Role of HbA1c as a Marker of Dyslipidemia in Patients with Type 2 VDiabetes Mellitus visiting Tertiary Health Care Center

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Abstract

Introduction: 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 diagnostic value of HbA1c in predicting diabetic dyslipidemia.

Methods: This was a cross-sectional study where the sera were analyzed for HbA1c, fasting blood glucose (FBG), total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL) and low-density lipoprotein cholesterol. SPSS version 23.0 was used to analyze the data.

Results: The levels of HbA1c did not differ significantly between males and females whereas male patients had significantly higher fasting blood glucose than females. There was a highly significant correlation between HbA1c and FBG. Both HbA1c and fasting blood glucose exhibited direct correlations with cholesterol, TG and LDL and inverse correlation with HDL; the magnitude of significance for all these lipid parameters being greater with HbA1c than fasting blood glucose.

Conclusions: HbA1c can provide valuable information about the circulating lipids beside its primary role in monitoring long term glycemic control.

INTRODUCTION

Type 2 Diabetes Mellitus (Type 2 DM) has rapidly developed into a major public health problem in South Asia as a result of rapid economic development, urbanization, and transitions in nutritional status.[1] Type 2 DM is characterized by hyperglycemia, insulin resistance, and relative impairment in insulin secretion. Patients typically present with a combination of varying degrees of insulin resistance and defective insulin secretion. It is often accompanied by hypertension, dyslipidemia and central obesity, referred to as the metabolic syndrome.[2] DM is characterized by metabolic abnormalities and long term macro and microvascular complications. The lipid abnormalities are more prevalent in DM because major key enzymes and lipid metabolism pathways are affected due to deficiency of insulin production and secretion.[3]

HbA1c has been used as a marker of glycemic control in DM. It has been observed that there is a direct correlation between HbA1c and the severity of coronary heart disease (CHD) in diabetic patients.[4] Dyslipidemia, frequently occurring in patients with Type 2 DM, might play a critical role in accelerated macrovascular atherosclerotic disease formation and may contribute significantly to the excess risk of CHD in patients with Type 2 DM. Elevated level of HbA1c has been identified as a significant risk factor for cardiovascular diseases and stroke in subjects who may have diabetes.[5]

The rationale of this study was to detect the lipid abnormality in patients with Type 2 DM incorporating HbA1c as the marker since early detection and treatment

of hyperlipidemia can prevent the progression of lipid abnormalities and minimize the risk of cerebrovascular accident and cardiovascular disorder.

METHODS

This was a cross-sectional study done in the Department of Biochemistry of Shree Birendra Hospital, Chhauni, Kathmandu, Nepal from November 2022 to January 2023. The study was initiated after taking approval from the Institutional Research Committee of Nepal Army Institute of Health Sciences (NAIHS) (Regd no. 665). Written consent was obtained from 120 participants, expressing their willingness to participate in the study. Venous blood samples were collected after at least eight hours fasting in EDTA vials and serum separator tubes. HbA1c was measured using Bio rad D10 analyzer (NGSP, IFCC certified). Sera were analyzed for fasting blood glucose (FBG), total cholesterol, triglyceride (TG), high density cholesterol (HDL) and low density cholesterol (LDL) using Cobas c 311 (Roche Diagnostics, USA). The impact of glycemic control on various parameters was evaluated by categorizing patients into three categories: < 6% (Good glycemic control), > 6 - 9% (Poor glycemic control) and > 9% (Worse glycemic control). The data were analyzed by SPSS version 23.0. Pearson's correlation test was performed to examine various correlation. Independent samples Student's t-test (2-tailed) was used to compare the means of different parameters between males and females. P values < 0.05 were considered as statistically significant.

RESULTS

The mean age standard deviation of male and female subjects was 61.8 ± 11.4 years and 57.2 ± 11.6 years respectively. Depending on three cutoff values, the mean HbA1c standard deviation of subjects were 5.8 ± 0.2 of good glycemic control, 7.5 ± 0.7 of poor glycemic control and 12.4 ± 2.3 of worse glycemic control. Among the participants, 63.5% of the females and 47% of the males had poor glycemic control whereas 36.5% of the females and 24% of the males had worse glycemic control (Table 1).

