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Original Research Article

Study of HbA1c as a biomarker of dyslipidemia in type 2 diabetes patients

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ABSTRACT

Background: In type 2 diabetes mellitus, lipid abnormalities that are all recognized as major risk factors for coronary artery disease and other macro vascular complications. Present study was aimed to study HbA1c as a biomarker of dyslipidemia in type 2 diabetes patients. **Material and Methods:** Present study was hospital-based case control study, conducted in 100 subjects of age group of 20-85 years, newly diagnosed diabetic cases not on statins and compared with 100 healthy age and gender matched non diabetic individuals. **Results:** Present study included 100 type 2 diabetic cases and an equal number of age and gender matched controls. Mean glycated haemoglobin levels were significantly higher among diabetics as compared to controls (8.56% vs 5.64%; $p<0.01$). Mean lipid parameters like triglycerides (142.4 vs 126.74 mg%), total cholesterol (168.48 vs 155.67 mg%) and LDL levels (112.37 vs 78.22 mg%) were significantly higher among diabetics as compared to non-diabetics ($p<0.05$). While mean HDL levels were significantly lower (39.99 vs 52.68 mg%; $p<0.01$). Prevalence of dyslipidaemia was observed in 89% cases as compared to 37% controls. The difference was statistically significant ($p<0.01$). On Pearson correlation analysis, significant correlation was observed between all lipid parameters i.e. triglycerides, total cholesterol, LDL levels with glycated haemoglobin levels while inverse correlation was observed with HDL ($p<0.01$). Poor glycemic control was significantly associated with prevalence of dyslipidaemia. Prevalence was 88.4% in subjects with poor glycemic control as compared to 52.8% in subjects with good control (p-0.03). On regression analysis, raised glycated haemoglobin levels were observed as a significant predictor of development of dyslipidaemia among type 2 diabetic cases.

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Conclusion: A high prevalence of dyslipidemia was observed among cases of diabetes. We also observed a significant correlation between HbA1c and lipid profile parameters.
Keywords: dyslipidemia, diabetes mellites, HbA1c, lipid profile, glycemic control

INTRODUCTION

Diabetes mellitus is the most prevalent metabolic disease in the world. Diabetes mellitus has been known since antiquity. In India, diabetes is not an epidemic anymore but has turned into a pandemic. The International Diabetes Federation estimated that the number of diabetic patients in India will be more than doubled from 19 million in 1995 to 40.9 million in 2007. It is projected to increase to 80 million by 2030.[1] The largest increase of the diabetic population occurs in the most economically productive age group. Currently up to 11% of India's urban population and 3% of rural population above the age of 15 has diabetes mellitus. The most prevalent is Type 2 diabetes mellitus (T2DM), which constitutes 95 percent of diabetic population in the country.[2]

In type 2 diabetes mellitus, lipid abnormalities are almost the rule and is associated with a cluster of interrelated plasma lipid and lipoprotein abnormalities that are all recognized as major risk factors for coronary artery disease and other macro vascular complications. These lipid abnormalities are not only quantitative but also qualitative abnormalities of the lipoproteins which are potentially atherogenic.[3]

The level of circulating HbA1c is taken as the gold standard of glycemic control, and regulating it is imperative for avoiding T2DM complications. HbA1c values not only reflect glycemic control but are also the main factor in determining the risk of diabetes- related complications[4] and mortality[5]. There are several conflicting results in the literature, such as a Turkish study that found a significant relationship between total cholesterol (TC), LDL, triglycerides (TGs) and HbA1c[6], while others reported no considerable relationship[7]. Present study was aimed to study HbA1c as a biomarker of dyslipidemia in type 2 diabetes patients

MATERIAL AND METHODS

Present study was hospital-based case control study, conducted in department of General Medicine, at Grant Government Medical College and Sir J.J. Group of Hospitals, Mumbai, India. Study duration was of 2 years (January 2019 to December 2021). Study approval was obtained from institutional ethical committee.

