



STUDY OF GLYCATED HEMOGLOBIN IN DIABETES MELLITUS AND ITS ASSOCIATION WITH DYSLIPIDEMIA

General Medicine

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ABSTRACT

Introduction Diabetes mellitus is a metabolic disorder characterized by the hyperglycemia and disturbance of carbohydrate, lipid, and protein metabolism due to insulin resistance or relative insulin deficiency. Patients with type 2 Diabetes mellitus have an increased prevalence of dyslipidemia, which contribute to their high risk of cardiovascular disease (CVDs). A timely intervention to normalize the circulating lipids could reduce the chances of cardiovascular complications. Glycated hemoglobin (HbA1c) is an indicator of glycemic status over long term. Many studies have proposed, HbA1c to be used as biomarker of both glycemic control and dyslipidemia in type 2DM. **Materials and Methods** A total of 100 patients with Type 2 DM were included in this study. The whole blood and sera were analyzed for fasting blood sugar (FBS), HbA1c, total cholesterol (TC), triglycerides (TGs), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C). Dyslipidemia was defined according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines. Diabetes was defined as per American Diabetes Association criteria. The correlation of FBS, HbA1c with lipid ratios and individual lipid indexes were analyzed. The statistical analysis was done by SPSS statistical package version 20.0. **Result** There was significant association of HbA1c with dyslipidemia as per Chi-Square test. HbA1c was found to have significant positive correlation with Total Cholesterol, Triglycerides and LDL and significant negative correlation with HDL and HDL/LDL ratio. The mean TC, TG, LDL was significantly lower and HDL and HDL/LDL was significantly higher in patients with good glycemic control. **Conclusion:** This study suggests utility of HbA1c as a marker of dyslipidemia in addition to chronic hyperglycemia and hence should be analyzed accordingly and thus early diagnosis of dyslipidemia can be used as a preventive measure for the development of CVD in patient type 2 diabetes mellitus.

KEYWORDS

Dyslipidemia, Diabetes Mellitus, Glycated hemoglobin

INTRODUCTION

The incidence of diabetes mellitus (DM) is increasing substantially worldwide. Over the past three decades, the global burden of DM has swelled from 30 million in 1985 to 382 million in 2014, with current trends indicating that these rates will only continue to rise.¹ The latest estimates by the international diabetes federation project that 592 million (1 in 10 persons) worldwide will have DM by 2035.² In 2021 an estimated 7.4 crores individuals had diabetes in India. The direct costs of DM are primarily attributed to both macrovascular and microvascular complications such as coronary artery disease, myocardial infarction, hypertension, peripheral vascular disease, retinopathy, end-stage renal disease and neuropathy.^{3,4} There is strong link exists between DM and cardiovascular disease (CVD). CVD is the most prevalent cause of mortality and morbidity in diabetic populations.⁵ Cardio-vascular risk factors including obesity, hypertension and dyslipidemia are common in patients with DM, particularly those with T2DM. In addition, studies have reported that several factors including increased oxidative stress, increased coagulability, endothelial dysfunction and autonomic neuropathy are often present in patients with DM and may directly contribute to the development of CVD.⁵

In India, a rise in obesity and dyslipidemia with increasing urbanization have led to various lifestyle related disorders like T2DM, CVD and metabolic syndrome.⁶ Among dyslipidemic subjects, increased LDL-C, TG and hypo-HDL are established markers for CAD risk. Additionally, TG-rich lipoproteins like VLDL and IDL contribute to total atherogenic cholesterol.⁷ Elevated glycohemoglobin A1 (HbA1c) is an established predictor for developing atherosclerosis beyond the risk associated with diagnosed diabetes.^{8,9} Hence the present study was done at our tertiary care center to assess the correlations between lipid profile parameter as well as glycated hemoglobin HbA1c value with type 2 DM.

AIMS AND OBJECTIVES

- To study the correlations between lipid profile parameter glycated hemoglobin value to type 2 DM
- To assess the level of various lipid component in type 2 DM.
- To compare the lipid profile between uncontrolled and controlled

diabetics.

- To study the demographic profile of diabetic patients.

