and muscle together with impaired pancreatic β cell function leading to relative insulin deficiency[1]. According to IDF diabetes atlas 2014, worldwide diabetes has caused 2.9 million deaths in 2014. One person in every 12 across the globe has this disease and surprisingly one in two persons do not know that they have it[2]. No wonder diabetes is called “Silent Killer”. There is a higher risk of cardiovascular disease in people with type 2

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diabetes, these patients have more than two-fold increased risk for cardiovascular death compared with persons without diabetes[3]. Dyslipidemia, which is one of the most important risk factors for coronary artery disease, is more prevalent among adults with type 2 diabetes mellitus than in the general population with a four to six fold greater cardiovascular mortality[4]. Typical pattern of diabetic dyslipidemia include an abnormally high level of triglycerides (TG), a high proportion of small dense low density lipoprotein cholesterol (LDL), low high density lipoprotein cholesterol (HDL), and postprandial lipemia[5-7]. The higher prevalence of lipid abnormalities in diabetes mellitus has been attributed to insulin resistance or deficiency that affects key enzymes and pathways in lipid metabolism[8]. So, hyperglycemia, dyslipidemia and coronary artery disease relate well with each other in type 2 diabetes and it has been proposed that higher prevalence of cardiovascular disease in type 2 diabetes is due to chronic uncontrolled hyperglycemia[9,10] and hence strict control of hyperglycemia and dyslipidemia can be preventive. Studies have suggested HbA1c to be an independent risk factor for coronary heart disease[11] and stroke and it has also been seen that risk of cardiovascular disease increases by 18% with every 1% increase in value of HbA1c in diabetic[12]. Also, it has been calculated that a reduction of 0.2% in the value of HbA1c reduces mortality due to cardiovascular events by 10%[13]. In a country like Nepal where a significant number of people belong to below poverty line group and are unable to take the blood tests as frequently as advised, using HbA1c as a dual marker i.e. marker for hyperglycemia and dyslipidemia would be of much help while treating patients. It should be understood that HbA1c cannot replace the utility of lipid profile, but if presence of certain correlation is discovered between the two, HbA1c could be considered for early determination of dyslipidemia and hence could help in assessing CVS risk. Hence this study was undertaken to observe correlation of HbA1c with lipid profile in Nepalese population.

Methods

This study was a cross sectional study conducted in the department of biochemistry with collaboration of the department of internal medicine at B.P. Koirala Institute of Health Sciences, Dharan, Nepal for duration of one year. A total of 168 consecutive patients attending endocrinology OPD either diagnosed as type 2 diabetic as per American Diabetes Association guidelines 2013 or already taking treatment for type 2 diabetes were enrolled in the study. Dyslipidemia was defined as per the National Cholesterol Education Programme (NCEP) Adult

Treatment Panel (ATP) III guidelines. The patients were included irrespective of duration of disease. Patients having severe anaemia, taking statins for dyslipidemia, having any metabolic instability, any type of cutaneous or systemic infection, any CVS or renal complications and not intending to take part in the study were excluded. The ethical clearance was taken from the institutional ethical review board and informed consent was taken from the participants. Blood samples were collected after a minimum of 8 hrs of fasting. Venous blood was collected into two vials, 3ml blood in plain vial and 2ml in potassium-EDTA vial. Blood samples in plain vial were allowed to clot and were centrifuged at 3000rpm for 5 minutes to separate the serum. Different parameters of lipid profile viz TC, HDL-C, LDL-C, TG were measured in serum and HbA1C in whole blood by preparing haemolysate. Analysis was done in fully automated closed system-Roche/Hitachi cobas c 311. Data were in entered in Microsoft Excel 2007 and analysed using spss 20.

Normally distributed data has been presented as mean and standard deviation and non parametric data as median and inter quartile range. Pearson correlation test has been used to find correlation between parametric data and spearman rho test for non parametric data. Comparison of means has been done by student's t test in parametric data with two groups. Comparison of median values has been done by Mann Whitney U test in non parametric data with two groups. P value less than 0.05 has been considered significant.

Results

This study is a cross-sectional study involving 168 type 2 diabetic patients. The correlation of long term glycemic control represented by HbA1C has been found out with parameters of lipid profile viz. TC, HDL-C, LDL-C and TG. Out of 168 patients, there were 91 females and 77 males. The means±SD of age, TC, HDL-C, LDL-C, HDL/LDL ratio and HbA1C of patients were 52.2±11.9 years, 182.9±41.9 mg/dl, 41.6±8 mg/dl, and 94.9±20 mg/dl, 0.47±0.18 and 6.5±1.5 % respectively. The median of TG was 152.5 (109, 195) mg/dl. The differences in the levels of these parameters among male and female patients were calculated but were not found to be significant.

