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Correlation of Hemoglobin A1C Levels with Serum Lipid Profile in Patients with Type 2 Diabetes Mellitus.

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ABSTRACT

Uncontrolled hyperglycaemia of diabetes mellitus results in impaired lipid metabolism. A case-control study was conducted on 50 known type 2 diabetic patients (T2DM) and 50 age and gender matched healthy control to evaluate the role of glycated hemoglobin (HbA1c) in predicting diabetic dyslipidemia. The variation in mean values of fasting blood sugar (FBS), HbA1c, total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL) and high density lipoprotein (HDL) among Group A, Group B and Healthy controls was highly significant, p <0.001 and that of very low density lipoprotein (VLDL) was significant, p <0.05. The difference in mean values of serum lipid profile in Group A and Group B was statistically highly significance, p <0.001, except for HDL which was statistically significant, p <0.05. In T2DM patients with poor glycemic control (Group B), the correlation between HbA1C and TC, VLDL and FBS was highly significant (p <0.001) and with LDL, TG and HDL it was significant (p <0.05). The correlation was insignificant (p >0.05) in T2DM patients with good glycemic control (Group A). Hence, HbA1c can be used as a potential biomarker for predicting dyslipidemia in T2DM patients.

Keywords: Diabetes Mellitus, Dyslipidemia, Glycated haemoglobin, Lipid profile

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INTRODUCTION

Diabetes mellitus (DM) is the most common endocrine disease affecting mankind since ages. DM is a potential epidemic in India with more than 62 million individuals currently diagnosed with the disease [1,2]. Diabetes causes about 5% of all deaths globally each year. The chronic hyperglycemia of diabetes is associated with long term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, and blood vessels [3,4]

Epidemiological studies have demonstrated that diabetes mellitus is an independent risk factor for cardiovascular disease (CVD) and it amplifies the effect of other common risk factors such as smoking, hypertension and dyslipidemia [5].

Atherogenic dyslipidemia (diabetic dyslipidaemia) is characterized by three lipoprotein abnormalities *viz* elevated very low density lipoprotein(VLDL), small LDL particles, and low high density lipoprotein(HDL) cholesterol also known as "the lipid triad" [6]. The most common alteration of lipoprotein being hypertriglyceridemia (TG) caused by an elevation in VLDL concentration. All these lipid abnormalities lead to microvascular and macro vascular disease [7]. An early intervention to normalize circulating lipids has shown to reduce cardiovascular complications and mortality [8,9].

Glycated Hemoglobin (HbA1C) reflects the glycemic control of a patient during the 6-8 week period before the sample was obtained. The amount of HbA1C correlates well with fasting and postprandial blood glucose levels. The level of HbA1C value 7% is said to be appropriate for reducing the risk of cardiovascular complications [10]. Apart from classical risks factors like dyslipidemia, HbA1C has now been regarded as independent risk factor for CVD in subjects with or without DM. HbA1C predicts the risk of developing diabetic complications. Each one percent increase in absolute HbA1C is associated with 18% increase in CVD [11]. Hence, the study was conducted to find out the association between glycemic control (HbA1C as a marker) and serum lipid profile in type 2 diabetic (T2DM) patients and evaluate the importance of HbA1C as an indicator of dyslipidemia in type 2 diabetic patients.

