Volume : 4 | Issue : 10 | October 2015 • ISSN No 2277 - 8179

Research Paper

Hba1c: Its Evaluation As A Screening Biomarker of Dyslipidemia in Diabetes Type 2 Patients

Biochemistry

KEYWORDS : Type-2 DM, lipid profile, dyslipidemia,HbA1C.

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ABSTRACT

Diabetes mellitus(DM) is a globally prevalent disease associated with hyperglycemia due to insulin deficiency or insensitivity or both. Hb1AC is used to assess blood sugar level over 3-4 months of the treatment period. DM type 2 patients have invariably abnormal lipid profile known as dyslipidemia. It is one of the important complications of diabetes mellitus. HbA1C can predict the status of the lipid profile or dyslipidemia in addition to blood sugar control. Several studies have found the very positive correlation between HbA1C and lipid profile .So, HbA1C might be used to predict dyslipidemia in DM type 2 patients.

INTRODUCTION:

Diabetes mellitus (DM) is a universal endemic human disease with rapid rising prevalence in both developing and developed countries.[1] According to world health organization report 2005, around 171 million peoples were affected with diabetes worldwide in 2000 and would increase to 366 million by year 2050.[2]

In India alone, 31.7 million people had diabetes in year 2000 which latter on increased to 61.3 million in 2011 and is expected to reach 101.2 million by 2030 (International Diabetes Federation). [3] Thus India is the 2nd largest country in world diabetes prevalence.[3] The maximum burden of diabetes in society is mainly contributed by DM type 2 which accounts for about 90% cases of diabetes.[4] And it is said that DM type 2 will alone affect 300 million people worldwide by 2025.[5]

HbA_1C is used as a marker of glycemic control over 3-4 months in diabetes patients.[6] An elevated HbA_1C level indicates poor control of blood sugar or poor glycemic index. It predicts the risk for the development of diabetic complications in diabetic patients.[7,8] Dyslipidemia is one of the important diabetic complications which is a classical risk factor for cardiovascular disease (CVD). Each 1 % increase in the level of HbA_1C shows 18% increase in cardiovascular disease(CVD).[9] A positive relationship between HbA_1C and dyslipidemia had been seen in DM type-2.[10, 11] So this study is focused on evaluation of HbA_1C as a screening biomarker for dyslipidemia in DM type 2 patients.

REVIEW AND LITERATURE:

Diabetes Mellitus is a metabolic disease characterized by hyperglycemia resulting from defects in insulin secretion, action or both.[12] It has several complications which accounts for mortality and morbidity due to diabetes. It causes about 5% of all deaths globally every year.[13] DM is strongly associated with dyslipidemia and glycated hemoglobin HbA_1C.[14, 15] HbA_1C is formed by non enzymatic glycosylation mechanism in hemoglobin over the entire 90- 120 days life span of red blood cells as a result of hyperglycemia.[6]

HbA_1C is used as a marker of glucose control over 3-4 months in diabetes people.[6] It is expressed into percentage. HbA_1C between 6 to 7% is considered to be good control whereas HbA_1C between 7-8% and above 8% are considered as fair and poor control respectively.[16] It is a routinely used marker for the assessment of average blood sugar level over past 3-4 months of treatment evaluating the effect of medications and preventive measures in diabetes persons.

Dyslipidemia is important complications of diabetes mellitus characterized by increased level of total cholesterol, VLDL ,LDL-cholesterol, triglycerides, and decreased HDL-Cholesterol in blood.[17] Patients with DM type 2 are usually dyslipidemic even if under relatively good glycemic control as compared to patients of DM type 1.[18,19] HbA_1C predicts the risk for the development of diabetic complications in diabetic patients.[7,8] Dyslipidemia is a major risk factor for coronart artery disease and cerebrovascular events, a leading cause of mortality in patients with diabetes mellitus. It predisposes to atherosclerosis in diabetes which accounts for 80% of all diabetic mortality out of which 75% from coronary atherosclerosis and 25% from cerebral or peripheral vascular disease.[20]

In diabetes mellitus type 2, due to decreased insulin secretion or action, the activity of hormone mediated lipoprotein lipase increases and lipoprotein lipase activity decreases. glucose is not utilized for energy purpose by cells due to insulin deficiency or insensitivity which triggers the lipolysis by hormone sensitive lipase leading to increased formation of free fatty acids(FFA). These FFAs are then catabolised to acetyl coA into liver and other tissues. Due to deficiency of oxaloacetate ,the excess acetyl coA is converted into cholesterol, VLDL, and triglycerides. LDL increases either because of increased hepatic production of VLDL or decreased removal of VLDL and LDL from circulation. Serum concentration of triglycerides also increases because of decreased removal from circulation.[21] Whereas Serum HDL level decreases due to excess catabolism which accounts for negative relationship between HDL and LDL level. Hence hyperglycemia is related with derranged lipid profile and this may lead to dyslipidemia.

