

Association between Glycemic Control and Serum Lipid Profile in type 2 Diabetic Patients: Experience in a Medical College Hospital

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Abstract

Impaired lipid metabolism in diabetic patients can lead to cardiovascular complications. Poor glycaemic control is associated with a significant increase in the risk of both patient's morbidity and mortality. An early intervention to regulate circulating lipids has been found to lower the risk of cardiovascular problems and death. Glycated hemoglobin (HbA1c) is a reliable indicator of rising blood sugar levels. This hospital based observational study was conducted in the Department of Medicine, Sher-E-Bangla Medical College Hospital, Barisal from October 2014 to March 2015 over a period of 6 month to determine the correlation of glycemic control and lipid profile in patients with type 2 diabetes. A total of 110 type 2 diabetes mellitus (DM) patients of both sexes admitted to the Department of Medicine of Sher-E-Bangla Medical College Hospital, Barisal, were recruited for this study. Following standard procedures and protocols, fasting blood sugar (FBS), blood sugar two hours after breakfast, Glycosylated Hemoglobin (HbA1c) and fasting lipid profile were measured. The age of respondents ranged from 34 to 70 years with the mean age of 54.35±8.02 years. Among the patients male were 70 (63.6%) and female were 40 (36.4%). Mean age at diagnosis of DM and duration of DM was 47.07±6.03 years and 7.27±3.41 years, respectively. Mean body mass index (BMI), FBS and HbA1c were 25.02±5.22 kg/m², 8.06±2.01 mmol/L and 8.34±1.9 % respectively. Significant positive correlation of HbA1c and FBS with BMI, total cholesterol (TC), triglyceride (TG), low density lipoprotein (LDL-C) and negative correlation with high density lipoprotein (HDL-C) was found. Significantly higher TC, TG and LDL-C and lower HDL-C were found in poor glycemic control (HbA1c ≥ 7) group than good glycemic control (HbA1c < 7) group. The results of this study showed that, higher levels of glycemic parameters are significantly associated with dyslipidemia. These findings also indicate that HbA1c can be utilized for screening of high risk diabetic patients for early diagnosis of dyslipidemia and timely intervention with lipid lowering drugs.

Introduction

Diabetes mellitus (DM) is a metabolic disorder characterized by hyperglycaemia affecting about 347 million people worldwide.¹ More than 80% of deaths from diabetes occur in low and middle-income countries. About 50% of people with diabetes die of cardiovascular diseases including stroke.²

Diabetes, impaired glucose tolerance (IGT) and impaired fasting glucose (IFG), can now be found in almost every population in the world and epidemiological evidence suggests that, without effective prevention and control programs, the burden of diabetes is likely to continue to increase globally.^{3,4} The socio-economic consequences of diabetes and its complications could have a seriously negative

impact on the economies of developed and developing nations.⁵

Epidemiological studies have demonstrated that diabetes mellitus is an independent risk factor for cardiovascular disease and it amplifies the effects of other common risk factors such as smoking, hypertension and dyslipidemia.⁶ Dyslipidemia is one of the most common risk factors for coronary artery disease (CAD) which is more prevalent among adults with type 2 diabetes mellitus than in the general population with a four to six fold greater cardiovascular mortality.⁷ Patients with type 2 diabetes often exhibit an atherogenic lipid profile, which greatly increases their risk of CVD compared with people without lipid abnormalities in diabetes mellitus. The dyslipidemia seen in diabetes mellitus patients are characterized by

increased triglycerides level, high low density lipoproteins, and low high density lipoproteins. An early intervention to normalize circulating lipids has been shown to reduce cardiovascular complications and mortality.^{8,9}

Glycated hemoglobin or glycosylated hemoglobin (HbA1c) is a form of hemoglobin formed by the condensation of glucose with the N-terminal Valine residue of each β -chain of HbA1 to form an unstable Schiff-base, is measured primarily to identify the average plasma glucose concentration over prolonged periods of time (2-3 months). Normal level of glucose produces a normal amount of glycosylated hemoglobin. HbA1c serves as a marker for average blood glucose levels prior to measurement.¹⁰

In accordance with its function as an indicator for the mean blood glucose level, HbA1c predicts the risk for the development of diabetic complications in diabetes patients.¹¹ The United Kingdom Progressive Diabetes Study (UKPDS) has shown that in patients with type 2 diabetes, the risk of diabetic complications were strongly associated with previous hyperglycemia. Glycemic control with decreased level of HbA1c is likely to reduce the risk of complications¹². Estimated risk of Cardio Vascular Diseases (CVD) has shown to be increased by 18% for each 1% increase in absolute HbA1c value in diabetic.¹³ Even in non diabetic cases with HbA1c levels within normal range, positive relationship between HbA1c and CVD has been demonstrated.^{14,15} Some studies have shown that all the parameters of lipid profile have significant correlation with glycemic control.¹⁶

