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A correlative study of HbA1c with lipid profile in Assamese population.

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Abstract
Objective: *The study was conducted to verify the association of HbA1c with lipid profile in a group of Assamese people so as to take precautions from developing future cardiovascular disease(CVD).*
Methods: *HbA1c and individual Lipid parameters and lipid ratios (total cholesterol, triglycerides, HDL, LDL, VLDL, TC/HDL AND LDL/HDL) were estimated in eight nine Type2DM Assamese people with HbA1c ≥ 6.5 % and who had no previous history of CVD to ascertain the pattern of their association between HbA1c and lipid profile, if any.*
Results: *The study proves a significant positive correlation ($p < 0.05$) between HbA1c and TC, LDL, TC/HDL and LDL/HDL and a significant negative correlation ($p < 0.05$) between HbA1c and HDL.*
Conclusion: *The study thus shows that HbA1c and lipid parameters are independent risk factors for CVD. Their correlation at higher values is a significant risk factor for CVD predisposition in Type 2 diabetics.*
Keywords: HbA1c, Total cholesterol(TC), Triglycerides(TG), HDL, LDL, VLDL, TC/HDL, LDL/HDL, Cardiovascular disease(CVD).

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I. Introduction

Diabetes is a worldwide disease. According to the International Diabetic Federation (IDF) 2012 report, Out of 371 million diabetic people worldwide 63 million are Indian which means every sixth person is diabetic[1]. History of diabetes has been vast. Our ancient Indian scriptures have made some vivid illustration as well as description of the disease condition. In ancient Indian scriptures, diabetes was known as *madhumeha*[2]. Diabetes Mellitus (DM) is the diseased condition which is characterized by chronic hyperglycemia with

disturbances of carbohydrate, lipid and protein metabolism, resulting from defects in insulin secretion and or insulin action. Dyslipidemia is a prominent feature of Coronary heart disease in diabetic patients. Other features are hypertension, hyperglycemia and abnormal glycation of proteins, endothelial dysfunction, micro vascular disease autonomic neuropathy and defects in cardiac structure and function[3].

Diagnosis of DM is usually done by fasting plasma glucose(FPG) and Oral glucose tolerance test (OGTT). Use of HbA1c was restricted to monitoring the effect of treatment of diabetes. HbA1c is always considered as a stable indicator of glycaemia for the preceding three months[4]. Its potential utility in diabetic care was first reported in 1985 World Health Organization report[5] and by 2010 all the major expert committee and association across the globe including the American Diabetes Association(ADA) has recommended HbA1c for the diagnosis of Type 2 DM, besides its role in prognosis[6]**.** The Diabetes Complications and Control Trial (DCCT) established glycosylated hemoglobin (HbA1C) as the gold standard of glycemic control, with levels≤ 7% deemed appropriate for reducing the risk of vascular complications.It is found that with the change in plasma glucose concentration per 1% increase in HbA1C is approximately 2 mmol/L(35mg/dL)[7].

Elevated HbA1C has been regarded as an independent risk factor for coronary heart disease (CHD) and stroke in subjects with or without diabetes, like dyslipidemia[8]. So this study was proposed to see for the association of HbA1c and lipid parameters as this risk association is a significant risk factor for CVD. So, with all the above aspects, the study was undertaken to correlate HbA1c and lipid profile in Type 2 diabetic Assameese population. Also such type of study is not conducted in the Assameese population.

II. Materials and methods

The present study was conducted in Department of Biochemistry, Gauhati Medical College and Hospital in collaboration with the Out Patient Department of Endocrinology and Medicine of Gauhati Medical College and Hospital for a period of six months from January 2010 to June 2010.