Inclusion criteria

- 100 subjects of age group of 20-85 years, newly diagnosed diabetic cases not on statins and compared with 100 healthy age and gender matched non diabetic individuals, willing to participate in present study

Exclusion criteria

- Patients of Type 1 DM.
- Subjects who are on medications which can alter serum lipid profile level such as HMG CoA reductase inhibitor, Fabric acid derivatives, Nicotinic acid, Beta blockers, Diuretics
- Hypertensive patients, chronic alcoholics
- Pregnancy and gestational DM

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- Adverse renal and liver disease
- Acute and chronic inflammatory disease and malignancy

Study was explained to patients in local language & written consent was taken for participation & study. The information pertaining to various baseline characteristics was gathered via interview during predesigned schedule. Detailed history regarding age, duration of diabetes mellitus, hypertension, smoking, alcohol, drug intake and treatment was taken from patients and meticulous examination was conducted through clinical examination and reviewing of previous hospital records was done. Patients were subjected for investigations as required.

Venous blood samples were collected from all the subjects after at least 8 hours fasting. Diabetes was diagnosed as per the ADA criteria 2012. [8] The Serum was later used for analysing, Lipid Profile Panel Test-Serum Total cholesterol (TC), HDL-cholesterol (HDL-C), Triacylglycerol (TAG), Risk ratio (TC/HDL-C) by using Mindray BA-AT 80 (Human Diagnostics Reagents, Germany) and Indirect LDL-cholesterol and Non-HDL Cholesterol (Non-HDL-C) was calculated by Friedwald and Frederickson formula. HbA1c was estimated by using Ion exchange chromatography (Crest A Coral clinical system, USA).

For serum lipid reference level, National Cholesterol Education Programme (NCEP) Adult Treatment Panel III (ATP III) guideline was referred. According to NCEP- ATPIII guideline, hypercholesterolemia is defined as TC>200 mg/dl, high LDL-C when value >100 mg/dl, hypertriglyceridemia as TAG >150 mg/dl and low HDL-C when value <40 mg/dl. Dyslipidaemia was defined by presence of one or more than one abnormal serum lipid concentration.

The quantitative data was represented as their mean ± SD. Categorical and nominal data was expressed in percentage. The t-test was used for analysing quantitative data, or else non parametric data was analysed by Mann Whitney test and categorical data was analysed by using chi-square test. Pearson correlation co-efficient was used for computing correlation between quantitative variables. The significance threshold of p- value was set at <0.05. All analysis was carried out by using SPSS software version 21.

RESULTS

Present study included 100 type 2 diabetic cases and an equal number of age and gender matched controls. The mean age of the study cases was 53.93 years while that of controls was 54.45 years with no difference between cases and controls (p-0.68).

Slight male preponderance was seen among cases of diabetes with 56% males to 44% females. Controls were also gender matched (58% males to 42% females) (p-0.91). Most common associated co-morbidity among diabetics and non-diabetics was hypertension (24% and 23%). No difference was observed between cases and controls regarding prevalence of co-morbidities.

Mean glycated haemoglobin levels were significantly higher among diabetics as compared to controls (8.56% vs 5.64%; p<0.01).

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Table 1- General characteristics

	Cases	Controls	p- value
Mean age (mean ± SD)	53.93 ± 8.79	54.45 ± 9.36	0.68
Gender			0.91
Male	44 (44 %)	42 (42 %)	
Female	56 (56 %)	58 (58 %)	
Co-morbidity			0.112
Hypertension	24 (24 %)	23 (23 %)	
COPD	7 (7 %)	4 (4 %)	
CAD	4 (4 %)	0	
Hypothyroidism	0	3 (3 %)	
PID	1 (1 %)	2 (2 %)	
NIL	61 (61 %)	71 (71 %)	
Others			
Mean glycated haemoglobin	8.56 ± 2.71	5.64 ± 1.20	< 0.01

Mean lipid parameters like triglycerides (142.4 vs 126.74 mg%), total cholesterol (168.48 vs 155.67 mg%) and LDL levels (112.37 vs 78.22 mg%) were significantly higher among diabetics as compared to non-diabetics ($p<0.05$). While mean HDL levels were significantly lower (39.99 vs 52.68 mg%; $p<0.01$).

