Original Research Article

Glycosylated hemoglobin as a marker of dyslipidemia in type 2 diabetes mellitus patients in a tertiary care hospital

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Abstract

Introduction: In persons with diabetes, chronic hyperglycemia (assessed by glycosylated hemoglobin level) is related to the development of micro vascular disease; however, the relation of glycosylated hemoglobin to macro vascular disease is less clear. Glycosylated hemoglobin (HbA1c) is a more stable, accurate parameter of glucose homeostasis than fasting glycemia, thus providing prognostic information in diabetics. However, its role and relationship with CAD remains unclear in non-diabetics. Diabetic patients with accompanied (but often unnoticed) dyslipidemia are soft targets of cardiovascular deaths. Glycated hemoglobin (HbA1c) is a routinely used marker for long – term glycemic control. This investigation is an attempt to evaluate the association between HbA1c and various lipid parameters.

Aim and objectives: To know the prevalence of dyslipidemias associated with type 2 DM, To study the impact of the glycemic status on lipid profile in type 2 DM, To evaluate the efficacy of HbA1c as a marker of dyslipidemia in type 2 DM.

Materials and methods: Venous blood samples collected from 35 type 2 diabetic patients (20 males, 15 females) and serum analyzed for HbA1c, Fasting blood glucose, Total Cholesterol, triglycerides, HDL-C and LDL-C. L/H risk ratio is also calculated. A detailed history with thorough systemic examination was carried out. Hemogram, urinalysis, fasting and blood sugar after 2 h of major meal, HbA1c, lipid profile, performed.

Results: We used student t-test and Pearson's correlation coefficient to find the statistical significance. Result: serum concentration of glycated hemoglobin and all the parameters of lipid

profile except HDL-C were increased while HDL-C concentration decreased in both the types of DM as compared to that of control.

Conclusion: Dyslipidemia is more prominent in type-2 DM than that in type-1 DM. Glycemic control is poorer & its correlation with lipid profile is stronger in type-2 DM.

Key words

Diabetes mellitus, HbA1c, Fasting blood glucose, Total Cholesterol, Triglycerides.

Introduction

Diabetes is a metabolic disorder characterized by hyperglycemia, either due to insulin deficiency or insulin resistance. Despite some progress in the development of new anti-diabetic agents, the ability to maintain tight glycemic control in order to prevent complications of diabetes without adverse complications still remains a challenge [1]. This increase is mainly associated with increase in the prevalence of lipid and glucose abnormalities Indians are known to have relatively lower levels of lipids and lipoproteins, raised TG and low HDL Cholesterol and presence of metabolic syndrome explaining more than half of the excess burden of CAD. Diabetes mellitus is emerging as a global endemic both in developing and developed countries. It is characterized by metabolic abnormalities and long-term micro and macro vascular complications [2]. There is a high risk of CAD in people with type 2 diabetes. Individuals with coexisting diabetes and metabolic syndrome have a high prevalence of CAD. Dyslipidemia is one of the major risk factors for cardiovascular disease in diabetes mellitus Type 2 [1, 2]. The aim of the study was to understand the pattern of dyslipidemia among the Type 2 diabetic patients and to understand its association with Glycated hemoglobin (HBA1C) [3]. Early detection and intervention in diabetes is now considered one of the most important public health agendas. Strict control of blood sugar remains the pivot in the decreased incidence of complications. Good glycemic control is essential in preventing diabetic complications. Fasting plasma glucose (FPG) is a simple, easy, inexpensive, and widely available to general population and has been most frequently used to identify subjects at high risk of diabetes. The 2-h plasma glucose after oral glucose tolerance test (OGTT) is also useful to identify subjects of impaired glucose tolerance [4]. There is no natural cutoff between normal and abnormal lipid levels because lipid measurements are continuous. A linear relation probably exists between lipid levels and cardiovascular risk, so many people with "normal" cholesterol levels benefit from achieving still lower levels. Consequently, there are no numeric definitions of dyslipidemia; the term is applied to lipid levels for which treatment has proven beneficial [5]. Proof of benefit is strongest for lowering elevated low-density lipoprotein (LDL) levels. In the overall population, evidence is less strong for a benefit from lowering elevated TG and increasing low high-density lipoprotein (HDL) levels. HDL levels do not always predict cardiovascular risk. For example, high HDL levels caused by some genetic disorders may not protect against cardiovascular disorders, and low HDL levels caused by some genetic disorders may not increase the risk of cardiovascular disorders [6]. Although HDL levels predict cardiovascular risk in the overall population, the increased risk may be caused by other factors, such as accompanying lipid and metabolic abnormalities, rather than the HDL level itself. When LDL cholesterol levels are high, fatty deposits (called plaques) can build up in the arteries, the blood vessels that carry blood from the heart throughout the body. Overtime, plaques narrow the arteries, producing *atherosclerosis* [7]. This can cause heart disease, heart attack, peripheral artery disease (reduced blood flow in the limbs, usually the legs), or stroke. Low levels of HDL and high levels of triglycerides can also increase fat build-up in the arteries [8]. High levels of HDL cholesterol, however, protect the heart by

