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Original Article

Correlation between Glycated Hemoglobin and Dyslipidemia in Type-2 Diabetes Mellitus

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Abstract

Objective: To evaluate correlation between glycated haemoglobin and dyslipidaemias in patients with type-2 Diabetes Mellitus (DM).

Patients and Methods: Participants were selected from out-patient department of Sheikh Zayed Hospital, Lahore and Laboratory analysis was performed at department of chemical pathology, University of Health Sciences, Lahore. Total 60 patients of type-2 DM and 40 age and gender matched controls were included in study. Glycated haemoglobin (HbA_1c), fasting blood glucose (FBG) and lipid profile was performed after overnight fasting. Control group was labelled as Group-A and patient group was labelled as Group-B. Mean of all parameters from both groups was compared and checked for significance by independent sample t-test and Pearson correlation.

Results: There was no significant difference in mean values of all biochemical parameters between both genders, except total cholesterol, which was found higher in females (p-value 0.047). Only 3.3% (n = 02) patients had normal lipid profile, 76.6% (n = 46) had one-abnormal parameter of lipid profile, 28.3% (n = 17) patients had two-abnormal parameter of lipid profile and 58.3% (n = 35) had mixed type of dyslipidemia. HbA_1c was positively correlated with all parameters of lipid profile except HDL-C, which was negatively correlated.

Conclusion: There is positive correlation between level of glycemic control (HbA_1c) and severity of dyslipidemia in patients of type 2 DM.

Key Words: Cardiovascular diseases, Diabetes mellitus type 2, Dyslipidemia, Glycated haemoglobin.

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Introduction

Diabetes mellitus (DM) is cosmopolitan disease of the globe. DM is a group of metabolic disorders characterized by hyperglycemia either due to the lack of insulin secretion, or defects of insulin action or both.[1] Recent reports showed that there were 171 million people in the world with diabetes in year 2000 and this is expected to increase to 366 million by 2030.[2] It is associated with reduced life expectancy, significant morbidity due to specific diabetes related microvascular complications, increased risk of macrovascular complications (ischaemic heart disease, stroke and peripheral vascular disease), and lessened quality of life.

Glycated haemoglobin (HbA_1c) is usually used as a monitoring tool for measuring glycemic control in DM patients. It gives glycemic control status for last 120 days.[3] HbA_1c predicts risk for development of diabetic complication in diabetic patients. United Kingdom Prospective Diabetes Study (UKPDS) has revealed that risk of diabetic complications was strongly associated with previous hyperglycemia. Good glycemic control with decreased level of HbA_1c is likely to reduce risk of complications.[4] Estimated risk of cardiovascular disease (CVD) has shown to be increased by 18% for each 1% increase in absolute HbA_1c value in diabetics.[5]

The chronic hyperglycemia can damage several body organs due to microvascular and macrovascular complications.[6,7] Macrovascular complications of diabetes include cardiovascular disease (CVD) such as stroke, which is the cause of death in 50% of diabetics.[8,9] On the other hand, microvascular complications of diabetes include diabetic nephropathy, neuropathy, and retinopathy.[10] Cardiovascular risk of diabetes increases further if diabetes is related with dyslipidemia. However, this risk can be reduced by good management and control of both hyperglycemia and dyslipidemia.[11,12]

A few studies have previously tried to find relationship between HbA_1c levels, fasting blood glucose (FBG) and

lipid profile. Some of these have shown that all parameters of lipid profile have significant association with glycemic control.[13] On the other hand, some studies do not report significant correlation between glycemic control and parameters of lipid profile.[14] Positive relationship between HbA_1c and CVD has been demonstrated in non-diabetic subjects even within normal range of HbA_1c.[15,16]

These controversies motivated us to conduct this study, to find out correlation between glycemic control (HbA_1c), FBG and different parameters of lipid profile in type 2 diabetic patients coming to out-patients department of endocrinology at Sheikh Zayed Hospital, Lahore.

Patients and Methods

Prior to the start of study ethical permission was obtained from ethical committee of the Sheikh Zayed Hospital, Lahore. Total 60 patients of type 2 DM for > 05 years with overnight fasting were recruited from Sheikh Zayed Hospital, Lahore. Patients with renal disease, thyroidal illness, history of alcohol intake and improper fasting were excluded from study. Total 40 age and gender matched controls without history of any acute or chronic illness were also included. 02ml fasting blood samples were obtained after signing informed consent from all participants for the measurement of HbA_1c, FBG and Lipid profile. HbA_1c, FBG and Lipid Profile were performed on Monza Chemistry Analyzer by using Randox reagent kits. The instrument was properly calibrated and quality control (QC) levels were also run along with patient sample. HbA1c was performed by affinity Chromomatography technique. Statistical analysis was performed by using IBM – SPSS version 21.0. Independent sample t-test (2-tailed) was used to compare mean of all parameters. Pearson's correlation test was done to evaluate correlations of HbA1c with all other parameters. All values of different parameters were expressed using conventional units. p-value ≤ 0.05 was considered statistically significant.

