Association between glycaemic control and serum lipid profile in type 2 diabetic patients: Glycatedhaemoglobin as a dual biomarker

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ABSTRACT

Background: Patients with type 2 diabetes have an increased prevalence of lipid abnormalities, contributing to their high risk of cardiovascular diseases (CVD).

Glycated hemoglobin (HbA1c) is a routinely used marker for long-term glycemic control. 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 diabetic patients[2].Apart from classical risk factors like dyslipidemia, HbA1c has now been regarded as an independent risk factor for (CVD) in subjects with or without diabetes.

Objective The aim of this study was to find out association between glycaemic control (HbA1c as a marker) and serum lipid profile in type 2 diabetic patients.

Methods This study was conducted in specialized center for Endocrinology and Diabetes (SCED) on 320 type 2 diabetic patient , from May 2009 TO November 2010The variables such as age, sex, family history, physical examination, fasting blood glucose, renal function test, thyroid function test, lipids profile panel test , HbA1c and body mass index (BMI) were analyzed .Dyslipidemia was defined according to the National Cholesterol Education Programme (NCEP) Adult Treatment Panel (ATP) III guidelines. Diabetes was defined according to American diabetes association criteria We excluded from this study other causes of dyslipidemia other than DM like uremia,over weight, hypothyroidism and others causes.

We selected diabetic patient with Ideal body weight and normal renal function.

Results In our study 114 (81%) females out of 132 and 147 (83%) males out of 178 were found tobe dyslipidemic. HbA1c demonstrated positive and significant correlations with total cholesterol
(TC), low density lipoprotein cholesterol (LDL-C), high density lipoprotein
cholesterol (HDL-C) and LDL-C ratio, non-HDL-C and TC/HDL-C ratio.

Patients with HbA1c value > 7.0% had significantly higher value of TC,
Triglycerid (TG), LDL-C, LDL-C/HDL-C ratio, non-HDL-C and TC/HDL-C ratio as
compared to the patients with HbA1c ≤ 7.0%. However, there was no significant
difference in value of HDL-C between two groups.

Conclusion :HbA1c can be used as a potential biomarker for predicting dyslipidemia in type 2
diabetic patients in addition to glycemic control.

Keywords: Diabetes mellitus, Dyslipidemia, Glycated hemoglobin, Lipid Profile panel, Biomarker

Al-Kindy College Medical Journal Vol.11 No.2.Page:10-14

** Received at 1th June 2013, accepted in final 25th Feb 2016.*

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One hundred million persons have a history of diabetes (DM) worldwide(1).

Lifestyle modifications, dietary modification, regular physical activity and weight reduction are indicated for prevention of diabetes (2),(5),(15)and(25).

In addition to the established major risk factors, atherosclerosis in type 2diabetes is also related to alterations in lipid profile (3),(13)and(23).

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 (3),(4)and(12).

Estimated risk of CVD has shown to be increased by 18% for each 1% increase in absolute HbA1c value in diabetic population (6),(11)and(14).

Positive relationship between HbA1c and CVD has been demonstrated in non-diabetic cases even within normal range of HbA1c (7),(8),(9)and(10).

Apart from classical risk factors like dyslipidemia, elevated HbA1c has now been regarded as an independent risk factor for CVD (17), (22)and(27) .

Non-HDL-C was shown to be the stronger predictor of CVD in diabetic population by , The Strong Heart Study,

Moreover, NCEP ATPIII has recommended using Non-HDL cholesterol in assessing CVD risk in patients with diabetes

Hence, Non-HDL cholesterol can be of great value in determining dyslipidemia in diabetic subjects.

Gimeno-Orna JA et al (28)and(30) showed that the main lipid predictor of vascular events was mean TC/HDL-C ratio and the predictive power of the TC/HDL ratio was found to be higher than that of Non-HDL cholesterol and study concluded that TC/HDL-C can be used as a treatment guides for diabetic dyslipidemia

Patients and methods

A total of 320 type 2 diabetic patients (178 males and 137 females) visiting the specialized center for Endocrinology and Diabetes (SCED) from May 2009 to November 2010, aged 25-65 years were included in this study.

Venous blood samples were collected from all the subjects after
at least 8 hours fasting. The serum was later used for analyzing fasting bloodglucosse (FBG), lipid profile panel test, Serum total cholesterol(TC),HDL-

cholesterol(HDL-C), Triglycerid(TG),Risk ratio (TC/HDL-C).

