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A STUDY ON APO B100/APO A-I RATIO IN UNCONTROLLED TYPE 2 DIABETES MELLITUS

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ABSTRACT:

Objectives: Dyslipidemia, a very common complication of diabetes mellitus (DM), is associated with life threatening complication like coronary artery disease (CAD). Apolipoprotein A-I and apo B100 are the protein components of high density lipoprotein (HDL-C) and low density lipoprotein (LDL-C) respectively. Apo B100/apo A-I ratio represents the balance between pro-atherogenic and anti-atherogenic factors. Apolipoproteins have recently gained importance as they are said to be a better indicator of coronary artery disease as compared to other lipid and lipoproteins. This study was done to study the apo B100/apo A-I ratio in type 2 diabetes mellitus.

Methods: Fasting plasma glucose (FPG), glycated hemoglobin (HbA1c), extended lipid profile (total cholesterol (TC), triglyceride (TG), HDL, apoA-I and apoB100) were estimated in 34 non diabetic controls and 37 diabetic cases.The cases were further subdivided into 2 groups based on their glycemic control. LDL levels were calculated by Friedewald's formula. Statistical analysis was done using SPSS software version 11.5. P value less than 0.05 was considered significant.

Results: Poorly controlled diabetic cases had significantly lower levels of HDL and apoA-I and significantly higher levels of TG. Total cholesterol, LDL and apoB-100 were comparable in both the groups. ApoB100/apoA-I ratio was significantly elevated in poorly controlled diabetic. Apo B100/apo A-I ratio showed a strong positive correlation with glycated HbA1c

Conclusion: Diabetes mellitus is associated with dyslipidemia. Strict glycemic control is capable of partially improving dyslipidmia. Apo B100/apo A-I ratio can be used as an additional parameter for assessment of risk of CAD in diabetes mellitus.

Key words: Apolipoproteins, dyslipidemia, diabetes mellitus.

INTRODUCTION

Diabetes mellitus (DM) is rapidly emerging as a major health problem. Long standing diabetes is associated with a state of chronic hyperglycemia which is responsible for various life threatening complications like retinopathy, nephropathy and atherosclerosis. Epidemiologic studies have demonstrated that diabetes mellitus is an independent risk factor for cardiovascular disease and it amplifies the effects of other common risk factors, such as smoking, hypertension and dyslipidemia[1, 2]. Hyperlipidaemia is one of the most important risk factors for coronary artery disease (CAD) which is more prevalent among adults with type 2 DM than in the general population with a four to six fold greater cardiovascular mortality. The serum lipid abnormalities in type 2 diabetes are characterized by decreased high density lipoprotein cholesterol (HDL-C) and hypertriglyceridemia, whereas total cholesterol and low density lipoprotein cholesterol (LDL-C) levels are similar to those in non-diabetic population[3, 4, 5] .

Apolipoproteins A-I and B 100 levels, which are the protein component of HDL-C and LDL-C respectively, have been described as better predictors of atherosclerotic diseases than the lipid and lipoprotein concentrations[6] . The apo B 100/apo A1 ratio represents the balance between atherogenic particles, rich in apo B 100, and the antiatherogenic ones, rich in apo A-I, and it has been shown to be a better parameter for the prediction of cardiovascular risk than the lipids, lipoproteins, and lipid ratios [7, 8]. Various studies like Quebec Cardiovascular study, Prospective Epidemiological Study of Myocardial Infarction (PRIME) study, Apolipoprotein related mortality risk (AMORIS) study have confirmed that apolipoproteins as a stronger risk factor for development of CAD [9,10,11]. Moreover, the apolipoprotein concentrations are minimally influence from biological variables when compared with lipid measurements [12]. In contrast to the large number of studies demonstrating the predictive value of the apo B100/apo A-I ratio for CAD, few studies have been done which evaluates the importance of apo B100/apo A-I ratio in predicting the risk for development of CAD in diabetes mellitus. From this point of view, this study was undertaken to study the relationship of apolipoproteins with the severity of diabetes mellitus and also to establish whether apo B100/ apo A-I ratio can be used as an marker for prediction of CAD in type 2 DM.