MATERIALS AND METHODS

A case-control study was conducted in the Department of Physiology and Diabetic clinic of a tertiary care teaching hospital over period of two years from April 2012 to April 2014. The Institutional Ethics Committee clearance was obtained prior to starting the study. The study group comprised of 50 T2DM patients attending the Diabetic clinic in the age group of 30 to 70 years with at least five years of disease duration. The diagnosis of T2DM was made in patients with blood glucose level of >126mg/dL estimated after overnight fasting of at least eight hours. The control group comprised of 50 age and gender matched healthy individuals attending the master health check at hospital. T2DM patients with hypertension, chronic alcoholism, pregnancy and gestational DM, renal diseases, liver diseases, acute and chronic inflammatory diseases and malignancy were excluded from the study. In all the subjects, after taking informed consent, a detailed history and clinical examination was done. Subjects fulfilling the above mentioned criteria were included in the study. Fasting blood sample of about 6ml was collected from all the subjects and fasting blood glucose, serum lipid profile and HbA1C were analysed. Serum was used for biochemical analysis for lipid profile panel test which included serum total cholesterol (TC), TG, HDL, LDL and VLDL. LDL and VLDL were calculated parameters whereas TG, TC and HDL were measured parameters. LDL is estimated by Friedwald formula (1972), LDL = TC-HDL-TG/5 and VLDL was calculated by the formula, TG/5. Study subjects were again divided into two groups *viz* Group A with good glycemic control (HbA1C levels < 8%) and Group B with poor glycemic control (HbA1C levels > 8%).

The results were analysed using Statistical Package for Social sciences (SPSS) 19.0 version. Quantitative variables were expressed as the mean and standard deviation and qualitative as percentages. Comparison of mean of different variables between two groups was performed using Student's unpaired't' test. Comparison of mean of variables between all three groups was assessed by using one way ANOVA test. The strength of association between HbA1C and lipid parameters was assessed by calculating r value (Pearson's correlation coefficient). A p value <0.05 was considered as significant whereas < 0.001 was considered as highly significant.

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RESULTS

Among patients with T2DM, 17 patients were in Group A and 33 were in group B. The mean age in Group A, Group B and healthy controls was 52±12.64, 51.18±9.98 and 49.26±11.8 years respectively. The age and gender distribution was comparable in all the groups (Table 1). The variation in mean values of FBS, HbA1C, TC, TG, LDL and HDL among Group A, Group B and Healthy controls was highly significant, p <0.001 and that of VLDL was significant, p <0.05 (Table 2). The difference in mean values of serum lipid parameters in Group A and Group B was statistically highly significance, p <0.001, except for HDL which was statistically significant, p <0.05 (Table 2). In T2DM patients with poor glycemic control (Group B), the correlation between HbA1C and TC, VLDL and FBS was highly significant (p <0.001) and correlation with LDL, TG and HDL was significant (p <0.05). The correlation was insignificant (p >0.05) in T2DM patients with good glycemic control (Group A) (Table 3).

Table 1: Age and gender wise distribution of Type 2 Diabetes Mellitus (T2DM) and healthy control groups

Age (Years)	Gender				Total	
	Female		Male		T2DM	Control
	T2DM	Control	T2DM	Control		
31-40	1	2	5	5	6	7
41-50	5	3	15	16	20	19
51-60	2	4	11	10	13	14
>60	5	4	6	6	11	10
Total	**13**	**13**	**37**	**37**	**50**	**50**

Table 2: Comparison of mean values of variables in Type 2 Diabetes Mellitus (T2DM) and healthy control groups

Sl. No	Variables	T2DM			Healthy Control	F	$p^{\dagger}$
		Group A	Group B	p^*			
1	FBS	149.99 ± 6.58	207.02 ± 43.74	>0.05	100.74 ± 18.04	140.321	<0.001
2	HbA1c	7.36 ± 0.42	9.60 ± 0.99	NA	5.53 ± 1.45	116.337	<0.001
3	TC	214.24±31.95	255.97±28.08	<0.001	156.66±27.83	122.387	<0.001
4	TG	141.24±39.24	192.74±48.23	<0.001	144.48±37.28	15.494	<0.001
5	LDL	151.90± 31.28	185.66 ± 24.56	<0.001	95.20 ± 27.29	114.500	<0.001
6	VLDL	25.82±7.8	38.10 ± 11.75	<0.001	45.34 ± 22.98	7.672	<0.05
7	HDL	36.18±2.71	32.83±4.02	<0.05	47.84±22.86	9.117	<0.001

