

Lipids, lipoprotein (a) profile and HbA1c among Arabian Type 2 diabetic patients

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Abstract

The aim of this study was to assess lipids, lipoprotein (a) profile and HbA1c in Qatari's type 2 diabetes mellitus (DM) and to correlate the values with various risk factors. This case control study was conducted in Hamad General Hospital, Doha, State of Qatar from May 2004 to November 2005 in 214 cases (with diabetes) and 214 controls (without diabetes) aged 25 to 65 years, males and females and Qatari nationals.

Face to face interviews were based on a questionnaire that included variables such as age, sex, family history, physical examination, fasting blood glucose, lipids, Lp (a) HbA1c cholesterol total, HDL, LDL and triglycerides analysis.

The age, male gender, BMI , obesity, WHR were higher in diabetics, ($p < 0.001$). The prevalence of hypertension was associated with the presence of diabetes (29% for diabetics vs. 4% for control group , $p < 0.001$). The percentages of patients with Lp (a) above 300 mg/l were significantly different between the two groups (48% vs 23%, $p < 0.001$). Diabetic patients had significantly higher TC ($p < 0.001$); TG ($p < 0.001$), LDL ($p < 0.001$) and Lp (a) ($p = 0.0045$). In diabetic patients, Lp (a) correlates with total cholesterol ($r = 0.296$; $p < 0.05$), LDL-C ($r = 0.285$; $p < 0.05$), but marginally significant with

ApoB ($r=0.573$, $p<0.001$), TG ($r=0.288$; $p<0.05$), and LDL-C ($r=0.584$; $p<0.001$). Similarly, ApoA1 significantly correlated with TC ($r= 0.292$; $p<0.05$), LDL-C ($r= 0.305$; $p<0.001$) and HDL-C ($r=0.565$; $p<0.001$).

The present study revealed that obesity, consanguinity, total cholesterol, reduced HDL cholesterol and triglyceride were more prevalent in diabetic patients. Furthermore, this study has reported that diabetes state does not increase plasma Lp (a) concentrations and fail to show any association of Lp (a) levels with glycemic control in type 2 diabetic patients.

Introduction

One hundred million persons have a history of diabetes (DM) worldwide [1]. Lifestyle modifications, inclusive of dietary modification, regular physical activity and weight reduction are indicated for prevention of diabetes [2]. In addition to the established major risk factors, atherosclerosis in type 2 diabetes is also related to alterations in lipid and lipoprotein profile [3]. An epidemiological study has demonstrated that type 2 diabetes mellitus (DM) is a well known risk factor for the development of cardiovascular disease, cerebrovascular disease, and peripheral vascular diseases [4-11]. Plasma Lp (a) concentration is largely under genetic control [10]. In addition to the established major risk factors, atherosclerosis in type 2 diabetes is also related to alterations in lipid and lipoprotein profile [4-8,11]. Furthermore, Lp (a) is also an independent risk factor for deteriorating renal function in type 2 diabetic patients [12].

The aim of this study was to assess lipids, lipoprotein (a) profile and HbA1c in Qatari's type 2 diabetes mellitus (DM) and to correlate the values with various risk factors.

Subjects and Methods

This is a case control study conducted during a period of May 2004 to November 2005. The study was approved by the Research Ethics Committee at the Hamad Medical Corporation in accordance with the ethical standards laid down in the Helsinki declaration.

The study included 214 consecutive Qatari type 2 diabetic patients aged 25-65 years who were referred from Primary health care clinics to the specialized diabetic unit in the Hamad General Hospital, Hamad Medical Corporation and 214 nondiabetic healthy subjects aged 25-65 years were served as controls. The diagnosis of diabetes was based on a previous history of diabetes on American Diabetes Association criteria (Expert Committee on the diagnosis and classification of Diabetes Mellitus 1997) [13]. Diabetic patients were treated by diet and /or anti diabetic drugs . A total number of 214 diabetic patients selected by a simple random process from Diabetic Clinics at the Hamad General Hospital. Impaired glucose tolerance test was performed in nondiabetic subjects so as to exclude any DM cases among the controls because DM2 is often a silent disease and it is expected to be common among middle aged population.

