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Original Research Article

Study of Association Between Glycated Hemoglobin and Lipid Profile in Type 2 Diabetes Mellitus in Tertiary Care Center

Tilchan Pandey,[a,d] Jivan Khanal,[b,d] Krishna Chandra Godar [c,e]

ABSTRACT:

Introduction: Diabetes is one of the major burdens of non-communicable disease causing morbidity and mortality. Glycated hemoglobin (HbA1c) has been used as a tool to monitor glycemic control in patients with type 2 diabetes mellitus and elevated HbA1c value is considered an independent risk factor for dyslipidemia. **Methods:** A total of 120 patients with type 2 diabetes mellitus were enrolled in this cross-sectional study. Means with standard deviation were used for age, height, weight and fasting blood sugar and Pearson correlation test was applied to identify correlation between Glycated hemoglobin (HbA1c) and lipid profile. Comparison of means was done by Student 't' test in parametric data within the two groups. P value less than 0.05 was considered significant. **Results:** The mean HbA1c of male and female patients were 8.35±1.77 and 8.65±1.95 respectively. Among patients with good glycemic control, mean total cholesterol and mean high density lipoprotein were higher than poor glycemic control patients. Patients with poor glycemic control had higher mean triglyceride and low density lipoprotein than good glycemic control patients. Correlation coefficient for various components of lipid profile and HbA1c were: total cholesterol (r=0.189, p=0.038, n=120), triglyceride (r=0.418, p<0.01, n=120), low density lipoprotein (r=0.673,p<0.01,n=120) and high density lipoprotein (r=-0.683,p<0.01, n=120). **Conclusion:** There was a significant moderate correlation between HbA1c and lipid profile. Lipid profile values were significantly higher in poor glycemic control than good glycemic control patients. Hence, HbA1c can be considered as a surrogate marker for dyslipidemia in type 2 DM patients.

Key words: Diabetes Mellitus, Glycated Hemoglobin, Lipid profile

INTRODUCTION:

Diabetes Mellitus (DM) is an endocrine disorder with high blood sugar level with disturbances of carbohydrate, lipid and protein metabolism resulting from variable degree of insulin resistance and deficiency or both.[1] Abnormalities of lipid profiles in diabetic patients often termed "diabetic dyslipidemia", is characterized by high total cholesterol (TC), high triglycerides (TG), low high-density lipoprotein cholesterol (HDL-C), increased levels of low density lipoprotein (LDL) particles and increased levels of very low density lipoprotein choleserol (VLDL-C).[2]

Glycated hemoglobin (HbA1c) shows the average plasma glucose over previous eight to twelve weeks and has been used as a tool to monitor glycemic control in patients with type 2 diabetes mellitus. An HbA1c of ≥6.5% is recommended by American Diabetic Association as the cut-off point

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a- Lecturer, Department of Internal Medicine,
b- Associate Professor, Department of Internal Medicine,
c- Consultant Physician,
d- Lumbini Medical College and Teaching Hospital, Palpa, Nepal.
e- Crimson Hospital, Manigram, Rupandehi, Nepal.

Corresponding Author:
Dr. Tilchan Pandey
e-mail: tilchan_pandey@yahoo.com
ORCID: https://orcid.org/0000-0002-0682-4516

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for diagnosis of diabetes mellitus.[3]

Elevated HbA1c is an independent risk factor for dyslipidemia and coronary artery disease. It has also been seen that 18% Cardiovascular Disease (CVD) risk increase with every 1% increase in value of HbA1c in diabetic.[4] It has been suggested that a reduction of 0.2% in the value of HbA1c reduces mortality due to cardiovascular events by 10%. Studies done in the past have shown significant positive correlation of HbA1c with TC, LDL-C, and TG and significant negative correlation with HDL. The correlation between HbA1c and LDL and HDL were found to be strong as suggested by higher values of correlation coefficients 0.785 and -0.897 respectively.[5]

The aim of this study was to assess the relationship between HbA1c and serum lipid profile in type 2 Diabetic mellitus patients.

METHODS:

This was a cross sectional study conducted at Lumbini Medical College and Teaching hospital, Palpa in the department of Internal medicine from May 2019 to November 2019. The study was approved by Institutional Review Committee (IRC) and written consent was obtained from all the patients.

All patients aged > 30 years with a known diagnosis or newly diagnosed with Type 2 Diabetes mellitus as per American Diabetic Association (ADA) criteria[3] were included in the study. Necessary demographic, clinical and laboratory parameters like age, sex, diabetes, height, weight, blood sugar fasting and postprandial and various lipid profiles data were collected as in a preformed questionnaire through guided interview.

Following participants were excluded from this study:

Patients with known diagnosis of type-1 Diabetes mellitus, hypothyroidism, chronic renal failure, nephrotic syndrome, familial hypercholesteremia, cholestatic jaundice, alcohol consumption, patient on lipid lowering drugs for some other indications, beta blockers or thiazide diuretics, paraneoplastic syndrome, anemic patients and obese patients. Samples were collected from patients attending outpatient department and stable indoor patients from department of Internal medicine. Cases were enrolled into study through purposive sampling.