Results

Among sixty patients, 66% (n = 40) were females and remaining 34% (n = 20) were males. Out of forty controls, 47.5% (n = 19) were males and 52.5% (n = 21) were females. Mean age for patient group was 51.17±6.85 years (male=52.85+7.12 years and female= 50.32+6.63 years) and for controls mean age was 42.82+13.66 years (male =45.53+12.69 years and female = 40.38+14.35 years). The frequency of dyslipidemia in our study population was 98%. Only 02% showed normal lipid profile components. Most common type of dyslipidemia was increased levels of low density lipoprotein cholesterol (LDL-C) (68.3%) followed by hyper-triglyceridemia (55%), hyper-cholesterolemia (46.7%) and decreased levels of high density lipoprotein cholesterol (HDL-C) (Figure-1).

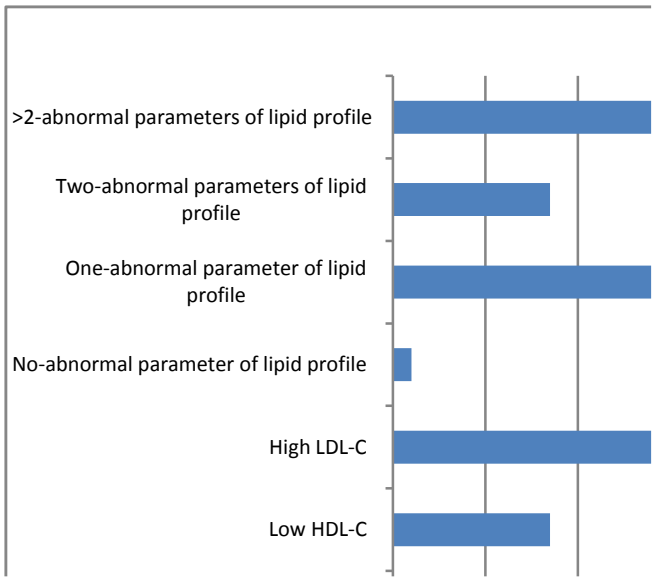

Figure-1: Frequency of Dyslipidemia in diabetic patients

In patient group (group-B) mean values of TC 42.33mg/dl, VLDL-C 11.89mg/dl, LDL-C 93.49mg/dl, Triglyceride 58.29mg/dl, HbA_1c 4.56% and FBG 89.52mg/dl were higher than control group (Group-A).

Mean age for males in total study population was 2.52 years higher than females. Mean levels (mg/dl) of VLDL-C, HDL-C, LDL-C, TG, FBG and HbA_1c (%) were relatively higher in females (Table-1).

Table-1: Comparison of lipid profile parameters and glycemic indices between group-A and group- B

Parameter	Group-A (n=40) Mean±SD	Group-B (n=60) Mean±SD	p-Value
TC (mg/dl)	158.30±19.01	200.63±54.60	0.000*
VLDL-C (mg/dl)	24.33±3.90	36.22±20.13	0.000*
HDL-C (mg/dl)	83.43±18.55	48.28±15.88	0.000*
LDL-C (mg/dl)	24.33±3.89	117.82±52.09	0.000*
TG (mg/dl)	121.78±15.92	180.07±90.50	0.000*
HbA1c (%)	4.49±0.50	9.05±1.86	0.000*
FBG (mg/dl)	87.85±6.11	177.27±65.73	0.000*

*p-value≤0.05 is considered statistically significant

We divided patient group (Group – B) further in to two sub-groups as good glycemic control (GGC) group and poor glycemic control (PGC) group. In GGC group patients had level of HbA_1c < 7% and in PGC patients had level of HbA_1c > 7%. We compared mean levels of lipid profile between these two groups. Mean difference of FBG was

found 53.0 mg/dl higher in group PGC and this was found statistically significant (Table-2).

Table-2: Biochemical Parameters categorize on the basis of HbA1c

Parameters	$HbA_1c < 7$ (GGC) (n=10)	$HbA_1c > 7$ (PGC) (n=50)	p-Value
Age (Years)	52.90±7.97	50.82±6.64	0.385
TC (mg/dL)	211.40±49.36	198.48±55.80	0.449
VLDL-C(mg/dL)	32.80±13.88	36.90±21.20	0.561
HDL-C (mg/dL)	53.60±23.35	47.22±14.01	0.423
LDL-C (mg/dL)	124.80±46.43	116.42±53.48	0.646
TG-C (mg/dL)	175.90±67.32	180.90±95.00	0.875
FBG-C (mg/dL)	133.10±34.60	186.10±67.12	0.001*

*p–value ≤0.05 is considered statistically significant, GGC: Good glycemic control, PGC: Poor glycemic control

HbA_1c was positively correlated with all components of lipid profile except HDL-C which showed negative correlation. FBG showed significant positive correlation with HbA_1c (Table-3).

