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Research Article

Glycated Hemoglobin as a Dual Marker: In Control of Glycemic Status and Diabetic Dyslipidemia

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ABSTRACT

Diabetes mellitus is associated with hyperglycemia and patients at an increased risk of cardiovascular disease. The present study was to evaluate the diagnostic value of Glycated hemoglobin (HbA1c) in predicting diabetic dyslipidemia. Clinically diagnosed cases of type 2 Diabetes Mellitus patients were included in the study with the age limit of 25-75 years. Out of which 28 diabetic patients with good glycemic control were included under Group A and 32 diabetic patients with poor glycemic control were included under Group B. Age and sex matched 60 male subjects are taken as control group. HbA1c demonstrate the positive and significant correlation with total cholesterol, triglycerides, LDLc, Non HDLc and a negative correlation with HDLc. There is also a good correlation between HbA1c and lipid ratios (TC/HDLc, LDLc/HDLc ratios). Poorly controlled diabetic patients (HbA1c value >7.0%) had a significant higher value of TC/HDLc and LDLc/HDLc as compared to the good glycemic controlled diabetic patients (HbA1c value <7.0%).Thus HbA1c can be used as a potential dual marker of glycemic control and dyslipidemia in type 2 diabetes mellitus.

Keywords: Diabetes mellitus, Glycated hemoglobin, lipid ratios.

INTRODUCTION

Diabetes is a global endemic with rapidly increasing prevalence in both developed and developing countries (1). DM is a group of metabolic disease characterised by hyperglycaemia resulting from defects in insulin secretion, insulin action or both (2). Uncontrolled diabetic patients are characterised by hyperglycemia, hyper insulinemia, protein glycation and oxidative stress which causes early appearance of diabetic complications (3).The chronic hyperglycaemia is associated with dysfunction, long-term damage and failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels (2).

People with type 2 Diabetes have a high risk of cardiovascular diseases (CVD). Diabetic patients often exhibit an atherogenic lipid profile, which greatly increases their CVD risk. However most of the individuals may also carry unnoticed dyslipidemia, characterised by increased levels of triglycerides and LDL and decreased HDL (1).

Glycated hemoglobin (HbA1c) is a routinely used marker for long-term glycemic control (1). The glycemic status of diabetic subjects can be assessed by HbA1c which is now regarded as an independent risk factor for cardiovascular events (2).Estimated risk of CVD has shown to be increased by 15-18% for each 1% increase in absolute HbA1c value in diabetic population (4). Positive relationship is demonstrated between HbA1c and CVD in non diabetic patients with normal range of HbA1c (5). The aim of the study is to evaluate the HbA1c as a marker of glycemic control and lipid profile.

METHODS

The study was conducted at SRM Medical College Hospital and Research centre, SRM Nagar, Potheri. The study was approved by ethical committee. 60 male clinically diagnosed cases of type 2 Diabetes Mellitus patients were included in the study with the age limit of 25-75 years. Out of which 28 diabetic patients with good glycemic control were included under Group A and 32 diabetic patients with poor glycemic control were included under Group B. Age and sex matched 60 male subjects are taken as control group.

Venous blood was collected from the subjects after an overnight or 12 hours of fasting samples were analyzed for fasting blood glucose, lipid profile and glycated haemoglobin.

Diabetes was defined as per American Diabetes Association (ADA) criteria (6). For serum lipid reference level, National Cholesterol Education Programme (NCEP) Adult Treatment Panel III (ATP III) guideline was referred (7).

STATISTICAL ANALYSIS

Data analysis was done using student t-test. Probability ($p<0.05$) were defined as significant.

RESULTS

Results of our study shows that HbA1c demonstrate the positive and significant correlation with total cholesterol, triglycerides, LDLc, Non HDLc and a negative correlation with HDLc. There is also a good correlation between HbA1c and lipid ratios (TC/HDLc, LDLc/HDLc ratios). Poorly controlled diabetic patients (HbA1c value >7.0%) had a significant higher value of TC/HDLc and LDLc/HDLc as compared to the good glycemic controlled

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Table : 1 Comparison of base line parameters between type 2 diabetes mellitus patients and control groups and the statistical significance of the differences

	Category	N	Mean	Std. Deviation	P-value
HbA1c	Control	60	5.732	0.443	<0.0001***
	Patient	60	9.675	2.466	
FBS	Control	60	94.98	8.73	<0.0001***
	Patient	60	198.35	60.78	

Table : 2: Comparison of lipid profile between type 2 diabetes mellitus patients and control groups and the statistical significance of the differences.

