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Original research article

LIPID INDICES IN TYPEII DIABETES MELLITUS AND THEIR ASSOCIATION WITH MACRO AND MICRO VASCULAR COMPLICATIONS

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ABSTRACT

Background: Type II Diabetes Mellitus patients can develop complications over a prolonged period of time. The alterations in lipid indices can be associated with these complications. **Aims**:To identify changes in lipid metabolism in type 2 DM in context with the glycemic status, its relative impact on the macro & micro vascular events, and the effects of insulin therapy on the lipid indices. **Methods and Material**: 158 Type II diabetics were selected as cases and 30 subjects without any coincidental illness as controls were selected for the study. Total cholesterol, Triglyceride, HDL-C, Cholesterol/ HDL-C ratio and Atherogenic Index (AI) were estimated and the data was statistically analyzed. **Results**: Atherogenic index and CHOL/HDL-C levels were significantly higher in diabetics than in controls. Both the indices were also found to be lowered in patients on treatment with insulin. The AI in patients with complications was also significantly higher than those without complications; however CHOL/HDL-C was not significantly different. Thus using the best cutoff values AI can be used as a better indicator for complications than using the ratio of CHOL/HDL-C. **Conclusion**: AI can be used to indicate the presence of increased cardiovascular risk in patients with type II DM, and as a guide for the aggressive therapeutic approach.

Keywords: Type II DM, Lipid indices, Atherogenic index, Micro and Macro vascular complications.

INTRODUCTION

Diabetes a metabolic disorder is characterized by hyperglycemia and a predisposition to micro and macro vascular diseases[1,15,19]. In patients with diabetes atherosclerosis occurs at an earlier age and is the chief cause of mortality in them [2,14]. Diabetes leads to impaired carbohydrate metabolism in association with derangement in lipid metabolism, virtually every lipid and

lipoprotein is affected in type II DM[1]. Elevated triglycerides associated with low HDLc levels, preponderance of small dense lipoproteins and increased apolipoprotein B in diabetics is the most prevalent pattern of dyslipidemia[3,4,5,16,17,18].

Hypertriglyceridemia, decrease in HDL are independent risk factors for coronary heart disease[4,17], small dense LDLc are also atherogenic as they are more likely to form oxidized LDL and are less readily cleared. Recently rather than the concentration of cholesterol in various lipoproteins the size and composition are shown to be important in atherogenesis. However as the sub fractionation of lipoproteins by the present method cannot be undertaken in all the clinical laboratories and recently as the AIP has been shown to correlate with the size and composition of lipoproteins[3,18]; Hence in the present study we observed the lipid profile and AIP and CHOL/HDL ratio, in type II diabetic patients in context with glycemic status and its relation to macro and micro vascular events and effects of insulin therapy on lipid indices.

MATERIALS &METHODS

After permission from the Institutional Ethical Committee, Total 178 subjects in between 30-80 yrs age were selected for the present study. 148 known diabetics on regular treatment as cases and 30 healthy subjects without any coincidental illness as controls. Patients with a history of smoking and alcoholism were excluded from the study; Cases were divided based on the level of glycemic control into HBA1c < 7 as good control (group I n=46), HBA1c 7-8 fair control (group II n=50) and HBA1c > 8 as poor control (group III n=52).

The above same Cases 148 were also categorized into group 1 consist of cases who had a history of complication in the past 10 years (n=62) and group2 who never had a history of complication in the past 10 yrs (n=86), to see its relation to the study parameters

The above same 148 cases were also divided into 2 groups, group I was the cases who were on oral therapy (i.e. oral hypoglycemic) (n = 95). Group II were patients who were on insulin therapy (n = 53). After an overnight fast, peripheral venous blood samples were collected in two vaccutainers 5ml in gel vaccutainer and 2 ml in the EDTA vaccutainer. Serum separated after centrifuge; was used to analyze fasting & the post prandial blood sugar by GOD-POD method, Total cholesterol by CHOD-POD method[6], Triglycerides by GPO-PAP method and HDL-c fraction which was assayed using the cholesterol CHOD-POD method[6].

The EDTA sample was used to measure HbA1C that was determined by HPLC method. LDL was calculated from Frieldwalds formula[7], CHOL/HDL-C ratio, AIP log (TG/HDL-C) [3] was calculated in different groups. Data obtained was analyzed by SPSS statistical software (v 17.0); ANOVA was used to compare the 3 groups and significance was estimated using the F value in between different groups.

