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GLYCATED HAEMOGLOBIN ACTSAS AN INDICATOR OF DISLIPIDEMIA IN PATIENTS WITH TYPE II DIABETES MELLITUS

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ABSTRACT

Diabetic patients with associated dyslipidemia are easy targets for cardiovascular diseases (CVD). Glycated hemoglobin predicts the risk for the development of diabetic complications. This study was an attempt to determine lipid abnormalities associated with Type-2 Diabetes Mellitus and association between glycated hemoglobin (HbA1c) levels and serum lipid profile to assess the importance of HbA1c as an indicator of dyslipidemia and future risk of cardiovascular disease in Bhola District, Barisal. In this cross-sectional study, 200 known patients of Type-2 Diabetes Mellitus within 35-85 years of age were randomly selected. They were investigated for HbA1c and lipid profile. The data were evaluated by Statistical Package for Social Sciences (SPSS) 16.0 version software. Independent samples t-test (2-tailed) was used to compare means of anthropometric, clinical and laboratory parameters and the effect of the glycemic control on their lipid profile was determined using correlation coefficient. Amongst the study group, 65% patients showed poor glycemic control, 35% with good glycemic control and 59.60% patient's haddyslipidemia.HbA1c was found to have significant positive correlation with total cholesterol (TCHO), low density lipoprotein (LDL-C) and triglycerides (TG) and significant negative correlation with high density lipoprotein (HDL-C). The mean value of TC, LDL-C and TG was found to be lower in patients with good glycemic control than those with poor glycemic control. These differences were significant at the level of $P<0.05$. These findings conclude that the glycemic control of the patient has got a strong impact on the serum lipid level and dyslipidemia is frequently encountered in those who have got poor glycemic control.

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INTRODUCTION

Diabetes mellitus is currently a global public health concern in the 21st century as its scale of challenge affect all people regardless of age or social class. The global prevalence of people living with diabetes mellitus among adults aged 27 -79 years by 2015 was estimated to be 415 million and the number is projected to raise up to642 million in the year 2040 if nothing is done to prevent the disease of which 318 million adults have impaired glucose tolerance (IDF, 2015).The development of type 2 diabetes (T2DM) is a complex process and accounts for 85 to 90 % of all the diabetes mellitus (DM) cases. It has remained a major concern of healthcare professionals from long time due its strong association with cardiovascular diseases (CVD) (Cheng, 2005).Diabetic patients have a greater likelihood of having dyslipidemia, hypertension, and obesity. Because early detection and prompt treatment may reduce the burden of diabetes and its complications, screening for diabetes may be appropriate under certain circumstances (American Diabetes Association, 2003).Typical pattern of diabetic dyslipidemia include an abnormally high level of triglycerides (TG), a high proportion of small dense low density lipoprotein cholesterol (LDL), low high density lipoprotein cholesterol (HDL) (Haffner, 2002; Goldberg, 2001; Ginsberg, 2006). The higher prevalence of lipid abnormalities in diabetes mellitus has been attributed to insulin resistance or deficiency that affects key enzymes and pathways in lipid metabolism. (Taskinen, 2002). So, hyperglycemia, dyslipidemia and coronary artery disease relate well with each other in type 2 diabetes and it has been proposed that higher prevalence of cardiovascular disease in type 2 diabetes is due to chronic uncontrolled hyperglycemia (Folli et al, 2011; Maritim et al., 2003) and hence strict control of hyperglycemia and dyslipidemia can be preventive. HbA1c to be an independent risk factor for coronary heart disease (Selvin et al., 2005) and stroke and it has also been seen that risk of cardiovascular disease increases by 18% with every 1% increase in value of HbA1c in diabetic (Selvin et al., 2004). Also, it has been calculated that a reduction of 0.2% in the value of HbA1c reduces mortality due to cardiovascular events by 10%.

In a country like Bangladesh where a significant number of people belong to below poverty line group and are unable to take the blood tests as frequently as advised, using HbA1c as a dual marker i.e. marker for hyperglycemia and dyslipidemia would be of much help while treating patients. It should be understood that HbA1c cannot replace the utility of lipid profile, but if presence of certain correlation is discovered between the two, HbA1c could be considered for early determination of dyslipidemia and hence could help in assessing cardiovascular diseases risk. The study was conducted to investigate the relationship between glycemic control and serum lipid profile and to investigate whether Glycated haemoglobin is a risk factor for cardiovascular disease.

MATERIALS AND METHODS

A hospital-based cross-sectional study was conducted from September 2017 to March 2018. The study populations were selected from the Diabetic Hospital, Bhola. A total of 200 T2DM patients (89 males and 111 females) with confirmed T2DM diabetes were selected.