Indirect LDL-cholesterol and Non-HDL Cholesterol(Non HDL-C) was calculated by Friedwald and Frederickson formula.

For serum lipid reference level, National Cholesterol Education Programme (NCEP) Adult Treatment Panel III (ATP III) guideline was referred. According to NCEP-ATPIII guideline, hypercholesterolemia is defined as TC>200 mg/dl, high LDL-C when value >100 mg/dl,

hypertriglyceridemia as TG >150 mg/dl and low HDL-C when value <40 mg/dl.

Dyslipidemia was defined by presence of one or more than one abnormal serum lipid concentration. Diabetes was defined according to American Diabetes Association (ADA) criteria.

Results

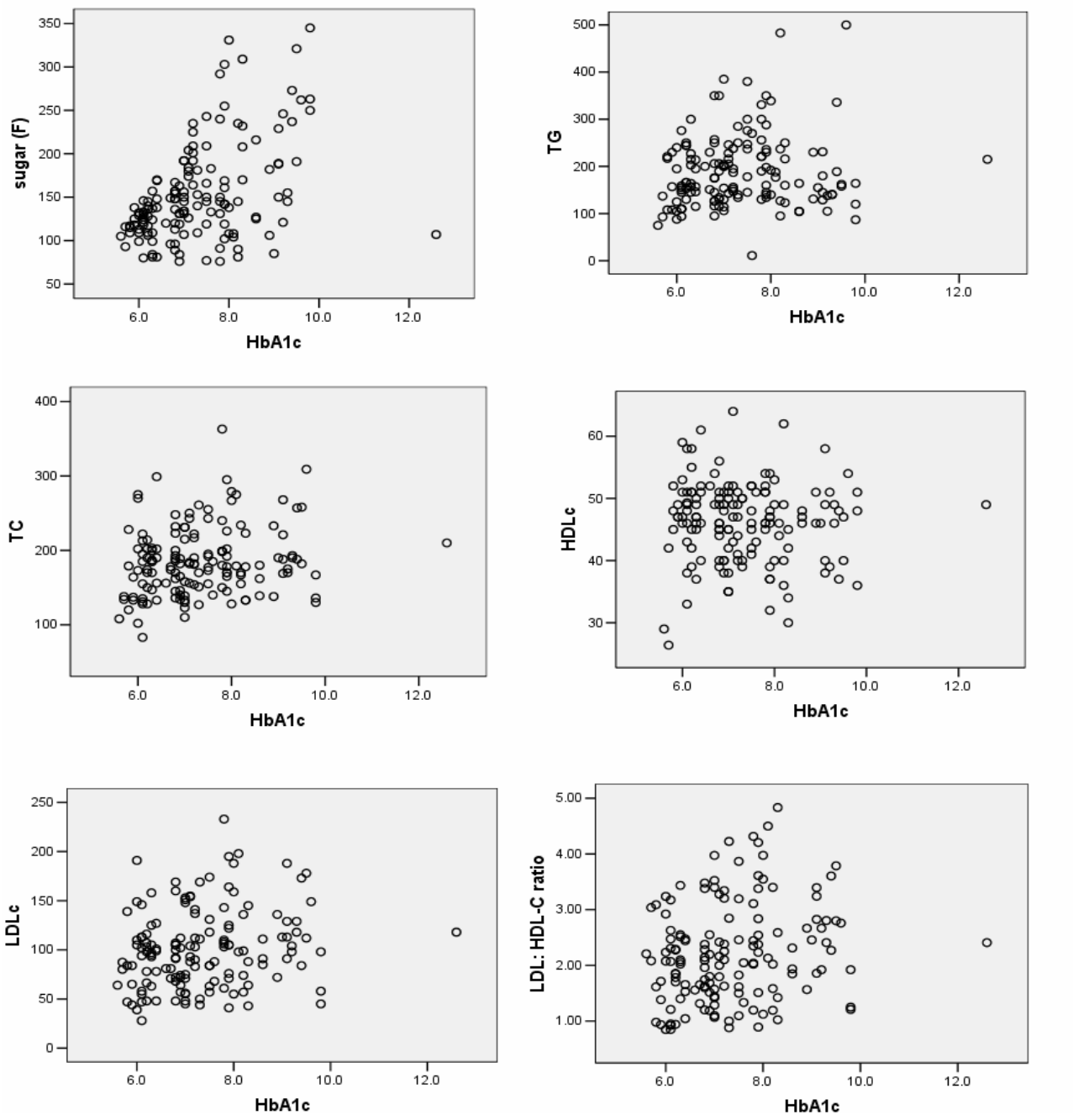
Among total 320 type 2 diabetic individuals included in this study, 178 were male and 132 were female.Hypercholesterolemia was found in 82 (25.6 %) individuals. Similarly, hypertriglyceridemia was found in 186 (58.2%) individuals, decreased HDL-C was found in 46 (14.3%) individuals and increased LDL-C was found in 140(45.6%) individuals. Among the diabetic individuals, 106(33.3%) individuals had only one abnormal lipid profile parameter, 88(27.5%) had two abnormal lipid parameter and 68(21. 2%) individuals had more than 2 abnormal lipid profile parameter. According to NCEP-ATPIII guideline, 114(81%) females out of 132 and 1470 (83%) males out of 178 were dyslipidemic.Diabetic patients were classified into 2 groups according to their glycemic index; first group consists of patients with HbA1c value ≤7.0 % and second group consists of patients with HbA1c value >7.0%. Patients with HbA1c value >7.0% had significantly higher value of TC (P=0.024), TG (P=0.030), LDL-C (P=0.011), Non-HDL-C(p=0.002), LDL-C/HDL-Cratio (p=0.002) and Risk ratio(p=0.001) as compared to the patients with HbA1c value ≤ 7.0% (Table 1).

