Original Research Article

Glycated hemoglobin as a marker of dyslipidemia in type II Diabetic patients

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ABSTRACT

Background: *Diabetes is an important public health problem and leading cause of cardiovascular problems its early detection and good glycemic control can reduce the complications associated with the disease.*

Objective: *This was a prospective study planned to evaluate the relationship of glycated haemoglobin (HbA1c) and lipid profile in type II diabetic Punjabi male population.*

Material and methods: *A total of 200 diabetes type II patient ranging from age group of 30 to 70 years were included in the study after taking a preinformed written consent. The glycated haemoglobin (HbA1c) & lipid profile were performed on fully automated analyzers. The statistical analysis was done by using SPSS statistics and correlation among HbA1c and lipid profile of type II Diabetic patients was established.*

Results: *The mean HbA1c was in the range of 7.54 ± 1.24%. There were 61% subjects with high total cholesterol (TC) levels and 96% were with raised LDL levels. The 68% of the subjects were having lower HDL level. HbA1c demonstrated significant positive relationship with total cholesterol, TC (r=0.995), triglyceride, TG (r=0.997), high density lipoprotein cholesterol, HDL-C (r=-0.940) and with low density lipoprotein cholesterol, LDL-C (r=0.993).*

Conclusion: *The study concluded that HbA1c apart from acting as important diagnostic marker for glycemic control can also be used as a positive predictor of dyslipidemia in type 2 diabetics.*

Keywords: *HbA1c, diabetes mellitus, glycemic control, lipid profile, dyslipidemia*

Introduction

Diabetes Mellitus (DM), often referred to as diabetes—is a condition in which the body either does not produce enough insulin, or does not properly respond to insulin. [1] The prevalence of type 2 diabetes is increasing at an alarming rate. Current projections suggest that the absolute number of cases worldwide may double over the next two decades. [2] DM has become an important public health problem worldwide, [3-5] which is estimated to be the third most challenging disease threatening public health after malignant tumors and cardiocerebral vascular diseases. [6] It is now the leading cause of cardiovascular, renal and other serious comorbidities not only in old but also young adult. [7-9] and estimated global number of individuals with diabetes will double from 171 million in 2000 to 366 million in 2030 among adults aged ≥20 years. [10] The global prevalence of diabetes in adults (20-79 years old) according to a report published in 2013 by the IDF was 8.3% (382 million people), with 14 million more men than women (198 million men *vs* 184 million women), the majority between the ages 40 and 59 years and the number is expected to rise beyond 592 million by 2035 with a 10.1% global prevalence. With 175 million cases still undiagnosed, the number of people

currently suffering from diabetes exceeds half a billion. [11] There are two major types of Diabetes type 1 and type 2. [12,13] Type 2 diabetes is the commonest form of diabetes and is characterized by disorders of insulin secretion and insulin resistance. [14] Early detection and intervention in diabetes is now considered one of the most important public health agendas. Strict control of blood sugar remains the pivot in the decreased incidence of complications. [1] Good glycemic control is essential in preventing diabetic complications. [15]

Early detection and intervention in diabetes is now considered one of the most important public health agendas. Strict control of blood sugar remains the pivot in the decreased incidence of complications. Good glycemic control is essential in preventing diabetic complications. [1,15] Fasting plasma glucose (FPG) is a simple, easy, inexpensive, and widely available to general population and has been most frequently used to identify subjects at high risk of diabetes. [16] The 2-h plasma glucose after oral glucose tolerance test (OGTT) is also useful to identify subjects of impaired glucose tolerance.