2.1 Selection of cases

Groups of eighty nine (89) non obese, non-hypertensive patients either sex of recently diagnosed, Type2DM patients in the age group of 20 - 60 were selected for the study that were having HbA1c ≥ 6.5 %. The patients were classified into three groups depending on their glycated hemoglobin (HbA1c); HbA1c < 7.0%, HbA1c≥7.0%< 10.0% and HbA1c ≥ 10.0%. The selected patients had no history of any cardiovascular events and were not on lipid lowering drugs. Alcoholics and subjects with renal disorders, hepatic disorders, Patients with known diagnosis of type-1 DM, Hypothyroidism, Familial

hypercholesteremic syndromes, Hypertensive using beta blockers or thiazide, Diuretics, BMI more than 30 were excluded from the study.

2.2 Selection of Controls

This group consists of normal healthy individual selected randomly among people from different sectors of the society belonging to diverse occupation and socioeconomic status. Among the subjects selected, healthy individuals, of either sex within the age group of 20 and 60 years were included as normal controls.A proper smoking and alcoholic history was takenfrom the subjects of the study. Ethical committee Clearance and written consent from all the participants of the study were obtained.

2.3 Test included

- Fasting blood sugar
- Serum creatinine
- Blood urea, Serum uric acid
- HbA1c
- Total cholesterol (TC)
- Triglyceride (TG)
- HDL cholesterol
- LDL cholesterol
- VLDL cholesterol
- TC/HDL ratio
- LDL/HDL ratio.

2.4 Procedure

8 hours fasting sample were used for estimation of serum total cholesterol (TC), triglyceride (TG), High Density Lipoprotein cholesterol (HDL), Low Density Lipoprotein cholesterol (LDL), Very Low Density Lipoprotein cholesterol (VLDL),fasting blood sugar and serum uric acid. For serum creatinine, blood urea and HbA1c non fasting sample were used. All the tests done in the present study were performed using Vitros 350 dry chemistry analyzer manufactured by Ortho Clinical Diagnostics of Jhonson & Jhonson, USA. TC, TG, and HDL were estimated by direct methods. LDL by Friedewald'sformula.VLDL by the formula TG/5 and the ratios TG/HDL and LDL/HDL were calculated. HbA1c estimated by Biorad D-10 based on HPLC.

2.5 Statistical analysis

The statistical analysis was done manually. Expression of the final result is in Mean± Standard deviation (SD) form. The statistical significance of difference between the various groups was determined by using the student's t test, and a p value was determined by one way ANNOVA and value of $p < 0.05$

is considered significant. Pearson correlation coefficient(r) was determined online.

III. Results and Observations

The study was conducted with 50 subjects as controls with 30 male and 20 female. While in the Patient group out of 89 Type 2 diabetic patients 51 were male and 38 were females.

TABLE 1.

	TEST	**CONTROL**
FBS(mg/dl)	167±62.1	78±15.1
Creatinine(mg/dl)	0.77±0.13	0.75±0.14
Urea(mg/dl)	25.87±4.29	24.9±4.27
HbA1C %	10±2.6	5.9±0.3
TC(mg/dl)	177±47.6	151±25.6
TG(mg/dl)	188±82.7	109±28.9
HDL(mg/dl)	37±13.4	46±12.9
LDL(mg/dl)	104±52.9	83±29.8
VLDL(mg/dl)	38±16.5	22±5.8
TC/HDL	6±4.8	3.6±1.7
LDL/HDL	4±4.1	2.1±1.4

Table 1 shows the MEAN±SD values for HBA1c, TC, TG, HDL, LDL, VLDL, TC/HDL AND LDL/HDL in both the Control andthe patient group.

TABLE 2.7

CORRELATION BETWEEN	**Control HbA1c<6.5%**	**HbA1c < 7.0%**	**HbA1c ≥7.0%<10.0 %**	**HbA1c ≥10.0%**
HbA1c & TC	r = 0.0138	r = 0.9178	r = 0.9838	r = 0.9365
HbA1c & TG	r = 0.2925	r = -0.587	r = 0.0661	r = 0.1902
HbA1c & HDL	r = 0.5065	r = -0.9026	r = -0.9835	r = -0.9879
HbA1c & LDL	r = -0.2636	r = 0.7611	r = 0.9167	r = 0.8195
HbA1c & VLDL	r = 0.2925	r = -0.5705	r = 0.0674	r = 0.192
HbA1c & TC/HDL	r = -0.312	r = 0.9066	r = 0.9936	r = 0.8787
HbA1c & LDL/HDL	r = -0.3424	r = 0.897	r = 0.9543	r = 0.8337