Table1. Biochemical Parameters categorized by patients' glycemic control (HbA1c)

Parameter	Glycated Hemoglobin (HbA1c) ≤7.0 (n=82)	>7.0 (n=85)	P-value
	Mean ± SEM	Mean ± SEM	
TC	174.89 ±5.29	181.78 ±5.19	0.024*
TAG	173.05 ±7.88	199.36 ±9.07	0.03*
HDL-C	46.79± 0.84	45.71± 0.68	0.322
LDL-C	91.63± 4.27	107.86 ±4.60	0.011*
Non-HDL-C	127.03 ±4.72	149.20 ±5.32	0.002*
Risk ratio (TC/HDL-C)	3.76±0 .098	4.31±0 .127	0.001*
LDL-C/HDL-C	1.98±0 .089	2.43±0 .107	0.002*
FBG	123.56 ±3.03	175.0± 6.79	0.000*

*statistically significant

Figure 1. Correlations between HbA1c and FBG & Lipid profile Panel



Discussion

In this study, we have evaluated the pattern of lipid profile parameters in diabetic subjects and its correlation with HbA1c.

This study reveals high prevalence of hypercholesterolemia, hypertriglyceridemia, high LDL-C and low HDL-C levels which are well known risk factors for cardiovascular diseases.

Insulin affects the liver apolipoprotein production. It regulates the enzymatic activity of lipoprotein lipase (LpL) and Cholesterol ester transport protein.

All these factors are likely cause of dyslipidemia in Diabetes mellitus(16)and(18). Moreover, insulin deficiency reduces the activity of hepatic lipase and several steps in the production of biologically active LpL may be altered in DM (19)and(21).

The main disorder in lipid metabolism was hypertriglyceridemia in our study. This finding is Inconcord with other study (20).

In the study of Sehran et al in Pakistan, 54% diabetic individuals had elevated LDL-C and > 50% individuals had increased TG. These findings are similar to our study.

We also observed significant correlations between HbA1c and TC, LDL-C and LDL-C/HDL-C ratio. HbA1c level was eminent as showing positive correlation with TC, LDL-C and TG in diabetic patients (24)and(26).

A higly significant correlation between HbA1c and FBG in our study is similar with various previous studies (21),(23) and(30) .

Conclusion

Significant correlation between HbA1c and various circulating lipid parameters and significant difference of lipid parameters in two groups (≤7.0% and >7.0%) of glycated hemoglobin indicates that 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 (30). It has been estimated that reducing the HbA1c level by 0.2% could lower the mortality by 10%(29) and (30).

HbA1c can be used as a potential biomarker for predicting dyslipidemia in type 2 diabetic patients in addition to glycemic control hence early diagnosis can be accomplished through relatively inexpensive blood testing.

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