Study of Association between HbA1c Level and Lipid Profile in Type 2 Diabetes Mellitus.

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ABSTRACT

Background: Atherosclerosis leading to ischemic heart disease remains the major cause of death and premature disability in developed countries and its prevalence is rising constantly in developing countries. Dyslipidaemia due to insulin resistance, the major cause of coronary atherosclerosis and ischemic heart disease is frequently associated with type 2 diabetes mellitus. Type 2 diabetes mellitus is an emerging pandemic with the number of patients increasing rapidly in both developed and developing countries around the world. **Methods:** In this study lipid abnormalities associated with type 2 diabetes mellitus were studied and association between HbA1C level and extent of dyslipidaemia detected. In this cross-sectional study 100 known cases of type 2 diabetes mellitus will be selected. They will be investigated for HbA1C and lipid profile. The data obtained will be analyzed by appropriate statistical methods. **Results:** In the present study, dyslipidaemia was found to be present in 89% patients of type 2 diabetes mellitus. Of these, 21% had single abnormal lipid parameter while 68% had combined dyslipidaemia. There was highly significant correlation between HbA1C & total cholesterol, HbA1C & LDL cholesterol, HbA1C & triglycerides, HbA1C & Tc/HDL ratio and HbA1C & non HDL cholesterol. Also, highly significant inverse correlation between HbA1C & HDL cholesterol was found. **Conclusion:** Prevalence of dyslipidaemia was alarmingly high in type 2 diabetes mellitus patients. Thus, HbA1C can be considered as a marker of dyslipidaemia in type 2 diabetes mellitus.

Keywords: Dyslipidaemia, Type 2 Diabetes Mellitus, Correlation, Risk factor.

INTRODUCTION

Over the last decade, cardiovascular diseases have become the single largest cause of death worldwide. By 2030, 33% of all deaths will be caused by cardiovascular diseases accounting for 24.2 million deaths worldwide. High cholesterol levels account for some 56% of ischemic heart disease and 18% of strokes, amounting to 4.4 million deaths annually.[1]

In patients of type 2 Diabetes mellitus, hyperlipidemia increases the risk of micro-vascular complications, while dyslipidemia is a major risk factor for macro-vascular complications.[2, 3] In national survey in India 54% of diabetics developed complications in the most productive years of their lives before the age of 50 years.[4, 5]

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Majority of patients with a longer duration of Various studies done on different population with different ethnicity, different eating and working habits and different life-styles have shown varying prevalence and patterns of dyslipidemia in type 2 diabetes mellitus but have consistently shown good correlation between HbA1$_C$ and individual lipid parameter. Difference in study results could be due to different cut-off of HbA1$_C$ and individual lipid level to label it as normal or abnormal.

Various studies done in the different parts of the world showed different mean values for various lipid parameters but all of them concluded very high level of prevalence of dyslipidemia among type 2 diabetes mellitus patients with different pattern. All of them showed that with worsening HbA1$_C$, lipid profile of the patient was worsening further.

The present study was conducted to study prevalence and pattern of dyslipidemia associated with type 2 diabetes mellitus and to study the association between HbA1$_C$ level and extent of dyslipidemia in type 2 diabetes mellitus.

MATERIALS AND METHODS

The study was a cross-sectional study. The study was done on 100 patients of type 2 diabetes mellitus, who were non obese, non hypertensive with no other cardiovascular, renal or thyroid ailments attending

(reporting to) outdoor patient departments or admitted in various wards of Guru Nanak Dev Hospital attached to Government Medical College, Amritsar. They fulfilled following inclusion and exclusion criteria.

Inclusion criteria:

> Patients who are already a known case, whether on treatment or not or newly diagnosed to be suffering from type 2 diabetes mellitus, diagnosed according to American Diabetes Association criteria, 2007. [6]

Exclusion criteria:

> Patients on hypolipidemic drugs
> Type 1 diabetes mellitus or other diseases associated with hyperglycemia
> Smokers
> Alcoholics
> Females on oral contraceptive pills
> Anemia
> Nephrotic syndrome
> Chronic renal failure
> Cirrhosis or other liver diseases
> Pregnancy, Lactation
> Hyperthyroidism / Hypothyroidism

After selecting the subjects fulfilling the above mentioned criteria, their informed written consent was taken for their participation in the study.

Detailed history was taken regarding presenting complaints, symptoms of type 2 diabetes mellitus, its duration and complications and treatment. Personal history was taken especially for dietary habits, alcohol consumption, smoking, exercise or any other addiction.

Patients were thoroughly examined to look for signs suggestive of liver, kidney or thyroid dysfunction and insulin resistance and hyperlipidemia. Examination was done for cardiovascular, respiratory, abdominal and central nervous system and was recorded as per the Performa.

