

Original Research Article

HbA1c as screening biomarker of dyslipidemia in type 2 diabetes mellitus patients

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ABSTRACT

Background: Patients with diabetes are considered to be at high risk for dyslipidemia and hypertension and therefore vulnerable to cardiovascular diseases. This study describes the possible role of Glycated Hemoglobin (HbA1c) and serum lipid profile as a biomarker for detecting cardiovascular diseases. The aim of present work is to study the role of HbA1c as a screening biomarker for dyslipidemia in patients with type 2 Diabetes Mellitus (T2DM).

Methods: Present study consists of 100 Type 2 DM patients between age 30-75 years along with age and sex matched 100 healthy controls. Fasting Blood samples were collected from all participants for measuring lipid profile, blood sugar (FBS) and HbA1c.

Results: Present study revealed a significantly increased level of glycated hemoglobin (HbA1c) in cases compared to control. HbA1c showed direct and significant correlations with cholesterol, triglycerides and LDL and inverse correlation with HDL in cases when compared to controls.

Conclusions: HbA1c can be used as a potential biomarker for the prediction of Dyslipidemia and CVD.

Keywords: Dyslipidemia, HbA1c, Type 2 diabetes mellitus

INTRODUCTION

Diabetes mellitus is a major health problem for India. It is associated with the development of a variety of complications that have a significant impact on morbidity and mortality.¹ The long-term complications of type 1 and type 2 diabetes include the microvascular complications of retinopathy, nephropathy and neuropathy, but the major health problem in type 2 diabetes is the increased risk of macrovascular complications, such as coronary artery disease, cerebrovascular disease and peripheral artery disease.² In India alone, 31.7 million people had diabetes in year 2000 which latter on increased to 61.3 million in 2011 and is expected to reach 101.2 million by 2030

(International Diabetes Federation).³ Thus India is the 2nd largest country in world diabetes prevalence.³ The maximum burden of diabetes in society is mainly contributed by DM type 2 which accounts for about 90% cases of diabetes.⁴ It is said that DM type 2 will alone affect 300 million people world-wide by 2025.⁵

Diabetes mellitus is a multifaceted group of metabolic diseases characterized by the increased level of glucose in the blood (hyperglycemia). This condition is due to non-utilization of glucose by body cells due to insulin resistance shown by the cells or due to insulin deficiency.⁶⁻⁸ This results in abnormalities in carbohydrate, protein and fat metabolism.⁹ Dyslipidemia and obesity are the most common complex metabolic

disorders accounting for the highest toll of health resources globally by its increasing incidences. This consequently leads to Type 2 Diabetes Mellitus (T2DM) and Cardiovascular Disorders (CVDs) with variable reports about the role of metabolic factors on glycemic control. The current study is designed to determine the association of Dyslipidemia and Obesity with glycated hemoglobin (HbA1c) in T2DM and non-diabetic subjects.¹⁰ The best index of long-term control of blood glucose level is measurement of Glycated hemoglobin or glyco-hemoglobin.¹¹

Recently, elevated HbA1c has been regarded as an independent risk factor for coronary heart disease (CHD) and stroke in subjects with or without diabetes.^{12,13} The impact of poor glycaemic control is so grave that increased maternal HbA1c could impair foetal long axis cardiac function, whereas improving glycaemic control can substantially reduce the risk of cardiovascular events in diabetics.¹⁴⁻¹⁶

Proteins are frequently glycated during various enzymatic reactions when the conditions are physiologically favorable. However, in the case of hemoglobin, the glycation occurs by the non-enzymatic reaction between the glucose and the N-terminal end of the β -chain, which forms a Schiff base.^{17,18} During the rearrangement, the Schiff base is converted into Amadori products, of which the best known is HbA1c. Vaag has suggested that improving glycaemic control in patients with type 2 diabetes may be more important than treating dyslipidaemia for the prevention of both microvascular and macrovascular complications.¹⁹

METHODS

This retrospective study was conducted at department of biochemistry at Gayatri medical college, Marikavalasa, Visakhapatnam, India. Study includes 100 type 2 diabetes mellitus patients of age group 35-75 year who visited medicine OPD of GVP Medical hospital along with 100 age and sex matched healthy controls.

