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Original Article

Lipoprotein (a) in Sudanese diabetic patients correlated with glycosylated heamoglobin

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ABSTRACT

Background: Diabetes mellitus (DM) is the most common endocrine-metabolic disorder in children and adolescents. It is characterized by high incidence of cardiovascular disease (CVD). The cause of increased risk of CVD in diabetes is multi-factorial, important factors include dyslipidaemia and poor glycaemic control. Problem: The Sudanese diabetic patients may have high frequency of dyslipidaemia, which may contribute significantly to accelerated coronary atherosclerosis. Aim: This study aim is correlation of lipid profile with glycosylated haemoglobin (HbA1C) in Sudanese diabetic patients. Materials and methods: In this cross-sectional study, the lipid profile and HbA1C levels of 219 Sudanese diabetic patients were diagnosed after informed or verbal consent. Enzymatic methods and chromatographic technique were applied to measure lipid profile and HbA1C, respectively. Results and Discussion: All Sudanese diabetic patients participated in this study had a lipoprotein (a) Lp (a) concentrations >30mg/dl, this level exceeded the cut-off value of Lp (a). However, Lp (a) concentration at the level ≥ 100mg/dl represent 33.3% of the total diabetic cases. This indicates a high risk for those patients. Greater than 40% of diabetic patients were having HbA1C level >9.0%, hence they were at increased risk of cardiovascular complications, because they were considered having poor glycaemic control. Lp (a) seen to be a determinant risk factor of all diabetic patients. Diabetic patients under study were at poor glycaemic control. Addition of Lp (a) to the routine lipid profile to assess cardiovascular risk in diabetic patients may enhance management of diabetes mellitus.

1. Introduction

Diabetes mellitus (DM) is a significant worldwide health burden with a growing prevalence globally (1, 2, 3). It is an endocrine disorder that affects over a 100 million people all over the world and it has reached an epidemic status (4, 5). The prevalence of DM is increasing at alarming rate (6, 7, 8). It is expected that more than one billion people will suffer from DM by the end of 21st century (9, 10).

DM is an independent risk factor for cardiovascular disease (CVD). It is characterized by high incidence of CVD (11, 12). Nearly 80% of diabetic patients die as a result of CVD. The cause of the increased risk of CVD is multi-factorial; important factors include dyslipidaemia and poor glycaemic control (13, 14).

The rate of formation of glycosylated haemoglobin (HbA1C) is directly proportional to the plasma glucose concentration. HbA1C assay, a measure of chronic glycaemia, is critical to the study of diabetic control and complications (15). The benefits of measuring HbA1C is that it gives more reasonable and stable view of what is happening concerning glycaemia over a course of time (i.e.; three months) (16).

Lipids disorders are common in patients with DM, and play crucial roles in the development of diabetic cardiovascular complications (17). Patients with diabetes have lipids abnormalities that placed them at high risk for cardiovascular and cerebrovascular events (18). Individuals with DM have an absolute risk of major coronary events similar to that of non-diabetic individuals with established coronary heart disease (CHD). After an acute coronary event, diabetic subjects develop congestive heart failure more frequently and have a higher mortality rate than non-diabetic individuals (12).

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The term dyslipidaemia is used to describe the lipids abnormalities associated with insulin resistance syndrome (19,20). These abnormalities include an elevated triglycerides, and small dense, atherogenic low-density lipoprotein (LDL-cholesterol) particles and low levels of high-density lipoprotein (HDL-cholesterol). High triglycerides and low HDL levels have a greater adverse impact on risk for vascular disease in women (19, 20).

Atherosclerosis, a chronic condition characterized by the formation of lipid-rich plaques within the walls of medium and large arteries, underlies many forms of vascular disease (21). Atherosclerosis is an inflammatory disorder that may be initiated by several factors (22). Many factors increase the risk of an individual developing severe or premature atheroma (1). Increasing evidence suggested that the postprandial state is a contributing factor to the development of atherosclerosis (11).

Lipoprotein (a) Lp(a) which was first described more than 40years ago, is an LDL-like molecule synthesized by the liver and is composed of protein, lipid, and carbohydrate (23). It is a macromolecular complex found in human plasma that combines structural elements from the lipoprotein and blood clotting systems associated with premature CHD (24). It consists of an apolipoprotein B (Apo B-100) particle attached by a disulfide bridge to apolipoprotein (a) (25, 26).