Table 1: Distribution of subjects according to gender and HbA1c cut off values

Glycemic control	HbA1c criteria	Female	Male	Total
Good	< 6%	0	6 (10.5%)	6
Poor	6 - 9%	40 (63.4%)	27 (47.4%)	67
Worse	> 9 %	23 (36.5%)	24 (42.1%)	47
		63	57	

All the patients were categorized into four age groups: < 50 years (24), > 50 - 60 years (41), > 60 - 70 years (36) and > 70 years (19). Alterations in serum biochemical parameters in various age groups are shown in Table 2.

Table 2. Serum Biochemistry categorized by patients' age group

	Age of patients			
Parameters	< 50 years	51 - 60 years	61 - 70 years	> 70 years
Hba1c (%)	9.4 ± 2.5	8.9 ± 2.5	9.7 ± 3.1	9.6 ± 3.7
Total Cholesterol (mg / dl)	195.3 ± 48.3	195.3 ± 54.4	203.8 ± 54.2	186.6 ± 46.9
Triglyceride (mg / dl)	251.5 ± 147.2	273.3 ± 158.8	233 ± 137.0	182.6 ± 67.2
HDL (mg / dl)	39.3 ± 14.5	37.1 ± 8.7	37.4 ± 7.0	38.9 ± 10.8
LDL (mg / dl)	100.6 ± 38.9	102.3 ± 35.0	104.8 ± 37.0	91.7 ± 40.0
Fasting Blood Glucose (mg / dl)	192.8 ± 120.1	163.4 ± 62.9	210.5 ± 114.8	208.8 ± 131.8

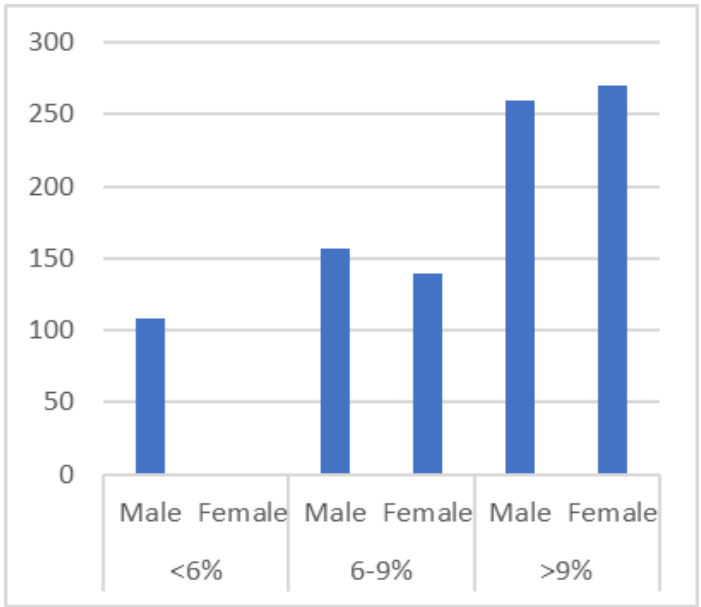
The levels of HbA1c was slightly higher and of HDL significantly higher in females as compared to male patients (Table 3). Among the circulating lipids, total cholesterol, LDL and triglycerides were higher in male patients, whereas the level of HDL was higher in females than males.

