Correlation Of Glycemic Control With Dyslipidemia In Type II Diabetes Mellitus

[1]Rupal Dosi, [2]Jigar Patel, [3]Shreyans Doshi, [4]Preeti Panchal, [5]Rushad Patel

[1] Professor, Department of Medicine, Medical College Baroda.
[2] Resident, Cardiology, Sri Jayadeva Institute of Cadiology, Bangalore.
[3] Ex-Intern, Medical College, Baroda .
[4] Assistant Professor, Department of Preventive and Social Medicine, Medical College Baroda.
[5] Resident, Internal Medicine, Cleveland Clinic Foundation, Ohio, USA.

ABSTRACT:

Background: Dyslipidemia is a well-known complication of type 2 diabetes mellitus. Understanding dyslipidemia and its relation to glycemic control is paramount to better management of patients with diabetes. The study aims to explore the correlation of diabetes control and lipid profile in a cohort of patients at a center in Western India. **Methods:** A total of 50 adult patients with a known diagnosis of type 2 Diabetes Mellitus were subjected to a detailed history, clinical exam and laboratory work-up. The focus was on glycemic status and lipid profile. Various parameters of the lipid profile were compared with glycemic control, in the form of glycosylated hemoglobin (HBA1C). They were also divided into two groups using a cutoff of HBA1C of 8 %. The two groups were then compared amongst themselves. And findings were compared with data from previous similar studies. **Results:** The mean age of the patients studied was 55.32 and duration of diagnosis was 7.78 years. The Pearson's Correlation index for HBA1C with lipid parameters showed a negative correlation with HDL whereas it was positive for the remaining parameters. **Interpretation and Conclusions:** Dyslipidemia is an important aspect of the vascular complications of diabetes and is thus a major therapeutic focus. Our study shows that HBA1c may be a useful tool not only for assessing long term glycemic control, but also predicting and monitoring lipid control. Future studies are needed to confirm and further delineate these findings.

Key-words: HbA1C, Lipid Profile, Dyslipidemia.

Corresponding Author: Dr. Rupal Dosi, Professor, Department of Medicine, Medical College Baroda, Gujarat, India. Email: rupal265@yahoo.com

INTRODUCTION:

Diabetes in India is a problem of burgeoning proportions and is estimated to continue to grow at an alarming rate.[1] The disease and its complications that follow are proven to be a significant strain on the lives of patients as well as the resources of a health care system.[2] Macrovascular complications, especially coronary artery disease is well known and of special concern due to mortality and morbidity. The increase in lipid and glucose abnormalities is a driving force in the manifold increase in incidence of coronary artery disease (CAD) that has been reported in the country.[3] Glycosylated hemoglobin is extremely useful not only as a marker of glycemic status over the long term but also as a diagnostic tool today. However, it may still be under utilized in developing countries due to limitations of cost and availability. An increase in the level of cholesterol and lipids in patients with diabetes with CAD as compared to those without CAD has been observed.[4] Elevated HBA1c has been suggested an important risk factor for CAD

in patients with Diabetes.[5] This is further supported by an association between the severity of ischemic heart disease and levels of HBA1c.[6] Each 1% increase in HBA1c has been estimated to correspond to a 25 % increase in diabetes associated mortality, a 35 % increase in the macrovascular complications and an 18 % increase in risk of myocardial infarction.[7]

Dyslipidemia is likely to play an important role in the accelerated atherosclerotic disease process observed in diabetics,[8] and is thus a well-known target for therapy in Diabetes Mellitus. Interventions targeting stabilization of glycemic levels and reduction of blood lipids have been shown to reduce cardiovascular disease and associated mortality in patients with type 2 DM.[9] Unlocking the relation between glycemic levels and lipid profiles could further our understanding and potential therapeutic strategies to reduce the risk of dyslipidemia and atherosclerosis in patients with type 2 DM. We aimed to compare lipid profiles between poorly controlled (HbA1c>8%) and well controlled (HbA1c<8%) diabetic subjects to explore the association of glycemic status with hyperlipidemia.[10]

MATERIAL AND METHODS:

This observational cross sectional study, which was carried out at a tertiary care hospital in an urban setting in Gujarat, India, included 50 subjects having type-2 diabetes mellitus, presented either to diabetes clinic, outpatient department or various wards. Written informed consent was obtained from all the participants at the time of enrollment.