Lp (a) is involved in lipid transport (27). It is an independent risk factor for the development of CHD (28, 21, 29). Increased Lp (a) concentration is predictive for CAD, the major cause of morbidity and mortality (30, 31, 32). Compared to non-diabetic the incidence of coronary artery disease (CAD) is twice in diabetic men and four times in diabetic women (33, 34).

Problem of Study:

Cause of the increased risk of CVD in diabetes mellitus is multi-factorial. Appropriate interventions to address each of these risk factors are imperative to lower the risk of CVD in people with diabetes mellitus. Therapeutic strategies for management of diabetic patients should give equal emphasis to the control of hyperglycaemia and dyslipidaemia.

Objective of Study:

To determine the magnitude of dyslipidaemia correlated with HbA1C in Sudanese diabetic patients.

MATERIALS AND METHODS:

This research was designed as cross-sectional prospective study. Known long-term diabetic patients defined by history were considered as participated subjects in this research. Two hundred and nineteen diabetic patients from different ages and sexes were included in this study, after informed or verbal consent. Each subject of the participants was asked for his age, duration of disease, residence, smoking and hypertension and whether he or she is under medication of lowering cholesterol or not. A well designed questionnaire has been prepared for this purpose.

Normal subjects (381 persons) with no personal or family history of diabetes were examined for lipid profile and HbA1C to compare means and cut-off values with those values of diabetic patients. They were asked for age, duration of disease, residence, smoking and hypertension and any medication. In this cross-sectional study, the lipid profile, HbA1C and lipoprotein levels of the diabetic patients, male and female were measured, after informed or verbal consent. Results were compared with those of healthy controls, male and female. Venous blood samples sufficient for analysis of HbA1C and lipid profile were obtained from the diabetic patients and control. Serum samples were obtained after 12 hours in fasting for measurement of lipid profile. All parameters were analyzed using commercially available test methods. Test kits (chemical and enzymatic methods) were purchased from Human Gesellschaft for Biochemica and diagnostica mbH, Germany, to test lipid profile. Column chromatographic spectrophotometric ion-exchange method was obtained from Cypress Diagnostic, Belgium to examined HbA1C.

Statistical analysis of data carried out using SPSS Windows version 15. Results expressed as mean, standard deviation and coefficient of variation. Differences in means were tested using the Student t-test and tests were considered significant when p values were < 0.05.

Control sera that obtained from Human Gesellschaft for Biochemica and diagnostica mbH, Germany, were applied for quality control purposes to test precession, reproducibility and accuracy of the test methods.

RESULTS

Table: 1, shows Lp (a), HbA1C, triglycerides, LDL, HDL and ApoA in the diabetic and non-diabetic subjects. Table: 2, shows differences in variables of diabetic patients among gender. Table 3, shows Lp (a) mean value of diabetic patients associated with theirs' pathological obtained values. Table 4, shows means of the obtained values of diabetic patients associated with theirs' HbA1C levels. Table 5, shows comparison of means of the obtained values of diabetic patients with Lp (a) levels. Figure 1, illustrates correlation of Lp (a) with HbA1C of diabetic patients.

There was significant correlation of Lp (a) with HbA1C ($P<0.05$) in all diabetic patient. There was significant association of Lp (a) mean value in diabetic patients with HbA1C $\geq$ 9%, ($P<0.01$). Analysis of variance (ANOVA test) to estimate the regression between Lp (a) and HbA1C was applied. The r2 and P value were (0.023) and (<0.05), respectively. Lp (a) $\geq$ 100mg/dl was significant ($P<0.01$) when compared to HbA1C $\geq$9%.