Table 2- Mean comparison of lipid profile fractions among study groups

	Cases	Controls	p- value
TGs	142.40 ± 48.43	126.74 ± 63.72	0.047
Total Cholesterol	168.48 ± 30.44	155.67 ± 35.49	0.01
HDL	39.99 ± 6.28	52.68 ± 9.06	< 0.01
LDL	112.37 ± 31.58	78.22 ± 22.20	< 0.01

Raised triglycerides, total cholesterol and LDL levels were seen in 29%, 17% and 45% cases of type 2 diabetics as compared to 12%, 8% and 20% controls while low HDL was observed in 57% cases as compared to 31% controls ($p<0.01$).

Table 3- Distribution of lipid profile derangements among cases and controls

	Cases	Controls	p- value
Raised TGs	29 (29 %)	12 (12 %)	0.01
Raised Total Cholesterol	17 (17 %)	8 (8 %)	0.02
Low HDL	45 (45 %)	20 (20 %)	< 0.01
Raised LDL	57 (57 %)	31 (31 %)	< 0.01

Prevalence of dyslipidaemia was observed in 89% cases as compared to 37% controls. The difference was statistically significant ($p<0.01$).

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Table 4- Prevalence of dyslipidaemia among cases and controls

Dyslipidaemia	Cases	Controls	p- value
Yes	11 (11 %)	63 (63 %)	< 0.01
No	89 (89 %)	37 (37 %)	

On Pearson correlation analysis, significant correlation was observed between all lipid parameters i.e. triglycerides, total cholesterol, LDL levels with glycated haemoglobin levels while inverse correlation was observed with HDL (p<0.01).

Table 5- Correlation of glycated haemoglobin with lipid profile fractions

Pearson co-relation		
HbA1c	**r- value**	**p- value**
TGs	0.98	<0.01
TC	0.91	<0.01
HDL	-0.92	<0.01
LDL	0.92	<0.01
VLDL	0.94	<0.01

Poor glycemic control was significantly associated with prevalence of dyslipidaemia. Prevalence was 88.4% in subjects with poor glycemic control as compared to 52.8% in subjects with good control (p-0.03).

Table 6-. Association of glycemic control with dyslipidaemia

Glycemic Control	Dyslipidaemia		Total	p- value
	No	Yes		
Good (HbA1c: <6.5%)	50 (47.2 %)	56 (52.8 %)	106 (100 %)	0.03
Moderate (HbA1c: 6.5%-8%)	19 (37.3 %)	32 (62.7 %)	51 (100 %)	
Poor (HbA1c: >8%)	5 (11.6 %)	38 (88.4 %)	43 (100 %)	
Total	74 (37 %)	126 (63 %)	200 (100 %)	

On regression analysis, raised glycated haemoglobin levels were observed as a significant predictor of development of dyslipidaemia among type 2 diabetic cases.

Table 7- Logistic regression analysis for prediction of dyslipidaemia among diabetics

Logistic Regression: Dyslipidaemia (Y/N)								
Variables	**B**	**S.E.**	**Wald**	**df**	**P value**	**Odds Ratio**	**95% CI**	
							Lower	**Upper**
HbA1c	0.32	0.083	14.957	1	<0.01	1.377	1.171	1.62
Constant	-1.62	0.552	8.619	1	0.003	0.198		

DISCUSSION

Glycated hemoglobin (HbA1c) levels are routinely measured in diabetics to monitor their glycemic control. The goal is to achieve a level below 7% (IDF guidelines).[7] Levels of HbA1c can be affected by multiple factors, including sugar intake, exercise and adherence to medications. Some studies have reported that HbA1c could potentially be utilized as a possible biomarker for predicting dyslipidemia and cardiovascular disease (CVD). [8,9]

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The mean age of the study cases was 53.93 years while that of controls was 54.45 years. Slight male preponderance was seen among cases of diabetes with 56% males to 44% females. Controls were also gender matched (58% males to 42% females). Khan et al.,[11] in a study on diabetic subjects observed 58% males to 42% females with mean age of 59.76 years. Reddy A et al.,[12] in their study of 490 Type 2 Diabetes mellitus patients observed 52% males to 48% females with mean age of 53.17 years. Similar findings were noted in present study.

