ORIGINAL RESEARCH PAPER

General Medicine

CORRELATION BETWEEN GLYCEMIC CONTROL AND LIPID PROFILE IN NEWLY DIAGNOSED TYPE2 DIABETES MELLITUS IN TERTIARY CARE HOSPITAL

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ABSTRACT

Introduction: As per the International Diabetes Federation, 422 million people are living with diabetes across the world, and it is expected to rise to a whooping figure of 592 million in 2035, of which 79.4 million diabetics will be from India. Worsening of glycemic control deteriorates lipid & lipoprotein abnormalities in Diabetes Mellitus. Glycated hemoglobin (HbA1c) is a gold-standard measure of long-term glycemic control.

Objective: to study the pattern of dyslipidemia and to determine the correlation of Glycated hemoglobin (HbA1C) with dyslipidemia in newly diagnosed type 2 diabetes mellitus patients.

Material and method: A cross-sectional study was carried out among 200 newly diagnosed type 2 Diabetes Mellitus patients from Feb 2019 to July 2019 in the Department of Medicine of a tertiary care teaching hospital in south-eastern Rajasthan. Venous blood samples were collected from all the subjects after at least 8 hours fasting. The Serum was later used for analyzing Fasting Blood Glucose (FBG), Lipid Profile and HbA1c.

Results: 70 (76.09%) females and 84 (77.8%) males were found to have dyslipidemia. Patients with HbA1c values greater than 7.0% had significantly higher values of FBG, TG, LDL, VLDL and risk ratio TC/ HDL, LDL/HDL. There was a significant positive correlation between HbA1c with TG, LDL and VLDL.

Conclusion: The study revealed a significant correlation between HbA1c and various circulating lipid parameters. This implies that HbA1c can be used as a potential biomarker for predicting dyslipidemia in patients with T2DM.

INTRODUCTION:

Over the past few decades, Non-communicable diseases (NCDs) have emerged as the leading causes of death globally, killing more people each year than all other causes combined.[1] One of the important diseases in this respect is diabetes, which is considered a "disease of urbanization".[2,3,4] The increasing modernization, sedentary lifestyle and unhealthy dietary habits in rural and urban India has taken its toll on the health of the general public, especially the youth.[5]

As per the International Diabetes Federation, 422 million people are living with diabetes across the world, and it is expected to rise to a whooping figure of 592 million in 2035, of which 79.4 million diabetics will be from India.[6] India is declared as the "diabetic capital" of the world by WHO.[7] An estimation of WHO in 2016 shows, 1.6 million deaths were directly caused by diabetes and another 2.2 million were attributable to consequences of high blood sugar levels and number of death caused by diabetes is expected to be double by 2030. Almost half of deaths attributable to high blood glucose occur before the age of 70.[8]

The patients with Type 2 diabetes mellitus may often remain asymptomatic for a longer period of time with abnormalities like insulin resistance, hyperinsulinemia, hyperglycemia, dyslipidemia, and hypertension tend to cluster and are often referred to as the "metabolic syndrome".[9,10] Worsening of glycemic control deteriorates lipid & lipoprotein abnormalities in Diabetes Mellitus.[11] The pattern of lipid profile in Type 2 diabetes mellitus is called "diabetic dyslipidemia" or "atherogenic dyslipidemia" comprising high plasma triglyceride (TG), low high density lipoproteins (HDL) and increased low density lipoproteins (LDL) particles. Some studies have also shown that dyslipidemia in diabetic patients is more atherogenic.[12,13] Patients with type 2 diabetes carrying apolipoprotein E 4 genotype were found to have a greater cardiovascular risk owing to metabolic variation in lipid metabolism leading to higher cholesterol and LDL.[14]

Glycated hemoglobin (HbA1c) is a gold-standard measure of long-term glycemic control with the ability to reflect the cumulative glycemic history of the preceding 2–3 months and consider better predictor than fasting or 2-h glucose.[15] HbA1c predicts the risk for the development of diabetic complications in diabetes patients. Recently, elevated HbA1c has been regarded as an independent risk factor for coronary heart disease and stroke in subjects with or without diabetes.[16,17] It is estimated that there is an 18% increased risk of CVD for each 1% rise in absolute HbA1c levels in the diabetic population. This positive correlation between HbA1c and CVD has been demonstrated in non-diabetic cases, even within the normal range of HbA1c.[18]

Very few studies have evaluated the effect of glycemic control on dyslipidemia particularly in south-eastern Rajasthan. With this background the present research was planned to study the pattern of dyslipidemia and to determine the correlation of Glycated hemoglobin (HbA1C) with dyslipidemia in newly diagnosed type 2 diabetes mellitus patients.