Inclusion criteria included patients diagnosed with type 2 diabetes mellitus, age more than 40 years and no clinical evidence of coronary artery disease. Pregnant patients, patients diagnosed with hemolytic anemia, patients on hypolipidemic therapy and known cases of secondary causes of hyperlipidemia were excluded.

A detailed evaluation of all the enrolled subjects was undertaken. Special attention was given to symptoms of diabetes and its complications. Medication history, past records, including glycemic control was carefully recorded. A focused physical examination, including general examination and thorough systemic evaluation and fundus examination was included.

Laboratory studies, including a hemogram, urine examination, fasting blood glucose [GOD-PAP Method] and 2 hours post-prandial blood glucose levels [GOD_PAP Method], Glycosylated hemoglobin (HBA1c) [HPLC Method], serum Creatinine, Fasting Lipid profiles [CHOD_PAP, Enzymatic Method 3rd generation direct assay] were undertaken for all subjects. Electrocardiograms, Chest X-rays and abdominal ultrasounds were also performed.

The impact of glycemic control on various parameters was evaluated by calculating the Pearson's correlation coefficient. The patients were also divided into two categories on the basis of HbA1c levels; < 8% good glycemic control (n=18), HbA1c levels >8% (n=32) poor glycemic control. The data was then tabulated and analyzed statistically. Students Unpaired t test was applied to the two groups HBA1c <8 and >8.

RESULTS:

A total of 50 patients were studied. The mean age of the patients was 55.32 years, and male: female ratio 1.95:1. The mean BMI was 27.51 and the duration of diabetes was 7.78 years. 32 (64%) patients had HbA1c> 8% and& 18 (36%) patients had HbA1c% ≤ 8%. Studying the correlation between the glycemic control as estimated by HBA1c and various parameters of the lipid profile was the principal aim of the study and Pearson's correlation coefficient was calculated accordingly. The results are displayed in table-1. Seen as a positive correlation trend between HBA1c and Total cholesterol, LDL cholesterol and VLDL cholesterol was seen, whereas there was a negative correlation for HBA1c and HDL cholesterol. The

correlation between HBA1c and total cholesterol and LDL was found to be statistically significant.

Also a comparison between the two groups (based on HBA1c using a cutoff of 8%) was undertaken using Students T test for unpaired data (table 2). The total cholesterol and LDL was statistically significantly higher in patients with higher Hba1c.

DISCUSSION:

Diabetes is a modern global pandemic, driven by the rising rates of obesity and reduced physical activity with a focus on South Asia.[11] Indians in part due to apparent inherent genetic susceptibilities in combination with industrialization and lifestyle changes have been shown to be particularly prone to type 2 diabetes.[13] Dyslipidemia has been observed well in type 2 diabetic subjects[14,15] and is an important focus of management in diabetic care.[16] HBA1c is an important tool to monitor glycemic control over a longer period as compared to a single time venous or finger stick methods. Moreover, reduction of HbA1C has been shown to reduce diabetic complications, making it a suitable target for drug therapy. Each 1% reduction in HbA1c was associated with a reduction in risk of 21% for any endpoint related to diabetes, 21% for deaths related to diabetes, 14% for myocardial infarction, and 37% for micro vascular complications.[17] Studies correlating HBA1C and lipid profiles are few[18] although some investigators suggest the importance of glycemic control in normalizing dyslipidemia.[19]

The classical abnormalities in blood lipids seen in patients with type 2 DM include elevated triglycerides, low HDL cholesterol and increased small dense LDL cholesterol particles. These abnormalities may be the result of the unbalanced metabolic state of diabetes i.e. hyperglycemia and insulin resistance.[20] Higher levels of LDL are explained in part by its decreased catabolism, reduced activity of and lipoprotein lipase enzyme as well as cholesterol ester transfer protein.[16,21]

Studying the lipid profile of the subjects with type 2 diabetes and correlating them with glycemic control, using HBA1c as a marker of glycemic control was the primary aim of the study.