Table 3: Distribution of biochemical parameters according to gender

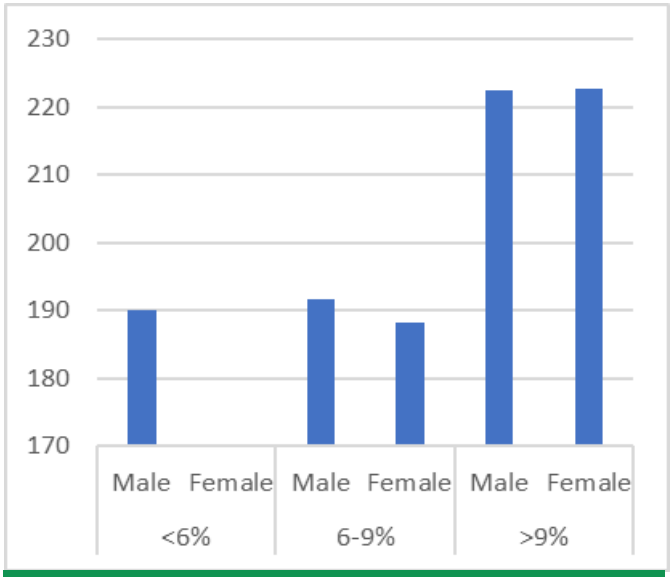
Parameters	Gender of Patients	
	Male	Female
Hba1c (%)	9.3 ± 3.2	9.4 ± 2.6
Cholesterol (mg / dl)	201.7 ± 54.2	191.8 ± 49.2
TG (mg / dl)	249.3 ± 150.6	236.4 ± 132.1
HDL (mg / dl)	35 ± 9.3	40.65 ± 9.8
LDL (mg / dl)	103.5 ± 39.8	98.8 ± 34.4
FBG (mg / dl)	194.6 ± 114.0	186.9 ± 97.2

The comparative effects of glycemic control in male and female diabetic patients are shown in Figure 1.

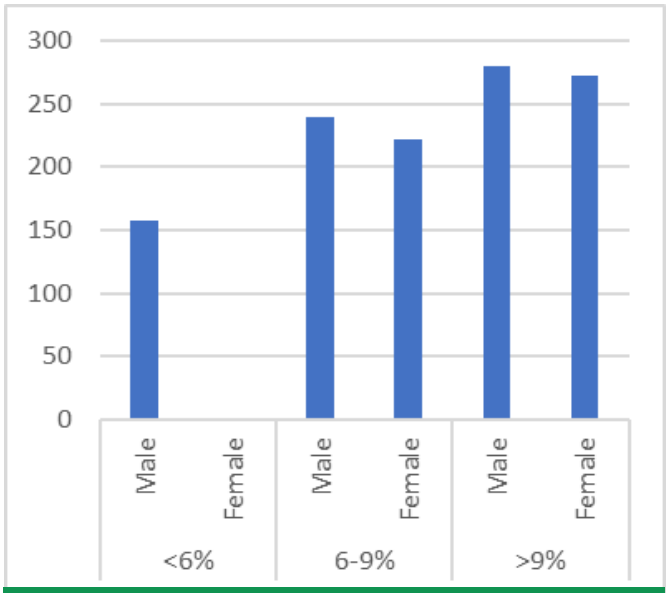
Figure 1 Distribution of various parameters with respect to glycemic control in male and female diabetic patients



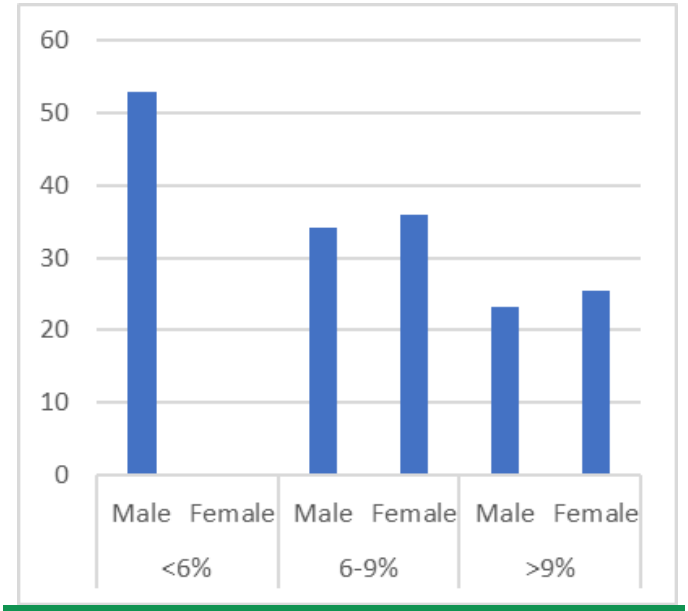
A. Fasting Blood Glucose (mg/dl)



