Original research article

A prospective study and Correlation between Glycosylated Haemoglobin and Serum Lipid Profile in Patients with Type 2 Diabetes Mellitus in KBN Hospital, Karnataka, India

Dr. Anand Shankar[1], Dr. Girish Ronad[2], Dr. Ravi Kumar[3]

[1]Assisstant Professor, Department of General Medicine, Faculty of Medicine, Khaja Banda Nawaz University, Kalaburagi. Karanataka. India.

[2]Assisstant Professor, Department of General Medicine, Faculty of Medicine, Khaja Banda Nawaz University, Kalaburagi. Karanataka. India.

[3]Resident, Department of General Medicine, Faculty of Medicine, Khaja Banda Nawaz University, Kalaburagi. Karanataka. India.

Corresponding Author: Dr. Girish Ronad

Abstract

Introduction: Patients with type 2 diabetes have an increased prevalence of lipid abnormalities, contributing to their high risk of cardiovascular diseases (CVD). This study is an attempt to evaluate the diagnostic value of Glycosylated hemoglobin (HbA1c) in predicting diabetic dyslipidemia**.**

Aims & Objectives: To study the correlation between glycosylated hemoglobin (HbA1c) and serum lipid profile in Type 2 Diabetics

Material and Methods: This is a cross sectional study conducted at Department of General Medicine, Khaja Banda Nawaz University, Kalaburagi,Karnataka from December 2018 to February 2019. In our study 50 patients of Type 2 diabetes mellitus were taken for the study after applying inclusion and exclusion criteria, and after obtaining written and informed consent from them. HbA1c and Fasting Lipid profile were done using appropriate tests. Correlation (Pearson's) test was used to interpret the result

Results: Mean total cholesterol was 155.76±13.41, mean total triglyceride was 180.52±17.21, mean LDL was 99.09±12.72, Mean HDL was 36.94±4.28 and mean HbA1c was 9.76±1.46. HbA1c negatively and significantly correlated with HDL (r= - 0.13). HbA1c positively and significantly correlated with total cholesterol (r=0.20) and LDL (r=0.24), did not show any show correlation with VLDL (r=0.03) and total triglycerides (r=0.02).

Conclusion: It was concluded from the results of this study that HbA1c can also be used as predictor of dyslipidaemia in Type 2 Diabetics in addition to as a glycaemic control parameter**.**

Keywords: Type 2 diabetes, Cardiovascular diseases, Glycosylated haemoglobin, Dyslipidaemia.

Introduction

Diabetes mellitus (DM) refers to a bunch of disorders of metabolism that share the phenotypic sign of hyperglycaemia. Different variants of DM are caused due to the interaction of various genetic factors with environmental factors. Depending on the pathogenic process leading to hyperglycaemia DM is classified, as Type I, Type II, Gestational Diabetes and Other specific types as maturity onset diabetes of youth (MODY), lipodystrophy diabetes, secondary diabetes due to pancreatitis, hemochromatosis, drug-induced, infectious, insulin receptor antibodies. [1]

Type II diabetes mellitus (T2DM) is a chronic disease that develops due to defective insulin