HbA1c predicts the risk for development of microvascular and macrovascular complications in diabetic patients. The World Health Organization (WHO) and American Diabetic Association guidelines introduced the use of HbA1c for diagnosis and assessment of glycemic control of DM^{17, 18}. Numerous studies were conducted to establish positive correlation between HbA1c and other glycemic parameters. But very few studies have been conducted so far, not only in our community but also in the world, to assess the impact of HbA1c with parameters of serum lipid profile values in type 2 diabetic subjects. Findings of those studies conducted previously were not identical. Clearly, there is a need to investigate further to discover the relationship between glycemic control and lipid profile parameters.

If strong impact of long term glycemic control on lipid profile parameters could have been established, HbA1c could be used as dual biomarker. This will help clinician to assess glycemic and lipid profile status and to predict long term complications by measuring HbA1c alone in type 2 diabetic subjects.

So, this study was conducted to see the correlation between glycaemic control and serum lipid profile in type 2 diabetic patients and to evaluate the utility of glycated haemoglobin (HbA1c) as an indirect marker of dyslipidaemia.

Methods

This hospital based observational study was conducted in the Department of Medicine, Sher-E-Bangla Medical College Hospital, Barisal from October 2014 to March 2015 over a period of 6 months. A total of 110 type 2 diabetes mellitus patients of both sexes admitted to the Medicine units of Sher-E- Bangla Medical College Hospital, Barisal, were selected for this study using a convenient sampling technique. Patients with nephropathy, hypothyroidism, familial lipid disorders, or who were taking lipid-lowering medications were excluded from this study. Informed written consent was taken from each study subject. Following standard procedures and protocols, fasting blood sugar, blood sugar two hours after breakfast, Glycosylated Hemoglobin (HbA1c) and lipid profiles were measured.

The data were collected by using a printed questionnaire. All statistical analyses were carried out using the SPSS software. Continuous variables were presented as means and standard deviation. Categorical data were presented as frequency with percentage. Chi-Square tests were performed for comparing categorical variables and t-tests for normally distributed continuous variables between two groups, Pearson correlation analyses were performed to detect any associations between continuous variables. A p value<0.05 was considered statistically significant.

Results

Majority of the patients incorporated in this study belongs to age group 51-60 years (43.6%), followed by 25.5% in age group 61-70 years. The age of respondents ranged from 34 to 70 years with the mean of 54.35 \pm 8.02 years. Among the patients' male were 70 (63.6%) and female were 40 (36.4%). Mean age of diagnosis of DM and duration of DM was 47.07 \pm 6.03 years and 7.27 \pm 3.41 years respectively. Mean BMI, FBS and HbA1c were 25.02 \pm 5.22 kg/m², 8.06 \pm 2.01 mmol/L and 8.34 \pm 1.9 % respectively (Table-I).

Pearson's correlation test was done to find out correlation of glycosylated Hemoglobin (HbA1c) with BMI, FBS and lipid profiles. Significant positive correlation of HbA1c was found with BMI, TC, TG, LDL-C and negative correlation with HDL-C (Table-II).

Pearson's correlation test was done to find out correlation of fasting blood sugar (FBS) with BMI and lipid profiles. Significant positive correlation of FBS was found with BMI, TC, TG, LDL and negative correlation with HDL (Table-III).

Unpaired t test was done to compare the lipid profiles between good glycemic control and poor glycemic control. TC, TG and LDL-C were found significantly higher in poor glycemic control and HDL-C was significantly lower in poor glycemic control (Table - IV).

