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Biochemistry

IMPACT OF POOR GLYCEMIC CONTROL ON SERUM LIPID PROFILE IN TYPE II DIABETES MELLITUS – A COMPARATIVE STUDY ON SUBJECTS WITH TYPE II DIABETES MELLITUS BASED ON HBA1C LEVELS AT WAYANAD REGION

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ABSTRACT Diabetes represents a spectrum of metabolic disorders, which has become a major health challenge worldwide. Diabetes is pandemic in both developed and developing countries. One of the most common problems in diabetic subjects is atherosclerotic cardiovascular disease which is induced by lipid abnormalities. Total 100 subjects were included in the study. Subjects were divided into two groups Group A and Group B. Group A consists of 50 non diabetic subjects with HbA1C<6.5%. Group B consists of 50 diabetic subject with HbA1C>6.5%. The samples were collected and processed as per standard protocol and analysed in BIO-RAD D-10 TM Hemoglobin A1c Program auto analyzer and COBAS INTEGRA 400 PLUS auto analyzer. The group B subjects with HbA1c value >6.5% exhibited a significant increase in FBS, TC, LDL-C, TG, HDL-C, TC/HDL-C ratio compared to group A subjects. The HbA1c showed significant positive relationship with TC (r=0.193), TG (r=0.13), HDL-C (r=0.014), LDL-C (r=0.073). Female diabetic subjects showed higher mean values for FBG, PPBS, TC, TG, and LDL-C than male diabetic subjects. The present study suggested that the glycemic control of the patient has got a strong impact on the serum lipid profile levels and atherosclerosis, CVD and CHD include heart attack and stroke. Subjects should be educated about regular monitoring of profiles and if found to be abnormal, should control blood glucose and cholesterol very effectively. In out diabetic study clearly added value of HbA1C can be monitoring long term glycemic control and as a potential indicator for dyslipidemia in group B subjects.

KEYWORDS :

INTRODUCTION

Diabetes represents a spectrum of metabolic disorders characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both; which has become a major health challenge worldwide (1). Diabetes is pandemic in both developed and developing countries. In 2000, there were an estimated 175 million people with diabetes worldwide and by 2030; the projected estimate of diabetes is 345 million.

By the year 2030, over 85 percent of the world's diabetic patients will be in developing countries. India has a high prevalence of diabetes mellitus and the numbers are increasing at an alarming rate. In India alone, diabetes is expected to increase from 40.6 million in 2006 to 79.4 million by 2030. The onset of diabetes among Indians is about a decade earlier than their western counterparts and this has been noted in Asian Indians in several studies. India has the largest number of diabetics in the world and the Government of India has rightly launched the national programme for control of diabetes, cardiovascular diseases and stroke in January 2008.

Diabetic patients have a greater likelihood of having dyslipidemia and obesity. Because early detection and prompt treatment may reduce the burden of diabetes and its complications, screening for diabetes may be appropriate under certain circumstances (1).

Epidemiological studies have demonstrated that type 2 diabetes mellitus (DM) is a well-known risk factor for the development of cardiovascular disease, cerebrovascular disease and peripheral vascular diseases. Dyslipidemia is a risk Factor for coronary artery disease, a leading cause of mortality in patients with diabetes mellitus. Dyslipidemia remains largely undiagnosed and under in high risk populations, such as patient with type-2 diabetes (2).

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 diabetes patients. Apart from classical risk factors like dyslipidemia, elevated HbA1c has now been regarded as an independent risk factor for cardiovascular disease in subjects with or without diabetes (3).

Estimated risk of cardiovascular disease has shown to be increased by 18% for each 1% increase in absolute HbA1c value in diabetic population. Positive relationship between HbA1c and cardiovascular disease has been demonstrated in non-diabetic cases even within normal range of HbA1c (4).

Apart from classical risk factors like dyslipidemia, elevated HbA1c has now been identified as an independent risk factor for cardiovascular disease in subjects with or without diabetes. Estimated risk of cardiovascular disease has shown to be increased by 18% for each 1% increase in absolute HbA1c value in diabetic population (4). Although new tests of glycation are now available, they are not without limitations of their own (5), very expensive and impractical for everyday use in developing countries like India. However the routinely used biomarker, HbA1c which is relatively cheap and affordable (in a developing country like India) has come under some critiques for not properly assessing the level of glycation and also dyslipidemia in certain haematological and biochemical conditions.

This study is an attempt to reassess the association of glycemic control and lipid profile using HbA1c whiles taking into consideration some of the factors affecting its use. This study will also afford health care providers attending to diabetic patients, the needed information as to when to use HbA1c in clinical monitoring of glycation and dyslipidemia.