MATERIAL AND METHODS

A hospital based observational and prospective study was conducted with 100 patients to analyze the glycated hemoglobin as a predictor of dyslipidemia in type 2 DM for a duration of 2 years. This study was done in the department of Medicine of GMERS Medical college and Hospital, Gotri which is a tertiary care center.

Inclusion Criteria

- All subjects with age ≥ 18 and ≤ 65 years diagnosed with Type 2 DM
- Provided written informed consent prior to any protocol-related procedures, including screening evaluations.

Exclusion Criteria

- Patients with Type 1 diabetes mellitus.
- History of metabolic acidosis or diabetic ketoacidosis
- Subjects with elevated thyroid stimulating hormone (TSH) level at screening with or without thyroid hormone replacement therapy.
- Patient on lipid lowering medications.

Clinical evaluation

The study was carried out at GMERS Medical college and Hospital, Gotri after due permission from the Institutional Ethics Committee. The patients were enrolled after taking written Informed Consent and a thorough history and physical examination was done as per proforma. Demographic details such as age, sex, weight, age of diagnosis, duration of treatment for type 2 diabetes mellitus and detail history of clinical features were recorded on pre designed proforma. The baseline demographic data and family history were obtained. 3 mL of venous blood sample was collected and the serum was used for analyzing fasting blood glucose (FBG), Total cholesterol (TC), HDL-cholesterol (HDL-C), Triglycerides (TG), HbA1C.

Statistical analysis

Statistical testing was conducted with the statistical package for the

social science system version SPSS 20.0. Continuous variables were presented as Mean $\pm$ SD or median (IQR) for non-normally distributed data. Categorical variables were expressed as frequencies and percentages. The comparison of normally distributed continuous variables between the groups was performed using Student's t test else Mann Whitney U test will be used for non-normal distribution data. Nominal categorical data between the groups will be compared using Chi-squared test, Fisher's exact test or Multivariate analysis as appropriate. For all statistical tests, a p value less than 0.05 was taken to indicate a significant difference. Results were graphically represented where deemed necessary.

OBSERVATIONS AND RESULTS

A hospital based observational and prospective study was conducted with 100 patients to analyze the glycated hemoglobin as a predictor of dyslipidemia in type 2 DM.

Distribution of patients according to Age & BMI

Majority of the patients (36%) were from the age group of 51-60 years followed by 25% from the age group of 61-65 years, 15% from the age group of 41-50 years, 12% from the age group of 31-40 years, 9% from the age group of 21-30 years and 3% from the age group of 18-20 years. The mean age of patients was 50.27 ± 12.75 years.

44 (44%) patients had BMI in the normal range while 53 (53%) and 3 (3%) patients were overweight and obese respectively. The mean BMI of patients was 25.28 ± 3.23 kg/m².

Distribution of patients according to Duration of Diabetes

12 (12%) patients had diabetes for 0-2 years while 25 (25%) and 40 (40%) patients had diabetes for 3-5 years and 6-9 years respectively. 23 (23%) patients had diabetes for ≥ 10 years. The mean duration of diabetes was 6.73 ± 3.60 years.

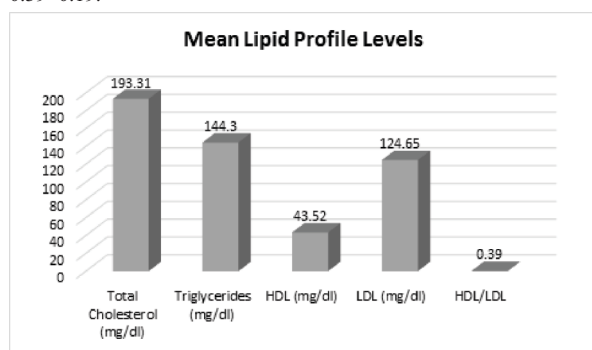
Mean Blood Glucose and HbA1c of patients

The mean Fasting Blood Sugar (FBS) of patients was 155.89 ± 12.38 mg/dl while the mean Postprandial Blood Sugar (PPBS) of patients was 224.57 ± 55.49 mg/dl.

56 (56%) patients had HbA1c < 7 (good glycemic control) while 44 (44%) patients had HbA1c ≥ 7 (poor glycemic control). The mean HbA1c level of patients was $7.17 \pm 1.45\%$.