MATERIALS AND METHODS

Subjects

The study was carried out in type 2 diabetes mellitus patients attending the Kasturba Hospital, Manipal. The study included a total of 71 subjects out of which 34 were healthy non diabetic controls (FPG less than 126 mg/dL) and 37 were diabetic cases (FPG <126 mg%/dL). In order to study the effect of uncontrolled diabetes on the lipid profile, the diabetic patients were further sub divided into two groups. Group I had 17 patients with a glycated haemoglobin (HbA1c) level up to 8% of total haemoglobin (Hb). Group II had 20 uncontrolled diabetic patients with HbA1c levels of more than 8% of total Hb. Age and sex matched non diabetic controls were selected for comparison. Informed consent and ethical committee clearance was obtained for the study. Exclusion criteria included patients with complications of diabetes mellitus like retinopathy, nephropathy, patients on lipid lowering agents, smokers and hypertensive patients.

Biochemical determination

Auto analyzers were used for determination of various biochemical parameters like fasting plasma glucose levels (FPG) (Glucose oxidase-peroxidase method), glycated hemoglobin (HbA1c), total cholesterol (TC) (CHOD-PAP method), triglyceride (TG) (GPO-PAP method), HDL-C (enzymatic method), apo A-I and apo B100 (immunoturbidimetric method). LDL-C was calculated using Friedwald's formula.

Statistical analysis

Statistical analysis was done using using the statistical package for social science (SPSS) version 11.5. One way analysis of variance (ANOVA) was used to compare the mean values in the three groups followed by multiple comparison post hoc test. Pearson's correlation was applied to correlate between parameters. A p value of < 0.05 was considered statistically significant.

RESULTS

The results of the study are shown in the table 1. The poorly controlled diabetic patients showed significant alteration in the lipid profile. The changes in the total cholesterol, LDL-C and apo B100 levels between the three groups were comparable with no statistical significance. The triglyceride levels were increased in the diabetic patients. This increase was more significant between the uncontrolled diabetes and the controls ($p < 0.01$). The HDL-C ($p < 0.01$) and the apo A-I ($p < 0.001$) levels were significantly decreased in poorly controlled diabetics. The decrease in the HDL-C and apo A-I levels in group 1 but was not statistically significant. The apo B100/ apo A-I ratio was comparable between group I diabetics and the controls. However there was a significant increase in the apolipoprotein ratio in poorly controlled group II diabetics which was statistically significant (p value <0.001) (Figure 1). As expected our study showed significant relation between apolipoproteins and their corresponding lipoproteins (Figure 2 and 3). Apo B100/apo A-I ratio showed a strong positive correlation with HbA1c ($r = 579$, $p < 0.001$) (Figure 4)

TABLE 1: FPG, Gly Hb, Fasting lipid profile, apo B100, apo A-I and apo B100/apo A-I ratio in controls and diabetic cases with the mean ± standard deviation

	Controls (n = 34)	*Cases*	
		Group I (n = 17)	*Group II(n = 20)*
FPG (mg %)	96.68 ± 13.7	149.12 ± 18.32	247 ± 72.25
Gly Hb (% of Hb)	5.97 ± 0.90	7.54 ± 0.53	10.39 ± 1.72
Triglyceride (mg %)	131.71 ±72.99	173.41 ± 79.52	238.15 ± 160.52**
Total Cholesterol (mg %)	184.18 ± 46.90	169.82 ± 43.79	184.45 ± 43.95
HDL (mg %)	45.00 ± 14.09	37.35 ± 11.57	31.85 ± 10.10 *
LDL (mg %)	112.34 ± 38.3	97.79 ± 39.49	104.97 ± 41.56
Apolipoprotein-A1	135.42 ± 31.72	122.79 ±= 30.93	97.47 ± 34.41**
Apolipoprotein-B100	82.05 ± 23.59	78.02 ± 25.36	80.83 ± 22.17
Apo B100/Apo A-I ratio	0.629 ± 0.205	0.662 ± 0.234	1.085 ± 1.003**