Routine investigations were performed with urine protein and sugar and microscopy, blood urea, serum creatinine, serum bilirubin, serum total proteins and serum albumin, hepatic enzymes – SGOT, SGPT, alkaline phosphatase, electrocardiography, etc. to know the general condition of the patient and to rule out renal or hepatic disease.

All the patients were investigated for $HbA1_C$ assay by Cation exchange resin method, total cholesterol by monozyme kit, HDL cholesterol by Phosphotungstate method, triglycerides by Lyphozyme kit and LDL cholesterol by Friedwald method. Patients were divided in two groups with reference to $HbA1_C$ level:

Group A: $HbA1_C$ level < 8%; 50 subjects
Group B: $HbA1_C$ level ≥ 8%; 50 subjects

To find out the prevalence of dyslipidemia, National Cholesterol Education Programme (NCEP) Adult Treatment Panel III (ATP III) guideline was taken as reference: [7]

Independent sample 't' test was applied to mean values of fasting blood sugar, post-prandial blood sugar, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, Tc/HDL ratio and non HDL cholesterol of both the groups to find out whether the difference was statistically significant or not. The difference was considered statistically significant when the result was $P < 0.05$.

To find out correlation between $HbA1_C$ and fasting blood sugar, post-prandial blood sugar, total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, Tc/HDL ratio and non HDL cholesterol, Pearson's correlation coefficient was used. $R > 0.5$ indicated strong direct correlation while $r < -0.5$ indicated strong inverse correlation.

RESULTS

The cross-sectional study was conducted in the Department of Medicine, Guru Nanak Dev Hospital, attached to Government Medical College, Amritsar. In this study 100 patients of type 2 diabetes mellitus were selected according to the inclusion and exclusion criteria. The patients were divided in two groups, Group A of 50 patients with $HbA1_C$ level < 8% and Group B with $HbA1_C$ level ≥ 8%.

In both the groups there was equal distribution of male and female patients ie. 25 male and 25 female patients in each group.

For Group A mean ± SD for age was 60.26 ± 11.72 yrs with SEM of 1.66 while for Group B it was 60.56 ± 10.54 yrs with SEM of 1.54. When t-test was applied, 't' value was 1.33, and p value was 0.89, which was statistically insignificant.

Table 1 shows the mean and standard deviation of Group A ($HbA1_C$ < 8%) type 2 diabetic patients' age (60.26±11.72), Body mass index (27.31 ± 2.09), Total cholesterol (183.84 ± 17.18), HDL (45.24 ± 4.39), LDL (106.02 ± 17.17), Triglycerides (162.88 ± 23.35), TC/HDL ratio (4.11 ± 0.65) and non-HDL (138.60 ± 18.84).

Also the mean and standard deviation of Group B ($HbA1_C$ ≥ 8%) type 2 diabetic patients' age (60.56 ± 10.90), Body mass index (27.98 ± 1.49), Total cholesterol (191.72 ± 16.73), HDL (41.70 ± 5.63), LDL (113.92 ± 19.33), Triglycerides (180.50 ± 22.97), TC/HDL ratio (4.70 ± 0.88) and non-HDL (150.02 ± 20.45).

As shown in [Table 1], the age of patients did not show any statistically significant difference for the Group A ($HbA1_C$ < 8%) and Group B ($HbA1_C$ ≥ 8%) (p= 0.89) (t = 0.133). When t-test was applied to data of body mass index, 't' value was 1.853 at p= 0.067, which was statistically insignificant.

As shown in [Table 1], the data of the Group A and Group B regarding Total cholesterol, Triglycerides, LDL cholesterol showed statistically significant difference based on the 't' test and p value. Also there was statistically significant difference in the

two groups for HDL cholesterol, non-HDL cholesterol and Tc/HDL ratio.

Table 1: Mean ± SD of Type 2 Diabetic patients in Group A and Group B with t and p value.

Parameter	Group A (n=50) HbA1$_C$ < 8% Mean ± SD	Group B (n=50) HbA1$_C$ ≥ 8% Mean ± SD	t value	p value
Age (yrs)	60.26 ± 11.72	60.56 ± 10.90	0.133	0.89
Body mass index (kg/m²)	27.31 ± 2.09	27.98 ± 1.49	1.853	0.067
Total cholesterol (mg/dl)	183.84 ± 17.18	191.72 ± 16.73	2.323	0.0222
HDL cholesterol (mg/dl)	45.24 ± 4.39	41.70 ± 5.63	3.509	0.0007
LDL cholesterol (mg/dl)	106.02 ± 17.17	113.92 ± 19.33	2.158	0.0334
Triglycerides (mg/dl)	162.88 ± 23.35	180.50 ± 22.97	3.804	0.0002
Tc/HDL ratio	4.11 ± 0.65	4.70 ± 0.88	3.827	0.0002
Non HDL cholesterol (mg/dl)	138.60 ± 18.84	150.02 ± 20.45	2.904	0.0046