In our observational cross-sectional study, the mean HBA1c was 9.14 %, total cholesterol 179.28 mg/dl, LDL 101.07 mg/dl, VLDL 33.82 mg/dl, HDL 40.09 mg/dl and Triglyceride 169.05 mg/dl, these findings are consistent with previous studies.[22,23] A significant correlation between HbA1c level and LDL level (r =0.4416, CI 0.1861-0.6411) seen in our study is similar to the findings described by Nasir Ahmed et al,[23] Adsani et al[24] and Ahmed khan et al.[25] Similarly a negative correlation trend was shown between HBA1c and HDL levels (r=-0.2698, CI -0.5999to -.0092) and a positive correlation trend for HbA1c and Triglycerides (r=0, 4382, CI -0.0173 to 0.5039).

In poorly controlled diabetes patients hyperglycemia leads to non-enzymatic glycosylation of LDL, which has been suggested, to result in its increased incorporation in the arterial wall.[26] Moreover the ability of LDL to interact with the LDL receptor is impaired by glycosylation of lysine groups on Apo lipoprotein B decreasing its metabolism via the LDL receptor pathway.[27] Low-density lipoprotein (LDL) cholesterol is a focus of current guidelines for determination of the risk of cardiovascular diseases.[28,29]

Our study supports that HBA1c can be a useful tool to predict and monitor dyslipidemia in diabetes.[30] Today HBA1c is used by clinicians to monitor the long term glycemic control. Regular monitoring of blood lipid parameters is also recommended in patients with diabetes. Considering the economic implications in a resource limited setting for repeated investigations, our study suggests that HBA1c may be used as a criterion to prioritize the use of a lipid profile. A large, long term study to confirm this is recommended.The small size of the study population, inability to perform apo-

lipoprotein analysis (apo A and apo B fraction estimation) as well as the single point study design rather than a follow up to understand progression of diabetic complications were limitations, mostly due to logistic hurdles which can be overcome in further studies.

Diabetes, hypertension and obesity contribute to a well-known strongly atherogenic environment, leading to a significant increased cardiovascular risk in susceptible patients. Dyslipidemia is an important target to decrease the risk of cardiovascular disease in such patients. Unlocking the important connection between the glycemic control and dyslipidemic parameters would help increase our understanding and potentially assist in designing therapeutic targets and strategies.

CONCLUSION:

Our study displayed a significant correlation between the total cholesterol and LDL & HDL cholesterol with the glycemic control in patients with type 2 diabetes mellitus in a tertiary care hospital in western India. Dyslipidemia in type 2 diabetics is well known, however, we have a long way to go in understanding its connection with glycemic indices (in our study measured by HBA1c). Furthermore HBA1c may prove to be useful as a predictive tool for blood lipids besides its current status as a marker of long term glycemic control. Further studies are needed to confirm these findings and their impact on micro and macrovascular complications.

Conflict of Interest: None.

Source of funding: Nil.

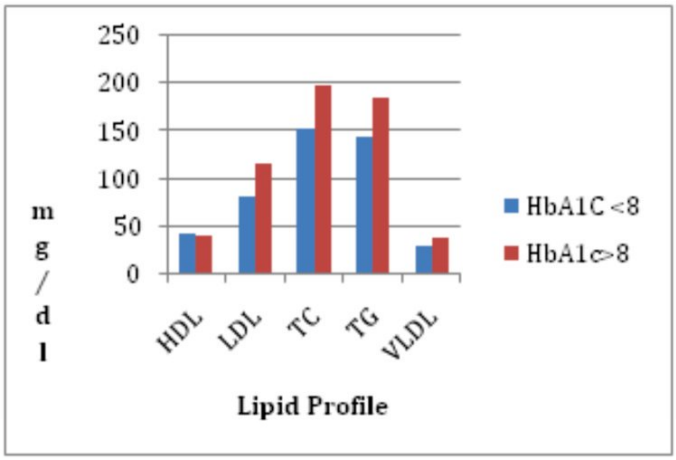
Table 1: Comparison clinical and laboratory features of two groups based on HBA1c, using a cutoff of 8%.

