Egypt. Acad. J. Biolog. Sci., 5(1): 107 – 112 (2013) C. Physiology & Molecular Biology
Email: egyptianacademic@yahoo.com ISSN: 2090-0767
Received: 25 / 5 / 2013 www.eajbs.eg.net

Lipoprotein (a) level and other laboratory variables in diabetic patients

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ABSTRACT

Objective: to evaluate the clinical and diagnostic significant of lp (a) levels and other lipid and apolipoprotein profiles in diabetic patients compared with different categorization of diabetic patients.

Method: Case control study determined the levels of lp (a), apolipoprotein A1, apolipoprotein B, Total Cholesterol (TC), Triglyceride (TG), Low Density Lipoprotein (LDL), High Density Lipoprotein (HDL) and fibrinogen in 100 diabetic patients with both types (40 were Insulin Dependent Diabetic Mellitus, IDDM and 60 were Non-Insulin Dependent Diabetic Mellitus NIDDM) and compared with normal healthy subjects.

Results: lp (a), apolipoprotein B, TC, TG and LDL were significantly higher in patients than control healthy subjects ($p<0.05$), apolipoprotein A1 and HDL were significantly lower in patients than control healthy subjects ($p<0.05$). No significant difference found in Fibrinogen between patients and controls. Lp (a) levels in obese patients significantly higher than in normal weight ($p<<0.05$). lp (a) in patients with Coronary Heart Disease (CHD) was significantly higher than patients without CHD ($p<0.05$). Lp (a) was significantly higher in NIDDM than in IDDM ($p<0.05$).

Conclusion: The study confirmed that the Lp (a) and other lipid and apolipoprotein parameters were significantly raised (good lipid decreased (apo A1 and HDL)) in diabetic patients compared to healthy subjects, and lp (a) are important diagnostic marker that can be used for early detection of atherosclerotic cardiovascular disease (CVD) in diabetic patients.

Keywords: Lipoprotein (a), Apolipoprotein A1, Apolipoprotein B, CHD, IDDM and NIDDM.

INTRODUCTION

Lipoprotein (a) [Lp (a)] is a plasma lipoprotein consisting of a LDL-like particle with a molecule of apolipoprotein B100 covalently linked to a very large additional glycoprotein known as apolipoprotein (a). Elevated Lp (a) levels constitute an independent risk factor for cardiovascular disease in the general population (Nordestgaard *et al.,* 2010). Apolipoprotein (a) is characterized by a high degree of genetic polymorphism, with many isoforms in plasma (Marcovina *et al.,* 1993). Lp (a) has atherogenic and thrombotic properties and is considered to be a major risk factor for the development of atherosclerotic disease. Lp (a) has been considered as an independent risk factor for atherosclerosis. Lp (a) is a variant of LDL and is similar to LDL in lipid composition (Davies *etal,* 1992). It consists of one or two molecules of apoprotein (a) [apo (a)} linked to apoprotein B-100 by a disulfide bridge (Scanu, 1992). Apo (a) is a distinctive glycoprotein of Lp (a) and is structurally homologous to plasminogen (a key protein) (Scanu, 1992), (Jurgens *et al.,* 1994) and (Ridker *et al.,* 1995) for the fibrinolytic system. Many epidemiologic and prospective studies have revealed elevated levels of Lp (a) in persons with Coronary Heart Disease (CHD) (Bostom, 1996) and (Ramirez *et al.,* 1992) suggesting the importance of Lp (a) in

the underlying mechanisms for the development of atherosclerosis in diabetics. But its may has not been determined in these subjects (Khan & Abdul Baseer, 1998). Many studies have shown that Lp (a) levels are closely associated with premature CHD (Garg, 1992). This study was conducted to evaluate the clinical and diagnostic significant of lp (a) levels and other lipid and apolipoprotein profiles in diabetic patients compared with different categorization of patients.