Mean Lipid Profile Levels of patients

The mean Total Cholesterol and Triglycerides values of patients were 193.31 ± 47.74 mg/dl and 144.30 ± 61.93 mg/dl respectively while mean High Density Lipoprotein (HDL) and Low-Density Lipoprotein (LDL) levels in patients were 43.52 ± 13.17 mg/dl and 124.65 ± 43.22 mg/dl respectively. The HDL/LDL ratio in patients was 0.39 ± 0.19 .



Graph 1: Mean Lipid Profile Levels of patients

Distribution of patients according to Dyslipidemia

85 (85%) patients had dyslipidemia whereas 15 (15%) patients did not have dyslipidemia.

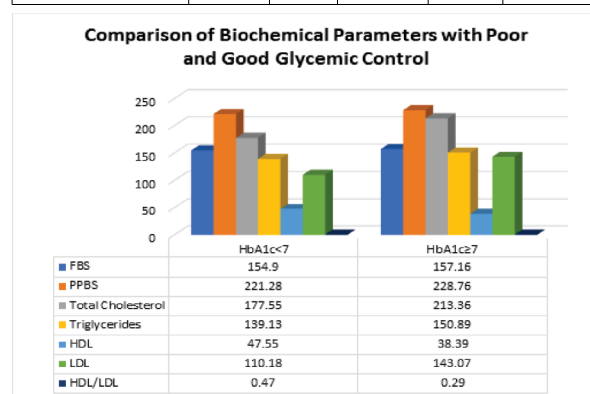
Comparison of Biochemical Parameters with Poor and Good Glycemic Control

The difference in FBS (154.90 ± 13.26 vs. 157.16 ± 11.17 mg/dl) and PPBS (221.28 ± 53.92 vs. 228.76 ± 57.79 mg/dl) was statistically not significant between the groups as per Student t-test ($p < 0.05$). The mean Total Cholesterol (177.55 ± 42.52 vs. 213.36 ± 46.92 mg/dl), Triglycerides (139.13 ± 73.43 vs. 150.89 ± 43.05 mg/dl), LDL

(110.18 ± 38.79 vs. 143.07 ± 41.90 mg/dl) was significantly lower and HDL (47.55 ± 13.68 vs. 38.39 ± 10.56 mg/dl) and HDL/LDL (0.47 ± 0.19 vs. 0.29 ± 0.13 mg/dl) was significantly higher in patients with good glycemic control as per Student t-test ($p < 0.05$).

Table 1: Comparison of Biochemical Parameters with Poor and Good Glycemic Control

Parameters	HbA1c < 7		HbA1c ≥ 7		p Value
	Mean	SD	Mean	SD	
FBS	154.90	13.26	157.16	11.17	>0.05
PPBS	221.28	53.92	228.76	57.79	>0.05
Total Cholesterol	177.55	42.52	213.36	46.92	<0.05
Triglycerides	139.13	73.43	150.89	43.05	<0.05
HDL	47.55	13.68	38.39	10.56	<0.05
LDL	110.18	38.79	143.07	41.90	<0.05
HDL/LDL	0.47	0.19	0.29	0.13	<0.05



Graph 2: Comparison of Biochemical Parameters with Poor and Good Glycemic Control

Association of HbA1c with Dyslipidemia

A significantly higher number of patients without dyslipidemia had good glycemic control as compared to patients without dyslipidemia. There was significant association of HbA1c with dyslipidemia as per Chi-Square test ($p < 0.05$).

Correlation of HbA1c with Lipid Profile parameters

HbA1c was found to have significant positive correlation with Total Cholesterol ($r = 0.268$; $p < 0.05$), Triglycerides ($r = 0.283$; $p < 0.05$) and LDL ($r = 0.794$; $p < 0.05$) and significant negative correlation with HDL ($r = -0.886$; $p < 0.05$) and HDL/LDL ratio ($r = -0.694$; $p < 0.05$).

Correlation of BMI with lipid profile parameters

The BMI showed significantly negative correlation ($r = -0.28$, $p < 0.05$) with HDL-C value, while the others parameters like TC ($r = 0.08$, $p < 0.05$), TG ($r = -0.11$, $p > 0.05$), LDL-C ($r = 0.1$, $p > 0.05$), HDL-C/LDL-C ($r = -0.22$, $p < 0.05$) did not show any significant correlation with BMI.