The subjects were interviewed by an Arabicspeaking trained nurse and all patients gave informed voluntary consent to participate in the study. Face to face interviews were based on a questionnaire that included variables such as age, sex, family history, consanguinity, physical examination, fasting plasma glucose, lipids, cholesterol total, Lp (a), HDL, LDL, triglycerides HbA1c analysis. Degree of consanguinity among the studied subjects was noted as 1st degree and 2nd degree. First degree consanguinity is defined as marriages between 1st cousins and 2nd degree is marriages between second cousins. The Height and weight were recorded and obesity was defined as body mass index (BMI) of ≥ 30 kg/m², where $BMI = \text{Weight(kg)} / \text{Height}^2 \text{ (m}^2\text{)}$. Waist to hip ratio (WHR) was calculated from measurements of the waist circumference taken at the mid point between umbilicus and xiphoid and hip circumference, at the widest point around the hips, respectively. Blood pressure was measured using mercury sphygmomanometer with subjects in a seated position. Systolic and diastolic pressures were determined at the time of the appearance and disappearance of Korotkoff sounds, respectively. Hypertension was defined according to World Health Organization (WHO) criteria as SBP > 135 mmHg and/or DBP > 85 mmHg and/or the use of antihypertensive medication [14].

Laboratory procedures

Blood samples were obtained after at least a 12 hours overnight fast. Blood glycated hemoglobin (HbA1c) was measured on Roche Cobas Integra 800 automated biochemistry analyzer (Basle Switzerland). Fasting plasma glucose (FPG), total cholesterol (TC), high density lipoprotein (HDL)-cholesterol, low density lipoprotein (LDL)cholesterol, triglyceride (TG) apolipoprotein A1 (apo-A1), apolipoprotein B (Apo-B) concentrations were assessed by automated analyzer (Roch / Hitachi 917 analyzer, Roche Diagnostic). HDL cholesterol was quantified after precipitation of apoB containing lipoproteins with magnesium / phosphotungstate. LDL cholesterol was calculated by the Friedwald formula 15. The respective intra and inter assay coefficients of variation (CVs) for each of the assay were: FPG 1.4 and 2.0%, TC 1.2% and 2.1%, TG 1.5% and 3.6%, LDL-C 1.0% and 2.1%, HDL-C 2.8% and 3.5%, apo-A1 2.4% and 3.4% and Apo-B 2.9% and 3.3%. Lp (a) was quantitatively estimated in plasma by an enzymatic immunoassay (ELISA) and reagents provided by Linco Research, Inc., Missouri, USA. The intra and interassay coefficients of variations of Lp (a) were 2.7% and 5.3%, respectively.

Student-t test was used to ascertain the significance of differences between mean values of two continuous variables and confirmed by nonparametric Mann-Whitney test. Chi-square and Fisher's exact Spearman correlation test were used an appropriate. The level $p \leq 0.05$ was considered as the cut off value for significance.

Results

Table 1 shows the socio-demographic and clinical characteristics of the diabetic patients and non-diabetic controls. The age, male gender, BMI, obesity, WHR were higher in diabetics, ($p < 0.001$). The prevalence of hypertension was associated with the presence of diabetes (29% for diabetics vs. 4% for control group , $p < 0.001$).

Table 1. Clinical characteristics of diabetics patients and healthy non diabetic controls.

| Variable | Healthy Controls (n= 214) | Diabetic Patients (n= 214) | P-Value |
|-------------------------------------|------------------------------|-------------------------------|---------|
| Age (in years) | 45.8±7.3 | 46.6±7.1 | NS |
| Range | (40-65) | (40-67) | |
| Gender (%) | | | |
| Male | 112 (52.4) | 94 (43.9) | NS |
| Female | 102 (47.6) | 120 (56.7) | |
| Obesity (%) | 98(45.7) | 117(54.5) | 0.025 |
| Consanguinity (%) | | | |
| None | 134(62.6) | 109(51.0) | |
| Second Degree | 29(13.6) | 32(14.9) | 0.036 |
| First Degree | 51(23.8) | 73(34.1) | |
| Smoking (%) | | | |
| Non smoker | 150(70.0) | 163(70.2) | |
| Ex-smoker | 29(13.6) | 25(11.7) | NS |
| Smoker | 35(16.4) | 26(21.1) | |
| Cardiovascular disease (CAD) | -- | 23 (12.7) | -- |
| BMI (kg/m ²) | 28.3±4.8 | 30.6±4.7 | 0.005 |
| WHR | 0.90±0.12 | 0.96±0.15 | 0.001 |
| Fasting plasma glucose (mmol/l) | 5.23±0.45 | 10.61±3.26 | <0.001 |
| HbA1c | -- | 8.9±1.7 | -- |
| Duration of Diabetes (years) | -- | 7.6± 4.8 | -- |
| Systolic Blood Pressure (mm Hg) | 126.7±16.9 | 132.4±15.7 | 0.0003 |
| Diastolic Blood Pressure (mm Hg) | 81.4± 9.6 | 82.3± 9.1 | NS |
| Hypertension (%) | 4 | 29 | <0.001 |
| Plasma creatinine (mmol/l) | 86.9±11.9 | 97.3±25.5 | <0.001 |
| Protein excretion rate | 0.02±0.03 | 0.1±0.25 | NS |

