

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

Background: Type 2 diabetes mellitus (DM) is one of the modern pandemics. Evidence has emerged supporting the benefits of glycemic control as well as control of blood pressure and lipid levels in the prevention or delay in onset and severity of complications due to DM. Type 2 DM is a common secondary cause of dyslipidemia, in particular, if glycemic control is poor which, in turn, is an important risk factor for atherosclerosis and coronary heart disease. Glycosylated Hb (HbA1c) is a better indicator of blood glucose as compared to fasting blood glucose and postprandial blood glucose. **Aims and Objectives:** (i) To know the prevalence of dyslipidemias associated with type 2 DM, (ii) To study the impact of the glycemic status on lipid profile in type 2 DM, (iii) To evaluate the efficacy of HbA1c as a marker of dyslipidemia in type 2 DM. **Material and Methods:** Patients having diagnosed with Type 2 DM with no clinical evidence of coronary artery disease and more than 40 years old were enrolled in the study. 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, chest X-Ray, electrocardiogram, and echocardiogram were performed. **Results:** About 30% male patients and 47% female patients had HbA1c $\leq 8\%$ while remaining had HbA1c $> 8\%$. 54% patients had low-density lipoprotein (LDL-C) < 100 mg/dl, 18% had LDL-C between 100 and 129, and 28% had LDL-C ≥ 130 mg/dl. 61% male patients had LDL-C < 100 mg/dl, 18% had LDL-C between 100 and 129, and 21% had LDL-C ≥ 130 mg/dl. 41% female patients had LDL-C < 100 mg/dl, 18% had LDL-C between 100 and 129, and 41% had LDL-C ≥ 130 mg/dl. **Conclusion:** HbA1c level showed the direct correlation with level of LDL-C, TG, and TC while it had negative correlation with high-density lipoprotein (HDL) level in the form of patients with HbA1c level $> 8\%$ had higher frequency of raised LDL, raised TC, raised TG and low HDL as compared to those with HbA1c $\leq 8\%$.


KEY WORDS: Glycosylated Hb; Diabetes Mellitus; Atherosclerosis; Dyslipidemia

INTRODUCTION

Type 2 diabetes mellitus (DM) is one of the modern pandemics. It is estimated to affect 220 million people by the

year 2020. Diabetes today is an important single disease in the medical specialty and is special subject in chronic medicine. It is one of those diseases that cannot be cured but can only be controlled so as to prevent its long-term microvascular and macrovascular complications.^[1]

The type 2 diabetic patients are prone to certain complications, and evidence has emerged supporting the benefits of glycemic control as well as control of blood pressure and lipid levels in the prevention or delay in onset and severity of complications due to DM. The development of various complications depends on the control of the blood glucose level.^[1-3]

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The Glycosylated Hb (HbA1c), a product of interaction between glucose molecule and hemoglobin, assesses the effectiveness of glucose control over previous 3 months. Thus, it is a better indicator of blood glucose as compared to fasting blood glucose and postprandial blood glucose which reflects the immediate control only.

About 50% of all type 2 diabetic patients have dyslipidemia. Lipid abnormalities are more common with type 2 diabetes than with type 1 diabetes. Type 2 DM is a common secondary cause of dyslipidemia, in particular, if glycemic control is poor which, in turn, is an important risk factor for atherosclerosis and coronary heart disease.^[1-3]

Dyslipidemia plays an important role in the diabetic complications, and there is a pronounced acceleration of atherosclerosis. Diabetic patients with accompanied (but often unnoticed) dyslipidemia are soft targets of cardiovascular complications.^[4,5]

There is a significant good correlation between the lower HbA1c levels and the reduced incidence of microvascular complications like retinopathy and nephropathy in both type 1 and 2 DM, this correlation is not that significant in macrovascular complications of diabetes like coronary heart disease and stroke, here the better control of hypertension and lipids and smoking cessation are equally important.^[1,6]

An early intervention to normalize circulating lipids has been shown to reduce the diabetic complications and mortality. This study was carried out to know the frequency of dyslipidemia in our patients and also to determine that whether patients with good glycemic control (HbA1c \leq 8%) are having better lipid profile than poorly controlled group. A good correlation between two would help us in cautiously looking for the dyslipidemia and related complications in very early stage in patients with poor glycemic control and also encourage taking necessary measures very well before the diabetic complications develop. This can help diabetic patients to lead a prolonged and good quality life.^[1-3,7]

Aims of Study

1. To know the prevalence of dyslipidemias associated with type 2 DM.
2. To study the impact of the glycemic status on lipid profile in type 2 DM.
3. To evaluate the efficacy of HbA1c as a marker of dyslipidemia in type 2 DM.