Lp (a) was correlated to LDL ($P<0.05$) and ApoB ($P<0.01$). Negative correlation was observed when Lp (a) was correlated with cholesterol, triglycerides, HDL and ApoA. This correlation was significant when Lp (a) was correlated with HDL and ApoA ($P<0.01$). Significant correlation was observed when HbA1C was correlated with cholesterol and LDL of diabetic patients ($P<0.05$). However, correlation was not significant with HDL, ApoB, ApoA and

triglycerides. Positive correlation was observed when mean of HbA1C of diabetic patients was compared with cholesterol, LDL and triglycerides. There was negative correlation between HbA1C and HDL, ApoB and ApoA means. HbA1C ≥ 9% was significantly (P<0.05) associated with cholesterol, and significantly (P<0.01) associated with LDL, HDL and triglycerides.

Table 1: Means ± standard deviations of variables

	Diabetic Patients (n=219)	Controls (n=381)
Age	55.7±12.6years	41.6± 11.14 years
Lp(a)	82.5±34.2mg/dl	16.4± 5.8 mg/dl
HbA_{1c}	10.4±4.5%	4.3± 0.7%
Cholesterol	(4.88±1.55mmol/L)	(4.11±0.82mmol/L)
Triglyceride	(2.2±0.66mmol/L)	(1.16±0.55mmol/L)
LDL	(3.1±1.76mmol/L)	(1.18±0.47mmol/L)
HDL	(1.15±0.36mmol/L)	(1.93±0.95mmol/L)
ApoB	(1.48±0.6g/L)	(1.34±0.12g/L)
ApoA	(1.62±0.1g/L)	(1.75±0.23g/L)

Table 2; Mean ± standard deviation of variables among gender

	Diabetic Male (n = 98)	Diabetic Female (n = 121)
Age	56.4 ± 13years	55.2 ± 12.2years
Duration of DM	11.2±6years	9.8±4.9years
Lipoprotein Lp(a)	79±35 mg/dl	85.3±33.3 mg/dl
HbA_{1c} (%)	10 ±4.5%	10.7±4.6%
Cholesterol	(4.72± 1.26mmol/L)	(5.01±1.6mmol/L)
Triglycerides	(2.1±0.62mmol/L)	(2.28±0.69mmol/L)*
LDL	(3.17±2.25mmol/L)	(3.05±1.23mmol/L)
HDL	(1.17±0.35mmol/L)	(1.14±0.36mmol/L)
ApoB	(1.49±0.70 g/L)	(1.476±0.51 g/L)
ApoA	(1.59±0.58g/L)	(1.64±0.64g/L)

(* P <0.05)

Table 3: Lp (a) means of diabetic patients associated with pathological obtained values of the estimated variables

Pathological value of variables	Lp(a) in mg/dl Mean ±SD	N (out of 219)	%
HbA_{1c} ≥9%**	91± 35	129	59%
Cholesterol ≥6.2mmol/L	89.8±29	28	13%
Triglyceride ≥2.5mmol/L	79±32	87	40%
LDL ≥3.07mmol/L	87.2±34	94	43%
HDL<0.93mmol/L**	95.9±34	59	27%
ApoB ≥1.65g/L**	92±33.6	64	29%
ApoA<1.56g/L**	94.4±35	88	40%

(P value < 0.01)**

Table, 4: Means of the obtained values of diabetic patients associated with HbA_{1c} levels.

	HbA_{1c} ≥9% (n=129)	HbA_{1c} <9% (n=90)
Age	54.6±12.9years	57.4±12years
Duration of DM	10.3±5.5years	10.5±5.2years
Lipoprotein Lp(a) **	91±35mg/dl	69.7±27mg/dl
Cholesterol*	(5.08±1.62mmol/L)	(4.61±1.23mmol/L)
Triglycerides**	(2.34±0.64mmol/L)	(2.02±0.65mmol/L)
LDL**	(3.35±2.07mmol/L)	(2.73±1.0mmol/L)
HDL**	(1.09±0.34mmol/L)	(1.24±0.36mmol/L)
ApoB	(1.48±0.63g/L)	(1.47±0.59g/L)
ApoA	(1.58±0.63g/L)	(1.66±0.59g/L)