secretion and is frequently associated with insulin resistance. [2] It is also characterized by progressively decreasing beta-cell function over time. [3,4] It contributes to about 90- 95 % of all diagnosed cases of DM in adults and currently affects more than 61.3 million Indian people that is more than 8% of the adult population. The age of onset of T2DM is 42.5 years on an average. Diabetes accounts to 1 million deaths in India every year. [5] The prevalence of dyslipidaemia was 39.9%, 46.8%, and 59.3% in participants with normal glucose, prediabetes, and type 2 diabetes mellitus (T2DM). Women had a lower dyslipidaemia prevalence than men (38.7% vs. 43.3%). [6] The feature of chronic hyperglycaemia is a forecaster of development of complications associated with diabetes. These can be divided into micro-vascular, macro-vascular and other complications. Micro-vascular complications of diabetes include diabetic neuropathy, diabetic nephropathy and diabetic retinopathy. [7] The complications of DM categorized under macro-vascular complications include cardiovascular disease, cerebrovascular disease and diseases related to peripheral vessels. Along with these complications, weight gain related with diabetes lead to further worsening of the disease. Other complications include acute metabolic complications, diabetic ketoacidosis. [8] The most common pattern of abnormality in patients with Type 2 diabetes mellitus is increased triglyceride levels, decreased HDL levels and increased concentration of low – density lipoproteins (LDL) particles. These LDL particles have been identified as a major risk factor for chronic heart disease (CHD) by the National Cholesterol Education Programme (NCEP) Adult Treatment panel (ATP) III. It has been shown that reducing the plasma LDL cholesterol levels sharply reduces the risk of subsequent clinical Coronary Heart Diseases in both patients with pre-existing Coronary Heart Diseases and in patients free of Coronary Heart Diseases. While LDL cholesterol is a strong risk factor for coronary artery disease (CAD). [9] Glycosylated haemoglobin (HbA1) is a term used to describe a series of stable minor haemoglobin components formed slowly and non-enzymatically from haemoglobin and glucose. [10] The glycation of haemoglobin can occur at various sites present on the polypeptide chains of the haemoglobin molecule with different carbohydrate molecules. More recently HbA1c is defined as Hb that is irreversibly glycated at one or both N- terminal valines of the β-chain. The remaining GHbs have glucose, glucose-6-phosphate, fructose-1,6-diphosphate, or pyruvic add bound to one of the 44 additional sites occurring at s-amino group of lysine residues or at the NH_2 terminal of the α -chain. [11] Formation of HbA1c is irreversible and the blood levels depend on both of the life span of red blood cell (average 120 days) and blood glucose concentration. The rate of formation of HbAlc is directly proportional to the ambient glucose concentration. The amount of HbAlc therefore represents the integrated values of glucose over the last three months and provides an additional means of assessing glycaemic control. [12] Hence, the study has been planned to evaluate the value of HbA1c as marker of dyslipidaemia in Type 2 Diabetics

Material and Methods:

This is a cross sectional study conducted at Department of General Medicine, Khaja Banda Nawaz University, Kalaburagi,Karnataka from December 2018 to February 2019. Total 50 patients of Type 2 diabetes mellitus were taken for the study after applying inclusion and exclusion criteria, and after obtaining written and informed consent from them.

Inclusion criteria

- Adults aged above 30 years and having Type 2 Diabetes Mellitus

Exclusion criteria

- Patients with hypothyroidism, nephrotic syndrome, cholestatic liver disease, chronic kidney disease

- Patients with BMI >30kg/m^2
- Patents on lipid lowering drugs
- Patients on OCP's, steroids and thiazide diuretics

HbA1c and Fasting Lipid profile: Total cholesterol, Triglycerides, HDL and VLDL cholesterol were measured using Erba blood analyser were done using appropriate tests.

- LDL cholesterol was calculated using friedwald formula.
- HbA1c was estimated by appropriate standard kits.
- Dyslipidaemia was defined according to NCEP-ATPIII guidelines.

Statistical Analysis:
The data was analysed with SPSS version 25.0. The mean, SD and correlation(Pearson's) test was used to interpret the results. Correlation coefficient (r) ≥ + 1 is taken as positive correlation, ≤ −1 is taken as negative correlation and between −1 and + 1 as no correlation. Correlation (Pearson's) test was used to interpret the result.

Result
In our study, among 50 Type 2 diabetic individuals included in this study, 24 were male and 26 were female.

Table 1: Sex Distribution of study population

	Total	**Males**	**Females**
No. of patients	50	24	26
Percentage	100	48	52
Chi-Square test p=value	0.112		

Table 2: Lipid profile of study population based on gender

Lipid profile	**Total**	**Male**	**Female**
Hypercholesterolemia	**9**	**4**	**5**
Hypertriglyceridemia	**26**	**10**	**16**
Low HDL	**28**	**13**	**15**
High LDL	**21**	**10**	**11**
No abnormality	**6**	**4**	**2**

In table 2, lipid profiles were taken into consideration, 9 patients had TC levels > 200 mg /dl, 26 patients had TG levels > 150 mg/dl, 28 patients had LDL levels > 100 mg/dl and 21 patients had HDL levels < 40 mg/dl.