MATERIALS AND METHODS

This study which was carried out at GMERS Valsad Hospital included 50 subjects (indoor) having type-2 DM, presented to diabetes clinic, outpatient department and various wards of Medicine Department.

Patients having diagnosed with Type 2 DM with no clinical evidence of coronary artery disease and more than 40 years old.

Pregnant women, patients taking hypolipidemic drugs and who had other causes of secondary hyperlipidemia.

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. 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 h of major meal, HbA1c, lipid profile, chest X-Ray, electrocardiogram and echocardiogram were performed. Appropriate statistical test was used data analysis.

RESULTS

Out of 50 patients, 66% were male and 34% 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.

About 46% of patients were having DM for <5 years, 32% for 5-10 years while 22% patients were having DM for more than 10 years.

Around 30% male patients and 47% female patients had HbA1c \leq 8% while remaining had HbA1c >8%. 54% patients had low-density lipoprotein (LDL-C) <100 mg/dl, 18% had LDL-C between 100 and 129, and 28% had LDL-C \geq 130 mg/dl. 61% male patients had LDL-C <100 mg/dl, 18% had LDL-C between 100 and 129, and 21% had LDL-C \geq 130 mg/dl. 41% female patients had LDL-C <100 mg/dl, 18% had LDL-C between 100 and 129, and 41% had LDL-C \geq 130 mg/dl.

Nearly 52% patients had high-density lipoprotein (HDL) <40 mg/dl, 34% had HDL between 40 and 50, and 14% had HDL >50 mg/dl. While in male patients, 52% had HDL <40 mg/dl, 30% had HDL between 40 and 50, and 18% had HDL >50 mg/dl and in female patients, 53% had HDL <40 mg/dl, 41% had HDL between 40 and 50, and 6% had HDL >50 mg/dl.

About 72% patients had triglycerides (TGL) <200 mg/dl, 26% had TGL between 00 and 399 and 2% had TGL \geq 400 mg/dl.

In male patients, 79% had TGL <200 mg/dl, 18% had TGL between 200 and 399 mg/dl and 3% had TGL ≥400 mg/dl. In female patients, 59% had TGL <200 mg/dl, 41% had TGL between 200 and 399 mg/dl.

Around 62% patients had total cholesterol <200 mg/dl, 30% had total cholesterol between 200 and 239 and 8% had ≥240 mg/dl. In male patients, 64% had total cholesterol <200 mg/dl, 30% had total cholesterol between 200 and 239 mg/dl and 6% had ≥240 mg/dl. In female patients, 59% had total cholesterol <200 mg/dl, 29% had total cholesterol between 200 and 239 mg/dl and 12% had total cholesterol ≥240 mg/dl.

Correlation between HbA1c and LDL, HDL, TGL and total cholesterol is shown in Figures 1-4, respectively.

Out of total 23 patients having duration of type 2 DM <5 years, 4% had TGL level ≥200 mg/dl, 48% patients had HDL <40 mg/dl, 30% patients had LDL level ≥100 mg/dl and 22% patients had total cholesterol ≥200 mg/dl.

Out of total 16 patients having duration of type 2 DM between 5 and 10 years, 31% had TGL level ≥ 200 mg/dl, 44% patients had HDL <40 mg/dl, 44% patients had LDL level ≥100 mg/dl and 37% patients had total cholesterol ≥200 mg/dl.