(For a larger image of table, click [here](#))

NS: not significant.

Data are expressed as mean (M) ±Standard deviation (SD.) or percent.

P values were obtained using Student's t test, or Mann-Whitney and chi-square test.

| Variable | Healthy Controls (n=214) | Diabetic patients (n=214) | P value |
|------------------------------------|-----------------------------|------------------------------|---------|
| e+sterol (mmol/l) | 4.62±1.05 | 5.24±1.03 | <0.001 |
| Total TG (mmol/l) | 1.21±0.56 | 2.05±1.29 | <0.001 |
| HDL cholesterol (mmol/l) | 1.09±0.33 | 0.87±0.23 | <0.001 |
| LDL cholesterol (mmol/l) | 3.07±1.08 | 3.39±0.87 | 0.0008 |
| ApoA1 (g/l) | 1.29±0.21 | 1.31±0.27 | NS |
| Apo B (g/l) | 1.02±0.25 | 1.03±0.24 | NS |
| Lp (a) (mg/l) | | | |
| Mean ± (S.D) | 264.9 (221.7) | 328.1 (236.1) | 0.0045* |
| Median | 203 | 291 | |
| Range | 20-1080 | 20-1290 | |
| >300 mg/l (%) | 23 | 48 | <0.001 |
| Total cholesterol/C-HDL | 4.76±1.93 | 6.60±2.32 | <0.001 |
| C/LDL/C-HDL | 3.27±1.70 | 4.36±1.71 | <0.001 |

(For a larger image of table, click [here](#))

NS: Not significant (P>0.05)

Lp (a) levels are expressed as Mean ± (S.D) as well as median values and range. A cut off levels of Lp (a) of 300 mg/l was used to categorize subjects with elevated Lp (a) levels (Percentage).

P values were obtained using Student's t test, or Mann-Whitney test (*) and chi-square test.

Table 3: Spearman correlation coefficient between Lp (a), lipid profile, and parameters of glycemic control

| Variable | Total cholesterol | Total TG | LDL-C | HDL-C | ApoA1 | ApoB | Lp (a) | HbA1c | Fasting glycemia |
|-----------------------------|-------------------|----------|---------|---------|--------|--------|--------|--------|------------------|
| Controls (n= 214) | | | | | | | | | |
| Total cholesterol | 1.00 | | | | | | | | |
| Total TG | 0.579** | 1.00 | | | | | | | |
| LDL-C | 0.782** | 0.454** | 1.00 | | | | | | |
| HDL-C | 0.243 | -0.148 | -0.293* | 1.00 | | | | | |
| ApoA1 | 0.278 | 0.086 | 0.299* | 0.118 | 1.00 | | | | |
| ApoB | 0.733** | 0.579** | 0.664** | -0.221 | -0.235 | 1.00 | | | |
| Lp (a) | 0.059 | 0.075 | 0.086 | -0.288* | -0.016 | 0.279* | 1.00 | | |
| HbA1c | -0.142 | 0.092 | 0.244 | -0.250 | 0.236 | -0.041 | 0.225 | 1.00 | |
| Fasting Glycemia | 0.348** | 0.351** | 0.290* | 0.058 | 0.032 | 0.183 | -0.267 | -0.053 | 1.00 |

