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A Correlation between Glycosylated Haemoglobin & Lipid Profile in Type 2 Diabetes Mellitus with & Without Complications

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Abstract

Objective: *To determine whether the prevalence of dyslipidaemia & associated complications are associated with hyperglycaemia or poor glycaemic control.*

Methods: *This was a prospective and analytical study. Type 2 diabetes mellitus patients who were attending the out patients clinic. 50 patients and 50 healthy subjects were included in the study. 50 clinically and biochemically confirmed cases of type 2 diabetes mellitus with and without complications of long duration, of both sexes and aged 35 to 75 years were selected.*

Results: *The mean age of cases was 51.46±12.71 and 52.48±12.76 in controls. The FBS level was significantly (p=0.0001) higher among cases (122.26±68.39) compared with controls (79.28±11.84). The PPBS was also higher (p=0.0001) among cases (188.20±87.27) than controls (124.12±10.96). The level of HbA1C was higher among cases (7.47±1.90) compared with controls (5.48±0.41). The increased level of TC, TG, LDL and VLDL was observed among cases than controls (p<0.01). However, decreased level of HDL was found among cases compared with controls (p>0.05). Overall, 40% of the cases had any one of the complications.*

Conclusion: *The rate of complications are higher in case of poor glycaemic control as compared to good glycaemic control in type 2 diabetes mellitus patients, thus, HbA1c can be used as a predictor of dyslipidemia in patients with type II diabetes in addition to its importance as glycemic control parameter.*

Keywords: *Dyslipidaemia, Hyperglycaemia, Diabetes*

INTRODUCTION

Diabetes mellitus (DM) today is a growing epidemic that has the potential to cripple health services in all the parts of the world (Sicree et al, 2003). In India, the number of diabetic patients have increased tremendously over the last decade making the capital of diabetic patients. It is a major cause of disability and premature death mainly through cardiovascular disease and other chronic complications (National Kidney Foundation, 2002). There were 285 million diabetic s worldwide in 2010 and it is estimated to reach 439 million in 2030 (Gerstein et al, 2001).

Diabetes mellitus is characterized by hyperglycemia, glycosuria, hyperlipidemia, negative nitrogen balance and sometimes ketonemia (Powers, 2008). Major consequence of hyperglycemia is excessive non enzymatic glycosylation of various body proteins including hemoglobin, albumin, collagen and elastine. Apart from hyperglycemia, DM is also characterized by oxidative stress, inflammation and insulin resistance. Chronic hyperglycemia from any cause can lead to a number of complications like cardiovascular, renal, neurological or ocular pathology, inter-current infection and lower extremity complications. After adjusting for age, the death rate of people with T2DM is about twice as high as their non-diabetic peers. Nearly 50-80% of all diabetics die of cardiovascular disease, stroke, or renal failure (Agewall et al, 1997).

There are two major types of diabetes mellitus: Type 1 diabetes mellitus which is primarily a result of pancreatic (3-cell destruction due to an immune-mediated process that is likely incited by environmental factors in genetically predisposed individuals (Harjutsalo et al., 2006). The more prevalent form, type 2 diabetes, accounts for more than 90% of cases (Olefsky, 2001). Type 2 diabetes usually begins as insulin resistance, a disorder in which the cells do not use insulin properly. As the need for insulin rises, the pancreas gradually loses its ability to produce it (Cohen, 2006).

Glycated hemoglobin (HbA1c) is a routinely used marker for long-term glycemic control as an indicator for the mean blood glucose level. HbA1c predicts the risk for the development of diabetic complications in diabetes patients. Apart from classical risk factors like dyslipidemia, elevated HbA1c has now been regarded as an independent risk factor for CVD in subjects with or without diabetes. Estimated risk of CVD has shown to be increased by 18% for each 1% increase in absolute HbA1c value in diabetic population (Selvin et al, 2005).

Lipids are a chemically diverse group of compounds that are poorly soluble in the aqueous environment of the cell. The main ones are cholesterol, triglyceride and phospholipid. Cholesterol is essential for growth and viability of cells. It can be obtained from the diet or synthesized de novo. The absorption of triglyceride is essentially complete whereas that of cholesterol varies between 30-50%. Endogenous synthesis of cholesterol in the liver is controlled by the rate limiting step involving the microsomal enzyme 3-hydroxy-3-methylglutaryl-CoA (HMG-

CoA) reductase.The present study was designed to determine whether the prevalence of dyslipidaemia & associated complications are associated with hyperglycaemia or poor glycaemic control.

MATERIAL AND METHODS

Study Design: This was a prospective and analytical study.

Study site: This study was conducted in the Department of Medicine and Biochemistry, Govt. Medical College, Jhansi.

Study subjects: Type 2 diabetes mellitus patients who were attending the out patients clinic of Medicine Department.

Sample size: 50 patients and 50 healthy subjects were included in the study. 50 clinically and biochemically confirmed cases of type 2 diabetes mellitus with and without complications of long duration, of both sexes and aged 35 to 75 years were selected.

