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LIPID CHANGES IN PATIENTS WITH TYPE II DIABETES MELLITUS AND THEIR RELATION WITH MICRO AND MACRO VASCULAR COMPLICATIONS

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Abstract:
Background: *Patients with type II diabetes may develop complications over a longer period of time. These complications may be related to changes in lipid markers.*
Aims: *To identify changes in lipid metabolism in type 2 diabetes in the context of glycemic status, its relative impact on macro and microvascular events, and the effect of insulin therapy on lipid indexes.*
Place and Duration: *In the Medicine Unit-II of Jinnah Hospital Lahore for one-year duration from March 2019 to March 2020.*
Methods and material: *158 patients with type II diabetes and 30 patients without coincidental illness were selected as a control group for the study. Total cholesterol, triglycerides, HDL-C, Cholesterol / HDL-C ratio, and atherogenic index (AI) were estimated, and the data were statistically analyzed.*
Results: *The atherogenic index and CHOL / HDL-C levels were significantly higher in diabetics than in the control group. It was also found that both indices were lowered in patients treated with insulin. The AI of patients with complications was also significantly higher than those of patients without complications; however, CHOL / HDL-C was not significantly different. Therefore, using the best AI cut-off values can be used as a better complication rate than the CHOL / HDL-C ratio.*
Conclusion: *AI may be used to indicate the presence of increased cardiovascular risk in patients with DM type II and as a guide to an aggressive therapeutic approach.*
Key words: *type II diabetes mellitus, lipid indices, atherosclerotic index, micro and macrovascular complications.*

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INTRODUCTION:

Diabetes mellitus, a metabolic disorder, is characterized by hyperglycemia and a predisposition to micro- and macrovascular diseases. In diabetic patients, atherosclerosis occurs at an earlier age and is the leading cause of mortality in them[1-2]. Diabetes mellitus leads to impaired carbohydrate metabolism in combination with impaired lipid metabolism, virtually every lipid and lipoprotein is affected by Type II DM disease[3-4]. Elevated triglycerides associated with low HDLc levels, the predominance of small dense lipoproteins, and increased apolipoprotein B in diabetics are the most common patterns of dyslipidemia. Hypertriglyceridemia, a decrease in HDL are independent risk factors for coronary heart disease, small dense LDLs are also atherogenic because they form oxidized LDL more often and are less well removed. Recently, it has been shown that, rather than cholesterol concentration in various lipoproteins, size and composition are important in atherosclerosis[5-6]. TG and TG-related ratio corresponded to glycemic status. In this study, we observed significantly lower rates of TG, VLDL, and rates in diabetics taking insulin compared to other treatments. However, total cholesterol and LDL-c are significantly higher in insulin-treated patients without a significant increase in HDL-c. Insulin treatment has been shown to improve diabetes-related dyslipidaemia. Insulin therapy increases the expression of the Apo A1 gene and inhibits the production of VLDL. Various fractions of lipids and lipoproteins have been shown to be associated with diabetes complications. In this study, we found significantly higher levels of total cholesterol, TG, VLDL and AIP, and lower HDL-c in patients with complications. However, the LDL-c and Chol / HDL-c ratios are not significantly different. To assess the importance of these different markers, the best cut-off values were calculated by ROC analysis. AIP is the only indicator that has shown significant sensitivity and specificity in identifying diabetic complications, and TG is another relatively better marker. All other markers showed poor sensitivity. However, since sub fractionation of lipoproteins by the present method cannot be performed in all clinical laboratories, AIP has recently been shown to correlate with lipoprotein size and composition; Therefore, in this study, we observed the lipid profile and the AIP and CHOL / HDL ratio in patients with type II diabetes in the context of glycemic status and its relationship with macro and microvascular events and the effect of insulin therapy on lipid indices.

MATERIALS AND METHODS:

This study was held in the Medicine Unit-II of Jinnah Hospital Lahore for one-year duration from March 2019 to March 2020. After obtaining the approval of the Institutional Ethics Committee, a total of 178 people aged 30 to 80 were selected for this study. 148 known diabetics treated regularly as cases and 30 healthy volunteers without any accidental disease as controls. Patients with a history of smoking and alcoholism were excluded from the study; Cases were classified according to the level of glycemic control with HBA1c <7 as good control (group I n = 46), HBA1c 7-8 sufficient control (group II n = 50), and HBA1c> 8 as poor control (group III n = 52). The same 148 cases were also classified into Group 1, which included those who had complications in the last 10 years (n = 62) and Group 2 who had never had complications in the last 10 years (n = 86), to see its relationship with the study parameters. The same 148 cases were also divided into 2 groups, group I were people who were on oral therapy (ie oral hypoglycemia) (n = 95). Group II includes patients treated with insulin (n = 53). After an overnight fast, peripheral venous blood samples were collected in two vacutainers of 5 ml in vacutainer gel and 2 ml in EDTA vacutainer. Serum separated after centrifugation; was used for the analysis of fasting and postprandial blood sugar by GOD-POD method, total cholesterol by CHOD-POD method, triglycerides by GPO-PAP method and HDL-c fraction determined by CHOD-POD cholesterol method. The EDTA sample was used for the measurement of HbA1C which was determined by HPLC. LDL was calculated from the Friedl walds formula, CHOL / HDL-C ratio, log AIP (TG / HDL-C) 3 was calculated in the different groups. The obtained data were analyzed with the SPSS statistical software (version 17.0); ANOVA was used to compare the 3 groups, and significance was estimated using F values between the different groups.

