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A correlative study of HbA_1C and lipid profile parameters among type 2 diabetic population in a rural hospital in puducherry.

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Abstract:
***Background**: Diabetes Mellitus (DM) is characterized by chronic hyperglycemia with disturbances of Carbohydrate, Lipid and Protein metabolism resulting from defects in insulin secretion, insulin action or both. Obesity is an independent risk factor for cardiovascular disease, including coronary artery disease and congestive heart failure, in both men and women. Glycated hemoglobin (HbA_1C) is a routinely used marker for long-term glycemic control. Elevated HbA1c has been regarded as an independent risk factor for coronary heart disease (CHD) and stroke in subjects with or without diabetes.*
***Aim&Objectives:**To evaluate the level of HbA_1C and lipid profile in type 2 diabetes mellitus patients. To find out the correlation between HbA_1C and lipid profile parameters in type 2 diabetic population.*
***Methodology:**This Cross sectional study was conducted among type 2 diabetic patients and control subjects and they were divided into three groups.Group 1- control subjects = 28, Group 2– Type 2 DM with good control = 28 and Group 3– Type 2 DM with poor control = 28.The serum sample was used for the measurement of total Cholesterol, Triglycerides, HDL, LDL and VLDL.Fasting and postprandial (2 hour) blood sugar (FBS & PPBS) were estimated by Glucose Oxidase-Peroxidase (GOD-POD) enzymatic end point method. HbA_1C was estimated by using Ion exchange chromatography (Crest A Coral clinical system, USA). Urine examination was done for benedicts test and proteinuria.Statistical Analysis was done by using SPSS version 75.0.*
***Results**:Our study showed significant correlation between HbA_1C and lipid profile parameters between the two groups (less than 7% and more than 7% of HbA_1C). The results suggested the importance of glycemic control in order to manage dyslipidemia and risk for cardiovascular disorder in type 2 diabetes.*
***Conclusion:**This dual biomarker- HbA_1C, glycemic control as well as lipid profile can be used for screening of high risk patients for early diagnosis of dyslipidemia thereby the cardiovascular and peripheral complications can be prevented by timely intervention of the disease.*

Keywords: *DM,HbA_1C, CHD and Dyslipidemia*.

I. Introduction

Diabetes Mellitus (DM) is characterized by chronic hyperglycemia with disturbances of Carbohydrate, Lipid and Protein metabolism resulting from defects in insulin secretion, insulin action or both[1]. Obesity is becoming a worldwide epidemic. Obesity is an independent risk factor for cardiovascular disease, including coronary artery disease and congestive heart failure, in both men and women[2]. Disorders of lipid metabolism are common and prominent in diabetes, and are important risk factors for the high frequency of atheromatous complications in the disease [3]. Coronary heart disease in diabetic patients is associated with numerous pathological features including hypertension, hyperglycaemia and abnormal glycation of proteins, dyslipidaemia, endothelial dysfunction, microvascular disease autonomic neuropathy and defects in cardiac structure and function[4].

Diabetic dyslipidaemia includes multiple lipoprotein disorders. Most of this account focuses on type 2 diabetes; untreated type 1 diabetes can cause severe hypertriglyceridaemia, but lipid levels are nearly normal in non-obese patients with well-controlled type 1 diabetes [5]. A central feature of the metabolic syndrome is insulin resistance,which results in hyperglycemia and hyperinsulinemia, and eventually leads to the development of diabetes. Central obesity is the most important predisposing factor for insulin resistance[6].Both obesity and the metabolic syndrome are associated with high mortality mainly related to cardiovascular disease[7].Overweight, obesity and metabolic syndrome have recently emerged as strong independent risk factors for chronic kidney disease (CKD) and ESRD[8]. Patients with type 2 diabetes often exhibit an atherogenic lipid profile, which greatly increases their risk of CVD compared with people without

diabetes[9].There is a large body of evidence that GHB (glycatedhaemoglobin) relates to integrated preceding glycemic control and the uses of GHB provides an objective assessment of long term blood sugar control in a single index[10]. The magnitude of the HbA1C as a risk factor for the development of microangiopathy[11]. Glycatedhemoglobin (HbA_1C) is a routinely used marker for long-term glycemic control. In accordance with its function as an indicator for the mean blood glucoselevel, HbA1c predicts the risk for the development of complications in diabeticpatients[12]. Adult haemoglobin is heterogeneous and in addition to unmodified haemoglobin (HbA_0) there are minor components that are more negatively charged-called HbA_{1a}, HbA_{1b} and HbA_{1c} in the order of their elution in ion-exchange chromatography[13]. Rahbar showed, in 1968, that these minor haemoglobins are elevated in diabetes[14].Since these are post-translational modifications formed by the slow non-enzymatic attachment of glucose to haemoglobin over the lifetime of the red cell, the degree of haemoglobin glycation can be used as an index of average glycaemia over the preceding weeks and months[15]. Treatment goals have been set based on the relationship between HbA_1C and complications: the American Diabetes Association recommends the goal of diabetes therapy should be an $HbA_1C<7\%$, and treatment action should be taken when the values are consistently > 8%. As an aid to understanding the clinical meaning of GHb, the relationship between mean plasma glucose concentration and HbA_1C during the DCCT has recently been established: the change in plasma glucose concentration per 1% increase in HbA_1C was approximately 2 mmol/L (35mg/dL). The Diabetes Complications and Control Trial (DCCT) established glycosylated hemoglobin (HbA_1C) as the gold standard of glycemic control, with levels £7% deemed appropriate for reducing the risk of vascular complications[16]. Elevated HbA_1C has been regarded as an independent risk factor for coronary heart disease (CHD)and stroke in subjects with or without diabetes[17]. So, with all the above aspects, the study was undertaken to correlate the glycatedHb and lipid profile in type 2 diabetic population.