The level of glycated hemoglobin (HbA1c) provides a measure of the glycemic control of diabetes patients during the previous 2–3 months. [17] (HbA1c), an indirect measure of mean blood glucose, does not require fasting, and is more reproducible than FPG. [16] Glycated hemoglobin should be measured in all individuals with DM during their initial evaluation and as part of their comprehensive diabetes care. [18] It is the primary predictor of long-term complications of DM. [19] Measuring glycated hemoglobin, the "gold standard" method for assessing glycemic control, is therefore fixed firmly in the sights of the clinical target setters. [20]

Due to the recent advancement of HbA1c measurement, the American Diabetes Association (ADA) report in 2009[21] advocated that, the diagnosis of diabetes may be conveniently based on HbA1c≥6.5%.Diabetes is defined according to the 2010 American Diabetes Association (ADA) criteria : FPG≥7.0 mmol/l, HbA1c values ≥6.5%, or both, or treatment by oral antidiabetic drugs or insulin. [22] The advantages of using HbA1c to diagnose diabetes include greater convenience and preanalytical stability, lower CV (3.6%) compared to FPG (5.7%) and 2h OGTT (16.6%), stronger correlation with microvascular complications especially retinopathy, and a marker for glycemic control and glycation of proteins which is the direct link between diagnosis of diabetes and its complications.[23-28] The advantages of using HbA1c to diagnose diabetes include greater convenience and preanalytical stability, lower CV (3.6%) compared to FPG (5.7%) and 2h OGTT (16.6%), stronger correlation with microvascular complications especially retinopathy, and a marker for glycemic control and glycation of proteins which is the direct link between diagnosis of diabetes and its complications. [23-28]

The abnormalities like insulin resistance, hyperinsulinemia, hyperglycemia, dyslipidemia, and hypertension in type 2 diabetics tend to cluster and are often referred to as the "metabolic syndrome. [29] Elements of the metabolic syndrome are strong risk factors for cardiovascular disease. [30,31] An early intervention to normalize circulating lipids has been shown to reduce cardiovascular complications and mortality.[32] Estimated risk of CVD has

shown to be increased by 18% for each 1% increase in absolute HbA1c value in diabetic population. [33]

Classification of Lipid Levels from the National Cholesterol Education Program Expert Panel [34]

Level(mg/dl)	Classification
Total Cholesterol	
<200	Desirable
200-239	Borderline high
≥240	High
TG	
<150	Normal
150-199	Borderline high
200-499	High
>500	Very high
LDL-C	
<100	Optimal
100-129	Near or above optimal
130-159	Borderline high
160-189	High
>190	Very high
HDL-C	
<40	Low
>60	High
VLDL	
<30	Normal

HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride; VLDL-C, very-low-density lipoprotein cholesterol

Thus the aim of the study was to correlate the elevated glycated hemoglobin levels with presence of dyslipidemia in known diabetic patients.

Materials and Methods

The present study was conducted in the Department of Biochemistry in Punjab Institute of Medical Sciences, Jalandhar. About 200 male patients with type II Diabetes participated in the study. A preinformed written consent was taken from all the patients. The Lipid Profile -total cholesterol (TChol), high density lipoprotein (HDL-c), Triglycerides (TG) and Glycated haemoglobin (HbA1c) of each subject was measured on fully automated biochemistry analyzer. The low density lipoprotein (LDL) was calculated by using Friedewald formula: LDL= TChol – (TG/5) - HDL.

Measurement of parameters

- Total Cholesterol (TChol) was estimated in serum by CHOD-PAP: enzymatic photometric test method (Diaysis) on BS400 fully automated analyzer.
- Triglycerides (TG) were estimated in serum by Enzymatic Colorimetric Method (Diaysis) onBS400 fully automated analyzer.
- High density lipoproteins (HDL-C) was estimated in serum by HDL-C Immuno FS (fluid stable) Method (Diaysis) onBS400 fully automated analyzer.
- Low density lipoproteins (LDL-C) was calculated by friedwald's formula. LDL-C was not calculated for samples having TG >400 mg/dl.
- Glycated hemoglobin HbA1c was estimated in whole blood (EDTA) by particle enhanced Immunoturbidimetric test Method (Diaysis) onBS400 fully automated analyzer.

The statistical analysis was done and correlation among HbA1c and lipid profile of type II Diabetic patients was established by Pearsons's correlation test and SPSS ver.21.