Methodology: The present cross-sectional study was carried out from Feb 2019 to July 2019 in the Department of Medicine in a tertiary care teaching hospital in south-eastern Rajasthan. A total of 200 newly diagnosed type 2 diabetic patients visiting the OPD of Medicine Department, satisfying the inclusion and exclusion criteria were included in this study.

Inclusion criteria
• Patients diagnosed with Type 2 DM first time at OPD (Newly Diagnosed),
• Patients who were willing to participate in study

Exclusion criteria
• Patients with Type I DM,
• Previously detected type 2 DM patients (old cases) or patients on anti-diabetic medication,
• Pregnant and lactating females,
• Seriously ill patients requiring immediate hospitalization,
• Non co-operative patients or patients not proving written consent.

Before commencing the study, ethical clearance was taken

from the Institutional Ethics Committee. A written consent was obtained from all the study participants before the study. Venous blood samples were collected from all the subjects after at least 8 hours fasting. The Serum was later used for analyzing Fasting Blood Glucose (FBG), Lipid Profile and HbA1c. The patients were then divided into two groups based on the HbA1c levels i.e. good glycemic control (HbA1c< 7%) and poor glycemic control (HbA1c $\geq$ 7%). For serum lipid reference level, National Cholesterol Education Programme (NCEP) Adult Treatment Panel III (ATP III) guideline was referred.[19] According to NCEP-ATP III guidelines, hypercholesterolemia is defined as TC > 200 mg/dl, high LDL when value > 100 mg / dl, hypertriglyceridemia as TG > 150 mg/dl and low HDL when value < 40 mg/dl. Dyslipidemia was defined by presence of one or more than one abnormal serum lipid concentration.[20] Diabetes was defined as per American Diabetes Association (ADA) criteria.[21] Data thus collected was entered in MS excel 10 and analyzed using SPSS trial version 20. Pearson's correlation test was applied to determine various correlations. Independent samples t-test (2-tailed) was used to compare means of different parameters. P value < 0.05 was considered as statistically significant.

RESULTS:
Based on inclusion and exclusion criteria, 200 newly diagnosed type 2 diabetes patient (Male-108, Female-92) attending OPD of Medicine department during February 2019 to July 2019 were enrolled in study. Mean age of study participants was 50.83±11.06 years. The mean values of FBS, HbA1c, Cholesterol, TG, LDL, VLDL and HDL were 173.74 ± 38.46, 7.6 ± 2.1, 208.45 ± 38.4, 187.66 ± 23.36, 114.72 ± 19.26, 29.33 ± 8.48 and 41.42 ± 4.32 respectively. The mean value of HbA1c and FBG were slightly higher in females in comparison to male patients but the differences were not significant (p>0.05).

Hypercholesterolemia was found in 62.5% of patients similarly hypertriglyceridemia was found in 74.5% of patients. Abnormal LDL levels were found in 68.5% while HDL less than 40 mg/dl was in 48.5% of the study participants. According to the NCEP ATP III guideline, 70 (76.09%) females and 84 (77.8%) males were found to have dyslipidemia. (Table 1).

The patients were divided into two groups based on the HbA1c levels i.e. good glycemic control (HbA1c< 7%) and poor glycemic control (HbA1c >7%). Age at first diagnosis of diabetes was lower in poor glycemic control group but difference was not statistically significant (p=0.20). Patients with HbA1c values greater than 7.0% had significantly higher values of FBG (p=0.0001), TG p=0.0001), LDL (p = 0.0001), VLDL p=0.0001) and risk ratio TC/ HDL (p = 0.0001), LDL/HDL (p=0.0001). Difference in cholesterol (p=0.061) and HDL (p=0.054) was not significant in these two group. (Table 2)

There was a significant positive correlation between HbA1c with TG (r = 0.124, p = 0.006), LDL (r=0.142, p=0.001) and VLDL (r=0.131, p=0.004). Although the correlation of HbA1c was found positive with cholesterol (r = 0.063, p = 0.206) and negative with HDL (r = -0.024, p = 0.625) but these correlation was found to be statistically non-significant. (Table 3)

DISCUSSION:
The present study was carried out to determine the correlation between glycemic control (HbA1c) and lipid profile among newly diagnosed type 2 diabetic patients attending OPD of a tertiary care institute. People with type 2 diabetic have a higher risk of cardiovascular morbidity and mortality, and are disproportionately affected by CVD compared with subjects without DM. Early detection and treatment of dyslipidemia associated with DM may be one step in reducing the CVD risk.[22]