DISCUSSION

A. Age

In the present study, majority of the patients (36%) were from the age group of 51-60 years, 25% from the age group of 61-65 years, 15% from the age group of 41-50 years, 12% from the age group of 31-40 years, 9% from the age group of 21-30 years and 3% from the age group of 18-20 years. The mean age of patients was 50.27 ± 12.75 years. There were 53 (53%) male patients while female patients constituted 47% of the study population. This is similar to the studies of Sirsikar M et al¹⁰, Baranwal JK et al¹², Vinod Mahato R et al¹³ and Hussain A et al¹¹.

B. BMI

In our study, 44 (44%) patients had BMI in the normal range while 53 (53%) and 3 (3%) patients were overweight and obese respectively. The mean BMI of patients was 25.28 ± 3.23 kg/m². This is comparable to the study of Khaak M et al¹⁵. Khaak M et al¹⁵ case control study found diabetics Body mass index (BMI) was also significantly more than the controls (28.57 ± 1.97 vs 24.46 ± 2.32 $p < 0.001$).

C. Duration of Diabetes Mellitus

It was observed in the present study that 12 (12%) patients had diabetes

for 0-2 years while 25 (25%) and 40 (40%) patients had diabetes for 3-5 years and 6-9 years respectively. 23 (23%) patients had diabetes for ≥ 10 years. The mean duration of diabetes was 6.73 ± 3.60 years. The mean Fasting Blood Sugar (FBS) of patients was 155.89 ± 12.38 mg/dl while the mean Postprandial Blood Sugar (PPBS) of patients was 224.57 ± 55.49 mg/dl. 56% patients had HbA1c < 7 (good glycemic control) while 44% patients had HbA1c ≥ 7 (poor glycemic control). The mean HbA1c level of patients was $7.17 \pm 1.45\%$. This is concordant to the studies of Sirsikar M et al¹⁰ and Vinod Mahato R et al¹³.

D. Sex

Sirsikar M et al¹⁰ study estimating glycated hemoglobin and lipid profile in patients with type 2 DM observed mean value of HbA1c and FBS were slightly higher in males in comparison to female patients and the differences were statistically significant. Increased HbA1c, fasting and post prandial blood sugars was observed in patients with diabetes as compared to the controls, with a significant p value of < 0.001 . Vinod Mahato R et al¹³ observed mean value of HbA1c and FBG were slightly higher in females in comparison to male patients but the differences were not significant.

E. Lipid profile

In the present study, 85 (85%) patients had dyslipidemia whereas 15 (15%) patients did not have dyslipidemia. This is in concordance to the studies of Vinod Mahato R et al¹³ and Hussain A et al¹¹.

It was observed in our study that the mean Total Cholesterol and Triglycerides values of patients were 193.31 ± 47.74 mg/dl and 144.30 ± 61.93 mg/dl respectively while mean High Density Lipoprotein (HDL) and Low Density Lipoprotein (LDL) levels in patients were 43.52 ± 13.17 mg/dl and 124.65 ± 43.22 mg/dl respectively. The HDL/LDL ratio in patients was 0.39 ± 0.19 . This is consistent with the studies of Sirsikar M et al¹⁰, Baranwal JK et al¹², Vinod Mahato R et al¹³, Hussain A et al¹¹ and Khaak M et al¹⁵.

Sirsikar M et al¹⁰ observed among the circulating lipids, TC TG, LDL-C and VLDL were significantly higher. Hypercholesterolemia was found in 90% patients while hypertriglyceridemia was found in 92% patients, increased LDL-C was found in 73% patients and decreased HDL-C was found in 86% patients. Baranwal JK et al¹² cross sectional study observing correlation of HbA1c with lipid profile observed hypercholesterolemia, hypertriglyceridemia and increased LDL-C was seen in 36%, 50% and 33% of patients respectively.

Vinod Mahato R et al¹³ study observed among the circulating lipids, TC and LDL-C were significantly higher ($P < 0.05$) in female patients. Although the mean level of TG was slightly lower and of HDL-C slightly higher in females than males, these differences were statistically non-significant. Hypercholesterolemia was found in 27.8%, hypertriglyceridemia was found in 63.26% individuals, decreased HDL-C was found in 15.6% individuals and increased LDL-C was found in 47.6% individuals.