Table 3: Distribution of Lipid Profile and HbA1c

Parameters	**Mean ± SD**
Mean HbA1c	**9.76 ± 1.46**
Mean Total cholesterol	**155.76 ± 13.41**
Mean Triglycerides	**180.52 ± 17.21**
Mean HDL	**36.94 ± 4.28**
Mean LDL	**99.09 ± 12.72**

In table 3, Mean total cholesterol was 155.76±13.41, mean total triglyceride was 180.52±17.21, mean LDL was 99.09±12.72, Mean HDL was 36.94±4.28 and mean HbA1c was 9.76±1.46.

Table 4: correlation analysis between serum Lipid profile and HbA1c.

Parameters	Correlation coefficient (r)	p - value
Total cholesterol-HbA1c	0.207	0.021
Triglyceride-HbA1c	0.028	0.432
HDL-HbA1c	- 0.130	0.032
LDL-HbA1c	0.241	0.041
VLDL-HbA1c	0.031	0.589

In our study table 4, HbA1c positively and significantly correlated with total cholesterol (r=0.20), LDL (r=0.24), HbA1c negatively and significantly correlated with HDL (r= - 0.13), and did not show any show correlation with VLDL (r=0.03) and total triglycerides (r=0.02).

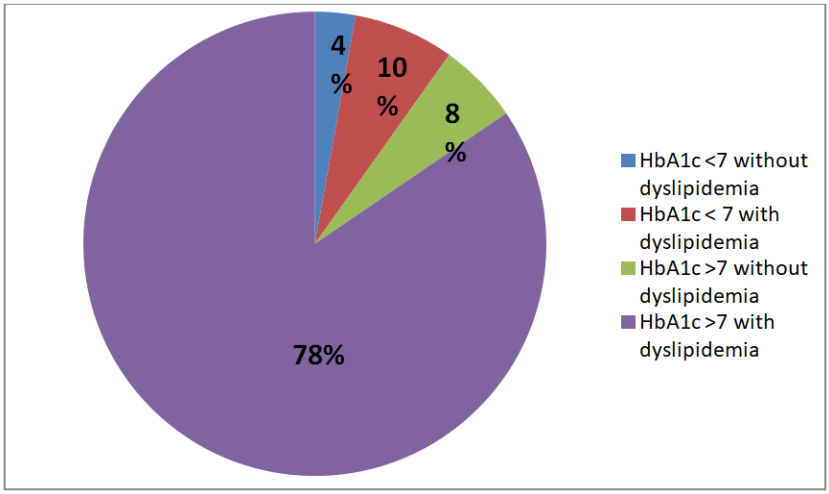

Figure 1: Lipid parameters categorized by patient's glycaemic control (HbA1c)