Results

The mean age of the patients was 48.6± 10.9 years, HbA1c levels had a mean of 7.56±1.25%, total cholesterol, triglycerides,

high density lipoprotein and low density lipoprotein were 210.4±16.4 mg/dl, 162.3 ± 16.9 mg/dl, 36.5 ± 6.5 mg/dl and 122.1 ± 10.9 mg/dl and respectively. Diabetes was defined as per American Diabetes Association (ADA) criteria. Results shows that 60% type 2 diabetics in this study had hypercholesterolemia, 56% Hypertriglyceridemia, 96% abnormal LDL levels and 68% of them the HDL was less than 40 mg/dl (Table 1).

Table 1: Mean ± SD of HbA1c & lipid profile of type 2 diabetics

Variables	Mean
Age (years)	48.6± 10.9 years
HbA1C (%)	7.56±1.25%
TChol (mg/dl)	210.4±16.4
TG (mg/dl)	162.3 ± 16.9
LDL-C (mg/dl)	122.1 ± 10.9
HDL-C(mg/dl)	36.5 ± 6.5

Further, it was concluded that glycated hemoglobin (HbA1c) was positively and significantly related with lipid profile i.e. total cholesterol (r=0.995), high density lipoproteins (r=-0.940), triglycerides (r= 0.997) and very low density lipoproteins (r=0.993).

Table 2. Correlation: HbA1c

T. Cholesterol	**r- value**	**0.995**
	p- value	**< 0.001**
TG	**r- value**	**0.997**
	p- value	**< 0.001**
LDL	**r- value**	**0.993**
	p- value	**< 0.001**
HDL	**r- value**	**-0.940**
	p- value	**< 0.001**

HbA1c-glycated haemoglobin, TC- total cholesterol, HDL- high density lipoproteins, LDL-low density lipoproteins, VLDL- very low density lipoproteins, TG- triglycerides

Discussion

This study has compared the lipid profile (TChol, TG, LDL-C and HDL-C) with glycated haemoglobin in type II Diabetic Punjabi males. The presence of dyslipidemia is evident with Diabetes. It is known that among patients with diabetes, physicians focus more on antihyperglycemic treatment, although blood pressure and lipid control are more effective in affecting patient-related end points.[35] In SHIELD (Study to Help Improve Early evaluation and management of risk factors Leading to Diabetes), a community-based population survey conducted in the United States, a multivariate analysis of self-reported data from 22,001 patients showed that dyslipidemia was independently associated with a higher likelihood of type 2 diabetes diagnosis (odds ratio, 3.95; *P* <0.0001). [36] Our study has also shown a positive correlation of dyslipidemia with total cholesterol(r=0.995), triglyceride (r=0.997) and LDL-C (r=0.993).The p value is statistically significant indicating that they act as positive predictor of dyslipidemia. The dyslipidemia becomes more evident as the levels of HbA1c increase i.e. lesser the control of glycemia higher is dyslipidemia In the UKPDS, a multivariate analysis found that LDL-C was the strongest independent predictor of CVD, followed by HDL-C, while modestly elevated TG levels did not predict CVD events, [37] helping to justify current national guidelines advocating LDL-C < 100 mg/dL as the primary target for the management of dyslipidemia in patients with type 2 diabetes. Serum TG levels are a surrogate for TG-rich lipoproteins (eg, VLDL-C), and non-HDL-C (LDL-C + VLDL-C or TC - HDL-C) reflects the concentration of cholesterol within lipoprotein particles considered atherogenic. [38,39] However in

our study HDL-C showed a negative correlation with the dyslipidemia (r=-0.940) acting as a protective marker for CVD (p<0.001) Khan et et al. [40] reported the impact of glycemic control on various lipid parameters and observed the significant alterations in all lipid parameters except LDL-C with regard to glycemic control. The severity of dyslipidemia increases in patients with higher HbA1c value. Elevated levels of HbA1c and dyslipidemia are independent risk factors of cardiovascular diseases and hence, diabetic patients with elevated HbA1c and dyslipidemia considered as high risk group for cardiovascular disease. Improving glycemic control can reduce the risk of cardiovascular events in diabetes. [41]

In this present study we have been able to significantly correlate HbA1c and various lipid parameters, higher mean values of lipid parameters and glycated hemoglobin indicates that HbA1c is an important tool for monitoring dyslipidemia in diabetic patients so that timely intervention with life style modifications or lipid lowering drugs can be started.

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