Table-I		
Baseline characteristics of the patients (n=110)		
	Frequency (f)/ (mean±SD)	Percentage
Age (years)		
31-40	7	6.4
41-50	27	25.5
51-60	48	43.6
61-70	28	25.5
Mean ± SD	54.35 ± 8.02 (34-70)	
Gender		
Male	70	63.6
Female	40	36.4
Age at diagnosis of DM (years)	47.07±6.03 (33-60)	
Duration of DM (years)	7.27±3.41 (1-16)	
BMI (kg/m ²)	25.02±5.22 (20.2-32.2)	
FBS (mmol/L)	8.06±2.01 (5.3-12.4)	
HbA1c (%)	8.34±1.9 (6.4-14.0)	

There was positive pearsons correlation between HbA1c and Fasting Blood Sugar(FBS) and which was statistically

Table-II		
Correlation of HbA1c with BMI, FBS and lipid profile		
Variables	r	p-value
BMI	0.45	<0.001
FBS	0.92	<0.001
TC	0.86	<0.001
TG	0.50	<0.001
LDL-C	0.83	<0.001
HDL-C	-0.27	0.004

significant($r=0.92$ & $p<0.001$) (Figure-1). The figure-2 is a scatter plot which depicted statistically significant positive

Table-III		
Correlation of FBS with BMI and lipid profiles		
Variables	r	p-value
BMI	0.51	<0.001
TC	0.87	<0.001
TG	0.44	<0.001
LDL-C	0.86	<0.001
HDL-C	-0.30	0.001

pearsons correlation between HbA1c and Serum Total Cholesterol (TC) ($r=0.86$ & $p<0.001$). In figure-3 there was a positive correlation between HbA1c and serum triglyceride level and which is statistically significant($r=0.50$ & $p<0.001$).

Table-IV			
Comparison of lipid profiles between good glycemc control and poor glycemc control patients			
Variables	Good Glycemc Control(n=31)	Poor Glycemc control(n=79)	P value
TC	134.10 ± 12.35	205.55 ± 38.43	<0.001
TG	121.45 ± 19.27	152.00 ± 52.84	<0.001
LDL-C	71.32 ± 11.26	141.33 ± 35.96	<0.001
HDL-C	38.48 ± 4.21	33.82 ± 5.54	<0.001

The figure-4 and figure-5 depicted statistically significant ($r=0.83$ & $p=0.004$) positive pearsons correlation between HbA1c and Serum LDL-C and statistically significant ($r=-0.27$ & $p<0.001$) negative correlation between HbA1c and HDL-C, respectively.

Discussions

This hospital based observational study was undertaken to find out correlation between glycosylated hemoglobin and level of different parameters of lipid profile in type 2 diabetes patients. A total number of 110 diagnosed diabetic patients who came to the Sher-E-Bangla Medical College and Hospital, Barisal, during the period of October 2014 to March 2015, were enrolled in this study.

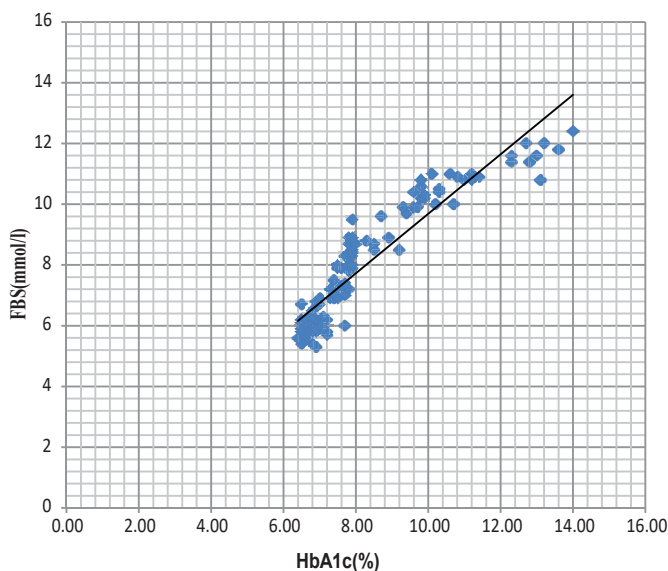


Figure - 1: Correlation of Glycosylated Hemoglobin(HbA1c) with Fasting Blood Sugar

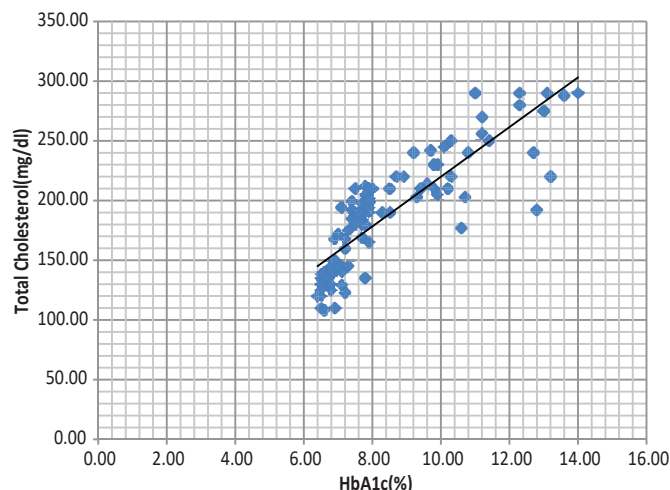


Figure - 2 : Correlation of Glycosylated Hemoglobin (HbA1c) with total Cholesterol