RESULTS:

Table 1 shows the mean and SD of the various lipid fractions tested. The mean ratio of total cholesterol, triglycerides, VLDL, AIP, CHOL / HDL was significantly higher in the patients than in the control group ($p < 0.001$). There was no significant increase in LDLc in patients compared to the control group ($p = 0.478$). Serum HDLc was significantly reduced in patients compared to the control group ($p = 0.002$). The multiple ANOVA comparison shows that total cholesterol was significantly higher in group III ($p = 0.003$) than in group I (= 0.422) and group II (= 0.092) compared to the control group; the increase was not significant compared to 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 reduced in group III ($p = 0.002$) than in group I (0.036) and group II (0.150) compared to the control group; the decrease was not significant in

comparison between group I and group II (0.981) and group III (0.0740) and group II and group III (p = 0.580).

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

TG and VLDL were significantly higher in group III (p = 0.001) than in group I (= 0.001) and group II (= 0.001) compared to the control group; 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 to the control group (p = 0.7333) and between groups (p = 0.717). ANOVA for AIP shows that AIP was significantly greater in Group III (less than 0.001), Group II (less than 0.001) compared to controls; and in Group III (less than 0.001) and Group II (less than 0.025) compared to Group I, but the increase was not significant between Groups II and III (0.231). The CHOL / HDL-c ratio was significantly greater in Group III (less than 0.001), Group II (less than 0.001) and Group I (less than 0.001) compared to the control group, and in Group III compared to Group I (less than 0.001). 0.001), but the increase was not significant between groups I and II (0.700) and groups II and III (0.086).

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%

ANOVA with respect to insulin therapy shows that total cholesterol (0.002), LDL-c (less than 0.001) was significantly higher in patients treated with insulin than in patients with other oral hypoglycemia (OHA), the increase in total cholesterol was significant compared to the control group (less than 0.001) than LDL-c (0.062). There was no significant increase in HDL-c in insulin-treated patients compared to OHA-treated patients (0.702). Insulin therapy showed a significant reduction in TG (0.033), VLDL (0.031), AIP (less than 0.001), CHOL / HDL ratio (0.046) in patients treated with insulin than on OHA. The complication ANOVA shows that the patients with complications did not show an increase in total cholesterol (0.934) and LDL-c (0.652) than the patients without complications, but the increase in total cholesterol (0.019) was significantly greater compared to the control group, but the increase in LDL-c was not significant compared to the control group (0.633). Complicated patients did not show a significant decrease in HDL than patients without complications (0.652), but the decrease was significant compared to the control group (0.006).

TG and VLDL showed a significant increase in patients with complications than without complications (less than 0.001) and controls (less than 0.001). The AIP was significantly greater in patients with complications than without complications (less than 0.001) and in controls (less than 0.001). The CHOL / HDL-c ratio did not differ significantly in patients with and without complications. At the best cut-off value, AIP is a much better marker for the identification of complications (sensitivity 80%, specificity 70%) than the CHOL / HDL-c ratio (sensitivity 50%, specificity 55%).

DISCUSSION:

Diabetes mellitus is the most common metabolic disorder, a social and economic burden to society due to the increased morbidity and mortality associated with its complications. Many markers are being studied for their association in the development of diabetic complications. The most common of these are different lipids, lipoproteins, and different ratios covering these complications[9-10]. Recently, subfractions of lipid particles are also involved in the atherogenic process. The main phenotype of diabetes mellitus, hyperglycemia, has been shown to be directly or indirectly related to the pathogenesis of complications; It has been shown that insulin therapy is associated with a reduction in the incidence of complications[11-12]. This study was undertaken to evaluate the value of various markers. Diabetes has been shown to affect all lipoproteins. The most common pattern of increasing TG, lowering HDL-c with increase in the current study, LDL-c confirms the changes in TG and HDL-c, but the increase in LDL-c was not significant and not in the TG range, to be expected as TG is the lipid component most affected by TG, an increase in TG levels can lead to an increase in LDL-c and cholesterol. Free fatty acid abundance appears to play an important role in the pathogenesis of low HDL in DM[13-14]. In the liver, free unsaturated fatty acids stimulate the synthesis of TG and the production of VLDL. Low HDL and elevated TG are also markers of the toxic metabolic situation of beta cells and beta cell failure. Hyperlipidemia is associated with hyperglycemia, and glycemic control reduces the risk of all complications of DM. Good glycemic control requires the continued combination of a proper diet, daily exercise, and usually anti-glycemic medications. Poor blood glucose control impairs endogenous insulin production, causing a vicious cycle that affects both carbohydrate and lipid metabolism in diabetic patients. Hyperglycemia has been shown to induce similar intracellular signals in endothelial cells as hyperlipidemia. In this study, we observed significantly higher levels of total cholesterol, TG, VLDL, and significantly lower levels of HDL-c in diabetic patients compared to controls, but TC and HDL-c did not differ significantly in different glycemic levels[15].

CONCLUSION:

The present study confirms that TG and VLDL abnormalities are more prominent than cholesterol and LDL in diabetic patients, and HDL is a better marker of lipid abnormalities than total and LDL cholesterol. AIP is a good marker for identifying complications associated with diabetes and is better correlated with the glycemic status of diabetics treated with insulin. And because AIP can be easily calculated from routine lipid testing, AIP can be routinely used as a marker for predicting complications.

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