		HbA1C<8%	HbA1C>8%	P VALUE
1	AGE(Years)	54.1	56	0.2555
2	SEX (M:F)	10:08	23:09	0.938
3	DURATION OF DISEASE (years)	3.35	7.7	0.00397
4	BMI (kg/m^2)	24.6	29.15	0.00012
5	SYSTOLIC BP (mm/hg)	136.2	137.5	0.4029
6	DIASTOLIC BP (mm/hg)	85.9	83.6	0.1888
7	HEMOGLOBIN (gm/dl)	11.3	11.1	0.3746
8	FBS (mg/dl)	174.9	197	0.0521
9	PP2BS (mg/dl)	255.1	268.4	0.2541
10	S.CREATININE (mg/dl)	1.1	1.6	0.0508
11	TOTAL CHOLESTEROL (mg/dl)	151.7	194.8	0.0003
12	LDL (mg/dl)	80.7	112.7	0.0017
13	VLDL (mg/dl)	28.5	36.8	0.1308
14	HDL (mg/dl)	41.3	39.4	0.4483
15	TRIGLYCERIDE (mg/dl)	143.4	183.5	0.1417
16	RETINOPATHY (%)	22%	56%	0.0064
17	NEPHROPATHY (%)	11%	31%	0.207
18	CARDIAC DISEASE (%)	22%	41%	0.992

Table-2: Correlation of HBA1C and Lipid Profile

Lipid Profile	r	P	Confidence Interval
Total cholesterol	0.4382	0.0015	0.1820 to 0.6386
LDL	0.4416	0.0013	0.1861 to 0.6411
HDL	-0.2698	0.0581	-0.5099 to 0.0092
Triglyceride	0.2623	0.0657	-0.0173 to 0.5039
VLDL	0.2681	0.0598	-0.0111 to 0.5085

Figure-1: Graph representing a comparison of lipid parameters in two groups based on the HBA1C value of 8%.



References:

1) Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030. Diabetes Care 2004;27:1047-53.
2) Ramachandran A, Ramachandran S, Snehalatha C, Augustine C, Murugesan N, Viswanathan V, et al. Increasing expenditure on health care incurred by diabetic subjects in a developing country: a study from India. Diabetes Care 2007;30:252-6.
3) Bulatao RA, Stephens PW. Global estimates and projections of mortality by cause. Washington DC: Population, Health and nutrition Department; World Bank; pre-working paper 1007, 1992.
4) Giansanti R, Rabini RA, Romagnoli F, Fumelli D, Sorichetti P, Boemi M, et al. Coronary heart disease, type 2 diabetes mellitus and cardiovascular disease risk factors: a study on a middle-aged and elderly population. Arch Genontol Geriatr 1999; 29(2):175-82.
5) Khan HA. Clinical significance of HbA1c as a marker of circulating lipids in male and female type 2 diabetic patients. Acta Diabetol 2007; 44:193-200.
6) Ravipati G, Aronow WS, Ahn C, Sujata K, Saulle LN, Weiss MB. Association of hemoglobin A(1c) level with the severity of ischemic heart disease in patients with diabetes mellitus. Am J Cardiol 2006;97(7):968-9.
7) America Diabetes Association. Standards of medical care in diabetes. Diabetes care 2004;27(Suppl 1): S15-S35.
8) Garg A, Grundy SM. Management of dyslipidemia in NIDDM. Diabetes Care 1990;13(2):153-69.
9) Jones PH. Clinical significance of recent lipid trials on reducing risk in patients with type 2 diabetes mellitus. Am J Cardiol 2007; 99(4A):133B-140B.
10) Saudek CD, Kalyani RR, Derr RL. Assessment of glycemia in diabetes mellitus: hemoglobin A1c. J Assoc Physicians India 2005 Apr; 53:299-305.
11) Misra A, Shrivastava U. Nutrients. Obesity and dyslipidemia in South Asians. Nutrients 2013 Jul 16; 5(7):2708-33.
12) Mohan V. Why are Indians more prone to Diabetes? J Assoc Physicians India 2004 June;