MATERIALS AND METHODS:

The present study was conducted in Major S D Singh Medical College and Hospital, Farrukhabad(Uttar Pradesh).between March 2015 and June 2015.The study protocol was approved by the ethical committee of the institute. 100 OPD diabetic type 2 male patients and 100 healthy male persons as control between age group 35-75 years were randomly selected for the study of the following parameters-

Volume : 4 | Issue : 10 | October 2015 • ISSN No 2277 - 8179

1.Blood Sugar by GOD-POD method.[22]
2. Glycated hemoglobin(HbA1C) by cation exchange resin method.[23]
3.Lipid profile(total cholesterol, triglycerides ,HDL-C and LDL-C)out of which total cholesterol(TC)[24],triglycerides(TG)[25]and HDL-C [26,27] are estimated by different enzymatic end–point methods .LDL-C estimation is based upon Friedewald,s formula.[28] as given below-

LDL-C=TC-HDLC-TG/5where VLDL =TG/5

All the above parameters were estimated in the clinical Biochemistry lab. of the hospital using commercially available standard kits. For serum lipid reference level, National Cholesterol Education Programme (NCEP) Adult Treatment Panel III(ATP III) guideline was used which defined hypercholesterolemia(total cholesterol >200mg/dl), high LDL-C when value >100mg/dl, hypertriglyceridemia when value >50 mg/dl and low HDL-C when value 40 mg/dl. Dyslipidemia was defined by the presence of one or more abnormal lipid parameters. HbA1C was expressed into percentage of total hemoglobin and values of lipid parameters into mg/dl. All values were expressed as mean ±S.D. Student t-test and Peerson's correlation coefficient were used to find the Statistical Significance. A P – value<0.05 is considered Statistically Significant.

RESULT AND DISCUSSION :

In the study, the mean values of HbA1C, TC,TG,VLDL-C,LDL-C and HDL-C were 11.06±1.84, 273.66±36.12, 208.12±30.12, 40.59±11.09, 163.11±53.25 and 37.04±5.81 respectively (Table1). The level of TC, TG, LDL-C and VLDL-C were found significantly increased (P<0.0001) while HDL-C level was significantly decreased as compared to control group (Table No.2). In addition ,it was also observed that glycated hemoglobin(HbA1C) was positively and significantly related with total cholesterol (r =+0.586), triglycerides (r =+0.927), LDL-C (r = 0.+574) and VLDL-C(r =+ 0.316). However, HDL-C (r = -0.193) showed negative correlation with insignificant P value(Table No.2)

TABLE NO.1

Mean ±SD Values of blood sugar, HbA1C and lipid profile of diabetes type 2 and controls		
Parameters	Type-2 diabetes(n=100) Mean±SD	Controls(n=100) Mean±SD
BloodSugar(mg/dl) Fasting	140±22.50	84.90±7.64
HbA1C(%)	11.06±1.84	5.20±0.94
Total Cholesterol,TC (mg/dl)	273.66±36.12	165.88±24.95
Triglycerides,TG (mg/dl)	208.12±30.12	117.56±22.52
HDL-C(mg/dl)	37.04±5.81	43.66±6.63
LDL-C(mg/dl)	163.11±53.25	97.96±21.21
VLDL(mg/dl)	40.59±11.09	23.41±4.55
Statistically significant at P value <0.0001		

TABLE NO.2

Correlation of HbA1C with lipid profile of diabetes type 2 patients		
Parameters	Correlation Coefficient	P -Value
TC(mg/dl)	+0.586	<0.001
TG(mg/dl)	+0.927	<0.001
HDL-C(mg/dl)	-0.193	NS*
LDL-C(mg/dl)	+0.574	<0.001
VLDL-C(mg/dl)	+0.316	<0.001
*NS-Statistically not Significantly, Statistically Significant at P value<0.0001.		

In the study, it was found that Serum total Cholesterol, triglycerides, VLDL and LDL-C were significantly higher in diabetic type 2 group than control group and were in borderline high risk range. While serum HDL-C was significantly lower in diabetic type 2 group than control group and was towards lower range of normal value. Thus the study showed the high prevalence of dyslipidemia, a well known risk factor for cardiovascular disease.[12] Thus the findings were in consistent with previous studies.[14, 15]

The cause of dyslipidemia in diabetes mellitus type 2 might be due to insulin insensitivity or resistance affecting the apoprotein production by the liver which regulates the enzymatic activity of lipoprotein lipase and cholesterol ester transport protein.[29] A highly positive significant relationship of HbA1C with dyslipidemia was observed in the present Study. Erclays et al also reported positive correlation of HbA1C level with total cholesterol and triglycerides level in diabetic persons. [10, 29, 30]

In diabetic persons, HbA1C≤ 7% was said to be appropriate for reducing the risk of cardiovascular complications.[9] The diabetic patients with higher HbA1C value could have significant increased level of TC,TG, LDL-C and HDL-C in comparison to patients with HbA1C value ≤ 7% which might be responsible for the increased severity of dyslipidemia in patients with higher HbA1C values as reported by khan et al.[11] Diabetic people can know about the status of their lipid levels by getting their HbA1C values. Until and unless HbA1C remained below 7%, lipid profile could be predicted to be normal. It had been reported that reducing the HbA1C level by 0.2% could lower the mortality by 10%.[20] Thus dyslipidemia could be ruled out by their HbA1C levels in diabetes mellitus type 2 patients.

CONCLUSION

HbA1C showed positive correlation with TC,TG,VLDL,LDL-C but negative correlation with HDL-C which showed that HbA1C might be used as a reliable biomarker in the screening of dyslipidemia in diabetes type-2 patients.

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