p value: * <0.01, ** < 0.001

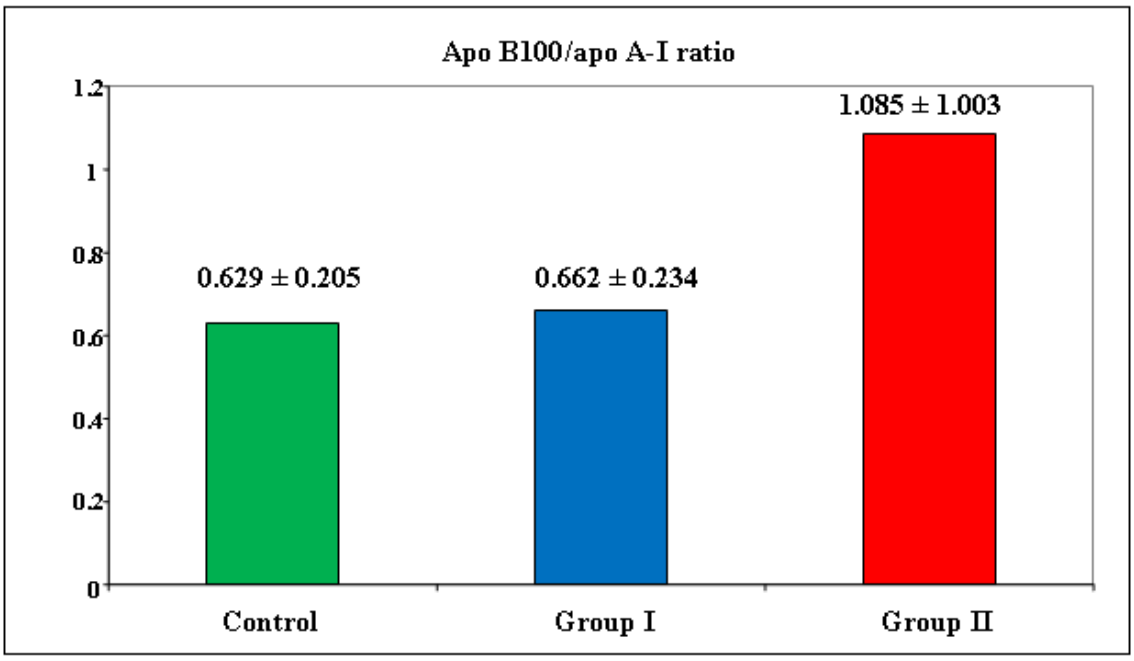

Figure 1: Graph depicting comparative significance of apo B100/apo A-I ratio between the normal controls and diabetic cases.

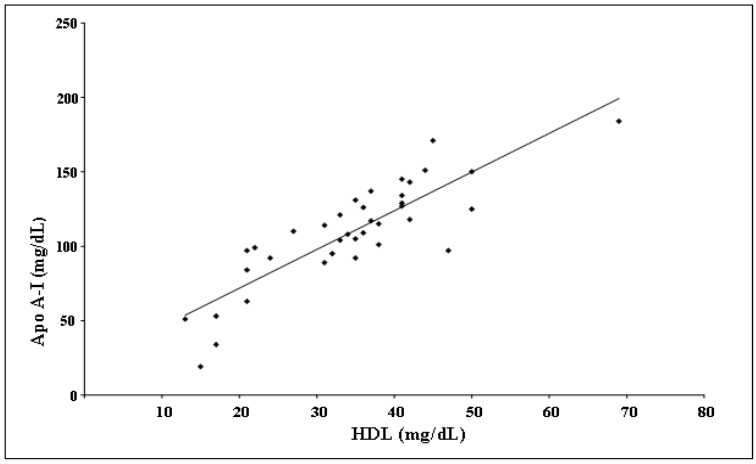

Figure 2: Correlation between Apo A-I and HDL (r = 0.854, p < 0.001)

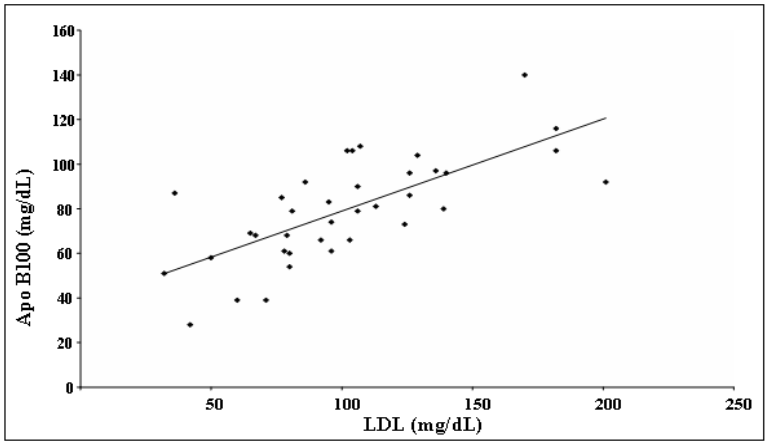

Figure 3: Correlation between apo B100 and LDL (r = 0.712, p < 0.001)