(For a larger image of table, click [here](#))

| Diabetic patients (n= 214) | | | | | | | | | |
|----------------------------|---------|---------|---------|---------|--------|--------|--------|--------|------|
| Total cholesterol | 1.00 | | | | | | | | |
| Total TG | 0.298** | 1.00 | | | | | | | |
| LDL-C | 0.815** | -0.12 | 1.00 | | | | | | |
| HDL-C | 0.284* | -0.267* | 0.190 | 1.00 | | | | | |
| ApoA1 | 0.292* | -0.131 | 0.305** | 0.565** | 1.00 | | | | |
| ApoB | 0.573** | 0.288* | 0.584* | 0.259* | 0.162 | 1.00 | | | |
| Lp (a) | 0.296* | 0.049 | 0.285* | -0.095 | -0.146 | 0.174 | 1.00 | | |
| HbA1c | 0.093 | 0.068 | 0.41 | 0.089 | 0.132 | 0.150 | -0.183 | 1.00 | |
| Fasting Glycemia | 0.271* | 0.276* | 0.210 | -0.045 | 0.085 | 0.269* | 0.101 | 0.488* | 1.00 |

(For a larger image of table, click [here](#))

- 2) level 50.0 eht ta tnacifngis si noitalerroC *-tailed)
- 2) level 10.0 eht ta tnacifngis si noitalerroC **-tailed)

Diabetic patients had significantly higher total cholesterol ($p < 0.001$), TG ($p < 0.001$); LDL cholesterol ($p < 0.001$), and Lp (a) ($p < 0.001$) but lower HDL cholesterol than non-diabetic controls ($p < 0.001$) (Table 2). As shown in Table 2, Lp (a) concentration are elevated in type 2 diabetic population compared to control one ($p = 0.0045$). The percentages of patients with Lp (a) above 300 mg/l were significantly different between the two groups (48% vs 23%, $p < 0.001$).

Table 3 summarize correlation matrix among Lp (a), lipids and glycemic control parameters. In diabetic patients, Lp (a) correlates with total cholesterol ($r = 0.296$; $p < 0.05$), LDL-C ($r = 0.285$; $p < 0.05$), but marginally significantly with ApoB ($r = 0.573$, $p < 0.001$), TG ($r = 0.288$; $p < 0.05$), and LDL-C ($r = 0.584$; $p < 0.001$). Similarly, ApoA1 with TC ($r = 0.292$; $p < 0.05$), LDL-C ($r = 0.305$; $p < 0.001$) and HDL-C ($r = 0.565$; $p < 0.001$). No significant correlation was found between Lp (a) and the parameters of glycemic control (HbA1c and fasting glycemia).

Discussion

In the present study, we have confirmed previous observations of an increased LDL and HDL cholesterol levels affect on diabetic patients [3-6,9-11,14,16-18]. The importance of LDL subfractions is increasingly recognized, with an increased proportion of small dense LDL particles being correlated with an increased risk of ischemic heart disease, [6,9,10], even after controlling for age and gender [17].

Most recent studies [5,6] reported that one confounder may be the concomitant use of lipid lowering therapy as part of the intensive cardiovascular risk factor management. The blood pressure lowering, diet, and lifestyle advice have shown to influence

lipoproteins, their effects on LDL subfractions have not been investigated in detail. Although, alteration of fat intake (as part of diet

This study was supported and funded by Hamad Medical Corporation Grant No. 231. We would like to thank Hamad Medical Corporation and Diabetic Association for generous support and help while this project conducted. tary/lifestyle alterations) can also result in a reduction in HDL cholesterol levels [4,9,11,17,18], a most recent study showed that dietary advice appears to be effective in bringing about modest beneficial changes in diet and cardiovascular risk factors months [4,9,16].

Changes in Lp (a) concentrations relative to diabetic control remain controversial, but most studies have failed to show any association of Lp (a) levels with glycemic control in patients with type 2 DM [6,11,17,18]. Our results showed that no strong link between either fasting glycemia or blood glucose control as assessed by HbA1c and plasma Lp (a) was found.

According to our results, there were significant correlations between Lp (a) levels and LDL-C in diabetic subjects. This result suggests that the atherogenicity of Lp (a) in diabetic men may depend on interaction of Lp (a) with environmental or other genetic factors such as LDL-C concentration [7,10,18].

In conclusion, the present study revealed that obesity, consanguinity, total cholesterol, reduced HDL cholesterol and triglyceride were more prevalent in diabetic patients and fail to show any association of Lp (a) levels with glycemic control in type 2 diabetic patients. There is a difference in the mean levels of Lp (a) between the study groups, although HbA1c did not correlate significantly with Lp (a) in subjects with or without type 2 diabetes.

Acknowledgements

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