Out of total 11 patients having duration of type 2 DM >10 years, 73% had TGL level ≥200 mg/dl, 73% patients had HDL <40 mg/dl, 82% patients had LDL level ≥100 mg/dl and 73% patients had total cholesterol ≥200 mg/dl.

DISCUSSION

Diabetes is a modern pandemic. Although the prevalence of both type 1 and type 2 DM is increasing worldwide, the prevalence of type 2 DM is rising more rapidly because of increasing obesity and reduced activity levels.

In our study, out of 50 patients, 66% were male and 34% were female. 44% of the patients were in age group of 40-50 years, 34% patients were in age group of 51-60 years and 22% patients were above 60 years of age. 46% of patients had duration of type 2 DM <5 years, 32% patients had duration of type 2 DM between 5 and 10 years and 22% patients had duration of type 2 DM more than 10 years.

Type 2 DM is known to have relation with BMI with higher prevalence among overweight and obese individuals. Mean BMI in our study was 27.12. There was a correlation between BMI and type 2 DM which is consistent with the result in the study conducted by Al-Adsani *et al.*, 2004.^[8]

The patients with type 2 DM can have many lipid abnormalities including high levels of LDL, TGL and TC and low levels

of HDL. These abnormalities may be the result of the unbalanced metabolic state of diabetes, i.e., hyperglycemia and insulin resistance.

In our study, out of 50 patients, 46% had LDL ≥100 mg/dl which is consistent with the studies conducted by Ahmed *et al.*, Abbottabad, Otieno *et al.* Nairobi and Al-Adsani *et al.*, Kuwait.^[8,9]

In our study, 52% of the patients had HDL <40 mg/dl and 38% of the patients had TC ≥200 mg/dl. The study Otieno *et al.* and Al-Adsani *et al.* revealed the same correlation^[8,10] Out of

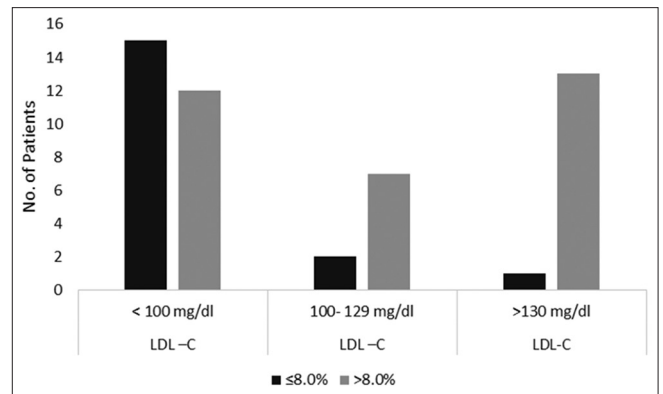


Figure 1: The relation between glycosylated hemoglobin and low-density lipoprotein

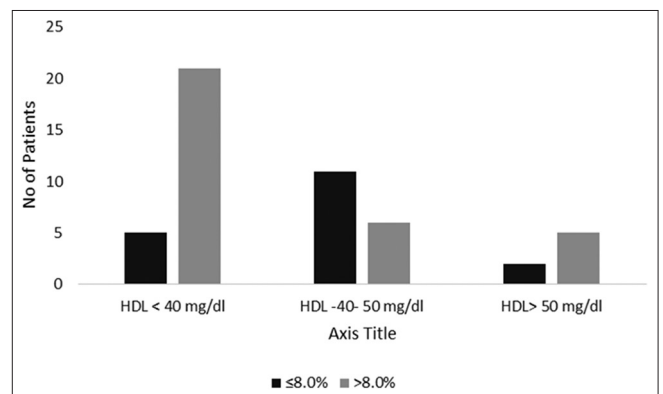


Figure 2: The relation between glycosylated hemoglobin and high-density lipoprotein