Studies have shown that among the metabolic abnormalities that commonly accompany diabetes are disturbances in the production and clearance of plasma lipoproteins. Defects in insulin action and hyperglycemia could lead to changes in plasma lipoproteins in patients with diabetes. Alternatively, especially in the case of type 2 diabetes, the obesity/insulin-resistant metabolic disarray that is at the root of this form of diabetes could, itself, lead to lipid abnormalities exclusive of hyperglycemia. A characteristic pattern, termed diabetic dyslipidemia, consists of low high-density lipoprotein (HDL), increased triglycerides, and postprandial lipemia.[13]

A study conducted by Kayode et al.,[14] showed that 57 diabetic patients out of 113 diabetic study subjects were having at least one lipid value or the other outside the clinical target, giving it a prevalence of 50.4%. The most frequent lipid combination was total cholesterol plus HDL-cholesterol. Vinod Mahato R et al.,[15] in their study observed that 92 (80.70%) females out of 114 and 150 (83.33 %) males out of 180 were found to be dyslipidemia. Similar findings were noted in present study.

Poor glycemic control was significantly associated with prevalence of dyslipidemia. Prevalence was 88.4% in subjects with poor glycemic control as compared to 52.8% in subjects with good control (p-0.03). On Pearson correlation analysis, significant correlation was observed between all lipid parameters i.e. triglycerides, total cholesterol, LDL levels with glycated hemoglobin and fasting blood sugar levels while inverse correlation was observed with HDL ($p<0.01$).

Vinod Mahato R et al.,[15] in their study observed that patients with HbA1c value > 7.0% had significantly higher value of TC, Triacylglycerol (TAG), LDL-C, LDL- C/HDL-C ratio, non-HDL-C and TC/HDL-C ratio as compared to the patients with HbA1c ≤ 7.0%. However, there was no significant difference in value of HDL-C between two groups. HbA1c can be used as a potential biomarker for predicting dyslipidemia in type 2 diabetic patients in addition to glycemic control. Singh G et al.,[16] in their study observed significant positive relationship of HbA1c with total cholesterol, TC (r=0.29), triglyceride, TG (r=0.26), high density lipoprotein cholesterol, HDL-C (r=0.19) and with low density lipoprotein cholesterol, LDL-C (r=0.5).

Sirivole MR et al.,[17] observed that poor glycemic control was associated with dyslipidemia in diabetic patients. This study showed a significant correlation between levels of glycosylated hemoglobin (HbA1c) and lipid profile. Samdani TS et al.,[18] observed that HbA1c had significant positive correlation with LDL-C (p=0.045) and negative correlation with HDL-C (p=0.024).

Thus, to summarize, very high prevalence of dyslipidemia was observed among cases of diabetes. We also observed a significant correlation between HbA1c and lipid profile parameters. Thus, better glycemic control reflected by HbA1c would also reflect better lipidemic state and vice versa. The results of the present study thus suggest the importance of glycemic control to manage dyslipidemia and risk for cardiovascular diseases in type 2

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diabetics. Hence, achieving the target HbA1c will contribute in improving the lipid state, and may lessen the diabetic complications in type 2 diabetic patients and also reduce the risk of development of atherosclerosis.

CONCLUSION

A high prevalence of dyslipidemia was observed among cases of diabetes. We also observed a significant correlation between HbA1c and lipid profile parameters. Thus, better glycemic control reflected by HbA1c would also reflect better lipidemic state and vice versa. Hence, achieving the target HbA1c will contribute in improving the lipid state, and may lessen the diabetic complications in type 2 diabetic patients and also reduce the risk of development of atherosclerosis.

The results of the present study suggest the importance of glycemic control to manage dyslipidemia and risk for cardiovascular diseases in type 2 diabetics. Glycated hemoglobin can thus be used as an indicator of glycemic control as well as a predictor of dyslipidemia in T2DM patients.

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