	Category	N	Mean	Std. Deviation	P-value
	Control	60	39.43	7.47	
TC	Patient	60	35.78	8.36	0.01*
LDLc	Control	60	163	26.75	0.000***
	Control	60	102	23.11	
HDLc	Patient	60	120	40.55	0.002*
	Control	60	93.92	32.29	
TGL	Patient	60	179.77	91.39	0.001*
	Control	60	4.0	0.99	
TCc/HDLc	Patient	60	5.4	1.71	<0.001**
	Control	60	2.5	0.81	
LDLc/HDLc	Patient	60	3.45	1.33	0.002*
	Control	60	121	25.69	
Non HDLc	Patient	60	155	45.65	0.000***

*** - *Extremely significant*
** - *Highly significant*
* - *Significant*
NS - *Not significant*

diabetic patients (HbA1c value <7.0%).Thus HbA1c can be used as a potential dual marker of glycemic control and dyslipidemia in type 2 diabetes mellitus.

DISCUSSION

In the present study we have estimated the diagnostic value of HbA1c. Diagnosis of diabetes rests on the measurement of plasma glucose levels. According to ADA FBS>126mg/dl is diagnostic value of diabetes (6).In our study the FBS increased significantly when compared control group and patients (Table:1). The diabetic patients with poor glycemic control had significantly higher FBS as compared to patients with good glycemic control as seen in (Table:3). Glycated hemoglobin (HbA1c) is a routinely used marker for long-term glycemic control. Studies have reported that HbA1c predicts the risk for the development of diabetic complications in diabetic patients. Elevated HbA1c levels have been regarded as an independent risk factor for CVD in subjects with or without diabetes (2). This study reveals that levels of HbA1c in diabetic patients are high in patient group when compared to the control group which was statistically significant p<0.0001.

This study also reveals high prevalence of hypercholesterolemia, hypertriglyceridimia, high LDLc, low HDLc and increased Non HDLc levels in DM patients which are well known risk factors for CVD (Table: 2). Type 2 diabetes mellitus is commonly associated with an abnormal lipoprotein phenotype which is characterised by increased TAG, decreased HDLc and an accumulation of small dense LDLc particles [(The so called atherogenic dyslipidemic phenotype)] (8). Our study also showed a significant increase in TC/HDLc and LDLc/HDLc ratios between control and patient groups and also in between controlled and uncontrolled diabetic group. An increased CAD risk was suggested due to the increase in total cholesterol/ HDLc ratio (9). Metabolic reasons for lower HDLc levels have not been fully documented. Decreased synthesis of HDLc has been found in one small study. Schmitt et.al; suggested that LDLc uptake by fibroblasts may be impaired in diabetic patients. This leads to increase in the LDLc/ HDLc ratio in type 2 diabetes(10). LDLc/ HDLc is actually a purer ratio than TC/ HDLc, because LDLc is a measure of good cholesterol, where as total cholesterol is the sum of HDL, LDL and VLDL. Non-HDL seems to be a better choice, as it includes triglyceride rich lipoproteins, which plays an important role in atherogenesis in type 2 diabetes (11).

A highly significant correlation between HbA1c and FBG is observed in our study which is similar to various studies (12). We also observed a significant correlation between HbA1c and TC/ HDLc and LDLc/ HDLc (Table: 4). Several investigations have reported significant correlation between HbA1c and lipid profile and suggested the importance of glycemic control in normalising dyslipidemia (13). Our study also showed a significant correlation between HbA1c and Non-HDLc. Non-HDLc was shown to be the stronger predictor of CVD in diabetic population (2&10).

The diabetes complications and control trial (DCCT)

Table: 3: Comparison of MEAN±SD of measured parameters between good controlled diabetic patients and poorly controlled diabetic patients.

	Category	N	Mean	SD	P-value
	Group A HbA1c<7%	28	146	17.55	
	Group B HbA1c>7%	32	246.5	45.36	<0.0001***
FBS					
TC/HDLc	Group A HbA1c<7%	28	4.4493	1.5971	
	Group B HbA1c>7%	32	6.3228	1.2890	<0.001**
LDL/HDLc	Group A HbA1c<7%	28	2.64	1.16	
	Group B HbA1c>7%	32	4.18	1.01	<0.001**
Non HDLc	Group A HbA1c<7%	28	129	41.58	
	Group B HbA1c>7%	32	178	40.49	<0.0001***

established HbA1c as the gold standard to assess glycemic control. As elevated HbA1c and dyslipidemia are independent risk factors of CVD, diabetic patients with elevated HbA1c and dyslipidemia can be considered as a very high risk group for CVD. Improving glycemic control can substantially reduce the risk of cardiovascular events in diabetics. It has been estimated that reducing HbA1c levels by 0.2% could lower the mortality by 10% (2).

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