II. Materials &Methods

In this cross sectional study, diabetic patients were evaluated and divided into groups.

Group 1 - control subjects = 28,Group 2 – Type 2 DM with good control = 28 and Group 3 – Type 2 DM with poor control = 28.Inclusion Criteria**:** Age 30-60years; Known Type II diabetic patients for -7 years;Glycated hemoglobin (HbA_1C) level less than 7 and on life style modifications, oral diabeticdrugs, insulin or combination of all three, associated with known complications of diabetesmellitus. eg. diabetic nephropathy, diabetic retinopathy, heart disease, and diabetic neuropathy.Exclusion Criteria: Type 1 diabetes mellitus, known type 2 diabetic for more than 7 years, pregnancy, liver disorders and infectious diseases, Hemolytic anemia, familial dyslipidemia, etc were excluded from our study.Ethical clearance from Institutional ethical committee and research committee was obtained.Assays**:**-Venous blood about 5ml was drawn from each subjects and it was separated into two parts. One portion was collected in an EDTA containing tube for HbA1c measurement and the other part in a non-anticoagulated plain tube for lipid profile.-After centrifugation, the serum sample was used for the measurement of total Cholesterol, Triglycerides, HDL, LDL and VLDL.-Serum lipid profile was measured by enzymatic kid method in fully automated analyzer.-Indirect LDL-cholesterol and Non-HDL Cholesterol (Non HDL-C) were calculated by Friedwald and Frederickson formula.-Fasting and post prandial (2 hour) blood sugar (FBS & PPBS) were estimated by Glucose Oxidase-Peroxidase (GOD-POD) enzymatic end point method.HbA_1C was estimated by using Ion exchange chromatography (Crest A Coral clinicalsystem,USA).Urine examination was done for benedicts test and proteinuria.

Statistical Analysis: Statistical Analysis was done by using SPSS version 75.0.Pearson correlation coefficient was calculated to find the linear relation between HbA1c and lipid profile. T-test, one way ANOVA and post HOC tests were done to analysis the parameters of FBS, PPBS, HbA1c, and lipid profile. $P<0.05$ was considered statistically significant.

III. Results

Table -1; Correlation between the control group and other parameters.

Control	Pearson correlation	BSF	BSPP	TC	TGL	HDL	LDL
HbA1C	r value	0.057	0.063	0.242	0.150	0.033	-0.180
	p value	0.772	0.751	0.214	0.447	0.866	0.359

*. Correlation is significant at the 0.05 level (2-tailed).

Table -2 Correlation between the group-1(HbA1C-<7) and other parameters **.**

Case (<7)	Pearson correlation	BSF	BSPP	TC	TGL	HDL	LDL
HbA1C	r value	-0.107	-0.112	0.717*	-0.252	.162	0.773*
	p value	0.588	0.570	0.0001	0.195	0.410	0.0001

*. Correlation is significant at the 0.05 level (2-tailed).

Table -3 Correlation between the group-2(HbA1C>7) and other parameters .

Case (>7)	Pearson correlation	BSF	BSPP	TC	TGL	HDL	LDL
HbA1C	r value	0.287	0.500*	0.715*	0.418*	0.500*	0.699*
	p value	0.139	0.007	0.0001	0.027	0.007	0.0001

*. Correlation is significant at the 0.05 level (2-tailed).

Table – 4 T-Test (standard deviation between two groups-control and group-1)

	Control Mean±SD	Case (<7) Mean±SD	t value	p value
BSF	89.07±12.13	88.2857±11.34	0.250	0.803
BSPP	120.71±16.76	168.50±20.99	-9.412	0.0001*
HbA1C	5.41±0.63	5.70±0.66	-1.653	0.104
TC	161.75±12.52	195.79±41.08	-4.194	0.0001*
TGL	117.36±21.44	136.82±57.83	-1.670	0.101
HDL	64.57±13.51	62.50±12.97	0.585	0.561
LDL	104.43±17.41	119.75±32.29	-2.210	0.031*

(*highly significant)

Table – 5 T-Test (standard deviation between two groups-control and group-2)

	Control Mean±SD	Case (>7) Mean±SD	t value	p value
BSF	89.07±12.13	124.54±21.68	-7.553	0.0001*
BSPP	120.71±16.76	267.50±49.82	-14.777	0.0001*
HbA1C	5.41±.63	8.74±.98	-15.162	0.0001*
TC	161.75±12.52	231.11±87.76	-4.140	0.0001*
TGL	117.36±21.44	162.11±32.34	-6.102	0.0001*
HDL	64.57±13.51	66.68±14.23	-0.568	0.572
LDL	104.43±17.41	125.25±29.17	-3.243	0.002*