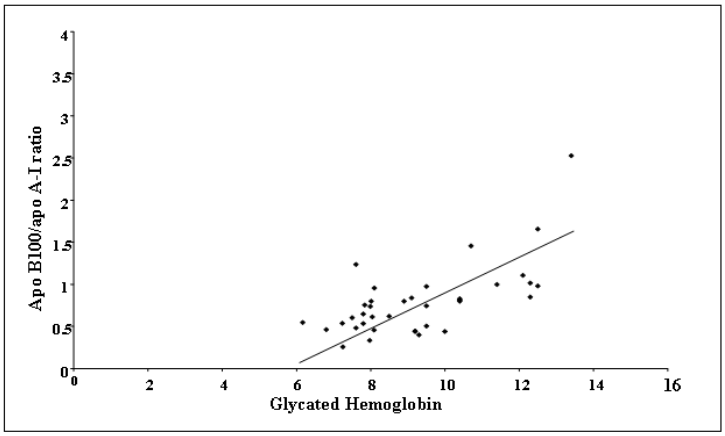

Figure 4: Correlation between Glycated Hemoglobin and Apo-B100/Apo A-I (r = 0.579, p < 0.01)

DISCUSSION AND CONCLUSION

Glucose and fatty acids are the two major fuels in the body. Disorder involving one is associated with altered metabolism of the other. Diabetes is associated with altered glucose metabolism and dyslipidemia. The most characteristic feature of diabetic dyslipidemia is hypertriglyceridemia characterized by increase in VLDL and chylomicronemia depending upon the glycemic control [4, 13]. This study was in accordance and showed the diabetic cases having hypertriglyceridemia. Well controlled diabetics had a lesser increase in their triglyceride levels as compared to poorly controlled diabetics. This proves that with good control of plasma glucose levels, triglyceride levels starts returning to normal. In this study special reference is given to Apo A-I and Apo B100 which are the major protein components of HDL and LDL respectively. A significant decrease in apo A-I and HDL-C level were observed in poorly controlled diabetic group compared to well controlled diabetic group. This suggests that though the apo A-I and HDL-C levels were significantly reduced in diabetics, improvement of glycemic control raises the Apo A-I and the HDL-C levels. However it was also observed that decrease in apo A-I levels was more significant than the decrease in HDL level. The decrease in HDL and Apo-A1 is due to impaired VLDL lipolysis, increased activity of hepatic lipase which increases the rate of HDL-C clearance and altered composition of HDL-C which includes non enzymatic glycosylation[13].

Diabetes mellitus affects the LDL metabolism by two opposing phenomenon. It decreases the LDL clearance to increase LDL levels and also directly removes the VLDL apo B to lower the LDL levels. The resultant concentration thus depends upon the relative magnitude of these two processes [13]. In this study, both the LDL-C and the apo-B100 levels in diabetic were comparable to those of controls. Apo B100/apo A-I ratio was significantly increased in group II diabetic cases. No difference in the apo B100/apo A-I ratio was seen between controls and well controlled diabetic. Therefore it can be assumed that diabetic patients who are under treatment and with well controlled plasma glucose levels, tends to show less chances of developing dyslipidemia. As in this case, in well controlled diabetic group, though the fasting plasma glucose was maintained at a higher level than the normal range, their apo B100/apo A-I ratio was almost same as those of controls. Therefore we can conlude that with increasing plasma glucose concentration the diabetics are at higher risk for developing CAD. The apoB100/apo A-I ratio showed a significance correlation with glycated hemoglobin indicating the adverse effect of prolonged hyperglycemia on the apolipoproteins. The use of these markers may be the next natural step in assessing the patient risk, and would represent an alternative to conventional lipid markers. However a large scale study and a long term follow up may be helpful to further evaluate the prognostic significance of apo B100/ apo A-I ratio in risk development of CAD in type 2 diabetes mellitus patients.

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