helping to remove the build-up of LDL from the arteries. Because people with diabetes are at high risk for cardiovascular disease, keeping blood sugar levels close to normal is important to prevent this and other serious complications. Regulating blood pressure and lipid levels is especially important to manage cardiovascular disease risk. The most typical lipid pattern in diabetes consists of high triglyceride levels, low HDL levels, and small, dense LDL particles, which easily stick to artery walls. This lipid pattern is linked with central obesity and insulin resistance [9].

Materials and methods

The study was conducted in 50 patients. Among them (20 were males and 15 were females). The detailed history was taken in detail about symptoms of diabetes and its complications. All previous records of patients were checked for duration of diabetes, past and present medications, glycemic control, previous admissions, and the presence of any complication. Inclusion Criteria: All diagnosed cases of Type 2 diabetes mellitus.

Exclusion criteria

- Age below 18 years
- Type 1 diabetics
- Patients on lipid lowering agents
- Acute coronary syndrome Stroke.

The lipid profile of the study was analyzed according to the ATP lll classification for identification of dyslipidemia, Low HDL 190 mg/dl, high cholesterol >200 mg/dl, and high TG >200 mg/dl. A detailed family history for diabetes and another associated condition like hypertension and IHD was taken. Personal history regarding dietary habits, sleep, appetite, substance abuse, bladder, and bowel habits were taken. Detailed menstrual and obstetric history was taken in female patients. Any signs of atherosclerosis were looked for. Thorough systemic examination was carried out. Hemogram, urinalysis, fasting and blood sugar after 2 hour of major meal, HbA1c, lipid profile

was done. Venous blood samples from all the subjects were collected in serum separator tubes after overnight fasting. The venous puncture was done in the cubital vein. Torniquet was used but was released just before sampling to avoid artificial increase in the concentration of serum lipids. Serum was separated within 2 hours of collection to prevent artificial changes in concentration of HDL. The blood was centrifuged at 5,000 rpm for 10 minutes. The supernatant clean serum was then pipetted out using dry piston pipettes with disposable tips and stored in dry thin walled vials at -20^{0}C until further analysis. Care was taken to exclude the hemolysed samples. The sera were analyzed for HbA$_1$c, FBS, TC, TG and HDL using an auto analyzer.

Results

Out of 35 patients, 20 were male and 15 were female. In male patients, 49% were in age group of 40-50 years, 30% were in age group of 51-60 years and 21% were above 60 years of age. In female patients, 35% were in age group of 40-50 years, 41% were in age group of 51-60 years and 24% were above 60 years of age. Biochemical Parameters Level of Diabetic Patients was as per **Table – 1**. Correlations of Dyslipidemia and Diabetic Complication among Diabetes Patients were as per **Table – 2**.