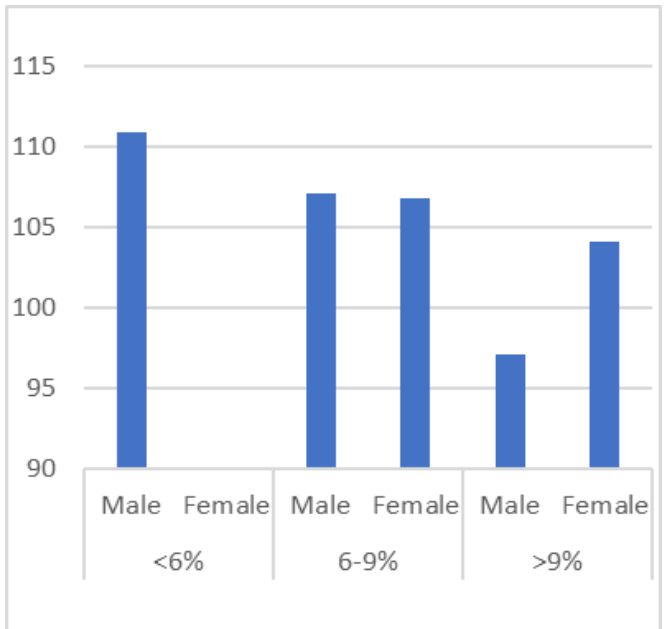
B. Cholesderol (mg/dl)



C. Triglyceride (mg/dl)



D. HDL (mg/dl)

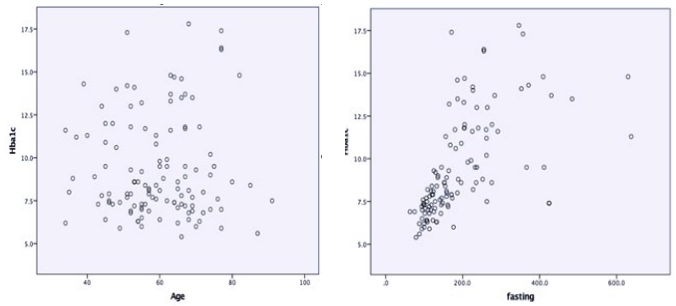


E. LDL (mg/dl)

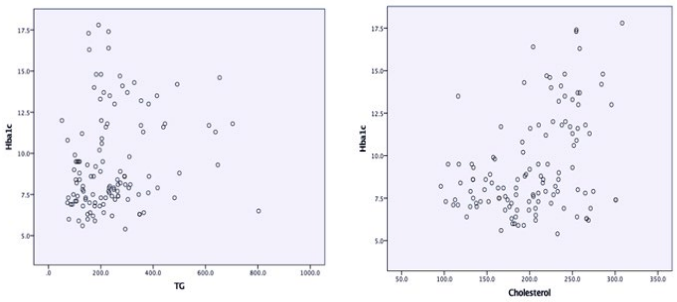
There was no significant correlation between patient age and HbA1c, whereas a highly positive correlation was observed between fasting blood glucose and HbA1c (r = 0.602, p < 0.05) (Fig 2).

