
The Pattern of Lipid Profile in Type 2 Diabetes Mellitus with Microalbuminuria

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Abstract:

Objectives: This study is designed to show the pattern of lipid profile in type 2 diabetes with microalbuminuria and without any evidence of cardiovascular disease.

Setting: Department of Pharmacology, College of Medicine, Al-Mustansiriya University, Baghdad- Iraq.

Design: A pilot, clinical and biochemical screening study.

Main outcome measures: 24 hour urinary albumin excretion, Electrocardiography and plasma TG, HDL, LDL, and VLDL.

Results: Diabetics with microalbuminuria were presented in this study without any clinical evidence of ischemic heart disease. Echocardiographic study showed significant alterations in left ventricular diameter in diabetics as compared with controls. However, the lipid profiles significantly differ in diabetics from that of controls. Multivariate correlation of lipid variables showed insignificant differences. However, lipid profile ratios tended to be significantly differ in diabetics from that in controls. Conclusion: Microalbuminuric diabetic patients showed disturbances in lipid metabolism to be involved all related variables without clinical evidence of ischemic heart disease

Key words: Type 2 diabetes, Microalbuminurea, Lipid profile

Introduction

Diabetes Mellitus(DM) is the fourth most common cause of death in USA ^[1]. The overall prevalence of (DM) approaches 8% of adult population of the USA and most of Europe ^[2].The most prevalent form of D.M. is type 2 (approximately 90% of diabetic patients) ^[3]. Type 2 diabetes is a chronic disease ,usually has a slow onset and it is associated or complicated with micro- and macro-vascular diseases ^[3].In addition diabetic dyslipidemia occurs more frequently in type 2 diabetes ^[4], since insulin has a major regulatory role in lipid and lipoprotein metabolism. Moreover, type 2 diabetic patients with albuminuria are 26 years more advanced in the atherosclerotic process {as assessed by intima-media thickness index} than non-diabetic population ^[5]. Type 2 diabetics usually present with concomitant elevation in plasma Triglyceride, very low-density lipoprotein, and small-dense low-density lipoprotein, and reduction in High-density lipoprotein ^[6].while the concentration of serum cholesterol and Low-density lipoprotein are similar or slightly lower than those of non-diabetic individuals {especially in those with good or fair glycemic control}.

This study was designed to show the pattern of lipid profile in type 2 diabetes with micro-albuminuria and with out of any evidence of cardiovascular disease.

Patients & methods:

This study was conducted at Department of Pharmacology, College of Medicine, Al-Mustansiriya University. The study samples included 30 male patients and 20 healthy male individuals referred by physicians during an 18-months period, (June, 1998 – Dec., 1999). All

patients included in the current study had the diagnosis of non-insulin dependent diabetes mellitus (type 2), with presence of complications to variable extent. None of them had cardiac disease at the onset of the study, as judged by clinical examination, and electrocardiography. Patients undergone a thorough physical examination and testing for the presence of microalbuminuria (>20 and <200 microgram/minute) ^[7]. Patients who had urinary albumin excretion <20 and >200 microgram/minute were excluded from the study.

Healthy subjects, all were normal on routine laboratory tests and medical examinations.

The anthropometric measures including the height (to the nearest centimeter), & weight (to the nearest Kilogram). Then the body mass index (BMI) was calculated by using Queller's equation ($BMI = \text{Weight (kg)} / \text{Height}^2 (\text{m}^2)$). The other measurements were waist circumference which was taken midway between the inferior margin of the last rib and the crest of the ilium in a horizontal plane and the hip circumference was measured in a horizontal plane at the level of maximal extension of buttock. Then the waist/hip ratio (WHR) as an index for central obesity was calculated.

Systemic blood pressure was measure at sitting position of the right arm after a resting period of at least five minutes on 3 occasions. The 5th phase of Kortokoff's sound was used as a cut off point of diastolic blood pressure. The mean value of the last two readings of the blood pressure was taken for each subject.

Total Urinary albumin excretion was determined by Lowry method ^[8].in which 24-hour urine collection for 2-3 occasions over 6 months period was obtained from each subject enrolled in the current study.