Hussain A et al¹¹ cross-sectional study determining the correlation between hemoglobin A1c (HbA1c) and serum lipid profile observed mean $\pm$ SD of FBS, HbA1c, TC, TG, HDL-C and LDL-C were 230.54 ± 100.58 , 9.84 ± 2.47 , 206 ± 53.51 , 256 ± 143.2 , 40.85 ± 13.62 , and 118.81 ± 51.78 respectively.

Khaak M et al¹⁵ case control study determining the correlation of plasma glucose levels with lipid profile in type 2 Diabetes Mellitus observed FPG was (11.23 ± 3.65 in diabetics vs 4.35 ± 0.68 in controls), HbA1c was (6.84 ± 0.482 vs 5.31 ± 0.487). Serum total cholesterol was (4.68 ± 0.96 vs 3.99 ± 1.01 $p < 0.001$), triglycerides (TG) were (2.42 ± 1.22 vs 1.56 ± 0.87 $p < 0.001$) and LDL-Cholesterol was (2.46 ± 0.77 vs 2.17 ± 0.72 $p < 0.05$). These parameters were significantly raised than in the control group.

Sugars

In our study, the difference in FBS (154.90 ± 13.26 vs. 157.16 ± 11.17 mg/dl) and PPBS (221.28 ± 53.92 vs. 228.76 ± 57.79 mg/dl) was statistically not significant between the groups as per Student t-test ($p < 0.05$). The mean Total Cholesterol (177.55 ± 42.52 vs. 213.36 ± 46.92 mg/dl), Triglycerides (139.13 ± 73.43 vs. 150.89 ± 43.05 mg/dl), LDL (110.18 ± 38.79 vs. 143.07 ± 41.90 mg/dl) was significantly lower and HDL (47.55 ± 13.68 vs. 38.39 ± 10.56 mg/dl) and HDL/LDL (0.47 ± 0.19 vs. 0.29 ± 0.13 mg/dl) was significantly higher in patients with good glycemic control as per Student t-test ($p < 0.05$).

Baranwal JK et al¹², Vinod Mahato R et al¹³ and Hussain A et al¹¹ noted similar observations in their studies.

Baranwal JK et al¹² observed mean value of TC, LDL and TG was found to be lower in patients with good glycemic control than those with poor glycemic control. But, mean value of HDL and HDL/LDL ratios was found to be higher in patients with good glycemic control than those with poor glycemic control and the differences were significant.

Vinod Mahato R et al¹³ study reported highly significant correlation was between FBG and HbA1c ($P = 0.000$). HbA1c also demonstrated direct and significant correlations with TC ($P = 0.017$), LDL-C ($P = 0.015$), LDL-C/HDL-C ratio ($P = 0.011$), Non-HDL-C ($P = 0.011$) and Risk ratio ($P = 0.005$).

Hussain A et al¹¹ cross-sectional study determining the correlation between hemoglobin A1c (HbA1c) and serum lipid profile observed hypercholesterolemia in 50.1% of patients; similarly hypertriglyceridemia was found in 74.8% of patients. Abnormal LDL-C levels were found in 62.8% of patients and HDL-C was less than 40 mg/dl in 51.9%.

It was observed in the present study that a significantly higher number of patients without dyslipidemia had good glycemic control as compared to patients with dyslipidemia. There was significant association of HbA1c with dyslipidemia as per Chi-Square test ($p < 0.05$). This finding was consistent with the studies of Baranwal JK et al¹², Hussain A et al¹¹, Kunikullaya KP et al¹⁴ and Artha IMJR et al¹⁶.

Baranwal JK et al¹² cross sectional study observing correlation of HbA1c with lipid profile observed level of HDL-C was low in 47% of females and 16% of males. Also, 63% of patients had good glycemic control as suggested by HbA1c level $< 7\%$.

Hussain A et al¹¹ cross-sectional study reported mean value of FBS, HbA1c, TC, HDL-C and LDL-C were slightly higher in female compared with male patients, but the differences were not statistically significant. Although the mean levels of TC and the TC/HDL-C ratio were slightly lower in women than in men, these differences were statistically non significant.