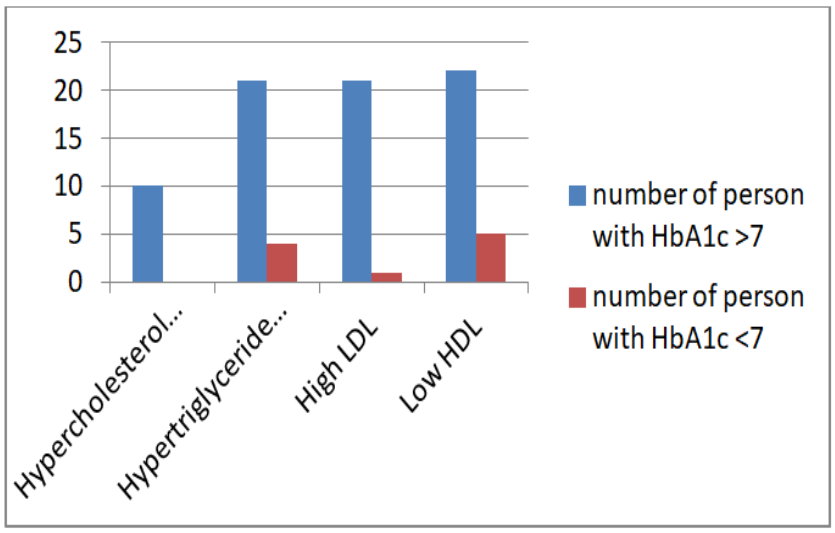

Figure 2: ***Correlations between HbA1c and Lipid Profile Parameters.***

Discussion

In the present study, we have evaluated the pattern of lipid profile parameters in diabetic subjects and its correlation with HbA1c. This study demonstrates the typical dyslipidaemia in diabetics characterized by high triglyceride, low HDL. Although there was no significant difference between male and female, the levels of TC and LDL were significantly higher in

female as compared to male Type 2 diabetic patients. This finding is in agreement with the previous studies. [13] Hyperlipidemia in females may be attributed to the effects of sex hormones on body fat distribution, which leads to differences in altered lipoproteins. [14] Another reason includes differences in coagulation, the pattern of obesity between men and women, and possible role for hyperinsulinemia. [15] In our study reveals high prevalence of hypercholesterolemia, hypertriglyceridemia, high LDL and low HDL levels which are well known risk factors for CVD and abnormality of cholesterol metabolism may lead to heart attacks. Insulin affects the liver apolipoprotein production. It regulates the enzymatic activity of lipoprotein lipase and Cholesterol ester transport protein. All these factors are likely cause of dyslipidemia in Diabetes mellitus. [16] Moreover, insulin deficiency reduces the activity of hepatic lipase and several steps in the production of biologically active lipoprotein lipase may be altered in DM. [17] The main disorder in lipid metabolism was hypertriglyceridemia in our study. This finding is in concord with our previous study. [18] In the study of Mahato RV et al, 54% diabetic individuals had elevated LDL and > 50% individuals had increased TG. [19] These findings are similar to our study. But in contrast to our present study, they reported low HDL in 73% individuals. In our study, a highly significant correlation between HbA1c and Lipid profile which is similar with various previous studies. [20] We also observed significant correlations between HbA1c and TC, LDL and HDL. In various studies, HbA1c level was eminent as showing positive correlation with TC, LDL and TG in diabetic patients. [21] HDL was shown to be the stronger predictor of CVD in diabetic population by 'The Strong Heart Study' (data evaluated by Liu et al), with hazard ratios of 2.23 and 1.80 respectively in male and female. [22] This study showed that increasing HDL cholesterol concentrations had significant, curvilinear relationships with CVD and CHD risk. Moreover, NCEP ATPIII has recommended using HDL cholesterol in assessing CVD risk in patients with diabetes. The measurement of HDL is simple which can be conducted even in non-fasting state of patients and can be determined regardless of TG concentration. Hence, HDL cholesterol can be of great value in determining dyslipidaemia in diabetic subjects. Risk ratio showed the strongest correlation with HbA1c in our study. In the prospective cohort study with inclusion of 418 Type 2 diabetic individuals with follow-up until the appearance of a cardiovascular event, Reddy AS et al, showed that the main lipid predictor of vascular events was mean TC/HDL-C ratio with hazard ratio (HR) of 1.46. In the same study, the predictive power of the TC/HDL ratio was found to be higher than that of HDL cholesterol and study concluded that TC/HDL-C can be used as a treatment guides for diabetic dyslipidemia. [23] Total number of apo-B containing particles and small LDL-C Particles are increased in diabetes and these metabolic abnormalities are better reflected by TC/HDL ratio and Non-HDL than LDL alone. [24] Significant association of HbA1c with various lipid parameters such as TC, HDL, LDL in present study suggests the importance of glycaemic control in order to control dyslipidaemia