There was a positive correlation between HbA1c and total cholesterol which was statistically significant (r = 0.396, p < 0.05). Likewise, the correlation between HbA1c and TG was positive and statistically significant (r = 0.183, p < 0.05). The relationship between HbA1c and HDL-C was inverse, giving a negative correlation, which was statistically significant (r = - 0.614, p < 0.05)

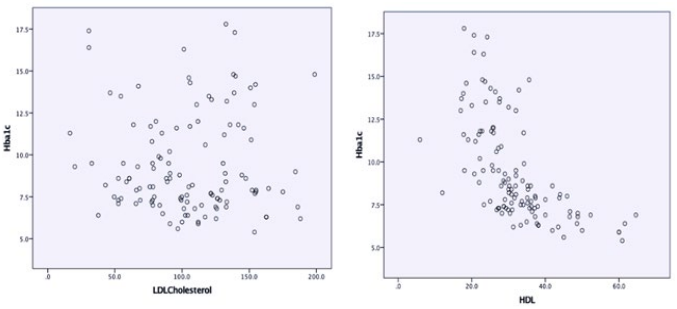
Figure 2. Correlations between HbA1c and age, FBG and serum lipid profile



R = 0.020, P = 0.830 R = 0.602, P = 0.000



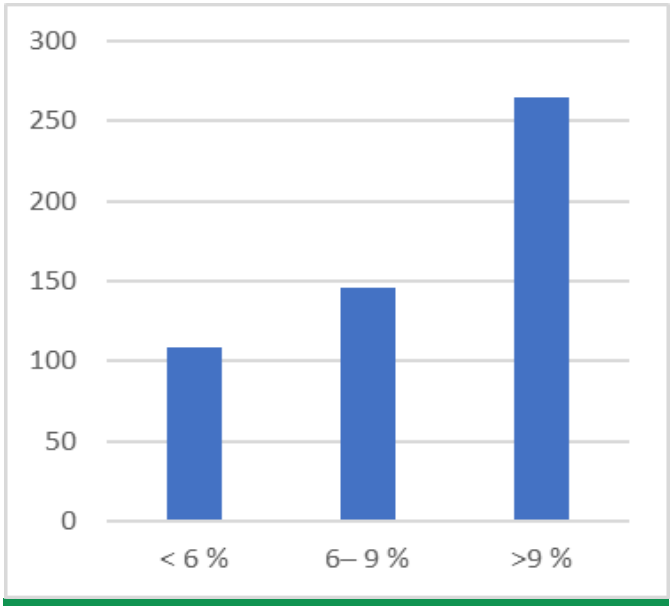
R = 0.183, P = 0.045 R = 0.396, P = 0.00



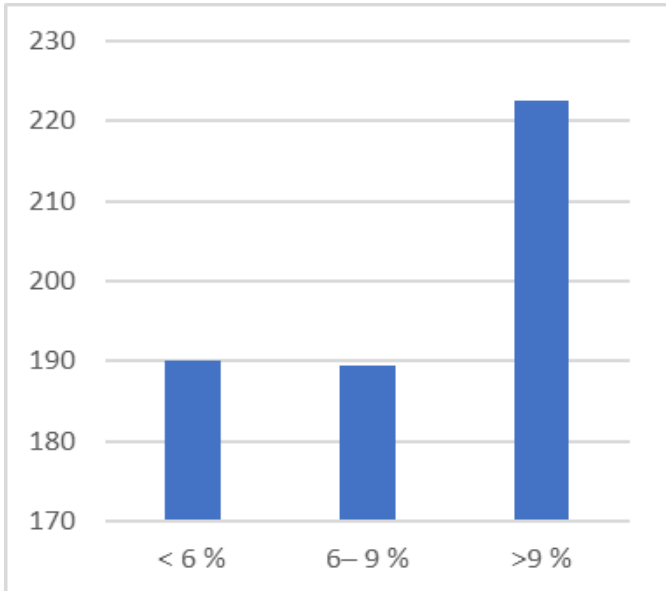
R = -0.004, P = 0.962 R = -0.614, P = 0.00

Diabetic patients with poor glycemic control had higher levels of FBG, total cholesterol, triglycerides and lower levels of HDL as compared to patients with good glycemic control as shown in Fig. 3.