Table 3: Correlation between HbA_1c and all biochemical parameters (n = 60)

Parameters	Correlation r-value	p-value
TC (mg/dL)	0.082	0.532
VLDL-C(mg/dL)	0.244	0.061
HDL-C(mg/dL)	-0.058	0.658
LDL-C(mg/dL)	0.029	0.826
TG (mg/dL)	0.173	0.187
FBG (mg/dL)	0.396	0.002*

*p-value ≤ 0.05 is considered statistically significant

Discussion

Despite many strategies for diagnosis and monitoring of DM, still this is a major challenge for public health around the globe. In conditions like uncontrolled DM the proportion of glycosylated haemoglobin increases substantially. This glycosylation of haemoglobin is result of non-enzymatic binding of haemoglobin A molecules with glucose which occurs only once during the life of single red blood cell. The levels of HbA_1c reflect the degree of glycemic control for last 120 days. So this is being used for diagnosis and monitoring diabetic control as well. The diabetic dyslipidemia is connected with raised levels of triglycerides, LDL-C and decreased HDL-C.[17]

In our study we evaluated correlation of HbA_1c with dyslipidemia. In Group-B 98.0% patients showed significant dyslipidemia. High LDL-C is most common followed by hyper-triglyceridemia, Hyper-cholesterolemia and Low LDL-C.

Al-alawi et al in 2014 reported high prevalence of hypercholesterolemia, hypertriglyceridemia, high LDL-C and low HDL-C. They revealed that increase LDL-C level is more frequent type of dyslipidemia.[18] It is well known that high LDL-C and low HDL-C levels are risk factors for development of cardiovascular diseases. Insulin effects the liver apolipoprotein production which is responsible for enzymatic activity of lipoprotein lipase and cholesterol esters transport protein. All these factors collectively cause dyslipidemia in DM.[19]

Hyper triglyceridemia can be due to alteration of lipoprotein in type- 2 DM. It is caused by hyperglycemia, insulin resistance which results in overproduction of VLDL-C, defective clearance of VLDL-C, decreased activity of lipoprotein lipase and decreased production of apolipoprotein B. Consumption of VLDL is altered which ultimately results in atherosclerosis. In type–2 DM, hyperglycemia increases the activity of hepatic lipase which leads to enhanced clearance of HDL-C while impaired catabolism of VLDL-C which causes decreased production of HDL-C.[20]

In present study, diabetic patients (n = 60) were divided into two groups as GGC group which included only 10 patients and PGC group which contained 50 patients. Severity of dyslipidemia was higher in patients with increased levels of Glycated hemoglobin (HbA_1c >7%). Elevated HbA_1c and dyslipidemia are sovereign risk factors of cardiovascular diseases. Through improvement in glycemic control, one can markedly diminish risk of cardiovascular events in diabetics. It has been assessed that reducing HbA_1c level by 0.2% could lower mortality by 10%.[6] Khan et al reported that impact of glycemic control is directly related to the severity of dyslipidemia.[21]

The dyslipidaemia in diabetic is frequent because insulin resistance or deficiency affects vital enzymes and lipid metabolism.[22,23] It affects the following processes: apoprotein production, regulation of lipoprotein lipase, action of cholesteryl ester, transfer proteins and hepatic and peripheral actions of insulin.[22] It has been suggested that composition of lipid particles in diabetic dyslipidaemia is more atherogenic than other types of dyslipidaemia. This means that even normal lipid concentrations might be more atherogenic in diabetic than in nondiabetic people.[22,24,25]

Pearson correlation was observed between HbA_1c and other components of lipid profile and FBG. A significant positive correlation was seen with FBG. Our findings were strongly matched with previous literature reports.[26,27] We also found positive but non-significant correlations between HbA_1c and cholesterol, triglycerides, LDL-C and VLDL-C in type-2 diabetic patients. HDL-C was found negatively correlated with HbA_1c. Previously many researchers have reported the

importance of HbA_1C for controlling dyslipidemia in patients with type-2 DM.[28,29]

Conclusion

Positive but non-significant correlation is found between glycemic control and severity of dyslipidemia in patients with type-2 DM. Thus by maintaining a good glycemic control, risk for the development of dyslipidemia and cardiac diseases can be reduced. Further studies should be conducted on a larger scale to significantly explore the role of HbA_1c in the development of dyslipidemia in type-2 Diabetic patients.

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Conflict of Interest

This study has no conflict of interest as declared by any author.

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Authorship Contribution:
Author 1,3: Conception, Synthesis and Planning of the research
Author 2,6: Active participation in active methodology
Author 4,5: Interpretation, analysis and discussion