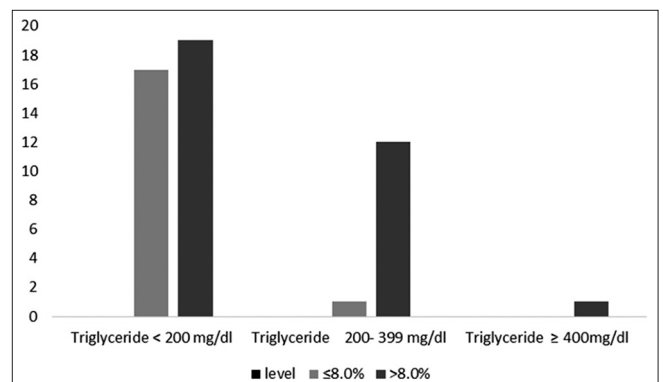


Figure 3: The relation between triglycerides and glycemic status

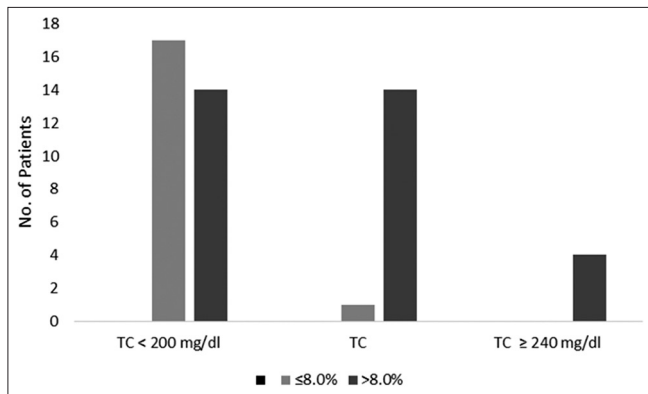


Figure 4: Relation between glycosylated hemoglobin and total cholesterol

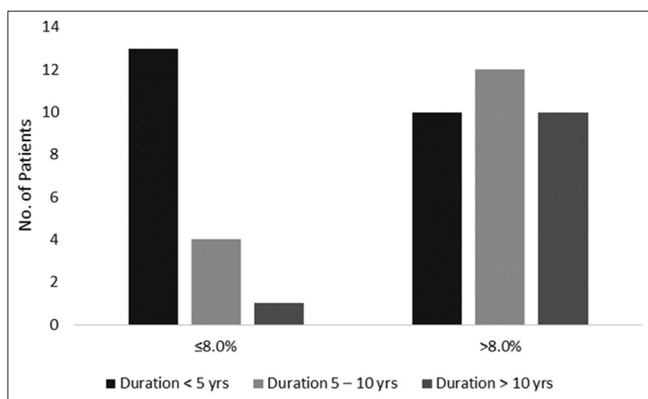


Figure 5: The relation between duration of Type 2 diabetes mellitus and glycemic status

Table 1: Distribution of patients according to BMI

BMI (kg/m ²)	Number of patients (n=50)	Male (n=33)	Female (n=17)
18-24.9	18	13	5
25-30	15	10	5
>30	17	10	7

BMI: Body mass index

Table 2: Correlation of duration of type 2 diabetes and diabetic complications in study population

Duration of diabetes	Retinopathy	Nephropathy	Cardiac dysfunction
<5 years	6	2	4
5-10 years	9	5	6
>10 years	7	5	7

Table 3: Correlation of glycemic status and diabetic complications in study population

Glycemic status	Retinopathy	Nephropathy	Cardiac dysfunction
≤8%	4	2	4
>8%	18	10	13

total 50 patients, 38% of the patients had TC ≥200 mg/dl. It is consistent with the study conducted by Ahmed et al.^[9]

Out of 18 patients having HbA1c ≤8%, 17% had LDL ≥100 mg/dl, while out of 32 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 ($P < 0.001$). The result is consistent with the studies conducted by Ahmed et al., Al-Adsani et al., and Ahmed et al.^[8,9]

Out of 18 patients having HbA1c ≤8%, 28% had HDL <40 mg/dl while out of 32 patients having HbA1c >8%, 65% of the patients had HDL <40 mg/dl. Thus, we found a significant negative correlation between HbA1c level and HDL level ($P < 0.001$). Ahmed et al., Al-Adsani et al., and Ahmed et al. revealed the similar correlation.^[8,9,11]

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 like Ahmed et al. and Ahemd et al.^[9,11]

In patients having HbA1c ≤8%, 6% of the patients had TG level ≥200 mg/dl, while those patients having HbA1c >8%, 41% had TGL ≥ 200 mg/dl. The correlation was significant ($P < 0.01$) as was in Ahmed et al. and Ahmed et al.^[9,11]

Thus, in our study, we found significant correlation between type 2 DM and various dyslipidemias. Furthermore, there was significant correlation between HbA1c level and different dyslipidemias. 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 dyslipidemias associated with type 2 DM have a major impact on the development of various complications.