RESULTS

Table 1: Mean ± SD of Various Parameters in Cases and Controls

	Controls	Group I	Group II	Group III	F value	Sig
T.Chol	153.6 ± 25.16	164.7 ± 27.2	172.2 ± 22.9	178.7 ± 35.67	5.414	<.001
HDL	38.5 ± 4.39	35.6 ± 4.54	36.08 ± 3.5	34.78 ± 4.4	5.16	.002
LDL	96.4 ± 15.27	96.4 ± 20.8	96.6 ± 20.11	103.04 ± 32.6	0.83	.478
VLDL	18.6 ±0.42	32.5 ± 5.05	38.7 ± 11.24	40.93 ± 13.4	38.70	<.001
TG	93.1 ± 9.49	163.3± 25.65	194.71 ±56.8	205.3 ± 67.2	38.93	<.001
AIP	0.38 ± 0.06	0.659±0.059	0.71 ± 0.11	0.75 ± 0.1	127.14	<.001
CHOL/HDL	4.02 ± 0.85	4.59 ± 0.30	4.76 ± 0.29	5.15 ± 0.89	20.46	<.001

Table 1 shows the mean and SD of different lipid fractions, studied. The mean of total cholesterol, triglycerides, VLDL, AIP, CHOL/ HDL ratio was significantly increased in patients than controls ($p<0.001$). There was no significant increase in LDLc in patients compared to controls ($p=0.478$). Serum HDLc was significantly decreased in patients when compared to controls ($p=0.002$).

Multiple comparison ANOVA shows that Total Cholesterol was significantly higher in group III ($p=0.003$), than group I(=0.422) and group II (=0.092)compared to controls; the increase was not significant in comparison of group I with group II(0.701) and group III(0.095),and group II with group III ($p=0.784$). HDL-c was significantly decreased in group III ($p=0.002$), than group I (0.036) and group II (0.150) when compared to controls; the decrease was not significant in comparison of group I with group II (0.981) and group III (0.0740), and group II with group III ($p=0.580$). TG and VLDL was significantly higher in group III ($p=0.001$), than group I (=0. 001) and group II (=0. 001) compared to controls; and in comparison of group I with group II (=0. 031) and group III (=0. 001), and group II with group III ($p=0.001$). LDL-c was not significantly higher in patients compared with controls($p=0.7333$) and in between the groups ($p=0.717$)

ANOVA for AIP shows that AIP was significantly more in group III (<0.001), group II (<0.001), & group I (<0.001) when compared to controls; and in group III (<0.001) and group II (<0.025) compared to group I but the increase was not significant between group II and group III (0.231). The CHOL / HDL-c ratio was significantly more in group III (<0.001), group II (<0.001), & group I (<0.001) when compared to controls, and in group III compared to group I (<0.001) but the increase was not significant between group I and group II (0.700) and group II and group III (0.086).

ANOVA in relation to insulin therapy shows that total cholesterol (0.002), LDL-c (<0.001) was significantly more in patients on insulin than patients with other oral hypoglycemic (OHA), increase in total cholesterol was significant in relation to controls (<0.001) than LDL-c (0.062). There was no significant increase in HDL-c in patients on insulin compared to patients on OHA (0.702). Insulin therapy showed a significant decrease in TG (0.033), VLDL (0.031), AIP (<0.001), CHOL/HDL ratio (0.046) in patients on insulin therapy than on OHA.

ANOVA in relation to complications shows that patients with complications showed no increase in total cholesterol (0.934) & LDL-c (0.652) than patients without complications, but the increase in total cholesterol (0.019) was significantly more compared to controls, but the increase in LDL-c was not significant when compared to controls (0.633). Patients with complications showed no significant decrease in HDL than patients without complications (0.652), but the decrease was significant when compared to controls (0.006). TG and VLDL showed a significant increase in patients with complications than without complications (<0.001), and controls (<0.001). AIP was significantly more in patients with complications than without complications (<0.001), and controls (<0.001). CHOL/HDL-c ratio was not significantly different in patients with and without complications.

At the best cutoff value AIP is a much better marker in identifying complications (sensitivity 80%, specificity 70%) than CHOL/HDL-c ratio (sensitivity 50%, specificity 55%).