MATERIAL AND METHODS

Subjects: A hundred Sudanese diabetic patients (40 type1 and 60 type 2) (61 male, 39 female), a mean average age of 46±1.6year (ranged from 4 to 78 year), were visiting outpatient clinic of Jabir Abu Alizz Diabetes Centre (Khartoum, Sudan) for treatment and follow up, were enrolled in the study. The patients compared with 50 healthy subjects as a control group of non-diabetic patients randomly selected as relatives of patients and other co-patients. The objectives of this study were verified for all patients and healthy subjects to obtain their consent.

Methods: blood samples collected from a subjects (patients and control) when they were fasting, (3ml) in plain containers using disposable syringes. All blood samples were allowed to clot at room temperature and then centrifuged at 4000 R.P.M to obtain the serum. Lipemic samples were cleared by ultracentrifugation. Fibrin formation due to centrifuging of serum samples before a complete formation of clot is avoided to prevent erroneous results. Some samples particularly those from patients receiving anticoagulant therapy, required increased clotting time. Specimens of about (500-600 µl) clear serum were preserved at 2-8°C prior to processing. Glucose (immediately determined), Cholesterol, Triglyceride, HDL, and LDL were measured spectrophotometrically. Apolipoprotein A1 Apolipoprotein B and Lipoprotein (a) were determined by quantitative immunoturbidimetry method. Fibrinogen was determined in plasma spectrophotometrically. Body mass index (BMI): was calculated from standard formula (Kg/m2). Statistical analysis: the data were analyzed SPSS version 19, analysis of variance and t-test used for analysis, and Pearson correlation. The probability $P<0.05$ consider significant.

RESULTS

Age and gender were matched between groups and Anthropometrics and Biochemical Characteristics of Patients and Control Subjects reported in Table 1. According to biochemical measurements, Lp (a)showed highly significant in patients both groups of diabetes compared to control group ($p<0.01$), and also showed significant difference in NIDDM compared to IDDM ($p<0.05$) there were significant difference when compared Total Cholesterol, Triglyceride, LDL, HDL apo A1 and apo B. ($p<0.05$). Lp (a) in different categorization of patients, showed no significance when compared with gender, but showed significant different when compared in different category of BMI and according to present and absent of hypertension ($p<0.05$) .The Table 2 and. Fig. 1 explain that lp (a) was directly proportional with age. According to data obtained from Table 3, lp (a) was directly correlated with FBG, LDL, and apo B significantly; and correlated inversely with HDL and apo A1 significantly ($p<0.05$), but no no significant correlation with TC and TG.

Table 1: Anthropometrics and Biochemical Characteristics of Patients and Control Subjects:

Character	**IDDM (n=40)**	**NIDDM (n=60)**	**Control (n=50)**
Age (year)	46±1.59	46±1.59	46±1.59
Gender (male, female)	(22, 18)	(39, 21)	(22, 28)
BMI	24±2.1	26±3.6	23.7±1.8
FBG	197.13±64.09*	202.23±65.19*	94.70±10.89
TC (mg/dL)	179.57±21.78*	182.80±28.56*	156.07±21.46
TG (mg/dL)	99.90±15.79*	100.53±25.58*	86.03±14.48
HDL (mg/dL)	48.87±6.92*	46.37±4.55*	59.00±4.81
LDL (mg/dL)	112.20±21.42*	113.70±21.90*	84.10±15.56
Apolipoprotein A1	119.33±13.87*	119.87±9.94*	141.30±10.21
Apolipoprotein B	118.87±13.47*	113.93±13.61*	92.23±12.9
Lp(a) (mg/dL)	30.03±7.51*	34.87±6.75**	20.27±6.51
Fibrinogen (g/L)	2.1±0.11	2.2±0.16	2.0±0.11

- n: number. * significant compare to control. ** significant compare to IDDM.
- The table shows the data as Mean±SD
- P-value ≤ 0.05 is considered significant