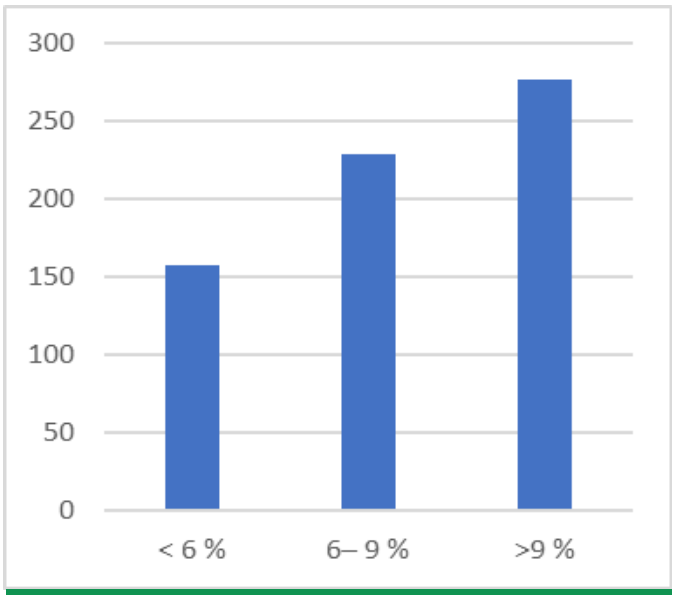
Figure 3. Distribution of various parameters according to glycemic control



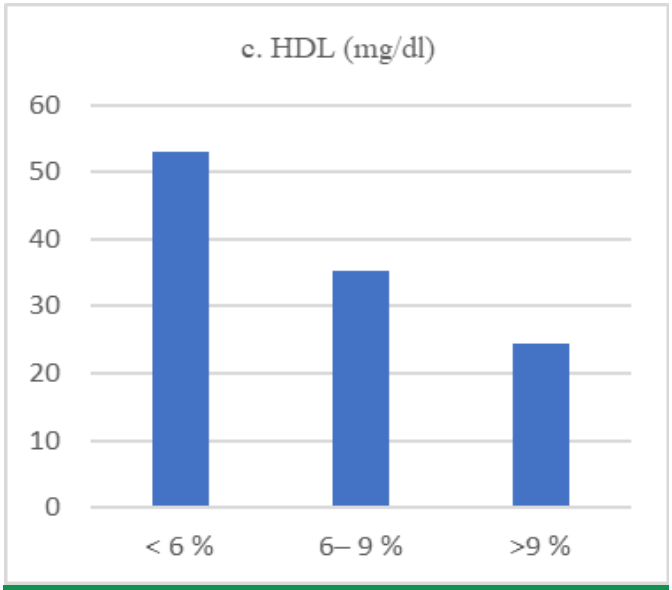
A. Fasting Blood Glucose (mg/dl)



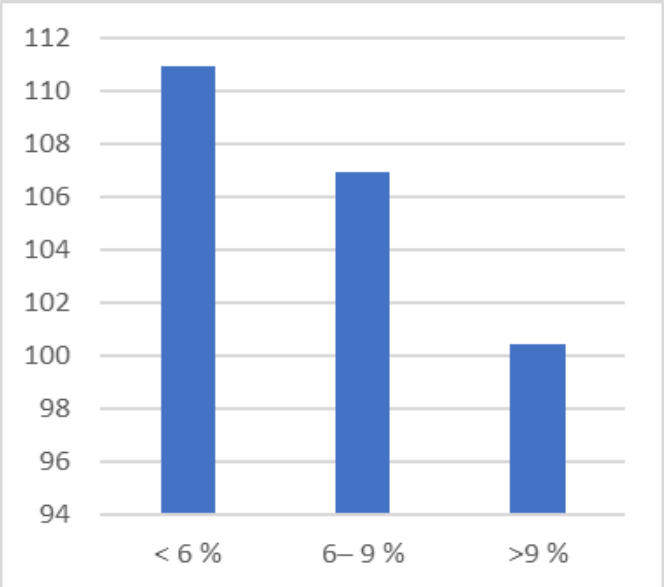
B. Total Cholesterol (mg/dl)