Inclusion criteria

Confirmed T2DM diabetes patients aged 35 to 85 years and regularly attended clinic were included in the study. Patients who qualified but not willing to participate in the study were not included in the study.

Ethical Consideration

The study was approved by the Department of Human Nutrition and Dietetics, Patuakhali Science and Technology University. Further written permission was obtained from the Medical Superintendent of the Diabetic Hospital, Bhola where samples were collected. Informed consent was obtained from study participants before the commencement of each interview, and no personal identification was registered. There was no any financial compensation or provision for the study participants.

Laboratory Investigations

Venous blood samples were collected from all the subjects after at least 8 hours fasting. Blood specimens were collected for HbA1c in Serum Separator Tube for fasting glucose (FBG) and lipid profile measurement. All the biochemical analyses were performed in the Laboratory of Bhola Diabetic Hospital, Bangladesh. Serum was used for analyzing lipid profile, which includes total cholesterol (TC), HDL-cholesterol (HDLC), triglycerides (TAG) and LDL-cholesterol (LDL-C) was calculated. The patients were classified into two groups depending on their glycated hemoglobin (HbA1c); Good Glycemic Control (GGC) group having HbA1c < 7.0% and Poor Glycemic Control (PGC) group having HbA1c>7.0%. For serum lipid reference level, National Cholesterol Education Programme (NCEP) Adult Treatment Panel III (ATP III) guideline was referred (http://www.nhlbi.nih.gov/guidelines/cholesterol/index.htm).

According to NCEP-ATPIII guideline, hypercholesterolemia is defined as TC>5.2 mmol/l, high LDL-C when value >2.6 mmol/l, hypertriglyceridemia as TG >3.8 mmol/l and low HDL-C when value <1.0 mmol/l. Dyslipidemia was defined by presence of one or more than one abnormal serum lipid concentration (Ram et al., 2011).

Statistical analysis

Finally, Statistical analysis was carried out by using student's't' test using SPSS 16 version. Pearson's correlation coefficient was also calculated to find the correlation between HbA1c and lipid parameters. Value of HbA1c was given as percentage of total haemoglobin and values of all other parameters were given in mmol/l. All Values are expressed as mean ± SD. The results were considered non-significant when P > 0.05.

RESULTS

In this cross sectional study, overall glycemic control was poor with only 35% of the study participants having good glycemic control while 65 % had poor glycemic control of HbA1c > 7% with mean HbA1c was 7.54 % (SD ± 1.37)) (Table: 1). The current showed significantly high level of poor glycemic as compared to studies conducted in Chennai India which reported 78.6% having ≥ 7% (Gopinath, 2013), Saudi Arabia reporting 78% with HbA1c ≥ 7% (Harrabi et al., 2014), in Cameroon and Guniea showing 74% of HbA1c ≥ 7% (Camara et al., 2015). Interestingly studies carried out in Germany and Japan showed 45% and 65% respectively having managed to achieve optimal HbA1c targets for T2DM patients. The current findings however were slightly lower compared to ADA Guidelines report (2008) that 26.3% of T2DM had good glycemic control. The difference between the current study findings and that of developed countries (Germany and Japan in this case) could be as a result of knowledge difference of participants between developing and developed countries, lack of uniform guidelines for assessing and management of glycemic control for physicians to set the cut off, and health insurance and the difference in health insurance access and coverage at primary care (Ali *et al*., 2012; Islam *et al*., 2015).Out of that 200 participants, the mean BMI was 26.23 kg/m2, Median ±SD (26.89 ± 3.42) kg/m2 , 51 (25.5%) were within the normal ranges of BMI (18.5 to 24.9 kg/m2) while 135 (67.5%) were classified as overweight (Table 1). Results further revealed that, participants mean fasting blood sugar was 8.26 , Std. Deviation ± 2.30 (mmol/L) with a median of 7.87 (mmol/L) with 181 (90.0%) uncontrolled fasting blood sugars levels above 6.1 mmol/L and 19 (9.5%) had optimal targets. Participants mean blood pressure was 122.42/79.78 mm/Hg. Total cholesterol mean 5.14, median 4.56, Std. Deviation ± 1.97 mmol/L. With regards LDL 42.5% of the study participants had dyslipidemia with a mean of 2.93 mmol/L and 28% had elevated Triglycerides with a mean of 1.49mmols/L (Table 1).