Sample size calculation:

From the previous study, correlation coefficient between HbA1c and lipid profiles (TC) was found to be 0.257(r).[4,5] With the help of this r value sample size was calculated using standard sample size calculation formula where alpha value 0.05 and beta value 0.2 were taken. The standard normal deviate for $\alpha = Z_{\alpha} = 1.960$, The standard normal deviate for $\beta = Z_{\beta} = 0.842$, $C = 0.5 * \ln[(1+r)/(1-r)] = 0.263$ total sample size $N= [(Z_{\alpha +} Z_{\beta)}/C]^2+3=117$

Technique of sample collection:

Venous blood was collected into two vials, three milliliter blood in plain vial and two milliliter blood in potassium-EDTA vial. Fasting blood sugar was labeled as per fasting for eight hours and post prandial blood sugar was assessed two hours after food intake. Glucose oxidase-peroxidase (GOD-POD) method was applied to measure fasting blood sugar and Nycocard Reader was used to estimate the glycated hemoglobin (HbA1c). Venous Blood sample was allowed to clot at room temperature in plain test tube and the serum was separated. Serum lipids (Triglyceride-TG, total Cholesterol-TC, and High-density lipoprotein cholesterol-HDL-C) measured directly and the value of Low-density lipoprotein cholesterol LDL-C was calculated using the Friedewald's formula.[6] All these parameters were analyzed using a fully automated chemistry analyzer (Siemens AdviaCentuar 1800) and ready-to-use reagent kits according to the manufacturer's instructions (Siemens Diagnostics, Germany). Interpretation of lipid profile value was done as per national cholesterol education program-Adult treatment panel III (NCEP-ATPII). According to these guidelines' recommendation normal, desirable, borderline and high-risk level of total cholesterol (TC) was defined as up to <200mg/dl, up to 200 mg/dl, 200-239mg/dl and >240mg/dl respectively. Triglyceride (TG) value up to 149 mg/dl, 150-199 mg/dl, 200-499 mg/dl and >500 mg/dl was defined as optimal normal, borderline, high and very high-risk level TG respectively. Low density lipoprotein (LDL) level was defined optimal risk when <100 mg/dl, near optimal 100-129 mg/dl, borderline high 130-159 mg/dl, high 160-189 mg/dl and very high >190 mg/dl respectively and low risk HDL as >60 mg/dl and high-risk level <40 mg/dl.[7] Optimal glycemic target was considered when FBS≤130mg/

dl and PPBS≤180mg/dl and uncontrolled DM when it was greater than the optimal target value.Glycemic status was divided into two groups; Good Glycemic Control (GGC) if HbA1c<7% and Poor Glycemic Control (PGC) if HbA1c ≥ 7% as per ADA criteria. [3]

For collecting the sample, this study used the structure questionnaires covering the age, gender, height, weight, Body Mass Index (BMI), Fasting Blood Sugar (FBS), Postprandial (PP), and lipid profile of patients. With this evidence, we collected 120 samples for this study. Data was analyzed with Statistical Package for Social Sciences (SPSS™) software version 16.

Normally distributed data were presented as mean and standard deviation. Pearson correlation test was done to identify the correlation between parametric data. Comparison of means was done by Student 't' test in parametric data with two groups. A p value less than 0.05 was considered significant.

RESULT:

In our study, there were a total of 120 patients. Age of the patients ranged from 30 to 90 years and more than half were older than 60 years. Demographic parameters are shown in Table 1. There was no statistically significant difference in age, height, weight, BMI, FBS, PPBS and HbA1c between the two genders.

Table 1. Demographic and clinical data in different genders.

Characteristics	Male Patient (n=66)	Female Patient (n=54)	
	Mean ± SD	Mean ± SD	P-value
Age	57.77 ± 16.13	61.89 ±15.46	0.556
Body Mass Index	22.32 ± 4.07	22.23 ± 5.45	0.910
Fasting Blood Sugar	153.40 ± 36.78	161.16 ± 42.21	0.291
Postprandial Blood Sugar	202.59 ± 54.49	218.66 ± 57.91	0.123
HbA_{1c}	8.35 ± 1.77	8.65 ± 1.95	0.374

A total of 96 (80%) patients had poor glycemic control (Table 2).

Table 2. Frequency and mean of poor glycemic control patients in different gender.

	N	%	Mean ± SD
HbA_{1c} ≥ 7%	96	80	9.05 ± 1.65
HbA_{1c} ≥ 7(male)	56	58.3	8.72 ± 1.66
HbA_{1c} ≥ 7(female)	40	41.7	9.50 ± 1.53

Among patients with uncontrolled DM, uncontrolled FBS was in 84 (70%) and uncontrolled PPBS in 69 (57.5%) patients. Their mean fasting and postprandial blood sugars were 170.87±39.42 and 229.98±54.36 mg% respectively. Lipid profile levels in DM patients are described in Table 3.