All subjects were asked to refrain from smoking, drinking alcoholic beverages or coffee prior to blood sampling of overnight fasting. A 5 ml of venous blood was obtained from anticubital vein for certain routine laboratory biochemical tests (including plasma nitrogen urea (PNU), plasma creatinine, and fasting plasma glucose (FPG)), and for markers of lipid metabolism (fasting plasma total cholesterol, total triglycerides, low-density lipoprotein, very low density lipoprotein and high-density lipoprotein).

Statistical analysis:

The results were presented as number, percentage, and mean + SD whenever possible. The data were analyzed by using Student's 't' test (unpaired two tailed), and correlation test taking $P < 0.05$ as the lowest limit of significance.

Results:

The characteristics of the study are shown in table 1 which shows no significant differences

($P > 0.05$) between controls and diabetics (regarding age, numbers of Smokers, number of alcohols, BMI, WHR, SBp, and DBp), but shows Significant difference ($P < 0.05$) between controls and diabetics (Regarding FBG, plasma nitrogen urea, and plasma creatinine).

Medical history of diabetic patients revealed that the median duration of diabetes was 10 years (mean \pm SD: 9.9 ± 4.96 year) and all cases were on therapeutic regimens of diet (n= 3), diet and oral hypoglycemic agents (n= 27).

Routine laboratory tests revealed that diabetics seemed to be uncontrolled as indicated by high plasma fasting glucose. Although plasma nitrogen urea and creatinine levels were significantly higher ($P < 0.05$) in diabetics than healthy individuals but still within the normal limits (Table 1).

Table 1: The characteristics of the study.

		Controls (n= 20)	Diabetics (n= 30)
Age (years) (mean \pm SD)		44.7 \pm 5.9	50.56 \pm 5.51
Smoking (No.)		10	19
Alcohol drinking (No.)		4	4
Blood Pressure (mmHg)	Systolic (mean \pm SD)	114.0 \pm 9.2	119.0 \pm 9.7
	Diastolic (mean \pm SD)	71.7 \pm 7.6	75.6 \pm 8.2
Weight (Kg)		70.77 \pm 8.12	72.05 \pm 10.68
Height (m)		1.72 \pm 0.06	1.69 \pm 0.05
Body mass index (Wt/h ²)		24.0 \pm 2.84	24.79 \pm 2.84
Waist circumference (cm)		88.08 \pm 7.56	91.26 \pm 8.12
Hip circumference (cm)		95.60 \pm 5.25	92.83 \pm 6.40
Waist/hip circumference ratio		0.916 \pm 0.067	0.978 \pm 0.044
Fasting plasma glucose (mmol/L)		4.67 \pm 0.91	11.25 \pm 3.07 **
Plasma Nitrogen urea (mmol/L)		8.169 \pm 2.041	10.046 \pm 2.135 *
Plasma creatinine (mmol/L)		61.5 \pm 12.34	73.0 \pm 13.5 *

The results are expressed as mean \pm SD of number of cases. * $P > 0.01$, ** $P < 0.001$

Microalbuminuria is demonstrated in diabetic patients (range; 31 – 95.7 $\mu\text{g}/\text{min}$) with normal renal function by the evidences of normal plasma nitrogen urea and creatinine. Microalbuminuria tended to be more frequent in diabetics who had duration of illness less than 15 years (Table 2).

The overall markers for lipid metabolism were significantly higher (for plasma total cholesterol, triglycerides low density lipoprotein, and very low density lipoprotein) and lower (for high density lipoprotein) among diabetics in comparison with controls (Table 3).

Table 2. The association of frequent microalbuminuria ($\mu\text{g}/\text{min}$) of patients with the duration of diabetes

Duration (year)	Microalbuminuria ($\mu\text{g}/\text{min}$)				Total
	30 – 39	40 – 49	50 – 59	≥ 60	
0 – 5	5	1	1	2	9
6 – 10	5	2	2	1	10
11 – 15	1	5	1	-	7
16 – 20	1	-	-	1	2
> 20	1	-	-	1	2
Total	13	8	4	5	30

Table 3: Plasma lipid profile (mmol/L) of this study.