C. Triglyceride (mg/dl)



C. HDL (mg/dl)



D. LDL (mg/dl)

DISCUSSION

The distribution of subjects according to gender showed that most of the patients with Type 2 DM experience poor or worse glycemic control irrespective of their gender (Fig. 1). Older patients (> 70 years) had HbA1c levels similar to the younger ones. However, there was neither a significant difference in HbA1c among the four age categories (Table 2) nor a direct correlation between age and HbA1c (Fig 2), which is supported by earlier study.[6] There was a slight decrease in various lipid components including total cholesterol, TG, LDL with advancing age (Fig. 1). The magnitude of hyperglycemia was significantly less in patients aged (51 - 60 years), whereas the average FBG levels in the remaining patients were almost similar. (Table 2).

Both male and female diabetic patients with uncontrolled diabetes had severe hyperglycemia and significantly increased TG, cholesterol and LDL (Fig. 1). The variation in HDL with respect to glycemic control did not differ among male patients. Whereas, female patients demonstrated proportionate decrements in HDL levels with increasing HbA1c cutoffs. High HDL levels protect against coronary artery disease development, as patients with high HDL tend to have lower prevalence of CHD risk factors.[7] Women with diabetes seem to have encountered an increased CHD mortality. Diabetic women might be subjected to additional changes in coagulation, vascular capability and CHD risk factors than diabetic men.[8,9]

A significant correlation between HbA1c and FBG (Fig.2) is in agreement with earlier reports. We also observed significant correlations between HbA1c and cholesterol, TG, HDL and LDL in diabetic patients which is in agreement with the findings of several other investigators who reported significant correlations between HbA1c and lipid profiles and suggested the importance of good management of diabetes in controlling dyslipidaemia.[10-13] Diabetic patients with poor glycaemic control exhibited a significant increase in cholesterol and TG and a decrease in HDL without any significant alteration in LDL (Fig. 3). The magnitude of impaired glycaemic control as defined by three different cutoff values of HbA1c was proportionally related with dyslipidaemia in terms of significantly higher cholesterol and TG and lower HDL levels (Fig. 3). The arbitrary cutoff values of HbA1c are based on earlier studies.[14-16] In diabetic individuals, Selvin et al found a linear association between CHD and HbA1c, indicating that the risk of CHD starts to rise even at HbA1c levels below 7.0%.[17] According to Grant et al those with HbA1c levels higher than 6.0% have considerably increased CVD risk factors.[18]

The risk of cardiovascular heart disease in people with diabetes is inversely related to HDL cholesterol and directly related to non-HDL cholesterol.[19] Another study on female type 2 diabetic patients has found that elevated triglycerides are associated with a higher risk of CHD.[20] Onat et al suggested that fasting triglycerides are predictive for future CHD independent of age, diabetes, total cholesterol and HDL.[21] It can be suggested that lipid parameters, such as total cholesterol, TG, HDL and LDL have a role in predisposing diabetes individuals to cardiovascular complications. Significant correlations between HbA1c and all these lipid parameters (Fig. 2) and a linear relationship between HbA1c and dyslipidemia (Fig. 3) point towards the usefulness of HbA1c for screening high-risk diabetic patients. Furthermore, a larger, multi centric study needs to be conducted for better outcomes in order to prevent risk of cardiovascular complications in patients with Type 2 DM.

CONCLUSIONS

The findings of this study suggest that HbA1c endures the ability of predicting serum lipid profile in both male and female diabetic patients. Diabetic patients with HbA1c > 6% - 9% and > 9% tend to have moderate and severe dyslipidaemia respectively. HbA1c as a marker of glycemic control as well as lipid profile indicator may be utilized for screening high-risk diabetic patients for timely intervention.

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CONFLICT OF INTEREST: None

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