Discussion

Out of 18 patients having HbA1c ≤8%, 17% had LDL ≥100 mg/dl, while out of 35 patients having HbA1c > 8%, 63% of the patients had LDL ≥100 mg/dl. Thus, we found a significant correlation between HbA1c level and LDL level ($P < 0.001$) [12]. In patients having HbA1c ≤8%, only 6% of the patients had TC level ≥200 mg/dl, while in patients having HbA1c level >8%, 56% of the patients had TC ≥200 mg/dl. Thus, our study showed a significant correlation between glycemic control and TC level ($P < 0.01$) which is consistent with the findings in studies [11]. Thus, in our study, we found significant correlation between type 2 DM and various dyslipidemia. Furthermore, there was significant

correlation between HbA1c level and different dyslipidemia. HbA1c had direct correlation with LDL, TC, and TG and had a negative correlation with HDL. The findings of the study clearly indicate that HbA1c is not only a useful biomarker of long-term glycemic control but also a good predictor of lipid profile. Type 2 DM increases the risk for atherosclerotic vascular disease. The glycemic control and various dyslipidemia associated with type 2 DM have a major impact on the development of various complications. Thus, in our study, we found significant correlation between HbA1c level and retinopathy. The result is consistent with UKPDS, DCCT studies In these studies, there was a significant correlation between HbA1c level and nephropathy and cardiac dysfunction. However, in our study, we could not show significant correlation between HbA1c and nephropathy and cardiac dysfunction [13]. Thus, in our study, we found significant correlation between diabetic complications like retinopathy and nephropathy with raised triglycerides and total cholesterol level. However, the correlation of these complications with HDL and LDL was not significant. For cardiac dysfunction, there was correlation with raised LDL, low HDL and high triglyceride level but no correlation we could obtain between total cholesterol level and cardiac dysfunction. The correlation between various dyslipidemias of type 2 DM and complications was present in various studies like [14]. In addition to the storage of lipids in the adipose tissue, adipocytokines like adiponectin, leptin, TNF, IL-6, resist in play an important role in tissue physiology and have been shown to be linked to obesity, insulin resistance and β-cell dysfunction. Present study showed a higher number of T2DM subjects with central obesity as compared to peripheral obesity, which could be due to higher rates of lipolysis in visceral fat than subcutaneous fat by catecholamine. This may in turn result into an increased FFA delivery to the liver, consequently stimulates hepatic glucose production by fatty acids (FA) causing interference in hepatic insulin removal, and may further accentuate insulin resistance [15].

Table – 1: Biochemical Parameters Level of Diabetic Patients.

Parameters (T = 35 subjects)	T2DM (n = 35) Mean ± SD (range)	p value
Fasting blood glucose (FBG)	210±18.9	<0.001[*]
Post Prandial blood glucose (PPBG)	233±0.8	<0.001[*]
HBA1C%	7.18 ± 1.75	<0.001
TC (mg/dl)	211.56 ± 52.01	<0.001
TG (mg/dl)	122.04 ± 73.30	<0.001
HDL-C (mg/dl)	44.24 ± 12.77	<0.001
LDL-C (mg/dl)	116.89± 3.88	<0.001

Table – 2: Correlations of Dyslipidemia and Diabetic Complication among Diabetes Patients.

Lipid profile	Retinopathy	Nephropathy	Cardiac dysfunction
LDL ≥100 mg/dl	6	11	8
HDL <40 mg/dl	7	8	11
TC ≥200 mg/dl	11	7	18
Triglyceride ≥200 mg/dl	10	9	16

Limitations of study

The study sample was small (*n* = 35) and it remains to be seen whether the observations seen by us were truly reflective of the universal population data. apo A and apo B fraction estimations were not done. Long-term follow-up

is required for better understanding of progression and interrelation of diabetes and its complications. Our study did not include the follow-up of the patients. All the patients enrolled were selected from tertiary care center and the majority of them had a long duration of diabetes more than 5 years, so a time bias was present in our study.

Conclusion

For cardiac dysfunction, it had correlation with raised LDL, raised TG and low HDL, but we could not get correlation of cardiac dysfunction with raised TC. In our study, we found significant correlation between duration of type 2 DM and various complications with these complications being more frequent in patients with duration of type 2 DM more than 5 years as compared to those with the duration <5 years. Thus, in our study, HbA1c was efficacious in predicting the dyslipidemia and various complications in type 2 DM patients.

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