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Correlation between Glycosylated Haemoglobin and serum lipid profile in patients with type 2 diabetes

Dr Deepthi Rao Gorukanti

Associate Professor, Department of General Medicine, Surabhi Institute of Medical Sciences, Mittapally village, Siddipet MDL & Dist, Telangana State

Dr Vallakoti Rajneesh

Assistant Professor, Department of General Medicine, Surabhi Institute of Medical Sciences, Mittapally village, Siddipet MDL & Dist, Telangana State

Dr P Shyam Prasad

Assistant Professor, Department of Orthopaedics, RIMS, Adilabad

Dr Ch Karunakar

Professor, Department of Medicine Surabhi Institute of Medical sciences, Mittapally village, Siddipet MDL & Dist, Telangana State
Corresponding Author: Dr Ch Karunakar

Abstract--Introduction: Dyslipidaemia is one of the major risk factor for cardiovascular disease in Type 2 Diabetes mellitus, characterized by elevated Total cholesterol (TC), Triglycerides (TG), Low density lipoprotein (LDL) and decreased High density lipoprotein (HDL). Haemoglobin A1c (HbA1c) is widely used as an index of mean glycaemia, a measure of risk for the development of diabetes complications and a measure of the quality of diabetes care. The aim of this study was to determine the impact of glycaemic control on lipid profile and to know utility of HbA1c as an indirect indicator of dyslipidaemia. Objectives: To assess the relationship between glycemic control (HbA1c) and serum lipid profile as well as to evaluate the importance of HbA1c as an indicator of dyslipidemia in patients with T2DM. Materials and Methods: The present study is a prospective, observational study which is conducted in the Department of General Medicine at Surabhi Institute of Medical Sciences over a period of 6 months. A total of 65 T2DM patients with dyslipidemia who had visited the hospital. Inclusion criteria: Adults aged above 30 years and having Type 2 Diabetes Mellitus with dyslipidaemia. Exclusion Criteria: Patients suffering from CVD, renal disorders, thyroid disorders, other endocrinopathies and patient who

had type 1 diabetes and those taking lipid-lowering agents were excluded from the study. Data insufficient of any patients. Results: In our study, among 65 Type 2 diabetic individuals, 42 were male and 23 were female. Distribution of Glucose Triad results of FBS, PPBS and HbA1c levels of patients presented as Mean \pm SD, mean FBS was 163.64 \pm 36.46 mg/dl, mean PPBS was 226.37 \pm 73.74 mg/dl and mean HbA1c was 7.85 \pm 0.74%. Mean total cholesterol was 193.64 \pm 14.65 mg/dl, mean total triglyceride was 231.64 \pm 15.64 mg/dl, mean LDL was 112.67 \pm 5.88 mg/dl, Mean HDL was 34.65 \pm 5.65 mg/dl. In our study, HbA1c positively and significantly correlated with total cholesterol (r=0.209), LDL (r=0.274), HbA1c negatively and significantly correlated with HDL (r= - 0.121), and did not show any correlation with VLDL (r=0.027) and total triglycerides (r=0.023). Conclusion: Due to the strong correlation with lipid profile, HbA1c could be the ideal marker for predicting dyslipidaemia in type 2 DM. Patients with higher HbA1c value and dyslipidaemia should be considered as a very high-risk group for CVD.

Keywords---Diabetes mellitus, Dyslipidemia, Glycosylated hemoglobin.

Introduction

Type 2 diabetes mellitus is a group of metabolic disorder that is characterized by hyperglycaemia resulting from insulin resistance and/or relative insulin deficiency. [1] Diabetes is associated with a greater risk of morbidity and mortality from cardiovascular disease (CVD). Serum lipids are frequently abnormal and are likely to contribute to the risk of coronary artery disease. [2] Worsening of glycaemic control deteriorates lipid and lipoprotein abnormalities and particularly of diabetes mellitus. [3]

The American Diabetes study (ADA) has designated HbA1c level of <7% as a goal of optimal blood glucose control [4] and the American Association of Clinical Endocrinologist has further recommended HbA1c level of <6.5%. [5] Criteria for abnormal lipid profiles were based on the ADA criteria, Hypercholesterolemia refers to a total cholesterol level \geq 200 mg/dl, Hypertriglyceridemia refers to a level is \geq 150 mg/dl, HDL was considered low when the level is < 40 mg/dl in males and < 50 mg/dl in females, LDL was considered high when the level is \geq 100 mg/dl. Dyslipidaemia was defined as the presence of one or more of the previous abnormalities in serum lipids. [6]