Table 2: Correlation between individual lipid parameters and HbA1$_C$ in all Type 2 Diabetic subjects.
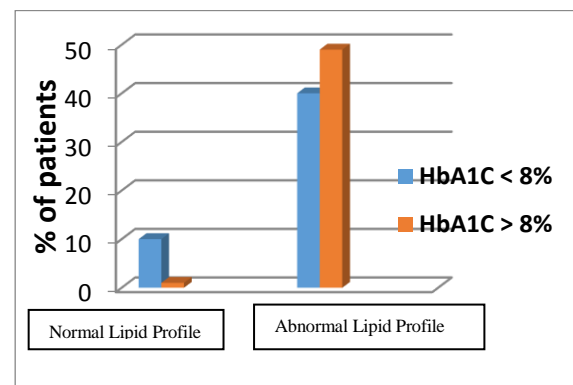
Parameter	Correlation coefficient	P value	Correlation
Total cholesterol	0.6368	<0.0001	Direct
HDL cholesterol	-0.5712	<0.0001	Inverse
LDL cholesterol	0.6172	<0.0001	Direct
Triglycerides	0.5237	<0.0001	Direct
Tc/HDL ratio	0.7217	<0.0001	Direct
Non HDL cholesterol	0.6906	<0.0001	Direct

The HbA1C level showed highly direct correlation with Total cholesterol (correlation coefficient 0.6368, P< 0.0001), LDL (correlation coefficient 0.6172, P<0.0001), Triglycerides (correlation coefficient 0.5237 P<0.0001), TC/HDL ratio (correlation coefficient 0.7217 P<0.0001) and non-HDL (correlation coefficient 0.6906, P<0.0001) as shown in [Table 2]. HDL was significantly and inversely correlated with HbA1C (correlation coefficient -0.5712 P<0.0001).

DISCUSSION

This cross-sectional study was done to find out prevalence and pattern of dyslipidaemia in type 2 diabetes mellitus patients and to evaluate association between marker of hyperglycemia – HbA1$_C$ and dyslipidaemia. In this study, prevalence of dyslipidaemia in diabetic patients by at least one abnormal lipid parameter was found to be 89% while 11% patients had normal lipid profile (Graph 1). This was concordant to the study done by Mahanto RV et al. in which they found the prevalence of dyslipidaemia among type 2 diabetic patients was 80.0% in females and 83.33% in males. [8] In another study, done by Jisieike-Onuigbo NN et al. they found prevalence of dyslipidaemia to be 90.7%. [9] Similar study was done by Okafor CI et al., they found the prevalence of dyslipidaemia to be 89%. [10] A study conducted by Singh and Kumar also was consistent with findings of 59% type 2 diabetics having hypercholesterolemia and 53% had hypertriglyceridemia. [11] Sreenivas et al. studied the impact of glycemic control on lipid profile by

categorizing the patients into 3 groups on the basis of HbA1$_C$ (4.5-6.5%, 6.6-8.5%, 8.6-16% respectively) and observed that worse glycemic control had significantly high TC, TG and LDL levels, but low HDL levels. [12]

Graph 1: Distribution of normal and abnormal lipid profile for Group A and Group B.

Hence, this study shows that quite a good number of diabetic patients have hypercholesterolemia, hypertriglyceridemia, high LDL and low HDL levels which are well established risk factors for cardiovascular diseases. Insulin plays an important role in production of liver apolipoprotein which further modulates enzymatic activity of lipoprotein lipase and cholesterol ester transport protein. This mechanism could be responsible for dyslipidaemia in Diabetes. [13] Also, insulin deficiency reduces the activity of hepatic lipase and therefore several steps in the production of biologically active lipoprotein

lipase may also be altered in Diabetes. [14] A highly positive significant correlation of HbA1$_C$ with dyslipidaemia was observed in the present study.

CONCLUSION

No significant difference was observed in the glycemic status of males and females. HbA1$_C$ showed positive correlations with TC, TG, LDL and VLDL and negative correlations were observed between HbA1$_C$ and HDL levels. So the conclusion drawn from this study is that HbA1$_C$ can be preferred as a good indicator for predicting the lipid profile of both male and female diabetic patients. Early diagnosis of dyslipidaemia can be reached with the glycemic parameter. Adequate preventive measures can be ensured for development of cardiovascular disease in type 2 diabetic patients.

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