According to, Diabetes complications and control trial (DCCT) established HbA1c as the gold standard of glycaemic control. The level of HbA1c value ≤7.0% was said to be appropriate for reducing the risk of cardiovascular complications. [25] In the present study, we divided diabetic patients into 2 groups as per the HbA1c cutoff of 7.0%. The diabetic patients with HbA1c value > 7.0% exhibited a significant increase in TC, TG, LDL, VLDL and without any significant alteration in HDL in comparison to patients with HbA1c value ≤7.0%. According to Sultania HA et al showed the impact of glycaemic control on various lipid parameters in which the diabetic patients were categorized into 3 groups according to their HbA1c levels: group 1, good glycaemic control (HbA1c 6%–9%) and group 3, worst glycaemic control (HbA1c>9%). Poor and worst glycemic control is considered as risk factor for complications in diabetes. Strict glycemic control lowers the risk of micro- and macrovascular complications of diabetes mellitus. [26] Severity of dyslipidaemia increases in patients with higher HbA1c value. As elevated HbA1c and dyslipidaemia are independent

risk factors of CVD, diabetic patients with elevated HbA1c and dyslipidaemia can be considered as a very high-risk group for CVD. Improving glycaemic control can substantially reduce the risk of cardiovascular events in diabetics. [27] It has been estimated that reducing the HbA1c level by 0.2% could lower the mortality by 10%. [28] According to Parveen et al. found a positive correlation between HbA1c and high triglycerides suggested that HbA1c can be used as a potent marker for dyslipidemia and mitigate the macro- and micro-vascular complications. [29] In this study, a significant correlation was observed between levels of glycosylated hemoglobin (HbA1c) and lipid profile. This may in turn help in predicting the lipid profile levels from the degree of glycemic control and therefore, identifying the patients with increased risk of diabetic complications. Lipid abnormalities are common in diabetic patients and frequently seen in patients with type-2 diabetic mellitus. The abnormal lipid profile observed in type 2 Diabetes mellitus is said to be related to insulin resistance as reported in previous studies, which leads to increased release of free fatty acids from fatty tissue, impaired insulin dependent muscle uptake of free fatty acids and increase fatty acid release to the hepatic tissue. [30] It has been closely associated with diabetic dyslipedemia, hypertension and enormous risk to cardiovascular diseases. Chronic hyperglycemia causes glycation of apolipoproteins and interferes with the normal pathways of lipoprotein metabolism. [31] It has been suggested that diabetes patients should join a fitness program and do regular exercise that comprises 30 mins of mild-intensity physical activity 4–6 times per week, with a minimum outlay of 200 Kcal. It is also suggested that every family physician be well aware of the relationship between HbA1c and hyperlipidemia in T2DM patients and check their patients' lipid profile and HbA1c at least twice a year to avoid future problems. There is a need for an educational program for diabetic patients regarding blood sugar control and the deleterious consequences of dyslipidemia. Awareness of this risk among family physicians and T2DM patients can play a pivotal role in controlling and avoiding the grave consequences of this complication for T2DM patients. The strength of the study is that we had the complete biochemical data of the patients and we computed a comparison, a correlation and a regression analysis. The present study had a few limitations, including being a retrospective study as well as having too small of a sample size and the fact that patients' dietary habits, lifestyle patterns, time since diagnosis with DM and duration of regular physical activity were undetermined. The patients included in our study were all taking different antidiabetic medications. However, we could not analyze the data according to the treatment modalities, and it is possible that such a patient grouping would have some impact on the study results. We have not tested the effect of glycemic control on various lipid ratios as study of these ratios have proven to be useful as markers for insulin resistance and CVD risk in T2D patients.

Conclusion

In conclusion, HbA1c showed positive correlation with serum Total cholesterol and LDL, negative correlation with HDL. These findings suggest that HbA1c can also be used as predictor of dyslipidaemia in Type 2 Diabetics in addition to as a glycaemic control parameter**.** So, HbA1c may be utilized for screening diabetic patient for risk of cardiovascular events and also for timely intervention with lipid lowering drugs**.**

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