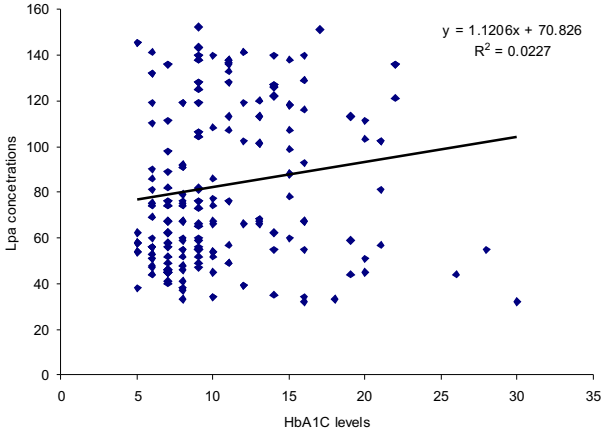
* P value <0.05, ** P value <0.01

Table 5: Comparison of means of the obtained values of diabetic patients in association with Lp(a) levels.

	Lp(a) ≥100mg/dl (n=75)	Lp(a) <100 mg/dl (n=144)
Age	55.4±13.1years	55.9±123years
Duration of DM	10.5±4.6years	10.4±5.8years
HbA1C % **	11.9±4.3%	9.6±4.5%
Cholesterol	(5.0±1.8mmol/L)	(4.8±1.3mmol/L)
Triglycerides	(2.17±0.59mmol/L)	(2.21±0.7mmol/L)
LDL	(3.46±2.35mmol/L)	(2.92±1.29mmol/L)
HDL**	(1.05±0.32mmol/L)	(1.2±0.37mmol/L)
ApoB*	(1.59±0.59g/L)	(1.42±0.60g/L)
ApoA**	(1.38±0.68g/L)	(1.74±0.54g/L)

* P value <0.05, ** P value <0.01,

Figure 1: illustrates correlation of Lp (a) levels with HbA_{1c} of diabetic patients



DISCUSSION:

In this study Lp (a), LDL, ApoB, triglycerides and HbA1C mean levels were increased and HDL and ApoA mean values were decreased in diabetic patients when compared to non-diabetic persons. These findings agreed with results of a study conducted by Valabhji, et al. in 2003. However, LDL mean level was not increased in diabetic patients of study population of Southern California (35).

Another study which was conducted by Makamto, et al. in 2005 found increased triglycerides and LDL levels and decreased HDL concentration in diabetic patients than non-diabetic persons in study population of Cameron.

Oyewole, et al in 2008 found triglycerides, total cholesterol and LDL levels were higher and HDL was lower in diabetic patients when compared to controls in Sierra Leone. Raised serum triglycerides and reduced HDL levels were found in diabetic patients when compared to non-diabetics, a study of Feher, et al in 1999. In contrast, total cholesterol and LDL concentrations were similar to those found in non-diabetic subjects, which differ from our findings. In respect to LDL level it is more consisting to the not raised cholesterol unlike our findings, so other components probably are responsible to the increased LDL level in our results.

Imani, et al in 2006 found means of ApoB, Lp (a), LDL and HDL were lower in diabetic children than in the control group in Isfahan. However, they found triglycerides mean level was higher in diabetic children than in control.

Lp (a) mean level in this study was not significantly higher in diabetic patients as compared to non diabetic controls. Our results are similar to results of study in Tunisian population (39).

In this study all diabetic patients had Lp (a) >30mg/dl. Cantin et al. in 2002 reported an Lp(a) cut- off value of 30mg/dl. One third of patients in this study had Lp(a) exceeded 100mg/dl which indicated high risk. Lp (a) mean level was not significantly, higher in the diabetic patients as compared to the controls (39). Increased Lp (a) concentration may synergistically contribute to Lp (a) pathogenicity. In addition, high Lp(a) and lipids disorder are the suggested risk factors for CHD and stroke morbidity and mortality (41, 23). Concentration of Lp (a) in human plasma vary from 0 to 30mg/dl (21). Lp(a) levels ≥ 20mg/dl are associated with an increased risk of incident non-fatal myocardial infarction, fatal myocardial infarction or sudden death (42).

In this study HbA1C mean level was 10.4%±4.5% for the diabetic patients under study and 4.3%±0.7% for the non-diabetic controls. These findings were comparable to other study results in Sudan and else where; mean level of HbA1C was 9.9%±1.40% and 6.4%±0.07% for diabetic patients and healthy controls respectively, a study done in Khartoum State, Sudan (43). From our findings, 42.5% of diabetic patients were having HbA1C level >9.0%, hence they were suggested at increased risk of cardiovascular complications, because they were considered having poor glycaemic control. In patients with DM the risk of diabetic complications was strongly associated with previous hyperglycaemia (44).