52:468-74.
13) Mohan V. Why are Indians more prone to Diabetes? J Assoc Physicians India 2004 June; 52:468-74.
14) Nasri H. Yazdani M. The relationship between serum LDL cholesterol, HDL cholesterol and systolic blood pressure in patients with type 2 diabetes. Kardiol Pol 2006;64 (12) : 1364-8;discusiion. 1369-71.
15) Arora M, Koley S, Gupta S, Sandhu JS. A Study on Lipid Profile and Body Fat in Patients with Diabetes Mellitus. Anthropologist 2007; 9(4):295-8.
16) Kalra S, Unnikrishnan AG. Diabetes and Dyslipidemia. J Pak Med Assoc 2013 Jun; 63(6):788-91.
17) DCCT Research Group. The absence of a glycemic threshold for the development of long-term complications: the perspective of the diabetes control and complications trial. Diabetes 1996;45(10):1289-98.
18) Smellie WS. Hyper- triglyceridaemia in diabetes. BMJ 2006; 333(7581):1257-60.
19) Ladeia AM, Adan L, Couto-Silva AC, Hiltner A, Guimaraes AC. Lipid profile correlates with glycemic control in young patients with type 1 diabetes mellitus. Prev Cardiol 2006;9(2):82-8.
20) Mooradian AD. Dyslipidemia in Type 2 Diabetes Mellitus. Nat Clin Pract Endocrinol Metab 2009 Mar;5(3):150-9.
21) Huang ES, Meigs JB, Singer DE .The effect of interventions to prevent cardiovascular diseases in patients with type-2 diabetes mellitus. Am J Med 2001;111(8):633-42.
22) Otieno CF, Mwendwa FW, Ogola EN, Amayo EO, department of medicine, university of Nairobi, Lipid profile of ambulatory patients with type 2 DM at Kenyatta hospital , Nairobi, East Afr J Med 2005 , Dec, S 173-9
23) Nasir Ahmed, Jahangir Khan, TahirSaeedSiddiqui. requency of dyslipidemia in type 2 DM in patients of Hazara division. J Ayub Medical College Abbotabad 2008;20(2).
24) Al- Adsani, Memon A, Suresh A, department of medicine, ministry of health, Kuwait, Pattern and determinants of dyslipidemias in type 2 diabetes mellitus patients in Kuwait, Acta Diabetol 2oo4, /sep,41,129-35.
25) Ahmed Khan, department of Biochemistry, College of Science, King Saud University, Saudi Arabia, clinical significance fo HbA1c as a marker of circulating lipids in male and female type 2 diabetic patients, ActaDiabetol 2007, Dec `193-200.
26) Taylor KG, John WC, Mathews KA, Wright AD. A prospective study on the effect of 12 months treatment on serum lipids and apolipoproteins A-I, A-II and B in type II (non insulin dependent) Diabetologia 1982; 23(6):507-10.
27) Kane JP, Havel RJ. Disorders of the biogenesis and secretion of lipoproteins containing the B apolipoproteins. In: Scriver CR, Beaudet AL, Sly WS, Valle D, eds. The metabolic and molecular basis of inherited disease, 7th ed. New York: McGraw-Hill, 1995.
28) Chehade JM, Gladysz M, Mooradian AD. Dyslipidemia in type 2 diabetes: prevalence, pathophysiology, and management. Drugs 2013 Mar; 73(4):327-39.
29) Stone NJ, Robinson JG, Lichtenstein AH, Goff Jr DC, Lloyd-Jones DM, Smith Jr SC, Blum C, Schwartz JS; for the 2013 ACC/AHA Cholesterol Guideline Panel. Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Disease Risk in Adults: Synopsis of the 2013 ACC/AHA Cholesterol Guideline. Ann Intern Med 2014 Jan 28.
30) Prabhavathi K, KirthanaK, Jaisri Goturu. Glycosylated Haemoglobin (HbA1c) – A Marker of Circulating Lipids in Type 2 Diabetic Patients. J Clin Diagn Res. 2014 Feb, Vol-8(2):20-23.

Cite this Article as: Dosi R, Patel J, Doshi S, Panchal P, Patel R. Correlation Of Glycemic Control With Dyslipidemia In Type II Diabetes Mellitus. Int Res Pub Med Sci 2015; 1(3):34-39.