Fasting venous blood samples were collected from all participants in EDTA and plain containers. Plain container Sample was centrifugated at central laboratory at 3000 RPM for 10 minutes. Serum glucose was estimated by GOD-POD method, TC, TG, and HDL are estimated by Enzymatic end point methods by full auto Analyzer (MEDICA EASY RA). LDL-C estimation is based upon Friedewald's formula $LDL-C = TC - HDLc - TG/5$ where $VLDLc = TG/5$. Glycated hemoglobin (HbA1c) is quantitatively measured by fluorescence Immunoassay using Ichromax fluorescence detection system in a sample of whole blood. Adult Treatment Panel III (ATP III) guideline was used which defined hyper cholesterolemia total cholesterol >200mg/dl, high LDL-C when value >100mg/dl, hypertriglyceridemia when value >150 mg/dl and low HDL-C when value <40 mg/dl.

Statistical analysis

Obtained results of case group were compared with control group for determination of significance of difference. P-value was calculated by using student t-test calculator. P-value less than 0.05 were considered as significant.

RESULTS

Table 1 shows the demographic data of cases and controls with Mean \pm SD of age in years. Table 2 shows Comparison of various biochemical parameters between cases and controls, all the biochemical parameters shows significantly ($p = <0.05$) increases in cases compared to controls. Table 3 shows the correlation of HbA1C with lipid profile of type 2 diabetes patients, HbA1C shows a significant positive correlation with lipid profile except HDL ($r = -0.18$, $p = 0.05$) it shows significant negative correlation with HbA1C.

Table 1: The causes of death.

Group	Number	Age	Group(yr)
Group 1(Case)	100	35-70	54.6 \pm 6
Group 1(Control)	100	35-70	51.4 \pm 7

Table 2: Comparison of various biochemical parameter case group and control group.

Parameter	Group (Case) [n=100]	Group (Control) [n=100]	p-Value
Fasting blood glucose (FBS) (mg/dL)	142 \pm 5.8	83.5 \pm 6.8	<0.05 (s)
S. Cholesterol (mg/dL)	284 \pm 11.3	148.6 \pm 8.3	<0.05 (s)
S. Triglyceride (mg/dL)	226 \pm 6.1	112.5 \pm 6.3	<0.05 (s)
S. HDL (mg/dL)	36.5 \pm 5.9	43.8 \pm 3.4	<0.05 (s)
S. VLDL (mg/dL)	45.3 \pm 4.1	22.5 \pm 5.8	<0.05 (s)
S.LDL (mg/dL)	195.4 \pm 9.7	85.6 \pm 7.9	<0.05 (s)
HbA1c (%)	11.5 \pm 0.9	5.4 \pm 0.4	<0.05 (s)

Note: S: Significant; NS: Non-significant

Table 3: Correlation of HbA1C with lipid profile of diabetes type 2 patients.

Parameter	Correlation coefficient	P-value
S. Cholesterol (mg/dL)	+0.53	<0.05 (s)
S. Triglyceride(mg/dL)	+0.89	<0.05 (s)
S. HDL(mg/dL)	-0.18	>0.05 (NS)
S. LDL(mg/dL)	+0.59	<0.05 (s)
S. VLDL(mg/dL)	+0.35	<0.05 (s)