The aim of the study is to investigate the relationship between glycemic control and serum lipid profile and to evaluate the role of HbA1c as an independent risk factor for cardiovascular diseases in type-2 diabetic patients.

MATERIALS AND METHODS

The work embodied in the study was carried out in the biochemistry department of the DM Wayanad Institute of Medical Science (DM WIMS), Meppadi, Wayanad, Kerala, during the period of October2016 to November 2016. DM WIMS is a well-equipped high tech hospital in the wayanad district. The subjects for the present study

are selected from the cases referred to department of biochemistry for evaluation of blood glucose levels, lipid profiles and HbA1C from subjects attending various OP departments of DMWIMS, Meppadi, Wayanad. Total 100 subjects were included in the study. Subjects were categorised into two groups, and termed as Group A and Group B. Group A consists of 50 non diabetic subjects with HbA1C <6.5%. Group B consists of 50 diabetic subjects with HbA1C >6.5%. There detailed diagnostic data was collected from subject medical records section of the hospital. Males and Females of age between 30 to 70 years were included in the study.

Majority of the subjects were on oral hypoglycemic drug, diet control and exercise for controlling hyperglycemia. Their HbA1c were quantitatively determined by ion-exchange High Performance Liquid Chromatography (HPLC). The test done on BIO-RAD D-10 TM Hemoglobin A1c Program auto analyzer. Blood glucose level and Lipid profile are quantitatively determined by enzymatic method. The tests were done on COBAS INTEGRA 400 PLUS auto analyzer.

STATISTICALANALYSIS

R software has been used for the statistical analysis. The correlations between HbA1C and lipid profile, blood glucose have represented using "Scatter Plots" and the corresponding correlation coefficients (r) have been found out.

RESULTS

Total 100 subjects were included in the study. Patients were categorised into two groups Group A and Group B. Group A consists of 50 non diabetic subjects with HbA1C <6.5%. Group B consists of 50 diabetic subject with HbA1C >6.5%. These detailed diagnostic data was collected from subject medical Records section of the hospital. Males and Females of age between 30 to 70 years were included in the study.

Table 1.Comparison of Mean, SD, P value of measured parameters between Group A and Group B Subjects.

Parameters	Group A(n=50) Mean ± SD	Group B(n=50) Mean ± SD	P value
Age	48.16 ± 12.48	54.82 ± 9.07	0.003**
HbA1c	5.50 ± 0.41	9.87 ± 1.44	0.000***
FBS	97.70 ± 7.47	204.01 ± 60.92	0.000***
PPBS	102.82 ± 17.59	267.88 ± 78.10	0.000***
Total cholesterol	175.08 ± 34.85	274.60 ± 36.34	0.000***
Triglyceride	122.20±43.032	256.64 ± 78.09	0.000***
HDLCholesterol	36.117 ± 7.19	42.02 ± 15.05	0.013**
LDL-Cholesterol	125.46 ± 39.74	215.82 ± 28.59	0.000***
C/H Ratio	4.48 ± 1.38	7.99 ± 2.07	0.000***

Each value is expressed as mean ± SD for each group.
*** Statistically highly significant.** Statistically significant

Table 2.Positive Correlations between HbA1c and, lipid profile, serum blood glucose in group B Subjects.

Parameter	Total Cholesterol	Triglycerides	High Density Lipoproteins	Low Density Lipoproteins	Total Cholesterol/HDL ratio	Fasting blood sugar	Postprandial blood sugar
HbA1c	r = 0.193 p = 0.00**	r = 0.13 p =0.0**	r = 0.014 p = 0.00**	r = 0.17 p = 0.00**	r= 0.073 p = 0.00**	r= 0.31 p = 0.00**	r = 0.34 p = 0.0**

Each value is expressed as mean ± SD for each group.
** Statistically highly significant.
r – Correlation coefficient

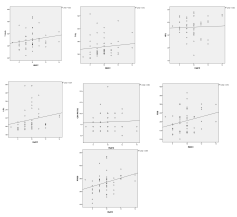

Figure: 1 Positive correlation between HbA1c and Lipid profile, FBS, PPBS in group B subjects (Scatter Plots).
Figure: 1 Positive correlation between HbA1c and Lipid profile, FBS, PPBS ingroup B subjects (Scatter Plots).
A). Positive correlation between HbA1c and Total Cholesterol
B). Positive correlation between HbA1c and Triglycerides.
C). Positive correlation between HbA1c and HDL-C.
D). Positive correlation between HbA1c and LDL-C.
E). Positive correlation between HbA1c and Total cholesterol/HDL ratio.
F). Positive correlation between HbA1c and Fasting blood glucose.
G). Positive correlation between HbA1c and Postprandial blood glucose.