Table 2: Lp (a) level according to genders, BMI andpresent or absent of CHD in diabetic patients:

Model	**Lp(a) level (mg/dL)**
Gender:	
Male	32.3±5.4
Female	32.8±6.3
BMI:	
Normal weight	26.2±4.5
Overweight	27.7±3.9
Obese	33.5±8.6 [a]
CHD:	
With CHD	24.8±6.2
Without CHD	36.9±9.5 [b]

- The table shows the data as Mean±SD
- BMI: Body Mass Index. CHD: Coronary Heart Disease.
- [a:] significant compared to normal weight. [b:] significant compared to patients without CHD.

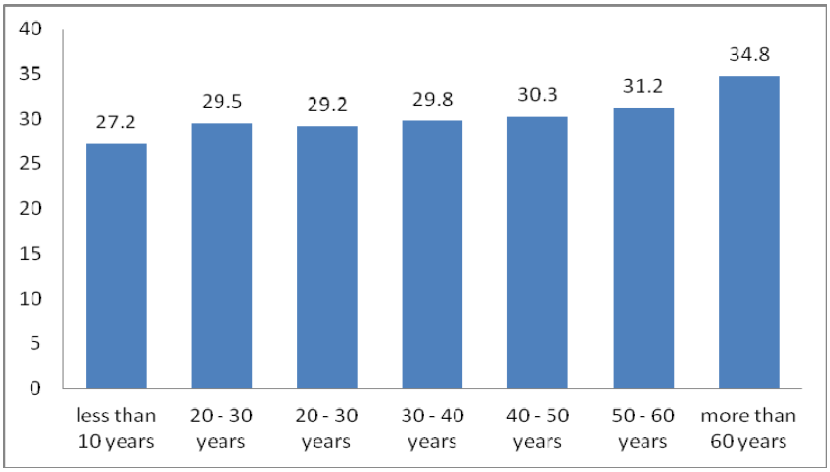

Fig. 1: Lp (a) mean levels in different age groups of patients

Table 3: Pearson correlation between Lp(a) and different biochemical variables in diabetic patients both types:

Variable	R	P value
FBG	0.47	<0.01**
TC	0.12	0.078
TG	0.10	0.120
LDL	0.23	0.037*
HDL	-0.25	0.016*
Apo A1	-0.36	<0.01**
Apo B	0.31	<0.01**

* Significant at p≤0.05.
** Significant at p≤0.01.

DISCUSSION

The major finding of the present study revealed increased level of Lp (a) in patients with diabetes mellitus compared with a healthy subjects; this finding agree with Ramirez *et al.,* 1992 and Khan *etal*.1998 Both reported that uncontrolled diabetes have high Lp (a) level, also suggested that metabolic abnormality contributes to the elevated coronary risk in diabetic subjects. But Taupin *et al.,* 1993 found no difference in Lp (a) concentrations between diabetics and non-diabetic subjects. Haffner *et al.,* 1992 reported slightly lower Lp (a) concentrations in diabetic patients than in non-diabetic subjects, but there was no statistical significance whereas Morishita *et al.*, 1996 showed significantly elevated levels of Lp (a) in patients with NIDDM. In the present study the level of lipid and apolipoprotein profiles, TC, TG LDL and Apo B showed significant increased in diabetic patients compared to control group. And significant decreased in the levels of both HDL and Apo A1 in diabetes compared to healthy subjects; no different in fibrinogen level in patients and controls. According to types of diabetes no significant different except in lp (a) level, which it was higher in DM1 compared to DM2. Khan *et al.,* 1998 agree with our finding, but he found no significant different between IDDM and NIDDM in lp (a) level. Alaupovic *et al.,* reported significantly high concentrations of triglycerides but normal levels of total cholesterol in diabetic patients in comparison with normal control subjects. Our data showed significant increased in Lp (a) level according to BMI in obese subjects compared to normal weight individuals, Tseng, 2004 disagree with this finding. Also according to the patients with CHD Lp (a) level showed significant increased. This agrees with Ramirez *et al., 1992* and Bostom *et al.,* 1996. Lp (a) showed proportion association with the age of patients in this study, this disagree with Boronat *et al.*, 2012. The elevated cardiovascular risk of diabetic patients is only partially explained by the presence of conventional cardiovascular risk factors, such as glycemic control, lipid abnormalities, hypertension and visceral obesity. This has suggested that additional risk factors, such as genetic risk factors, may favor the increased cardiovascular morbidity and mortality observed in diabetic patients (Nathan *et al.,* 2005) Among the genetic risk factors, Lp (a) and apo (a) polymorphism has been evaluated. As the process of atherosclerosis starts in childhood, the risk factors should be assessed and prevention of atherosclerosis should start in childhood (Buscaglia *et al.,* 1995) and (Gazzaruso *et al.,* 1996). Diabetes, the most common non-communicable disease in Sudan, is having an increasing impact on rates of morbidity and mortality. The spread of sedentary lifestyles and adoption of western Dietary habits-high in refined carbohydrates and fat – are driving an increase in the number of people with