Artha IMJR et al¹⁶ retrospective study observed lipid profile findings such as total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), and lipid ratio parameter (LDL-C to high-density lipoprotein cholesterol (HDL-C) ratio) were higher in patients in the poor glycemic control group ($p < 0.05$) and HDL-C was significantly lower in patients with poor glycemic control ($p = 0.001$).

It was observed in our study that HbA1c was found to have significant positive correlation with Total Cholesterol ($r = 0.268$; $p < 0.05$), Triglycerides ($r = 0.283$; $p < 0.05$) and LDL ($r = 0.794$; $p < 0.05$) and significant negative correlation with HDL ($r = -0.886$; $p < 0.05$) and HDL/LDL ratio ($r = -0.694$; $p < 0.05$). Similar observations were noted in the studies of Sirsikar M et al¹⁰, Baranwal JK et al¹², Vinod Mahato R et al¹³, Hussain A et al¹¹, Kunikullaya KP et al¹⁴, Khaak M et al¹⁵ and Artha IMJR et al¹⁶.

Sirsikar M et al¹⁰ study reported a highly significant positive correlation between FBG and HbA1c. The value of r was 0.7245, $P < 0.01$. There was a strong positive correlation HbA1c and PPBS with r value 0.7356., $p < 0.01$. HbA1c also demonstrated direct and significant correlations with cholesterol with r value 0.6445, TG with r value 0.5426, LDL-C with r value of 0.3584, VLDL r value 0.2245, L/H R value of 0.3416 with a strong positive correlation. Whereas HDL-C showed negative correlation with r value -0.4965.

Baranwal JK et al¹² cross sectional study observing correlation of HbA1c with lipid profile reported HbA1c was found to have significant positive correlation with TC, LDL, and TG and significant negative correlation with HDL and HDL/LDL ratio.

Vinod Mahato R et al¹³ study reported positive correlation of HbA1c with TAG ($P = 0.169$) and with that of HDL-C was negative ($P = 0.596$) but it was statistically non-significant. Also, HbA1c was found to be a predictor of hypercholesterolemia and high LDL-C by linear regression analysis. However, HDL-C and TAG did not show significant association with HbA1c. Patients with HbA1c value $> 7.0\%$

had significantly higher value of TC ($P=0.024$), TG ($P=0.030$), LDL-C ($P=0.011$), Non-HDL-C, LDL-C/HDL-C ratio and Risk ratio as compared to the patients with HbA1c value $\leq 7.0\%$.

Hussain A et al¹¹ cross-sectional study reported significant positive correlation between HbA1c and TC. HbA1c also demonstrated a significant correlation with TG. The correlation between HbA1c and HDL-C was negative and was found to be statistically nonsignificant. Furthermore, it was found that HbA1c was positively and significantly related to LDL-C and LDL-C/HDL-C ratio. However, HDL-C and FBS did not show any significant association with HbA1c in the regression analysis. Patients with HbA1c values greater than 7.0% had significantly higher values of cholesterol ($p = 0.004$), LDL-C ($p = 0.002$), LDL-C/HDL-C ratio ($p = 0.024$), FBS ($p = 0.64$), TG ($p = 0.097$), HDL-C ($p = 0.334$), and risk ratio ($p = 0.58$), compared with the first group.

Kunikullaya KP et al¹⁴ retrospective study reported HbA1c showed direct and significant correlations with cholesterol, TG and LDL and HbA1c was a good predictor of circulating lipid levels.

Khaak M et al¹⁵ reported serum FPG, HbA1c, Total Cholesterol, TG and LDL-Cholesterol were significantly increased in T2DM while HDL-Cholesterol levels decreased significantly.

Artha IMJR et al¹⁶ retrospective study reported significant positive correlation between LDL, total cholesterol, LDL-C, TG, and TC to HDL-C ratio, triglycerides, and TC/HDL-C ratio with HbA1c level. Meanwhile, a negative correlation was observed on HDL-C with the HbA1c level. Only TC/HDL-C ratio and LDL-C/HDL-C ratio parameters used as predictive models ($AUC > 0.7$), with cutoff point, sensitivity, and specificity of 4.68 (77%; 52%) and 3.06 (98%; 56%) respectively.

Limitation of study

The limitation of our study are the cross-sectional design and a small number of participants. The contribution of diet and socio-economic factors in influencing lipid profile and obesity were not considered. Similarly, waist circumference (WC) was not measured.