Number of Cases selected for the study were: 30 cases of diabetes without complications; 20 cases of diabetes with complications; 50 age & sex matched healthy individuals serve as control.

Data Collection and Analysis

Ethical clearance was taken before the commencement of the study. Written consent was obtained from the participants after they were given an explanation of the study details. The data was collected in a proforma which includes IPD/OPD no. various socio-economic parameters like name, age, sex, occupation, religion as well as detailed medical examinations and laboratory investigations. A brief questionnaire that included the history of diabetes, hypertention cerebrovascular accident, ischemic heart disease, as well as family history of diabetes and hypertension were introduced and recorded.

Sample collection and storage

Under aseptic conditions 10ml of venous blood was collected. Out of this, 1 ml was collected in EDTA bulb after overnight fasting for estimation of HbA1c and remaining sample was allowed to centrifuged (3,000 rpm, for 20 min at 4deg.C) to obtain serum. Urine was also collected in clean container for microalbumin & routine, microscopic test.

Biochemical measurements

These included: Hb/TLC/DLC/ESR, Fasting plasma glucose (GF), Postprandial blood glucose and glycated hemoglobin (HbA1c), Lipid profile: Total cholesterol, TAG, LDL-cholesterol, and HDL-cholesterol & VLDL; Renal function tests: serum creatinine and blood urea nitrogen (BUN). Serum sodium & potassium, Urine for microalbumin, Urine- Routine & Microscopic. These tests were performed at the Clinical Biochemistry Laboratory at the institute by the standard methods.

Statistical Analysis

Data were entered in a Microsoft Excel spreadsheet. All the entries were checked for any keyboard error. Data available were analysed by

simple statistical means like percentage, mean and total number. All data processing was done using SPSS 16.0. The mean and SD was estimated for each of the lipid parameters. The comparison between diabetic and non-diabetic cases was carried out by using the student "t-test". The p-value<0.05 was considered significant. All the analysis was carried out by using SPSS 16.0 version (Chicago, Inc., USA).

RESULTS

A total of 50 cases and 50 controls were included in the study. Out of the cases, there were 20 with complication and 30 without complication.

About half (52%) of cases and 26% of controls were in the age group 41-50 years. However, 22% of cases and 28% of controls were above 60 years. The mean age of cases was 51.46±12.71 and controls was 52.48±12.76. The difference in the age between cases and controls was statistically not significant (p>0.05), showing the comparability of the groups in terms of age. The male/female ration between cases and controls was similar (p>0.05) (Table-1).

The FBS level was significantly (p=0.0001) higher among cases (122.26±68.39) compared with controls (79.28±11.84). The PPBS was also higher (p=0.0001) among cases (188.20±87.27) than controls (124.12±10.96). The level of HbA1C was higher among cases (7.47±1.90) compared with controls (5.48±0.41). The increased level of TC, TG, LDL and VLDL was observed among cases than controls (p<0.01). However, decreased level of HDL was found among cases compared with controls (p>0.05) (Table-2).

Overall, 40% of the cases had any one of the complications. The complication was higher among 51-60 years (57.1%) than 41-50 (42.3), >60 (36.4%) and <40 (16.7%) years. The complication was higher among males (44%) compared with females (36%) (Table-3).

The level all the biochemical parameters were significantly (p<0.05) higher among the cases of complications compared with without complications (Table-4).

The median value of HbA1C was 6.00. There was significant lower level of PPBS and TG in the cases of HbA1C<6 than HbA1C above 6. There was no significant difference in glucose and lipid levels between the two categories of HbA1C (Table-5).

Table-1: Demographic distribution of cases and controls

	Cases (n=50)		Controls (n=50)		p-value[1]
	No.	%	No.	%	
Age in years					
<40	6	12.0	10	20.0	0.06
41-50	26	52.0	13	26.0	
51-60	7	14.0	13	26.0	
>60	11	22.0	14	28.0	
Mean±SD	51.46±12.71		52.48±12.76		
Gender					
Male	25	50.0	26	52.0	0.84
Female	25	50.0	24	48.0	

[1]Chi-square test

Table-2: Comparison of biochemical parameters between cases and controls

	Cases (n=50)	Controls (n=50)	p-value[1]
Glucose levels			
FBS	122.26±68.39	79.28±11.84	0.0001*
PPBS	188.20±87.27	124.12±10.96	0.0001*
HbA1C	7.47±1.90	5.48±0.41	0.0001*
Lipid levels			
TC	175.42±44.64	145.32±20.30	0.0001*
TG	156.32±87.35	80.08±34.25	0.0001*
HDL	41.90±9.08	45.48±11.55	0.08
LDL	102.36±37.22	84.80±18.20	0.003*
VLDL	31.15±17.48	15.94±6.78	0.0001*