Table 2 shows the correlation of HbA1c with TC, TG, HDL, LDL and the TC/HDL, LDL/HDL ratios in control and test group. r is the Pearson correlation coefficient. In test group, HbA1c values are divided into three groups according to glycemic control, HbA1c <7.0%, HbA1c≥7.0%<10.0%, HbA1c ≥10.0%. It is evident that HbA1c is showing a significant ($p<0.05$) positive correlation with TC and LDL. There is significant($p< 0.05$) negative Correlation of HbA1c with HDL. Ratios of lipid parameters are also showing significant($p<0.05$)positive correlation with HbA1c. The higher is the value of HbA1c better is the correlation. In the control group, correlation of HbA1c with lipid profile is not well seen.

IV. Discussion

Despite multiple clinical and biochemical evidences, there is large population of Type 2 diabetics who develop life threatening complications like nephropathy and CAD. Many a times it is silent MI in Diabetics[9]. Though many modalities for Type 2 diabetes diagnosis are employed, HbA1c has been found to be the gold standard for determining glycemic control. It gives the idea of glycemic control over preceding three months and estimation is also least effected by other factors.So, in this study HbA1c values are correlated with other lipid parameters to verify whether Type 2 diabetes without a known cardiovascular disease is associated with dyslipidemia, so that identifying and treating such person can prevent development of CVD. Therefore only recently diagnosed Type 2 DM patients were considered for the study. In the study, patient data were divided into three groups according to the HbA1c value. It is found that HbA1c is showing a significant($p<0.05$) positive correlation with TC and LDL. There is significant($p<0.05$) negative Correlation of HbA1c with HDL. Ratios of lipid parameters are also showing significant($p<0.05$)positive correlation with HbA1c. As the value of HbA1c increases, the correlation seems much better. So, in the groups having HbA1c ≥7.0% <10.0% and HbA1c≥10.0%, the correlation values are significant.

Diabetic dyslipidemia includes multiple lipoprotein disorders.Cause of dyslipidemia in Type 2 Diabetes could be deficiency or resistance to insulin as reported by Goldberg. Insulin has role in apolipoprotein production which regulates the enzymatic activity of lipoprotein lipase and Cholesterol ester transport protein[10,11].

The UKPDS study has shown that in patients with type 2 diabetes, the risk of diabetic complications were strongly associated with previous hyperglycemia[12]. Estimated risk of CardioVascular Diseases (CVD) has shown to be increased by 18% for each 1% increase in absolute HbA1c value in diabetic[13].

Z Yan et al found that compared with individual lipid indexes, the changes of lipid ratio can reflect impaired lipid metabolism at earlier stage, and

the most sensitive indicator is LDL/HDL ratio. Thus, LDL/ HDL ratio is helpful in assessing and reducing the risk of cardiovascular disease[14]. In our study also lipid ratios are showing strong positive correlation with glycemic control. Poor the glycemic control better is the correlation**.**

Khan et al showed similar impact of HbA1c values on various lipid parameters in which severity of dyslipidemia increases in patients with higher HbA1C values. High HbA1c and dyslipidemia are independent risk factors of CVD. So in diabetics, if we find dyslipidemia along with high HbA1c, it could be considered to be in high risk group for CVD development. Mortality rate can be lowered by 10% by reducing the HbA1c level by 0.2%[15, 16].Increase in HbA1c values is suggested to be an indicator of glycation of LDL cholesterol and its further predisposition to CVD events. The present study also showed that the severity of dyslipidemia increases with increased HbA1C values. Hence, good glycemic control through antidiabetic therapy along with lifestyle modifications can reduce the risk of atherosclerosis and related complications.

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