HbA1c is formed by the condensation of glucose with the N-terminal Valine residue of each β -chain of HbA to form an unstable Schiff-base, which is the most widely used biomarker for long-term glycaemic status, as well as an independent risk factor for coronary heart disease (CHD) and stroke. [7] Elevated cholesterol levels, are believed to be a major factor in promoting atherosclerosis, it is now recognized that triglycerides are an independent risk factor. Atherosclerosis is characterized by the deposition of cholesterol and cholesterol esters from the plasma lipoproteins into the artery wall. Diseases in which prolonged elevated

levels of VLDL, IDL, chylomicron remnants, or LDL occur in the blood (diabetes mellitus). The liver and many extra-hepatic tissues express the LDL (apo B-100) receptor. It is useful for atherogenic risk assessment in dysglycemic patients. [8]

HDL is synthesized and secreted from both liver and intestine. However, apo C and apo E are synthesized in the liver and transferred from liver HDL to intestine HDL, when the latter enters the plasma. Non-HDL is a simple, readily available, no-cost test obtained with the usual lipid profile and reflects the atherogenic risk in diabetic patients with hypertriglyceridemia and can conveniently measure CVD risk. [9] The aim of this study was to examine impact of glycaemic control on the lipid profile of type 2 diabetic patients, and to know importance of HbA1c as an indirect indicator of dyslipidaemia.

Material and Methods

The present is a prospective and observational study was conducted in the Department of General Medicine at Surabhi Institute of Medical Sciences over a period of 6 months. A total of 65 T2DM patients with dyslipidemia who had visited the hospital were selected for the present study.

Inclusion criteria: Adults aged above 30 years and having Type 2 Diabetes Mellitus with dyslipidaemia. Family history of patients with dyslipidaemia and hypertriglyceridemia.

Exclusion Criteria

Patients suffering from CVD, renal disorders, thyroid disorders, other endocrinopathies and patient who had type 1 diabetes and those taking lipid-lowering agents were excluded from the study. Data insufficient of any patients.

Patients with an established diagnosis of T2DM were selected according to the American Diabetes Association criteria established. These criteria set the following as values that are indicative of T2DM: HbA1C $\geq 6.5\%$, FPG ≥ 126 mg/dl, 2-hours plasma glucose ≥ 200 mg/dl during an oral glucose tolerance test (OGTT), or random plasma glucose ≥ 200 mg/dl with symptomatology. [10]

Biochemical data such as FPG, HbA1c, and lipid profile, along with age and gender, were also taken. All patients' anthropometric measurements (weight, height and BMI), blood pressure and laboratory results, including HbA1c levels, TC levels, TG levels, LDL-C levels and HDL-C levels, were collected. For all DM patients, blood samples were collected between 8:00 and 10:00 AM (12–14 h fasting), and plasma was used for estimating the glucose level. The FPG, and HbA1c and lipid profile levels were determined. We characterized the participants' glycaemic control as poor (HbA1c $>7\%$) or good (HbA1c $<7\%$). [11]

Statistical Analysis

The data was analysed with SPSS version 25.0. The mean, SD and correlation (Pearson's) test was used to interpret the results. Correlation coefficient (r) $\geq +1$ is taken as positive correlation, ≤ -1 is taken as negative correlation and between -1 and $+1$ as no correlation. Correlation (Pearson's) test was used to

interpret the result.

Result

In our study, among 65 Type 2 diabetic individuals included in this study, 42 were male and 23 were female.

Table 1
Sex Distribution of study population

	Total	Males	Females
No. of patients	65	42	23
Percentage	100	64.6	35.4
Chi-Square test p=value	0.264		

Table 2
Distribution of Glucose Triad

Parameters	Mean \pm SD
FBS (mg/dl)	163.64 \pm 36.46
PPBS (mg/dl)	226.37 \pm 73.74
HbA1C (%)	7.85 \pm 0.74

In table 2, distribution of Glucose Triad results of FBS, PPBS and HbA1c levels of patients presented as Mean \pm SD, mean FBS was 163.64 \pm 36.46 mg/dl, mean PPBS was 226.37 \pm 73.74 mg/dl and mean HbA1c was 7.85 \pm 0.74 %.

Table 3
Distribution of Lipid Profile and HbA1c

Lipid Profile	Mean \pm SD (mg/dl)
Total Cholesterol	193.64 \pm 14.65
Triglycerides	231.64 \pm 15.64
HDL	34.65 \pm 5.65
LDL	112.67 \pm 5.88
VLDL	46.32 \pm 3.12

In table 3, Mean total cholesterol was 193.64 \pm 14.65 mg/dl, mean total triglyceride was 231.64 \pm 15.64 mg/dl, mean LDL was 112.67 \pm 5.88 mg/dl, Mean HDL was 34.65 \pm 5.65 mg/dl.