From our findings, no significant difference was observed between HDL mean levels of diabetic male and female. However, our study showed 42% of diabetic patients having HDL level <40mg/dl (1.06mmol/L), which indicated more risk to CVD. Optimal HDL levels (<40mg/dl (1.06mmol/L) in men and <50mg/dl (1.3mmol/L) in women) should include lifestyle modifications, followed by the consideration of pharmacotherapy in high-risk diabetic patients (34). Low HDL level is common among diabetic patients at risk of adverse cardiovascular outcomes (45). Poor glycaemic control in DM can lead to decreased HDL cholesterol levels (38). Low levels of HDL in diabetic patients may be present because there was no association of VLDL triglycerides to form HDL particles. The reduction in HDL levels is due to the increased transfer of cholesterol from HDL to triglyceride-rich lipoproteins, with reciprocal transfer of triglyceride to HDL. Triglyceride-rich HDL particles are hydrolyzed by hepatic lipase and, as a result, are rapidly catabolized and cleared from plasma (46).

Our data reported that there was difference in ApoB mean level in diabetic patients and non-diabetic subjects, resembling data obtained in Chinese population (47). In Bahrainis and Kuwaiti populations, the ApoB levels were higher in diabetic than in non-diabetic women (48). However, in our study means of ApoB for the patients were increased in males than females. Our data did not agree with data presented by a study in Chinese population that diabetic patients having higher ApoB levels were more likely to be female and older (47).

ApoB ≥ 165mg/dl (1.65g//L) was found in 29% of diabetic patients. These findings support the idea that the addition of ApoB measurement to the routine lipid profile for assessing and monitoring patients at risk would enhance patient management (49).

Many lipoprotein disorders are characterized by increased serum ApoB concentrations and higher levels of ApoB were strongly and independently associated with an increased future risk of CHD (50, 51).

It was indicated that ApoB, a marker of LDL carrying particles, should be taken into consideration in addition to other lipid markers in Asian populations (47). Data demonstrated that ApoB is more strongly associated than LDL with risk of CHD among Chinese (47). Considerable evidence indicates that Apo B is a better index of reaching or not reaching treatment targets than LDL or cholesterol (52).

In this study no significant difference was observed between triglycerides mean levels of diabetic patients and non-diabetic persons, although, significant difference in triglycerides levels were observed between diabetic male and female. A study conducted in Cameron showed raised triglycerides level in diabetic patients than non-diabetic persons in both sexes (2). However, both diabetic men and women had higher serum triglycerides than their non-diabetic counterparts in a study population of Southern California (35).

Although no one of the patients in our study was reported having cholesterol-lowering medication, no significant difference

was observed between cholesterol means level in diabetic patients and non-diabetic persons. Our findings agreed with results of study conducted in a population of Southern California that diabetic patients did not have higher cholesterol concentration than non-diabetic persons (35). However, in Chinese and Greek populations cholesterol results showed increased levels in diabetic patients than non-diabetic persons (30, 47).

The difference between cholesterol mean values of male and female diabetic patients in Tunisian and Australian communities was not significant (6,39). In Bahrainis, Kuwaiti and Arabian Peninsula populations the total cholesterol was higher in diabetic than in non-diabetic women (48). In Cameroonians population, cholesterol level in men diabetic patients was higher than non-diabetic men. However, there was no difference between cholesterol level of diabetic and non-diabetic women (2). Generally diabetes does not lead to marked elevations of blood cholesterol (53).

CONCLUSSIONS:

Management of hyperglycaemia in diabetic patients is crucially important to the prevention of both acute and long-term complications. Lp (a) seen to be determinant risk factor of all diabetic patients. HbA_{1C} remains a suitable measure to assess hyperglycaemic control in diabetic patients. Lipids and lipoproteins levels for diabetic patients vary depending on the degree of glycaemic control assessed using HbA_{1C}. The diabetic patients under study were at poor glycaemic control. Therefore therapeutic strategies will be needed addressing hyperglycaemia and dyslipidaemia to control the consequence of diabetic complications. Addition of Lp (a) to the routine lipid profile to assess cardiovascular risk in diabetic patients may enhance management of diabetes mellitus.