(*highly significant)

Table – 6 One way ANOVA

	Control Mean±SD	Case (<7) Mean±SD	Case (>7) Mean±SD	F value	p value
BSF	89.07±12.13	88.2857±11.34	124.54±21.68	48.289	0.0001*
BSPP	120.71±16.76	168.50±20.99	267.50±49.82	146.974	0.0001*
HbA1C	5.41±0.63	5.70±0.66	8.74±.98	160.281	0.0001*
TC	161.75±12.52	195.79±41.08	231.11±87.76	10.583	0.0001*
TGL	117.36±21.44	136.82±57.83	162.11±32.34	8.720	0.0001*
HDL	64.57±13.51	62.50±12.97	66.68±14.23	.663	0.518
LDL	104.43±17.41	119.75±32.29	125.25±29.17	4.452	0.015*

This one way anova,revealed that except HDL all other parameters were significantly correlated.

IV. Discussion

Despite multiple clinical, electrographic and biochemical characteristics, there are subgroups of patients who progress to severe, life threatening nephropathy and CAD without much symptoms and signs, especially in patients with type 2 DM. who frequently suffer from MI with significantly increased risk of complications[18].

In the present study, diabetic patients were divided into two groups as per the HbA_1C cut-off of 7.0%. Which includes 56 known diabetic patients, the correlation between HbA_1C and lipid profile was estimated. Group-II (More than 7) expressed the significant increase in TC, LDL and TG in correlation with HbA_1C but there is no significant correlation between HbA_1C and HDL (Table-5 Table-6). In group-I, i-e. HbA_1C less than 7, hypercholesterolemia-10 patients (35.71%), hypertriglyceridemie-4patients (14.28%) and hyperlipoproteinemia-increased LDL-10patients (35.71%) (Table-2, Table-4).

In group-II, i.e HbA_1C more than 7, hypercholesterolemia-16 patients (57.14%), hypertriglyceridemia-16 patients (57.14%) and hyperlipoproteinemia-increased LDL-14 patients (50%) (Table-3, Table-5). There was a highly significant correlation between PPBS and HbA_1C in group two (Table-3, Table-5). Type 2 DM is commonly associated with an abnormal lipoprotein phenotype which is characterized by increased triglyceride and decreased HDL and accumulation of small dense LDL particles[19]. In our study also in one way ANOVA, fasting blood glucose is highly significant in group-II (more than 7%) (Table-6).

Measurement of plasma glucose levels gives the diagnosis of diabetes, according to ADA guidelines-FBS-more than 126mg/dl, is diagnostic value of diabetes[20]. In our study also, T test for group-II, more than 7%, indicated FBS increased significantly (Table-5). For long term glycemic control, we used HbA_1C as a routine marker and study shown that HbA_1C predicts the risk for the development of complications in DM. Elevated HbA_1C is also considered as an independent risk factor for CVD in subjects with or without DM[21]. In our study also, group-II HbA_1C was significantly correlated with lipid profile parameters in both T test and one way ANOVA.

Khan HA et al [22] showed the impact of glycaemic control on various lipid parameters in which severity of dyslipidemia increase in patients with higher HbA_1C value. As elevated HbA_1C and dyslipidemia are independent risk factors of CVD, diabetic patients with elevated HbA_1C and dyslipidemia can be considered as a very high risk group for CVD. Improving glycaemic control can substantially reduce the risk of cardiovascular events in diabetics[23]. It has been estimated that reducing the HbA_1C level by 0.2% could lower the mortality by 10%[24]. One African study, constituting 401 type 2 DM patients showed that 35% had increased total cholesterol and one more England study found that 73% had increased total cholesterol, i-e. all are having more than 200 mg/dl. In our study also there was a significant correlation between HbA_1C and total cholesterol in both the groups (Table-6).

Therefore, increased HbA_1C has been suggested as an indicator of glycation of LDL and subsequent predisposition to atherosclerosis. The present study also demonstrated that the severity of dyslipidemia increases with increased HbA_1C values. Hence, good glycemic control through anti diabetic therapy along with life style modifications can reduce the risk of atherosclerosis and related complications.

VI. Conclusion

Our study showed significant correlation between HbA_1C and lipid profile parameters between the two groups (less than 7% and more than 7% of HbA_1C.) The results suggested the importance of glycemic control in order to manage dyslipidemia and risk for cardiovascular disorder in type 2 diabetes. HbA_1C has the ability of predicting serum lipoprotein in both diabetic and non diabetic population irrespective of the gender. The DCCT also established HbA_1C as the gold standard of glycemic control.This dual biomarker- HbA_1C , glycemic control as well as lipid profile indicator can be used for screening of high risk patients for early diagnosis of dyslipidemia and by this,we can prevent and postpone the cardiovascular and peripheral complications by timely intervention of the disease.

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Conflicts of interest: None

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