Table 2: **Area under the curve, sensitivity and specificity, of various lipoproteins, AIP and CHOL/HDL-c ratios; calculated from best cut off value using ROC curve.**

	COMPLICATION			INSULIN		
PARAMETER	AUC	SENSITIVITY	SPECIFICITY	AUC	SENSITIVITY	SPECIFICITY
T.CHOL	0.552	52%	56%	0.654	57%	67%
HDLC	0.531	27%	70%	0.597	35%	79%
LDL	0.603	41%	64 %	0.285	55 %	75 %
VLDL	0.747	40 %	99.94%	0.625	24 %	90 %
TG	0.747	64 %	78 %	0.625	25.6 %	87 %
AIP	0.810	80 %	69.7%	0.712	62.8%	75.7%
CHOL/HDL	0.564	50 %	55 %	0.628	61.4%	62.8%

DISCUSSION

Diabetes mellitus is the commonest metabolic disorder, a social and economic burden to the society because of the increased morbidity and mortality associated with its complications[3, 8, 9, 10].

Many markers are studied for their association in the development of diabetic complications. The most common amongst them are various lipids, lipoproteins and different ratios involving these complications[3, 8, 10]. Recently lipid particle sub fractions have also been implicated in the atherogenic process[18]. The major phenotypic feature of diabetes mellitus, the hyperglycemia is shown to be directly or indirectly associated with the pathogenesis of complications; insulin therapy is shown to be associated with decreased incidence of complications[2]. The present study was undertaken to assess the value of different markers.

All Lipoproteins are shown to be affected in diabetes mellitus. The most prevalent pattern being increased TG, decreased HDL-c with an increase in the LDL-c[3,4,5,16,17,18], present study confirms the changes in TG and HDL-c, but the increase in LDL-c was not significant and not to the extent of TG, this can be expected as TG is most affected lipid component, increase in TG level may lead to increase in LDL-c and cholesterol[10] . The abundance of free fatty acids appears to play an important role in the pathogenesis of low HDL in DM. In liver free unsaturated fatty acid stimulate the TG synthesis and VLDL production. Low HDL and increased TG are also markers of beta cell toxic metabolic situation and beta cell failure[11,16,18].

Hyperlipidemia is associated with hyperglycemia and glycemic control reduces the risk for all complications from DM. Good glycemic control requires a continual combination of proper diet, daily physical activity, and usually antiglycemic drug therapy[9]. Poor control of blood glucose levels impairs endogenous insulin production, resulting in a vicious cycle, that affects both the carbohydrate and lipid metabolisms in patients with diabetes[2, 9]. Hyperglycemia is shown to induce similar intracellular signals in endothelial cells as hyperlipidemia[3].

In the present study we observed significantly higher total cholesterol, TG, VLDL and significantly lower HDL-c in poor diabetics compared to controls, however TC, HDL-c, are not significantly different in different grades of glycemic status. TG and the TG associated ratio paralleled glycemic status.

In the present study we observed significantly lower TG, VLDL and ratios in diabetics on insulin compared to other modes of treatment. However total cholesterol and LDL-c is significantly higher in patients on insulin therapy with no significant increase in HDL-c. Insulin treatment was shown to be associated with improvement in

dyslipidemia of DM. Insulin therapy increases the expression of Apo A1 gene and inhibits the production of VLDL[12].

Various lipid and lipoprotein fractions are shown to be associated with diabetic complications[2,13,14,18]. In the present study we found a significantly higher concentration of total cholesterol, TG, VLDL and AIP, and Lower HDL-c in patients with complications. However LDL-c and Chol/HDL-c ratios are not significantly different.

To assess the significance of these various markers the best cutoff values were calculated using ROC analysis. The AIP is the only indicator which showed significant sensitivity and specificity in identifying diabetic complications, TG is the next relatively better marker. All other markers showed poor sensitivity.

CONCLUSION

The present study confirms that the abnormalities in TG and VLDL are more prominent than Cholesterol and LDL in patients with diabetes and HDL is a better indicator of lipid abnormalities than total cholesterol and LDL.

AIP is a good marker in identifying complications associated with diabetes, and is better correlated with glycemic status in diabetics on insulin therapy. And as AIP can easily be calculated from routine lipid investigations, AIP can be routinely be used as a marker for prediction of complications.

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