Addition of ApoB to the routine lipid profile to assess cardiovascular risk in diabetic patients is of value. Measurements of Lp (a) or together with ApoB will be sufficient for the assessment of the lipid profile.

References

1 Ahmed S, Cannon CP, Murphy SA, Braunwald E. Acute coronary syndromes and diabetes: is intensive lipid lowering beneficial? Result of the PROVE IT-TIMI 22 trial. European Heart Journal 2006; 27 (19): 2323-29.

2 Makamto SC, Oben JE, Ngondi JL. Fezeu KLL, Kengne AP, Mbanya JC. Dietary control and lipid profile of type 2 diabetes mellitus patients in Yaoundé, Cameroon. Pakistan Journal of Nutrition 2005; 4 (5): 282-86.

3 Hamaoui K, Butt A, Powrie J, Swaminathan R. Concentration of circulating rhodopsin mRNA in diabetic retinopathy. Clinical Chemistry 2004; 50: 2152-55.

4 Ahmed SAE, Gadour MOE. The screening for diabetic nephropathy in diabetes clinic in Khartoum- Sudan. Sudan Journal of Medical Science 2008; 3 (4): 285-90.

5 Southerland JH, Taylor GW, Offenbacher S. Diabetes and periodontal infection: making the connection. Clinical Diabetes 2005; 23: 171-78.

6 McDermott R, Rowley KG, Lee AJ, Knght S, O'Dea K. Increase in prevalence of obesity and diabetes and decrease in plasma cholesterol in central Australian Aboriginal community. The Medical Journal of Australia 2000; 172: 480-84

7 Saudek CD, Derr RL, Kalyani RR. Assessing glycaemia in diabetes using self-monitoring blood glucose and haemoglobin A1C. The Journal of the American Medical Association 2006; 295 (14): 1688-97.

8 Boden WE, Taggart DP. Diabetes with coronary disease, a moving target amid evolving therapies? The New England Journal of Medicine 2009; 360 (24): 2570-72.

9 Bailes BK, Diabetes mellitus and its chronic complications (home study program). Association of periOperative Registered Nurses 2002; 76 (2): 265-82.

10 Khalangot M, Tronko M, Kravchenko V, Kulchinska J, Hu G. Body mass index and the risk of total and cardiovascular mortality among patients with type 2 diabetes: a large prospective study in Ukraine. Heart 2009; 95: 454-60.

11 Ceriello A, Postprandial hyperglycemia and diabetes complications, is it time to treat? Diabetes 2005; 54: 1-7.

12 Solano M P, Goldberg R B. Lipid management in type 2 diabetes. Clinical Diabetes 2006; 24: 27-32.

13 Batty GD, M Kivimaki M, Smith G D, Marmot M G, Shipley M J. Obesity and overweight in relation to mortality in men with and without type 2 diabetes/ impaired glucose tolerance. Diabetes Care 2007; 30: 2388-91.

14 Triplitt C, Alvarez CA, Practices for lowering the risk of cardiovascular disease in diabetes. Diabetes Spectrum 2008; 21: 177-89.

15 Steffes M, Cleary P, Goldstein D, Little R, Wiedmeyer HM, Rohlfing C, England J, Bucksa J, Nowicki M, et al. Glycosylated Hemoglobin HbA1C measurements over nearly two decades: sustaining comparable values throughout the diabetes control and complications trial and the epidemiology of diabetes interventions and complications study. Clinical Chemistry 2005; 51: 753-58.

16 Kilpatrick ES, Rigby AS, Atkin SL. Variability in the relationship between mean plasma glucose and HbA1c: implications for the assessment of glycaemic control. Clinical Chemistry 2007; 53: 897-901.

17 Garry SX. Lipid disorders in diabetes mellitus and current management, Current Pharmaceutical Analysis 2007; 3(1): 17-24.