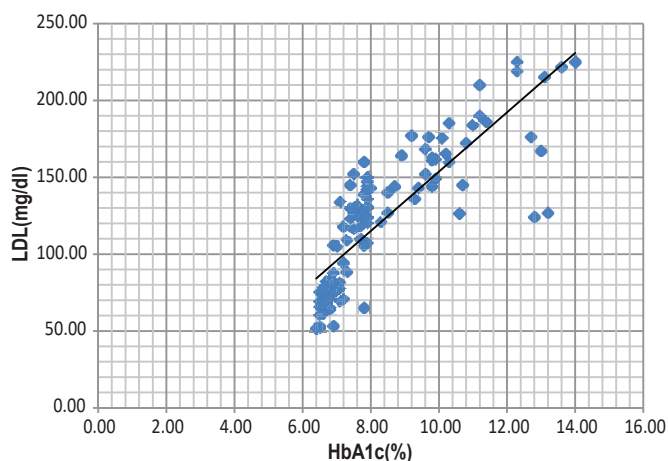


Figure - 4 : Correlation of glycoslated hemoglobin (HbA1c) with serum Low Density Lipoprotein Cholesterol(LDL-C)

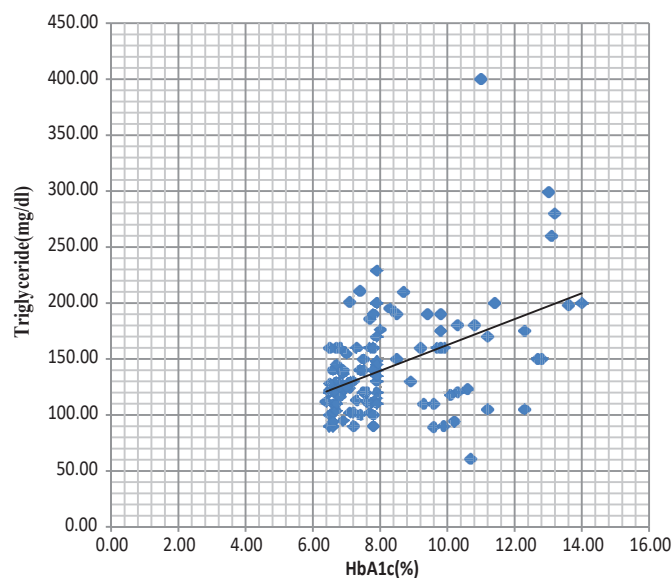


Figure - 3: Correlation of Glycosylated Hemoglobin (HbA1c) with serum Triglyceride

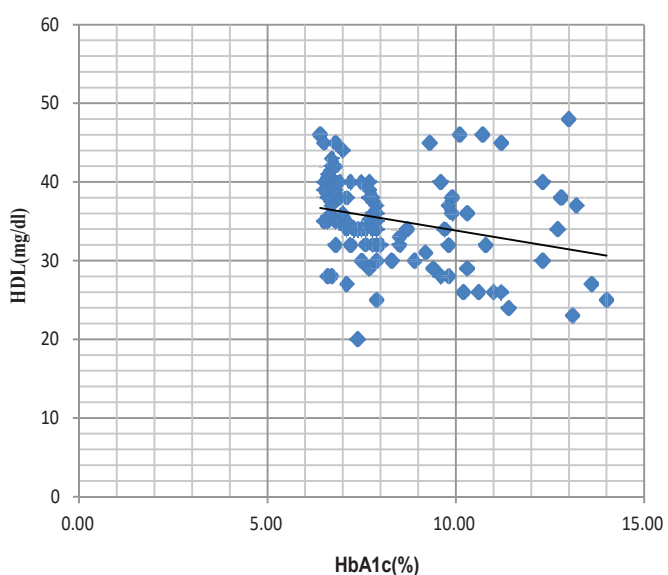


Figure - 5: Correlation of Glycosylated Hemoglobin (HbA1c) with serum High Density Lipoprotein Cholesterol (HDL-C)