In our study, out of total 18 patients having HbA1c level ≤8%, 22% of the patients had retinopathy, 11% of the patients had nephropathy and 22% of the patients had cardiac dysfunction. Out of 32 patients having HbA1c ≥8%, 56% of patients had retinopathy, 31% of the patients had nephropathy and 41% of the patients had cardiac dysfunction.

In patients having retinopathy, 18% had HbA1c level ≤8% while 82% of the patients had HbA1c >8% ($P < 0.05$). In patients having nephropathy, 17% of the patients had HbA1c ≤8% while 83% of the patients had HbA1c >8% ($P < 0.5$). In patients with cardiac dysfunction, 24% had HbA1c level ≤8% while 76% of the patients had HbA1c >8% ($P < 0.5$).

Table 4: Correlation of dyslipidemia and diabetic complications in study population

	Retinopathy	Nephropathy	Cardiac dysfunction
LDL \geq 100 mg/dl	11	6	10
HDL <40 mg/dl	14	7	11
TC \geq 200 mg/dl	12	6	7
Triglyceride \geq 200 mg/dl	9	4	8

HDL: High-density lipoprotein, LDL: Low-density lipoprotein

Thus, in our study, we found significant correlation between HbA1c level and retinopathy. The result is consistent with UKPDS, DCCT studies.^[5,6] 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.

In our study, out of total 23 patients having LDL \geq 100 mg/dl, 48% had retinopathy, 26% had nephropathy, and 43% patients had cardiac dysfunction ($P < 0.5$). Out of total 26 patients having HDL <40 mg/dl, 54% patients had retinopathy, 27% had nephropathy and 42% of the patients had cardiac dysfunction ($P < 0.5$).

Out of 19 patients having TC \geq 200 mg/dl, 63% patients had retinopathy ($P < 0.05$), 32% had nephropathy ($P < 0.5$) and 37% patients having cardiac dysfunction. Out of 14 patients having TGL \geq 200 mg/dl, 64% patients had retinopathy ($P < 0.1$), 26% patients had nephropathy and 57% patients had cardiac dysfunction ($P < 0.05$).

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 UKPDS, Krentz et al. and Kreisberg.^[12,13]

Limitations of Study

The study sample was small ($n = 50$) 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

In our study, we found a significant prevalence of dyslipidemias in type 2 diabetes. Out of 50 patients, 46% of the patients had LDL level \geq 100 mg/dl, 38% of the patients had TC level \geq 200 mg/dl, 28% of the patients had TG level \geq 200 mg/dl and 52% of the patients had HDL level below 40 mg/dl. HbA1c level showed the direct correlation with the level of LDL-C, TG and TC while it had a negative correlation with HDL level in the form of patients with HbA1c level $>$ 8% had a higher frequency of raised LDL, raised TC, raised TG and low HDL as compared to those with HbA1c \leq 8%. We found significant correlation between HbA1c level and duration of diabetes in the form of the HbA1c level was significantly high in patients with duration of type 2 DM \geq 5 years as compared to those with duration $<$ 5 years. There was a significant correlation between the duration of type 2 DM and dyslipidemias. The patients with duration of type 2 DM $>$ 5 years had a higher frequency of dyslipidemias as compared to those with duration of type 2 DM $<$ 5 years. We found a significant correlation between HbA1c level and retinopathy. However, the correlation of HbA1c with nephropathy and cardiac dysfunction was not significant ($P = 0.5$). In our study, we found 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 ($P = 0.5$). 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 dyslipidemias and various complications in type 2 DM patients.

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