18 Laaksonen DE. Role of physical exercise, fitness and aerobic training in type 1 diabetic and healthy men in relaxation to the lipid profile lipid per-oxidation and the metabolic syndrome. Journal of Sport Science and Medicine 2003; 2: 61-5

19 Koerbel G, Korytkowski M. Coronary heart disease in women with diabetes, Diabetes Spectrum 2003; 16: 148-53.

20 Goldberg RB, Kendal DM, Deeg MA, Buse JA, Zagar AJ, Pinaire JA, Tan MH, Khan MA, Perez AT, Jacober SJ, et al. A comparison of lipid and glycaemic effects of Pioglitazone and Rosiglitazone in patients with type 2 diabetes and dyslipidaemia. Diabetes Care 2005; 28: 1547-54.

21 Jones GT, Van Rij AM, Cole J, Williams MJA, Bateman EH, Marcovina SM, Deng M, McCormick SPA, et al. Plasma lipoprotein (a) (Lp(a)) indicates risk for 4 distinct forms of vascular disease. Clinical Chemistry 2007; 53: 679-85.

22 Ross R. Atherosclerosis an inflammatory disease. The New England Journal of Medicine 1999; 340 (2): 115-26.

23 Dieplinger B, Lingenhel A, Baumgartner N, Poelz W, Dieplinger H, Haltmayer M, Kronenberg F, Mueller T, et al. Increased serum lipoprotein (a) concentrations and low molecular weight phenotypes of apolipoprotein (a) are associated with symptomatic peripheral arterial disease. Clinical Chemistry 2007; 53: 1298-305.

24 Utermann G. The mysteries of lipoprotein (a). Science 1989; 246, 4932: 904-10.

25 Milionis HJ, Winder AF, Mikhailidis AF. Lipoprotein (a) and stroke. Journal of Clinical Pathology 2000; 53: 487-96.

26 Berglund L, Ramakrishnan R. Lipoprotein (a), an elusive cardiovascular risk factor. Arteriosclerosis, Thrombosis, and Vascular Biology 2004; 24: 2219-25.

27 Boffa MB, Marcovina SM, Koschinsky ML. Lipoprotein (a) as a risk factor for atherosclerosis and thrombosis: mechanistic insights from animal models. Clinical Biochemistry 2004; 37 (5): 333-43.

28 Hartmann M, Bergelen CV, Mintiz GS, Stoel MG, Eggebrecht H, Wieneke H, Fahy M, Neumann T, Palen JVD, Louwerenburg HW, Verhorst PMJ, Erbel R, et al. Relation between lipoprotein (a) and fibreniogen and serial intravascular ultrasound plaque progression in left main coronary arteries. Journal of American College of Cardiology Foundation 2006; 48: 446-52.

29 Anuurad E, Rubin J, Chiem A, Tracy RP, Pearson TA, Berglund L. High levels of inflammatory biomarkers are associated with increased allele-specific apolipoprotein(a) levels in African-Americans, The Journal of Clinical Endocrinology & Metabolism 2008; 93 (4): 1482-88.

30 Alamanos Y, Tsamandouraki K, Koutis A, Lionis C, Fioretos M. Obesity, hypertension, hypercholesterolemia and diabetes mellitus in women aged 20-69, living in a highland community of Crete. European Journal of Public Health 1991; 1(2): 65-7.

31 Widmann MD, Sumpio BE. Lipoprotein (a): a risk factor for peripheral vascular disease. Annals of Vascular Surgery 1993; 7 (5): 446-51.

32 Chan DC, Watts GF. Apolipoproteins as markers and managers of coronary risk. International Journal of Medicine 2006; 99 (5): 277-87.

33 Hirowatari Y, Yoshida H, Kurosawa H, Doumitu K, Norio T. Measurement of cholesterol of major serum lipoprotein classes by anion-exchange HPLC with per chlorate ion-containing eluent. Journal of Lipid Research 2003; 44: 1404-12.

34 Ashen MD, Blumenthal RS. Low HDL cholesterol levels. The New England Journal of Medicine 2005; 353 (12): 1252-60.

35 Valabhji J, Elkeles RS. Dyslipidaemia in type 2 diabetes: epidemiology and biochemistry. The British Journal of Diabetes and Vascular Disease 2003; 3 (3): 184-89.