	Controls (n= 20)	Diabetics (n= 30)
Total cholesterol	4.55 \pm 0.33	5.63 \pm 0.98 *
Triglycerides	1.43 \pm 0.55	2.61 \pm 1.05 *
High density lipoprotein (HDL)	1.45 \pm 0.43	0.92 \pm 0.47 **
Low density lipoprotein (LDL)	2.34 \pm 0.29	3.41 \pm 1.22 *
Very Low density lipoprotein (LDL)	0.286 \pm 0.11	0.522 \pm 0.21 *

The results are expressed as mean \pm SD of number of cases. * P<0.001, ** P<0.05

In addition, diabetic patients showed a significant variation in lipids ratios from controls pointed to high plasma triglycerides and low density lipoproteins and indicated that these patients were potentially at risk of cardiovascular events.(table 4).

Further analysis revealed that the duration of diabetes not correlated with ratios of cholesterol / HDL ($r=0.003$, $P= 0.9$), cholesterol / LDL ($r= -0.11$, $P= 0.5$), cholesterol / triglycerides ($r= 0.07$, $P= 0.6$), and LDL/ HDL ($r= 0.01$, $P= 0.9$).

Table 4: Results of lipid profiles ratios.

Lipids ratios	Controls (n= 20)	Diabetics (n= 30)
Cholesterol / HDL	3.26 ± 0.902	9.13 ± 8.13 ***
Cholesterol / LDL	1.950 ± 0.239	1.723 ± 0.406 *
Cholesterol / Triglycerides	3.705 ± 1.617	2.460 ± 1.104 **
LDL / HDL	1.720 ± 0.569	5.976 ± 6.312 ***

The results are expressed as mean±SD of number of cases.* P<0.02, ** P<0.01, *** P<0.001

Discussion:

Microalbuminuria It tended to be demonstrated in diabetic patients within first few years of onset of diabetes, and in this small sample study a cut-off-point of < 15 years duration of diabetes was the most frequent association of microalbuminuria, a comparable results were obtained by Rothman 1986(9).This observation may be served to use the

variable of microalbuminuria as an early diagnostic marker herald to the occurrence of complications other than diabetic nephropathy.

The positive correlation of plasma LDL-cholesterol with microalbuminuria gave a clue that this type of patients were potentially to develop IHD

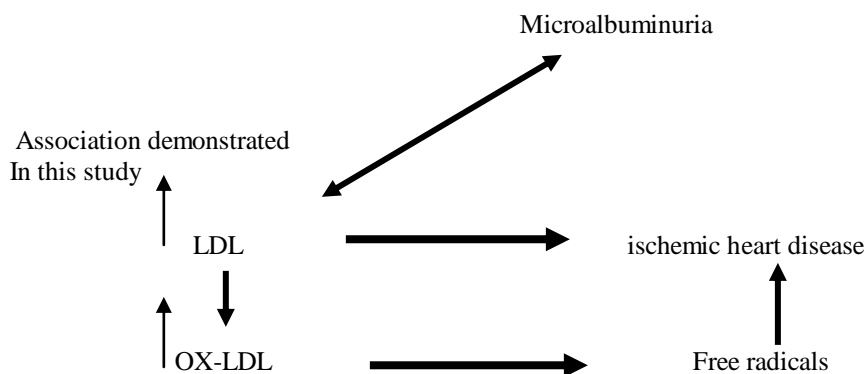


Diagram : Association of LDL with Microalbuminuria

It is important to interpret this observation not as just correlation between abnormalities in lipid profile with magnitude of microalbuminuria since the correlation was demonstrated with LDL-c, which is a precursor for generation of free radicals(10).

Regarding lipid profiles, the results reported in this study showed a significant unfavorable pattern of hypertriglyceridemia, cholesterolemia, low density lipoproteinemia, very low density lipoproteinemia and below control’s level of high density lipoproteinemia, similar observations had been reported by Okubo M. & Murase [1996] (11),and Brunzell, & Ayyobi [2003](12).

The ratio of LDL-c / HDL-c was significantly elevated in diabetics by more than three folds of controls. This association indicated that our diabetics selection was potentially at risk of IHD (13).

Conclusion:

Microalbuminuric diabetic patients showed disturbances in lipid metabolism to be involved all related variables without clinical evidence of ischemic heart disease.

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