Table 1. Distribution of glycemic control profile indicators of the study participants

Variables	Classes	Optimal targets	Min	Max	N	Percentage
HbA1c (%)	Good glycemic	<7%	5.08	13.78	70	35
	Poor glycemic	>7%			130	65
	Mean 7.54, Median 7.26, Std. Deviation ±1.37					
BMI (kg/m^2)	Underweight	<18	17.67	41.10	4.0	2.0
	Normal	18.5-24.9			51	25.5
	Overweight	25.0-29.9			135	67.5
	Obese	>30			10	5.0
	Mean 26.23, Median 26.89, Std. Deviation ± 3.42					
FBS (mmol/L)	Normal range	4-6.1	4.76	16.47	19	9.5
	Hyperglycemic	>601			181	90.5
	Mean 8.26 , Median 7.87 , Std. Deviation ± 2.30					
SBP (mm/Hg)	Optimal	<130	100	150	134	67
	Off optimal				66	33
	Mean 122.42 , Median 120.00 , Std. Deviation ± 13.97					
DBP (mm/Hg)	Optimal	<80	60	100	82	41
	Off optimal				118	59
	Mean 79.78, Median 80.00 , Std. Deviation ± 12.33					
T.Cho (mmol/L)	Optimal	<5	1.89	11.50	139	69.5
	Off optimal				61	30.5
	Mean 5.14, Median 4.56, Std. Deviation ± 1.97					
LDL (mmol/L)	Optimal	<2.6	0.59	8.68	115	57.5
	Off optimal				85	42.5
	Mean 2.93, Median 2.43, Std. Deviation ± 1.54					
HDL (mmol/L)	Optimal		0.10	2.18	117	58.5
	Below optimal	>1.2			83	41.5
	Mean 1.19, Median 1.03, Std. Deviation ±. 38					
TGS (mmol/L)	Optimal	<1.7	0.10	6.54	144	72
	Off optimal				56	28
	Mean 1.49 , Median 1.10, Std. Deviation ± .98					

Key: HbA1c (Glycated haemoglobin) BMI (Body Mass Index), FBS (fasting blood sugar), SBP (Systolic Blood Pressure), DBP (Diastolic Blood Pressure), Total Cholesterol), LDL (Low Density Lipoproteins), HDL (High DensityLipoproteins), TGS (Triglycerides)

Result indicated that among all diabetes patients overweight 58.6% had good glycemic control and 72.3% possessed poor glycemic control (Table 2). Among the respondents88.5% of participants with elevated fasting sugars had poor glycemic control. Although many of the participants with off optimal systolic and diastolic blood pressure 51.4% had good glycemic control. Above 67.1% of participants with optimal serum triglycerides had good glycemic control with 25.4% of participants having off optimal triglyceride levels having poor glycemic control.

Table 2. Comparison of the biochemical parameters of subjects with high and desirable HbA1c levels

Variables		Good control (< 7%)		Poor control (>7%)	
		N	%	N	%
BMI (kg/m2)	Underweight	3	4.3	1	0.8
	Normal	21	30.0	30	23.1
	Overweight	41	58.6	94	72.3
	Obese	5	7.1	5	3.8
FBS (mmol/L	Normal range	4	5.7	15	11.5
	Hyperglycemic	66	94.3	115	88.5
SBP (mm/Hg)	Optimal	53	75.7	81	62.3
	Off optimal	17	24.3	49	37.7
DBP (mm/Hg)	Optimal	34	48.6	48	41.0
	Off optimal	36	51.4	82	59.0
T.Cho (mmol/L)	Optimal	53	75.7	86	66.2
	Off optimal	17	24.3	44	33.8
LDL (mmol/L)	Optimal	41	58.6	74	56.9
	Off optimal	29	41.4	56	43.1
HDL (mmol/L)	Optimal levels	43	61.4	74	56.9
	Below optimal	27	38.6	56	43.1
TGS (mmol/L)	Optimal	47	67.1	97	74.6
	Off optimal	23	32.9	33	25.4

Among total 200, type 2 diabetic individuals included in this study, 89 were male and 111were female. The mean age ± SD of male and female subjects were 51.41± 6.40 and 50.39 ± 5.62 years respectively (Table 3). The mean value of HbA1c and FBG were slightly higher in females in comparison to male patients and the differences were significant. When lipid profiles were taken in to consideration, 200 patients it was seen that TCHO, LDL, TG were also higher in female than male and TCHO, TG showed significant relationship among the both genders. On the other hand, HDL was higher in male than female and there was no statistically significant difference in HDL levels among them (Table 3).