Table 4
Biochemical parameters of type 2 diabetes mellitus patients with glycated haemoglobin ≥ 7 and glycated haemoglobin < 7

Parameters	Glycated Haemoglobin (HbA1c)		p - value
	< 7 (n=29)	≥ 7 (41)	
FBS	153.58 \pm 36.75	172.46 \pm 43.75	0.002
Total cholesterol	183.75 \pm 14.38	193.48 \pm 15.83	0.041
Triglycerides	193.63 \pm 12.73	247.84 \pm 16.39	0.004
Mean HDL	34.84 \pm 4.17	35.84 \pm 4.83	0.037
Mean LDL	107.74 \pm 6.74	121.74 \pm 6.95	0.085

Table 5
Correlation analysis between serum Lipid profile and HbA1c

Parameters	Correlation coefficient (r)	p - value
Total cholesterol-HbA1c	0.209	0.024
Triglyceride-HbA1c	0.023	0.364
HDL-HbA1c	- 0.121	0.039
LDL-HbA1c	0.274	0.049
VLDL-HbA1c	0.027	0.635

In our study table 5, HbA1c positively and significantly correlated with total cholesterol ($r=0.209$), LDL ($r=0.274$), HbA1c negatively and significantly correlated with HDL ($r= - 0.121$), and did not show any show correlation with VLDL ($r=0.027$) and total triglycerides ($r=0.023$).

Discussion

The present study to evaluated the pattern of lipid profile parameters in type 2 diabetic patients with and its correlation with HbA1c. This study shows high prevalence of hypertriglyceridemia, high LDL- C, hypercholesterolemia and low HDL-C levels in type 2 diabetic patients. These are well known risk factors of cardiovascular diseases. Insulin affects liver apolipoprotein production. It regulates the enzymatic activity of lipoprotein lipase (LPL) and cholesterol ester transport protein. All these factor are likely cause of dyslipidaemia in DM. [12-15] In this study, most significant abnormal value of lipid profile was hypertriglyceridemia. Similar finding was shown by Regmi P et al [16] and Mahato RV et al. [17]

This study shows highly significant correlation between HbA1c and FBG which is similar to studies done by Ito C et al [18], Ko GT et al [19] and Rosediani et al. [20] This study also found significant correlation between HbA1c and TC, LDL- C as reported by Er ciyas F et al [21], Thambiah GE et al [22] in their studies.

The diabetes complications and control trial (DCCT) considered HbA1c as the gold standard of glycaemic control. The target HbA1c value for reducing cardiovascular complication was $\leq 7.0\%$. In this study, we classified diabetic patients in 2 groups

as per the HbA1c cut off of 7.0%. The patients with HbA1C value >7.0% showed significant increase in TC, LDL -C, TG and VLDL without any significant change in HDL-C in comparison to patients with HbA1c ≤7.0%. It is suggested that insulin resistance has a central role in the development of diabetic dyslipidemia. One of the causes is increased free fatty acid release from insulin-resistant fat cells. If the glycogen stores are adequate, these free fatty acids promote TG production which further stimulates Apolipoprotein (Apo-B) and very low-density lipoprotein. The apolipoprotein regulates the enzymatic activity of lipoprotein lipase (LpL) and Cholesterol ester transport protein. [23]

Khan HA et al [24] showed the impact of glycaemic control on various lipid parameters. Though there was no significant differences in LDL-C with regard to glycaemic control, alterations in other lipid parameters were statistically significant. Thus, this study suggests that severity of dyslipidaemia increases with higher HbA1c value and diabetic patients with increased HbA1c and dyslipidaemia should be considered as very high risk group for cardiovascular disease (CVD). Therefore, we should focus on improving glycaemic control which can essentially reduce the risk of cardiovascular events in diabetics. [25] It has been considered that reduction in HbA1c level by 0.2% could lower the cardiovascular mortality by 10%. [26]

In T2DM subjects, insulin resistance is considered the cause of dyslipidemia. The reasons for increased TG levels in T2DM patients is an inadequate secretion or function of insulin that causes enhanced hepatic secretion of very low-density lipoprotein (VLDL) along with the late removal of TG-rich lipoproteins, mainly due to enhanced substrate levels for TG synthesis. [27]

Conclusion

A significant correlation exists between HbA1c and lipid profile. Better glycemic control reflected by HbA1c would also reflect better lipidemic state. Achieving the target HbA1c will contribute in improving the lipid state, and hence may lessen the diabetic complications in type 2 diabetic patients. HbA1c can be used as an indicator of glycemic control as well as a predictor of dyslipidaemia in T2DM patients.

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