Note: S: Significant; NS: Non-significant

DISCUSSION

Diabetes mellitus (DM) is a hereditary, chronic and endocrine-metabolic disorder. 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. Alterations in lipid and lipoprotein profile contribute to atherosclerosis in type 2 diabetes. Control of blood glucose in patients with diabetes can be assessed by several methods. These include assessment of glycated hemoglobin (HbA1c), fasting blood sugar (FBS), and Lipid profile. The gold standard for assessment of glycaemic control at follow up is the glycated hemoglobin level. In the present study we have estimated the diagnostic value of HbA1c as a dual marker. Diagnosis of diabetes rests on the measurement of plasma glucose levels. According to American Diabetic Association FBS >126mg/dl is diagnostic value of diabetes. The mean value of HbA1c were higher in cases (11.5±0.9) in comparison to controls (5.4±0.4) and the differences were statistically significant <0.05. The mean value of FBS were higher in cases (142±5.8) than with controls (83.5±6.8) and the differences were statistically significant <0.05. A significant correlation between HbA1c and FBS found in this study is in agreement with earlier reports by Rosediani et al, Ito et al, Ko et al Ravipati et al and it is observed a direct correlation between HbA1c and the severity of coronary artery disease in diabetic patients.²⁰⁻²³ Another study in 2011 independently showed that cardiovascular disease (CVD) is significantly higher in people with high levels of HbA1c.²⁴ In this study, it was found that Serum total Cholesterol, triglycerides, VLDL and LDL-C were significantly higher in diabetic type 2 groups than control group and were in borderline high risk range. While serum HDL-C was significantly lower in diabetic type 2 group than control group and was towards lower range of normal value. Thus, the study showed the high prevalence of dyslipidemia, a well-known risk factor for cardiovascular disease.²⁵ Thus the findings were in consistent with previous studies.^{26,27} Thus reduction in HbA1c is associated with reduction in diabetes related risk complication.²⁸ Type 2 diabetic patients are at a much higher risk of cardiovascular diseases than the non-diabetic. Thus, the risk of cardiovascular events in diabetics can be reduced by improving the glycemic control.²⁹ Type 2 diabetic patients have markedly increased risk of coronary heart disease than similarly dyslipidaemic non-diabetic subjects. Low HDL and high VLDL cholesterol, high triglycerides are powerful risk indicators for coronary heart disease events in patients with type 2 diabetes mellitus. The cause of dyslipidemia in diabetes mellitus type 2 might be due to insulin insensitivity or resistance affecting the apoprotein production by the liver which regulates the enzymatic activity of lipoprotein lipase and cholesterol ester transport protein. A highly positive significant relationship of HbA1C with dyslipidemia was observed in the present study. Erclays et al also reported positive

correlation of HbA1C level with total cholesterol and triglycerides level in diabetic persons.³⁰⁻³² In diabetic persons HbA1C ≤7% was said to be appropriate for reducing the risk of cardiovascular complications.³³ The diabetic patients with higher HbA1C value could have significant increased level of TC, TG, LDL-C and HDL-C in comparison to patients with HbA1C value ≤7% which might be responsible for the increased severity of dyslipidemia in patients with higher HbA1C values as reported by Khan et al.³⁴ Diabetic people can know about the status of their lipid levels by getting their HbA1C values. Until and unless HbA1C remained below 7%, lipid profile could be predicted to be normal. It had been reported that reducing the HbA1C level by 0.2% could lower the mortality by 10%.³⁵ Thus, dyslipidemia could be ruled out by their HbA1C levels in diabetes mellitus type 2 patients. Changes occurring in diabetic dyslipidaemia include quantitative and qualitative changes. Quantitative changes include increase in LDL levels and decrease in HDL levels, due to increase in hepatic lipase activity and decrease in VLDL clearance. Qualitative changes include size difference in lipid parameters, non-enzymatic glycosylation of LDL and susceptibility of LDL cholesterol to form peroxides, thus increasing risk of atherosclerosis and cardiovascular complications among diabetic patients.³⁶ Hyperglycaemia increases complications in diabetes mellitus by generating reactive oxygen species, resulting on oxidative stress. Increased lipid peroxidation causes crosslink formation between single molecules of amino acids and LDL particles. In metabolically poorly controlled diabetic patients, glycation of LDL increases with hyperglycemia.³⁷ This elevated level of LDL is explained by decreased catabolism of LDL, decreased activity of cholesterol ester transfer protein and lipoprotein lipase activity.^{37,38} It has been suggested that non enzymatic glycosylation of the LDL particle itself result in its increased incorporation in the arterial wall.³⁹ Thus, plasma LDL levels are high and atherosclerosis occurs very early in life.³⁹ Because of its critical importance in atherogenesis, LDL cholesterol is a focus of current guidelines for determination of the risk of cardiovascular diseases. The above discussion clearly indicates the clinical significance of various lipid parameters in predisposing diabetic patients to cardiovascular complications. Significant correlations between HbA1c and all lipid parameters and a linear relationship between HbA1c and dyslipidemia point towards the usefulness of HbA1c for screening diabetic patients at high risk of developing CAD.

CONCLUSION

From present study it may be concluded that HbA1C might be used as a reliable biomarker in the screening of dyslipidemia in diabetes type-2 patients because it showed positive correlation with TC, TG, VLDL, and LDL-C but negative correlation with HDL-C. Patients with Type-2 DM are considered to be at more risk of Dyslipidemia and Hypertension, hence targets for CVD

and complications. The key findings of this study demonstrated that most of the microvascular and macrovascular complications in Type-2 DM patients arise with an increase in HbA1c, dyslipidaemia and hypertension. HbA1c can potentially be used as a potential biomarker for the predictor of Dyslipidemia and CAD.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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