Table 3. Comparison of BP, duration of DM, BMI, HbA1c, FBG and lipid profile of male and female T2DM patients

Variables	Female (n=111) Mean± SD	Male (n=89) Mean± SD	P value
Age	50.39 ± 5.62	51.41± 6.40	
BMI	26.93± 3.78	25.68±3.01	0.010**
Duration of DM (years)	1.10 ±.303	1.12±.323	0.721
SBP (mmHg)	122.48±13.22	122.96±14.92	0.953
DBP (mmHg)	79.23±11.60	80.45±13.22	0.490
HbA1c %	7.89±1.73	7.25±.89	0.001**
FBG (mmol/L)	8.29±2.03	8.25±2.50	0.021*
TCHO(mmol/L)	5.26±2.07	5.00±1.90	0.036*
LDL(mmol/L)	2.95±1.69	2.91±1.42	0.838
HDL(mmol/L)	1.15±.37	1.32±.39	0.238
TG(mmol/L)	1.79±.87	1.48±1.06	0.052*

* Significant at the 0.05 level (2-tailed); ** Significant at the 0.01 level (2-tailed).

To see the utility of HbA1c as a marker of dyslipidemia, we divided subjects into two groups, good and poor glycemic control groups depending upon the levels of HbA1c as <7% and >7% respectively. The mean value of TC, LDL and TG was found to be lower in patients with good glycemic control than those with poor glycemic control (Table 4). But, mean value of was found to be higher in patients with good glycemic control than those with poor glycemic control. These differences were significant at the level of p <0.05.

Table 4. Comparison of BP, duration of DM, BMI, HbA1c, FBG and Lipid profile of T2DM patients with HbA1c < 7 and HbA1c >7

Variables	HbA1c<7(n=130) Mean ± SD	HbA1c>7 (n=70) Mean ± SD	p-value
BMI	26.48 ± 3.22	25.77 ± 3.75	0.160
Duration of DM (years)	1.12 ± 0.33	1.09±0.28	0.423
SBP (mmHg)	124.15 ± 14.46	119.21±12.47	0.017**
DBP (mmHg)	81.42 ± 12.18	76.71±12.09	0.010**
FBG (mmol/L)	8.46 ± 2.18	8.16 ± 2.51	0.011**
TCHO(mmol/L)	5.24 ± 2.12	4.96 ±1.67	0.032*
LDL(mmol/L)	2.98 ± 1.61	2.83 ± 1.41	0.001**
HDL(mmol/L)	1.17 ± 0.39	1.22 ± 0.37	0.039*
TG(mmol/L)	1.52 ± 1.03	1.42± 0.89	0.050*

* Significant at the 0.05 level (2-tailed); ** Significant at the 0.01 level (2-tailed).

In this study, the pattern of lipid profile parameters in diabetic subjects and its correlation with HbA1c was evaluated. A highly significant correlation between HbA1c and FBS in this study is similar with various previous studies. Significant correlations were observed between HbA1c and TC, LDL-C and TG (Table 5). In various studies, HbA1c level was eminent as showing positive correlation with TC, LDL-C and TG in diabetic patients (Khaw et al., 2004, Ram et al., 2011, Masram et al., 2012).The Diabetes complications and control trial (DCCT) established HbA1c as the gold standard of glycemic control. The level of HbA1c value ≤7.0% was said to be appropriate for reducing the risk of cardiovascular complications (Rohlfing et al., 2002) .In the present study, diabetic patients were divided 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, LDL-C, TG without any significant alteration in HDL in comparison to patients with HbA1c value ≤7.0%. Severity of dyslipidemia increases in patients with higher HbA1c value. As elevated HbA1c and dyslipidemia are independent risk factors of CVD, diabetic patients with elevated HbA1c and dyslipidemia can be considered as a very high risk group for CVD. Improving glycaemic control can substantially reduce the risk of cardiovascular events in diabetics (Selvin et al., 2006).Significant correlations between HbA1c and the lipid parameters and a linear relationship between HbA1c and dyslipidemia point towards the usefulness of HbA1c for screening high-risk diabetic patients.

Table 5. Significant correlations with profile indicators and Glycated Haemoglobin in patients with Type 2 Diabetes

Variables	Correlation Coefficient	P value	Correlation
HbA1c an BMI	0.529	0.011	Direct
HbA1c and FBS	0.793	0.016	Direct
HbA1c and TCHO	0.872	0.001	Direct
HbA1c and TG	0.689	0.019	Direct
HbA1c and HDL	-0.838	0.001	Inverse
HbA1c and LDL	0.741	0.010	Direct

CONCLUSION

There were affirmative correlations of HbA1C with TC, TG, LDL and negative correlations between HbA1c and HDL levels. It was concluded that HbA1c can be utilized as an indicator of dyslipidemia in T2DM and could be additionally used as glycemic control parameter. Hence, early diagnosis of dyslipidemia can be used as a pre-emptive measure for the development of cardiovascular disease (CVD) in T2DM.

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CONFLICT OF INTEREST

There is no conflict of interest. All the authors are happy to be one of the authors of the paper.

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