Our study did not analyse the types and effect lipid lowering treatment in dyslipidemic patient.

CONCLUSION

HbA1c predicts serum lipid profile and provides valuable supplementary information about the extent of circulating lipids besides its primary role in monitoring long-term glycemic control. Dual biomarker capacity of HbA1c (glycemic control as well as lipid profile indicator) may be utilized for screening high-risk diabetic patients for timely intervention with lipid lowering drugs and thus preventing adverse cardiovascular events.

Significant correlation of level of HbA1c with parameters of lipid profile suggests utility of HbA1c as a marker of dyslipidemia in addition to chronic hyperglycemia and hence should be analyzed accordingly and thus early diagnosis of dyslipidemia can be used as a preventive measure for the development of CVD in patient type 2 diabetes mellitus.

Lipid profiles (LDL-C) and lipid ratios (LDL-C/HDL-C and TC/HDL-C ratio) show potential markers that can be used in predicting glycemic control in patients with T2DM.

REFERENCES:

1. Wild S, Roglic G, Green A et al. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care*. 2004; 27:1047–1053.
2. Aguirre F, Brown A, Cho NH et al. IDF Diabetes Atlas. 2013.
3. Bahia LR, Araujo DV, Schaan BD et al. The costs of type 2 diabetes mellitus outpatient care in the Brazilian public health system. *Value Health*. 2011; 14:S137–S140.
4. American Diabetes Association. Economic costs of diabetes in the U.S. In 2007. *Diabetes Care*. 2008; 31:596–615.
5. Matheus AS, Tannus LR, Cobas RA et al. Impact of diabetes on cardiovascular disease: an update. *Int J Hypertens*. 2013; 653789.
6. Singh AK, Singh SK, Singh N et al. Obesity and dyslipidemia. *Int J Biol Med Res*. 2011; 2(3):824–8.
7. Peters A. Clinical Relevance of Non-HDL Cholesterol in Patients with Diabetes. *Clinical Diabetes*. 2008; 26(1):1–7.
8. Khaw KT, Wareham N, Luben R et al. Glycated hemoglobin, diabetes, and mortality in men in Norfolk cohort of European prospective investigation of cancer and nutrition (EPIC-Norfolk). *BMJ*. 2001; 322:15–18.
9. Laakso M. Glycemic control and the risk for coronary heart disease in patients with non-insulin-dependent diabetes mellitus: the Finnish studies. *Ann Intern Med*. 1996; 124:127–130.

10. Sirsikar M, Supriya, Mohanty S et al. Role of glycated hemoglobin (HbA1c) as a dual marker to predict glycemic status and dyslipidemia in type II diabetes mellitus. *Int J Res Med Sci*. 2016; 4:4524–9.
11. Hussain A, Ali I, Ijaz M, Rahim A. Correlation between hemoglobin A1c and serum lipid profile in Afghani patients with type 2 diabetes: hemoglobin A1c prognosticates dyslipidemia. *Ther Adv Endocrinol Metab*. 2017; 8(4):51–57.
12. Baranwal JK, Maskey R, Majhi S et al. Association between level of HbA1c and lipid profile in T2DM patients attending diabetic OPD at BPKIHS. *Health Renaissance* 2015; 13(3):16–23.
13. Vinod Mahato R, Gyawali P, Raut PP et al. Association between glycaemic control and serum lipid profile in type 2 diabetic patients: Glycated haemoglobin as a dual biomarker. *Biomedical Research* 2011; 22(3): 375–380.
14. Kunikullaya KP, Goturu J. Glycosylated Haemoglobin (HbA1c) - A Marker of Circulating Lipids in Type 2 Diabetic Patients. *J Clin Diagn Res*. 2014; 8(2):20–23.
15. Khaak M, Nawaz A, Anis Khan J et al. Dyslipidemia in Type 2 Diabetes Mellitus. *JIMC*. 2018, Vol. 13, No.3.
16. Artha IMJR, Bhargava A, Dharmawan NK et al. High level of individual lipid profile and lipid ratio as a predictive marker of poor glycemic control in type-2 diabetes mellitus. *Vasc Health Risk Manag*. 2019; 15:149–157.