[1]Unpaired t-test, *Significant

Table-3: Age and gender distribution of cases according to complications

Age in years	No. of patients	With complication		Without complication		p-value[1]
		No.	%	No.	%	
<40	6	1	16.7	5	83.3	0.50
41-50	26	11	42.3	15	57.7	
51-60	7	4	57.1	3	42.9	
>60	11	4	36.4	7	63.6	
Total	50	20	40.0	30	60.0	
Gender						
Male	25	11	44.0	14	56.0	0.56
Female	25	9	36.0	16	64.0	

[1]Chi-square test

Table-4: Comparison of biochemical parameters according to complications

	With complication (n=20)	Without complication (n=30)	p-value
Glucose levels			
FBS	175.85±81.50	86.53±15.83	0.0001*
PPBS	270.35±81.97	133.43±26.64	0.0001*
HbA1C	9.21±1.93	6.31±0.43	0.0001*
Lipid levels			
TC	208.95±49.97	153.07±20.96	0.0001*
TG	219.75±98.42	114.30±44.09	0.0001*
HDL	45.30±12.01	39.63±5.61	0.02*
LDL	119.80±49.90	90.73±18.97	0.006*
VLDL	43.82±19.68	22.70±8.82	0.0001*

[1]Unpaired t-test, *Significant

Table-5: Comparison of biochemical parameters according to HbA1C

	Cases			Controls		
	HbA1C<6 (n=5)	HbA1C≥6 (n=45)	p-value[1]	HbA1C<6 (n=40)	HbA1C≥6 (n=10)	p-value[1]
FBS	76.00±9.95	127.40±70.21	0.11	77.92±11.06	84.70±13.86	0.10
PPBS	108.20±7.59	197.09±87.57	0.02*	122.68±11.61	129.90±4.84	0.06
TC	139.80±3.49	179.38±45.37	0.06	143.60±20.36	152.20±19.49	0.23
TG	78.40±24.15	165.16±87.60	0.03*	79.70±36.48	81.60±24.86	0.87
HDL	41.60±3.20	41.93±9.53	0.93	46.20±12.41	42.60±6.91	0.38
LDL	82.60±6.22	104.56±38.60	0.21	82.68±18.80	93.30±13.09	0.09
VLDL	15.60±4.98	32.88±17.53	0.03	15.85±7.21	16.30±4.94	0.85

[1]Unpaired t-test, *Significant, Cutoff value is 6 as Median in all the patients

DISCUSSION

Patients with type 2 diabetes often exhibit an atherogenic lipid profile, which greatly increases their risk of CVD compared with people without diabetes. An early intervention to normalize circulating lipids has been shown to reduce cardiovascular complications and mortality (Haffner et al, 1998). The lipid changes in diabetes mellitus are attributed to the associated hyperinsulinemia and insulin resistance. Diabetes is associated with characteristic triad of lipid alteration: hypertriglyceridemia, low HDL-C and increased concentration of small dense LDL-cholesterol particles. This occurs due to (1) increase in the release of free fatty acid from the insulin resistant adipose tissue, (2) increase in fatty acid synthesis in the liver, (3) increase in hepatic VLDL production, and (4) decrease in LPL activity resulting in reduced catabolism of chylomicrons and VLDLs (Windier, 2005). In this study, the HbA1C and lipid levels were compared in diabetes type-2 cases and controls. The mean values of HbA1C and lipid parameters were also compared between the groups as well as

between diabetes with and without complications in the present study. In the present study, in diabetic group, there was significant elevation of total cholesterol, TG, LDL and VLDL when compared to non-diabetic healthy individuals. This is comparable to the study done by Sapna et al (2008). The HDL-C was significantly lower in the diabetics when compared to non-diabetics in this study. Suryavanshi et (2006) also reported similar results.

ADA (American Diabetic association) has reported that well controlled type 2 diabetics have a mixed hyperlipidemia with high triglycerides, low HDL-C and high LDL-C levels (Perez et al, 2006). On the other hand, in poorly controlled type 2 diabetics have a mixed dyslipidemia resulting in high cholesterol and triglyceride level. It has also been reported that controlling dyslipidemia and good glycemic control delays atherosclerosis and prevent CHD (Alagozlu et al, 2005).

In the present study, there was no association between age and gender with diabetes with and without complication. However, increased level of HbA1c and lipid level was observed between with complication and without complication. Most of the studies have not compared this, so that findings of this study cannot be compared with other studies. Only PPBS and TG were significantly different between HbA1c<6 and HbA1c ≥6 in the present study. Khan et al. (2007) reported the impact of glycemic control on various lipid parameters and observed the significant alterations in all lipid parameters with regard to glycemic control. The severity of dyslipidemia increases in patients with higher HbA1c value. Elevated levels of HbA1c and dyslipidemia are independent risk factors of cardiovascular diseases and hence, diabetic patients.

CONCLUSIONS

The rate of complications are higher in case of poor glycaemic control as compared to good glycaemic control in type 2 diabetes mellitus patients, thus, HbA1c can be used as a predictor of dyslipidemia in patients with type II diabetes in addition to its importance as glycemic control parameter.

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