Table 3. Lipid profile level in DM patients.

	Cholesterol	TG	LDL	HDL
Optimal			28 (23.3%)	
Desirable	22 (18.3%)	13 (10.8%)	39 (32.5%)	1 (0.8%)
Borderline	8 (6.7%)	53 (44%)	17 (14.2%)	69 (57.5%)
High	90 (75%)	54(45%)	36 (30%)	50 (41.7%)
Total	120	120	120	120

Among poor glycemic control patients, mean serum value of TG, LDL were statistically significantly higher and mean HDL was statistically significantly lower (Table 4).

Table 4. Mean of lipid profiles among good and poor control DM patients.

	HBA1c		P value
	<7%	≥7%	
Total Cholesterol	281.21 ± 84.53	264.51 ± 70.74	0.322
TG	177.33 ± 12.25	215.26 ± 76.78	<0.01
LDL	103.04 ± 23.55	152.74 ± 56.02	<0.01
HDL	51.71 ± 3.91	44.36 ± 6.94	<0.01

Among various lipid profile, LDL cholesterol had moderate positive correlation and HDL cholesterol had moderate negative correlation with HBA1c values (Table 5).

Table 5. Correlations of HbA1c to lipid profile level.

		Total Cholesterol	TG	LDL	HDL
HbA1c	Correlation (r)	0.189	0.418	0.673	-0.683
	P-value	0.038	<0.01	<0.01	<0.01

Table 6. Lipid profiles correlation between male and female.

Variables	Male	P-Value	Female	P-Value
	Correlation		Correlation	
TG	0.36	0.003	0.49	<0.001
LDL	0.64	<0.001	0.70	<0.001
HDL	-0.58	<0.001	-0.83	<0.001
TC	0.24	0.051	0.13	0.34

Among various lipid profile in males, LDL cholesterol had moderate positive correlation whereas HDL cholesterol had moderated negative correlation. Among females, LDL had high positive correlation and HDL had high negative correlation (Table 6).

DISCUSSION:

The percentage of diabetic patients has increased from 19.04% in 2002 to 25.9% in 2009 in Nepal and is continuously growing ever since. A survey conducted in urban Nepal between 2001 and 2002 showed that the ratio of Male: Female diabetics were 1.56:1.[8] Our study with type 2 DM revealed male to female ratio of 1.22:1

The mean age of type 2 DM patients were 57.77±16.13 and 61.89±15.46 years for male and female respectively. A study done by Hussain et al.[4] showed mean age of 51.71±11.70 years for male and 50.97±10.23 years for female. Another study by Baranwal et al.[5] had nearly equal number of participants as ours and depicted mean age of male and female patients to be 52.7±11.9 and 51.84±12.1 years respectively thus revealing that more elderly people with type 2 DM visited our hospital. Presence of various risk factors, change in life style, poor dietary intake, low physical exercise may be an explanation for these observed differences.[9,10,11] With this realization an appropriate intervention to avoid or minimize these unhealthy behaviors is essential and warranted.

Most of our patients had poor glycemic control (n=96, 80%). Majority of them were male patients and mean HbA1c among poor glycemic control patients was 9.05±1.65 (Table 2). This result was supported by various other studies but many of these studies showed disagreement with gender preponderance.[4,5,6]

More than 80% patients had high TC, TG with low HDL. Similarly, 44.2% had high LDL levels. These findings were also supported by some studies.[2,5] Meanwhile, we also found that there was an increase mean TG, LDL and decrease in HDL levels in poor glycemic control than good glycemic control patients. The study by Alzahrani et al. revealed partial agreement with our study where there was raised TG level in high HbA1c group.[12]

We also studied the relationship of HbA1c with different lipid parameters. HbA1c showed significant positive relationship with TG (r=0.418, p<0.01) and LDL (r=0.64, p<0.01) and significant negative correlation with HDL (r=-0.683, p<0.01).

We observed a positive significant correlation between HbA1c with TC, LDL, and TG and a significant negative correlation of HbA1c with HDL. These findings are valid with regards to the metabolic effect of hyperglycemia and deficiency of insulin on various lipid parameters. Various studies done by many authors have mixed results of HbA1c with various lipids profile components.[2,4,5,6] These mixed findings were due to the differences in life style, genetic factors, behavioral and environmental factors.[14,15,16] Thus, measures to change unhealthy life style, promoting good and healthy diet, reducing body weight and performing regular physical exercise to improve or control diabetic dyslipidemia is mandatory.[17,18,19]

The present study is not without limitations. The study was done on a small sample size. Impact

of patients' dietary habits, lifestyle, regular physical activity/exercise, time and duration since diagnosis of DM were not determined in this study.

CONCLUSION:

There was a significant moderate correlation between HbA1c and various components of lipid profile in type 2 DM patients. Lipid profile values were significantly higher in poor glycemic control and uncontrolled DM patients. Thus, HbA1c can be considered as a surrogate marker of dyslipidemia control in type 2 DM patients.

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