36 Oyewole OI, Sessie S, Mansaray M, Kamara B. Changes in serum electrolytes and lipid profile in diabetic subjects in Freetown Sierra Leone. Sudan Journal of Medical Science 2008; 3 (4): 309-13.

37 Feher MD, Elkeles, RS. Lipid modification and coronary heart disease in type 2 diabetes: different from the general population? Heart 1999; 81: 10-11.

38 Imani S F, Hashemipour M, Kelishadi R. lipid profile of children with type 1 diabetes compared to control. Advance Research Yields Across Atherosclerosis Journal 2006; 2 (1): 36-8.

39- Ben Hamda BK, Masmoudi AS, Mandhouj O, Hammami S, Attia N, Smaoui M, Zidi MA, Nabli N, Chaaba R, Mahjoub S, Ben Farhat M, Hammami M, et al. Lipoprotein (a) and ischemic heart diseases in patients with type 2 diabetes. Archives de Institute Pasteur de Tunis 2002; 79 (1-4): 27-33.

40 Cantin B, Despres JP, Lamarche B, Moorjani S, Lupien PJ, Bogaty P, Bergeron J, Dagenais GR, et al. Association of the fibrinogen and lipoprotein (a) (Lp(a)) as a coronary heart disease risk factor in men (The Quebec cardiovascular study). American Journal of Cardiology 2002; 89 (6): 662-66.

41 D'Angelo A, Ruotolo G, Garancini P, Sampietro F, Mazzola G, Calori G. Lipoprotein (a), fibrinogen and vascular mortality in an elderly Northern Italian population. Haematologica 2006; 91 (12): 1613-20.

42 Eckardstein NA, Novel risk for atherosclerosis. Journal of American Medical Association, Middle East 2004; 14 (3): 36-8.

43 Mohieldein AH, Abdelkarim AM, Osman FM, Abdallah EA, Ali MM. HbA1C as a marker to reduce limb amputation in patient with type 2 diabetes mellitus. Sudan Journal of Medical Science 2008; 3 (3): 227-32.

44 Stratton, IM, Adler AI, Neil HAW, Matthews DA, Manley SE, Cull CA, Hadden D, Turner RC, and Holman RR. Association of glycaemia with macrovascular complications of type 2 diabetes (UKPDS 35): prospective observational study. British Medical Journal 2000, 321 (7258): 405-12.

45 Drexel H. Reducing risk by raising HDL-cholesterol: the evidence. European Heart Journal Supplements 2006; 8: 23-9.

46 Krauss RM. Lipids and lipoproteins in patient with type 2 diabetes. Diabetes Care 2004; 27: 1496-504.

47 Chien KL, Hsu HC, Su TC, Chen MF, Lee YT, Frank BH. Apolipoprotein B and non-high density lipoprotein cholesterol and the risk of coronary heart disease in Chinese. Journal of Lipid Research 2007; 48: 2499-505.

48 Al-Mahroos F, Al-Roomi K, McKeigue PM. Relation of high blood pressure to glucose intolerance, plasma lipids and educational status in an Arabian Gulf population. International Journal of Epidemiology 2000; 29 (1): 71-6.

49 Williams K, Tchernof A, Hunt KJ, Wagenknecht LE, Haffner SM, Suiderman AD. Diabetes, abdominal adiposity, and atherogenic dyslipoproteinaemia in women compared with men. Diabetes 2008; 57: 3289-96.

50 Contois JH, McConnell JP, Sethi AA, Csako G, Devaraj S, Hoefner DM, Warnick GR, et al. Apolipoprotein B and cardiovascular disease risk: Position statement from the AACC lipoproteins and vascular diseases division working group on best practices. Clinical Chemistry 2009; 55: 407-19.

51 Barter P. The role of HDL-cholesterol in preventing atherosclerotic disease. European Heart Journal Supplements 2008, 7: 4-8.

52 Miremadi S, Sniderman A, Frohlich J. Can Measurement of serum apolipoprotein B replace the lipid profile monitoring of patients with lipoprotein disorders? Clinical Chemistry 2002; 48: 484 – 88.

53 Goldberg IJ, Dansky HM. Diabetic vascular disease, an experimental objective. Arteriosclerosis, Thrombosis, and Vascular Biology 2006; 26: 1693-701.