In our study, a large proportion of type 2 DM patients have

hypercholesterolemia, hypertriglyceridemia, high LDL and low HDL levels which are well established risk factors for cardiovascular diseases. These findings are consistent with study by Mahato RV et al[23] and Wexler DJ et al.[24] The abnormal lipid profile observed in type 2 Diabetes mellitus is said to be related to insulin resistance as reported in previous studies, which leads to increased release of free fatty acids from fatty tissue, impaired insulin dependent muscle uptake of free fatty acids and increase fatty acid release to the hepatic tissue.[25]

In present study, we observed a significant correlation of HbA1c with LDL and TG. This finding is comparable to studies by Mahato RV et al[23], Khan HA et al[26] and Andersen G et al[27]. HbA1c level was inversely correlated with HDL in our study. This finding is also consistent to other studies.[20,23,26].

In our study, patients with HbA1c greater than 7.0% found with a significant increase in LDL, TG, and LDL/HDL ratio compared with those with HbA1c up to 7.0%. This finding is in accordance to study by Mahato RV et al[23] and Bhattacharjee P et al[20]. Selvin et al et al[16] reported in their study that improving glycemic control may substantially reduce the risk of cardiovascular events among type 2 DM patients. Khan HA et al[26] also reported that severity of dyslipidaemia increases in patients with higher HbA1c value. As dyslipidaemia and elevated HbA1c are independent risk factors of CVD, diabetic patients with elevated HbA1c and dyslipidaemia can be considered as a very high risk group for CVD. It has been reported that reducing the HbA1c level by 0.2% could lower the mortality by 10%.[22]

CONCLUSION:
The study revealed a significant correlation between HbA1c and various circulating lipid parameters. This implies that HbA1c can be used as a potential biomarker for predicting dyslipidemia in patients with T2DM. The results of our study suggest the importance of glycemic control in managing dyslipidemia and further reducing the risk for CVD in patients with T2DM.

Table 1 Serum lipid profile parameters of Type 2 Diabetes patients.

Parameters	Mean	SD
Age (years)	50.83	11.06
FBS (mg/dl)	173.74	38.46
HbA1c (%)	7.6	2.1
Cholesterol (mg/dl)	208.45	38.24
TG (mg/dl)	187.66	23.36
LDL (mg/dl)	114.72	19.26
VLDL (mg/dl)	29.33	8.48
HDL (mg/dl)	41.42	4.32

FBS-fasting blood sugar; HbA1c-hemoglobin A1c; TG-triglyceride; LDL-low density lipoprotein; VLDL- very low density lipoprotein; HDL-high-density lipoprotein.

Table 2: Association between Serum lipid profile parameters and Glycated hemoglobin (HbA1c) of the T2DM patients

Parameters	Glycated haemoglobin (HbA1c)				P value
	$\leq$ 7.0 (n=82)		>7.0 (n=118)		
	Mean	SD	Mean	SD	
Age (years)	51.64	11.24	49.67	9.78	0.20
FBS (mg/dl)	188.54	33.28	226.36	36.62	0.0001
Cholesterol (mg/dl)	202.09	38.86	212.87	40.64	0.061
TG (mg/dl)	173.47	22.88	197.52	28.62	0.0001
LDL (mg/dl)	103.29	9.60	122.63	13.82	0.0001
VLDL (mg/dl)	22.72	7.32	33.93	7.96	0.0001
HDL (mg/dl)	43.26	11.08	40.14	11.34	0.054
TC/HDL	4.67	1.08	5.30	1.06	0.0001
LDL/HDL	2.39	0.86	3.06	1.12	0.0001

FBS-fasting blood sugar; HbA1c-hemoglobin A1c; TG-triglyceride; LDL-low density lipoprotein; VLDL- very low density lipoprotein; HDL-high-density lipoprotein.