Table 3.HbA1c, Lipid profile Parameters, PPBS, FBS, between Male and Female in group B subjects.

Parameters	Males(n=20) Mean ± SD	Females (n=30) Mean ± SD
Age	54.47 ± 9.85	55.06 ± 8.65
HbA1c	9.66 ± 1.20	10.02 ± 1.58
FBS	200.80 ± 58.08	206.26 ± 63.71
PPBS	254.38 ± 53.70	277.33 ± 91.12
Total cholesterol	263.90 ±18.69	282.1 ± 43.5
Triglyceride	258.66 ± 85.31	255.23 ± 74.10
HDL-Cholesterol	34.90 ± 8.33	36.96 ± 6.29
LDL-Cholesterol	210.14 ± 24.87	219.80 ± 30.71
C/H Ratio	8.10 ± 2.5	7.86 ± 1.69

Each value is expressed as mean ± SD for each group.

DISCUSSION

In the present study we have evaluated the pattern of lipid profile parameters in diabetic subjects and its correlation with HbA1c. Abnormality of Cholesterol metabolism may lead to cardiovascular disease and heart attacks. Total cholesterol levels are different in the presence of risk factor for diabetes mellitus. The National Cholesterol Educational Program (NCEP) identified elevated LDL as a primary risk factor for coronary heart disease (CHD).

The group B subjects with HbA1c value >6.5% exhibited a significant increase in FBS, TC, LDL-C, TG, HDL-C, TC/HDL-C ratio compared to group A subjects(Table 1). These finding were in agreement with the previous studies (6, 7). Both lipid profile and diabetes have been shown to be the important predictors for metabolic disturbances including dyslipidemia, hypertension, and cardiovascular disease. Lipids play a vital role in the pathogenesis of diabetes mellitus. High prevalence of hypercholesterolemia, Hypertriglyceridemia and high LDL and Low HDL was found in group B subjects in this study, which are well known risk factors for cardiovascular diseases.

Table 2 and Figure 1 results show that highly significant correlation between HbA1c and FBS, PPBS was noted in this study. Similarly, significant correlations between HbA1c and TC, TG, HDL, LDL-C and TC/HDL-C ratio were observed (8).In this regard it is worth to state that apo-B containing particles and small LDL-C particles are increased in diabetes and these metabolic indicators are indirectly reflected by TC/HDL-C ratio rather than LDL-C alone. The significant association between HbA1c with TC/HDL-C ratio in the present study suggests the importance of glycemic control reflects an improved lipid status (9).

In diabetes many factors may affect blood lipid level, because of interrelationship between carbohydrate and lipid metabolism. Therefore, any disorder in carbohydrate metabolism leads to disorder in lipid metabolism.Goldberg (10) reported that the cause of Dyslipidemia in type 2 diabetes mellitus may be that insulin is not working properly which affects the liver apolipoprotein production. The apolipoprotein regulates the enzymatic activity of lipoprotein lipase (LpL) and Cholesterol ester transport protein (10),

Table 3 results show that Female diabetic subjects showed higher mean values for FBG,PPBS, TC, TG, and LDL-C than male diabetic subjects. The study suggests relative risk of cardiovascular disease is higher in diabetic women compared to men (11)
Severity of dyslipidemia increases in subjects with higher HbA1c value. As elevated HbA1c and Dyslipidemia are independent risk

factors of CVD, diabetes patients with elevated HbA1c and dyslipidemia can be considered as a very high risk group for CVD (11). Also, this study showed that HbA1c can be used as a potential biomarker for predicting dyslipidemia in diabetic patients (12). Thus, the result of the present study suggest the importance of glycemic control in order to manage dyslipidemia and risk for cardiovascular diseases in group B subjects at Wayanad region. Thus, it can be deduced that diabetic populations with higher blood glucose levels are more fain to cardiovascular diseases. Also, this study showed that HbA1c can be used as a potential biomarker for predicting dyslipidemia in diabetic patients.

CONCLUSION:

The present study suggested that the glycemic control of the patient has got a strong impact on the serum lipid profile levels and atherosclerosis, CVD and CHD including heart attack and stroke. Patients should be educated about regular monitoring of lipid profiles and if found to be abnormal, should control blood glucose and cholesterol very effectively. In out diabetic study clearly added value of HbA1C can be monitoring long term glycemic control and as an indirect indicator for dyslipidemia in group B subjects.

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