Note: FBS, Fasting blood sugar; HbA1c, Glycated hemoglobin A1c; HDL, High density lipoprotein; LDL, low density lipoprotein; TC, Total cholesterol; TG, Triglycerides; VLDL, Very low density lipoprotein. * p value for Student Unpaired 't' test, † p value for ANOVA

Table 3: Correlation of HbA1c values with lipid parameters and FBS in Group A and Group B Type 2 Diabetes Mellitus patients

Sl. No.	Group A			Group B		
	Parameters	r value	p value	Parameters	r value	p value
1	FBS	0.379	>0.1	FBS	0.554	<0.001
2	TC	-0.079	>0.1	TC	0.558	<0.001
3	TG	0.189	>0.1	TG	0.494	<0.01
4	LDL	-0.0003	>0.1	LDL	0.494	<0.01
5	VLDL	0.358	>0.1	VLDL	0.554	<0.001
6	HDL	-0.250	>0.1	HDL	-0.464	<0.01

Note: FBS, Fasting blood sugar; HbA1c, Glycated hemoglobin A1c; HDL, High density lipoprotein; LDL, low density lipoprotein; TC, Total cholesterol; TG, Triglycerides; VLDL, Very low density lipoprotein

DISCUSSION

T2DM is a well-known risk factor for the development of cardiovascular disease, cerebrovascular disease and peripheral vascular disease. Alterations in lipid and lipoprotein profile contribute to atherosclerosis in T2DM [5]. In the present study, hypercholesterolemia, hypertriglyceridemia, high LDL and low HDL has been demonstrated in patients with T2DM when compared to healthy controls. Similar findings

have been reported in various research studies like CARE, VAHIT and DIGAMI study [12]. The development of dyslipidemia in T2DM can be attributed to role of insulin in production of lipoprotein in the liver. Insulin regulates the enzymatic activity of lipoprotein lipase (LPL) and cholesterol ester transport protein [13]. Insulin deficiency reduces the hepatic lipase activity and causes defective clearance of LDL. In addition, the composition of LDL is altered in T2DM leading to production of small dense, triglyceride enriched LDL which have increased susceptibility for oxidization and play a major role in atherosclerotic process [14]. Hyperglycemia and insulin resistance together can lead to overproduction of VLDL triglyceride, defective clearance of VLDL triglyceride and decreased production of apolipoprotein B. The composition of VLDL is also altered causing increased propensity for atherosclerosis [14].

In normoglycemic subjects, a carbohydrate moiety is attached to a small proportion of haemoglobin A. Thus creating what is called as glycosylated or glycated haemoglobin. It has three distinct fractions *viz* A1a, A1b and A1c. The A1c fraction accounts for 60% of bound glucose. Non-diabetic individuals have HbA1c values in the range of 3-6% [14]. Similarly, prolonged hyperglycemia in DM leads to non enzymatic glycosylation of LDL particles and collagen fibers resulting in production of a Schiff base and formation of Amadori products. The glycated LDL binds with glycated collagen leading to heavy cholesterol deposition which is the possible first step in the pathogenesis of atherosclerosis leading coronary artery disease [15]. As in the present study, the increased levels of LDL has been correlated significantly with elevated HbA1C levels in T2DM patients with poor glycemic control [15,16]. Therefore, increased HbA1C has been suggested as an indicator of glycation of LDL and subsequent predisposition to atherosclerosis [15]. The present study also demonstrated that the severity of dyslipidemia increases with increased HbA1C values. Hence, good glycemic control through antidiabetic therapy can reduce the risk of atherosclerosis and related complications [17]. A longitudinal intervention study has demonstrated significant reduction in the LDL and Apo B and an increase in HDL and Apo AI in patients with improved glycemic control [16].

CONCLUSION

The diabetes complications and control trial (DCCT) established HbA1C as the gold standard of glycemic control [18]. However, based on our results, it can be concluded that HbA1C can also be utilized for screening high risk diabetic patients for early diagnosis of dyslipidemia and timely intervention with lipid lowering drugs.

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