Table 3: Correlation between Glycated haemoglobin (HbA1c) and Lipid Profile in Type 2 Diabetes Mellitus patients

Lipid Profile Parameters	HbA1c	
	Pearson's correlation	P value
Cholesterol	0.063	0.206
TG	0.124	0.006
LDL	0.142	0.001
VLDL	0.131	0.004
HDL	-0.024	0.625

REFERENCES:
1. Global Status Report on Non-communicable Diseases 2010. World Health Organization; 2011. Available from: http://www.who.int/nmh/publications/ncd_report_full2010/_en/.
2. Reddy KS. Prevention and control of non-communicable diseases: status and strategies. New Delhi: Indian Council for Research on International Economic Relations; 2003
3. Anand K, Shah B, Yadav K. Are the urban poor vulnerable to noncommunicable diseases? A survey of risk factors for non-communicable in urban slums of Faridabad. Natl Med J India. 2007;20(3):115–20.
4. Misra A, Pandey RM, Rama DJ. High prevalence of diabetes, obesity and dyslipidemia in urban slum population in northern India. Int J ObesRelatMetabDisord. 2001;25(11):1722–9.
5. Wild S, Bchir MB, RoglicG,Green A, Sicree R, King H. Global prevalence of diabetes. Diabetes care.2004;27:1047–53.
6. International Diabetes Federation. IDF Diabetes Atlas Update Poster. 6th ed. Brussels, Belgium: International Diabetes Federation; 2014.
7. Gupta V.Diabetes in Elderly patients.JK practitioner,2002;49:631-642.
8. https://www.who.int/news-room/fact-sheets/detail/diabetes accessed on 23/07/2019
9. Gong W, Lu B,Yang Z,Ye W, Du Y, Wang M, et al. Early-stage atherosclerosis in newly diagnosed, untreated type 2 diabe¬tes mellitus and impaired glucose tolerance. Diabetes Metab 2009; 35(6):458–62. doi:10.1016/j.diabet.2009.05.005PMID:19879790
10. Grundy, S.M. 1998. Multifactorial causation of obesity: implications for prevention. Am J. Clin. Nutr., 67:563S-572S.
11. Sreenivas Reddy A, Meera S, Ebenezer William, Kumar JS.Correlation between Glycemic Control & Lipid Profile in Type II Diabetic Patients: Hba1c as an indirect indicator of Dyslipidemia.Asian Journal Of Pharmaceutical & Clinical Research.vol 7, issue 2:2014:153-155.
12. Krauss RM. Lipids and lipoproteins in patients with type 2 diabetes. Diab Care.2004;27:1496-504.
13. Haffner SM. American Diabetes Association Management of dyslipidemia in adults with diabetes. Diab Care. 2003;26(1):s83-6.
14. Morbois-Trabut L, Chabrolle C, Garrigue MA et al (2006) Apolipoprotein E genotype and plasma lipid levels in Caucasian diabetic patients. Diabetes Metab 32:270–275
15. Zachary T,Bloomgarden. Cardiovascular Disease, Neuropathy and Retinopathy.Diabetes care 2009;32: e64- e 68.
16. Selvin E, Coresh J, Golden SH et al (2005) Glycemic control and coronary heart disease risk in persons with and without diabetes: the atherosclerosis risk in communities study. Arch Intern Med 165:1910–1916
17. Selvin E, Coresh J, Shahar E et al (2005) Glycemia (haemoglobin A1c) and incident of ischemic stroke: the Atherosclerosis Risk in Communities ARIC) Study. Lancet Neurol 4:821–826.
18. Syed I and Khan WA. Glycated haemoglobin – a marker and predictor of cardiovascular disease. J Pak Med Assoc 2011; 61: 690–695.
19. National Cholesterol Education Program (2002). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation.
20. Bhattacharjee P, Das P, Nath BK, Basumatary A, Das D. HbA1C and its correlation with lipid profile in acute myocardial infarction. International Journal of Contemporary Medical Research. 2018;5(4):D13-D16.
21. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetesd2018 Diabetes Care 2018;41(Suppl. 1):S13–S27.
22. Khaw K, Wareham N, Bingham S, et al. Association of hemoglobin A1c with cardiovascular disease and mortality in adults: the European prospective investigation into cancer in Norfolk. Ann Intern Med 2004; 141: 413–420.
23. Mahato RV, 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. Biomed Res 2011; 22: 375–380.
24. Wexler DJ, Grant RW, Meigs JB, et al. Sex disparities in treatment of cardiac risk factors in patients with type 2 diabetes. Diabetes Care 2005;28:514–520.
25. Boden G; Role of fatty acids in the pathogenesis of insulin resistance and NIDDM. Diabetes, 1997; 46(1):4755.
26. Khan HA, Sobki SH, Khan SA. Association between glycaemic control and serum lipids profile in type 2 diabetic patients: HbA1c predicts dyslipidaemia. Clin Exp Med 2007; 7: 24-29.
27. Andersen G, Christiansen J, Mortensen H, et al. Plasma lipid and lipoprotein in type 1 diabetic children and adolescent in relation to metabolic regulation, obesity and genetic hyperlipoprotenimia. Acta Paediatr Scand 1983; 72: 361–365.