obesity-related type 2 diabetes (Ahmed & Ahmed, 2001). Physician at primary health care should be motivated to identify the problem and implement necessary remedial and preventive measures focusing on weight control, controlling dyslipidemia and diabetes.

CONCLUSIONS

The study confirmed that the Lp (a) and other lipid and apolipoprotein parameters were significantly raised in diabetic patients compared to healthy subjects, and Lp (a) are important diagnostic marker that can be used for early detection of atherosclerotic cardiovascular disease (CVD) in diabetic patients.

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ARABIC SUMMARY

مستوي البروتين الدهني (a) وبعض المتغيرات المعملية عند مرضى السكر

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المقدمة:
الهدف: تقييم الاهمية الطبية لقياس مستوي البروتين الدهني (a) ومستويات البروتينات الدهنية والدهون عند مرضى السكر وقارنة القياسات بفئات مختلفة عند المرضى.
طرق القياس: دراسة مقارنة بين مرضى ومجموعة ضابطة تم فيها قياس مستويات كل من البورتين الدهني (a) ، البروتين الدهني A1 ، البروتين الدهني B ، مجموع الكوليسترول ، الدهون الثلاثية ، البروتين الدهني منخفض الكثافة ، البروتين الدهني مرتفع الكثافة والفبرينوجين في 100 من المرضى (40 من النوع الاول و 60 من النوع الثاني) وقورنت النتائج بمجموعة ضابطة تضم 50 شخص اصحاء.
النتائج: اوضحت النتائج زيادة ذات دلالة احصائية في مستويات كل من البروتين الدهني (a) ، مجموع الكوليسترول ، الدهون الثلاثية ، البروتين الدهني B والبروتين الدهني منخفض الكثافة عند المرضى مقارنة بالاصحاء ، وفي المقابل يوجد انخفاض ذو دلالة احصائية عند المرضى مقارنة بالاصحاء في مستوى كل من البروتين الدهني A1 و البروتين الدهني مرتفع الكثافة. لايوجد فرق مهم بين مستوى الفبرينوجين بين المرضى والاصحاء. مستوى البروتين الدهني (a) يزيد بدلالة احصائية عند المرضي ذوي السمنة المفرطة وعند المرضى الذين ظهرت لديهم امراض شرايين القلب ، وعند المرضى من النوع الثاني مقارنة بالنوع الاول.
الخلاصة: خلصت الدراسة لان مستوى البروتين الدهني (a) ومستويات الدهون البروتينية والدهون مرتفعة (الدهون الحميدة منخفضة) عند مرضى السكر مقارنة بالاصحاء ، وان البروتين الدهني (a) وؤشر مهم في تشخيص امراض القلب وتصلب الشرايين عند مرضى السكر.