Table 1: Biochemical parameters in males and females

	Male (77)	**Female (91)**	**'p' value**
AGE (years)	52.7±11.9	51.84±12.1	0.64[a]
TC (mg/dl)	176.3±42.4	188.4±41	0.06[a]

HDL (mg/dl)	40.9±9.2	42.1±6.9	0.32[a]
LDL (mg/dl)	95.1±19.8	94.7±20.3	0.9[a]
HDL/LDL	0.4±0.1	0.5±0.1	0.8[a]
HbA1C (%)	6.5±1.4	6.5±1.3	0.98[a]
TG (mg/dl)	130 (99, 179)	167 (124, 217)	0.05[b]
Hs-CRP (mg/dl)	1.6 (1.0, 2.8)	2.0 (0.9, 2.7)	0.33[b]
[a]Independent t test [b]Man whitney U test			

We classified dyslipidemia according to NCEP ATP III guidelines and found out that hypercholestrolemia, hypertriglyceridemia and increased LDL-C was seen in 36%, 50% and 33% of subjects respectively. Level of HDL-C was low in 47% of females and 16% of males. Also, 63% of patients had good glycemic control as suggested by HbA1c level <7%. HbA1c was found to have significant positive correlation with TC(r=0.257, <0.01), LDL (r=0.785, <0.01), and TG (r=0.272, <0.01) and significant negative correlation with HDL (r= -0.897, <0.01) and HDL/LDL ratio (r= -0.690, <0.01).

Table 2: Correlation of HbA1c with S.lipid profile

	TC[a]	**HDL[a]**	**LDL[a]**	**HDL/LDL[a]**	**Triglycerides[b]**
HbA1C[a]	0.257* p <0.01	-0.897* p <0.01	0.785* p <0.01	-0.690* p <0.01	0.272* p <0.01

[a]Pearson's correlation, [b]Spearman rho correlation.

* Correlation is significant at 0.01 level.

To see the utility of HbA1c as a marker of dyslipidemia, we divided subjects into two groups, good and poor glycemic control groups depending upon the levels of HbA1c as <7% and >7% respectively. The mean value of TC, LDL and TG was found to be lower in patients with good glycemic control than those with poor glycemic control. But, mean value of HDL and HDL/LDL ratios was found to be higher in patients with good glycemic control than those with poor glycemic control. These differences were significant at the level of p <0.05 (Table 3)

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Table 3: Comparison of lipid profile between subjects with good and poor glycemic control

HbA1c	<7	≥7	'p' value
TC[a] (mg/dl)	5.15±40.5	196.16±41.5	<0.01*
HDL[a] (mg/dl)	46.3±4.9	33.5±5.4	<0.01*
LDL[a] (mg/dl)	84.8±8.2	112.2±22.3	<0.01*
HDL/LDL[a]	0.55±0.11	0.33±0.19	<0.01*
Triglycerides[b] (mg/dl)	149 (106,182)	172 (119,233)	0.03ǂ

[a] Independent t-test , [b] Mann Whitney U test.

* Significant at level of p=0.01

ǂ Significant at the level of p=0.05

Discussion

This is a cross sectional study conducted with the aim to find out whether there is any association of glycemic control with the CVS risk factor, dyslipidemia in the individuals suffering from Type 2 Diabetes. We have also attempted to look into the pattern of dyslipidemia in our patients. Among the different parameters of dyslipidemia, hypertriglyceridemia came out to be the commonest one. Though there have been differences in the level of lipids among males and females, they were not statistically significant. Females have been found to have higher levels of total cholesterol, triglyceride and HDL-C which is in agreement with many studies[14-17].

It has been proposed that dyslipidemia is more prevalent among adults with type 2 diabetes mellitus than in the general population[4], and also that the composition of lipid particles in diabetic dyslipidemia is more atherogenic than other types of dyslipidemia[18]. This means that even normal lipid concentrations might be more atherogenic in diabetic than in non diabetic people. Also, as HbA1c has been found to be an independent risk factor for coronary heart disease[11] and stroke[12], combination of dyslipidemia and chronic uncontrolled blood sugar can be considered to be associated with higher CVS risk in these patients. As HbA1c level is routinely checked in T2DM patients, the correlation between HbA1c and parameters of lipid profile suggested by this study can be used in early diagnosis of dyslipidemia and treat it on time. Our study showed significant positive correlation of HbA1c with Total cholesterol, LDL-C, and Triglycerides and significant negative correlation with HDL and HDL/LDL ratio. The correlation between HbA1c and LDL-C and HDL-C was found to be strong as suggested by higher values of correlation coefficients

0.785 and -0.897 respectively. Khan et al and various other authors reported similar findings[18,19,20].

The Diabetes complications and control trial (DCCT) has established HbA1c as gold standard for glycemic control and its value ≤7.0% has been said to be associated with reduced risk of cardiovascular complications[21]. We divided subjects into two groups, good and poor glycemic control groups depending upon the levels of HbA1c as <7% and >7% respectively. The mean value of TC, LDL and TG was found to be lower in patients with good glycemic control than those with poor glycemic control. But, mean value of HDL and HDL/LDL ratios was found to be higher in patients with good glycemic control than those with poor glycemic control.

These correlations were significant hence possibility of dyslipidemia in patients with high HbA1c level should not be ignored. American Diabetes Association suggests looking into the HbA1c levels at least bi-annually or quarterly and level of lipids annually in patients with T2DM. As suggested by our study and so many other studies, raised level of HbA1c should be considered as suggestive of dyslipidemia and in such patients lipid profile level should be checked immediately.

Conclusion

Significant correlation of level of HbA1c with parameters of lipid profile suggests utility of HbA1c as a marker of dyslipidemia in addition to chronic hyperglycemia and hence should be analysed accordingly. Our study adds to the existing literature suggesting HbA1c as an indicator for dyslipidemia.

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