In this current study, it was observed that the mean age was 54.35 ± 8.02 years with range from 34 to 70 years. The majority of population were found >50 years. Probably aged populations were more prone to develop diabetes mellitus. Out of these 110 subjects 70(63.6%) were males and 40(36.4%) were females (Table-I). Khan et al conducted a study in 2007 and showed mean age was 58.69 ± 10.21 years and males were 51.7% and females were 49.3%.¹⁹ Mean BMI of the respondents was 25.02 ± 0.22 kg/m² with a Range of 20.2-32.2 kg/m². Most of the diabetic patients (51.80%) in this study was in the BMI range of 18.5-24.9 kg/m². Western pacific region of world health organization(WHO) states BMI >23 kg/m² in Asian population is associated with adverse metabolic outcomes.⁵

Results of this study showed that the levels of LDL-C, TC and TG were significantly higher in type 2 diabetic patients. These findings are similar with the previous studies.²⁰ High prevalence of hypercholesterolemia, hypertriglyceridemia, high LDL-C and low HDL-C was found in type 2 diabetics in this study which are well known risk factors for cardiovascular diseases. Goldberg reported that the cause of dyslipidaemia in type 2 diabetes mellitus may be that insulin is not working properly which affects the liver apolipoprotein production.^{21,22} The apolipoprotein regulates the enzymatic activity of lipoprotein lipase (LpL) and Cholesterol ester transport protein. Insulin impacts the liver apolipoprotein production which regulates the enzymatic activity of lipoprotein lipase and Cholesterol ester transport protein.

These could be the likely causes of dyslipidemia in Diabetes mellitus as reported by Goldberg.

The mean values of FBS, HbA1c, TC, TG, LDL-C were higher in males as compared to female type 2 diabetic patients. This observation is in conformity with a study conducted by byV Siva Prabodh et al²³ in 2012. Gender wise evaluation of the data shows that there is no statistically significant difference in glycemic parameters as well as lipid profile between males and females except in HDL values which are higher in females.

Statistically significant correlation was found between HbA1c and FBS. A significant correlation between glycemic parameters (HbA1c and FBS) and lipid profile parameters was found in this study. Strong direct correlation of HbA1c and FBS with TG, LDL,TC, and inverse correlation was found with HDL in both male and female. This correlation was statistically significant in both sexes except for HDL in female. Though HDL in female is also inversely correlated with glycemic parameters, it was not statistically significant. These Observations are in agreement with earlier studies^{24,25} published by Rosediani M and Ito C et.al.

In the present study, diabetic patients were divided into 2 groups as per the HbA1c cutoff value of 7.0%. The diabetic patients with HbA1c value $\geq 7.0\%$ exhibited a significant increase in TC, LDL-C, TG, with significant decrease in HDL-C in comparison to patients with HbA1c value $\leq 7.0\%$. Statistically significant differences of mean values of lipid profile parameters between subjects of good glycemic control and poor glycemic control were found. This findings are also similar to the study done by Gligor Ramona et al.¹⁶ Khan HA et al¹⁹ showed the impact of glycaemic control on various lipid parameters in which severity of dyslipidemia increases in patients with higher HbA1c value. As elevated HbA1c and dyslipidemia are independent risk factors of CVD, diabetic patients with elevated HbA1c 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.²⁶ It has been estimated that reducing the HbA1c level by 0.2% could lower the mortality by 10%.²⁷ The Diabetes complications and control trial (DCCT) established HbA1c as the gold standard of glycemic control. The level of HbA1c value $<7.0\%$ was said to be appropriate for reducing the risk of cardiovascular complications. Several studies have reported significant correlations between HbA1c and lipid profiles and suggested the importance of glycemic control in normalizing dyslipidemia.^{28,29}

The results of the present study suggest the importance of glycemic control in order to manage dyslipidaemia and risk for cardiovascular disease.

Limitations of the study

Small size of the study population was small and it was the single centre study. Study was conducted in a tertiary hospital which does not represent all groups of the general population. Sample population is not representative of whole nation.

Conclusions

Elevated total serum cholesterol, Triglyceride, LDL-C and low HDL-C were observed in type 2 diabetics with poor glycemic control compared to patients with good glycemic control. This indicates that HbA1c can be used as a potential biomarker for predicting dyslipidemia in type 2 diabetic patients in addition to glycemic control. So, HbA1c may be utilized for screening of risks of cardiovascular events of diabetic patients and also for timely intervention with lipid lowering drugs.

Declaration

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Conflict of interest : The authors declare no conflict of interests.

Availability of data and material : These are available upon reasonable request.

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