Hyperlipidemia in Non Insulin-Dependent Diabetes Mellitus

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Background: Hyperlipidemia is a risk factor of cardiovascular disease. No data exists in Jordan regarding blood lipid level in diabetics.

Objectives: To determine the prevalence of high plasma cholesterol and triglyceride levels among non insulin-dependent diabetes mellitus (NIDDM) and to study the effect of controlling blood sugar on the levels of plasma lipids.

Design and methods: A sample of 393 persons aged 30 years or more were selected from patients followed up at the endocrinology and general medicine clinics. Plasma glucose, cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL), and triglycerides, blood pressure, height and weight were measured and a pre-tested structured questionnaire was administered by the doctor.

Results: The prevalence rates of hypercholesterolemia (HC) and hypertriglyceridemia (HT) in NIDDM were 34% and 38% respectively. According to blood sugar control, HC and HT were found in 34% and 38% in patients with poor control of blood sugar, and in 32% and 35% in patients with good blood sugar control. Combined hyperlipidemia (HC and HT) was higher among diabetics (19%) than non-diabetics (7%).

Conclusions: In non diabetics, hypercholesterolemia and hypertriglyceridemia are highly prevalent with a pattern consistent with that of the United States and other developed countries. Dietary habits and lifestyle of the people have to be investigated and may provide an explanation for our findings. In diabetics, hypercholesterolemia, hypertriglyceridemia and combined hyperlipidemia are markedly increased and good control of blood sugar does not significantly affect their levels. Good control of blood sugar significantly affects the plasma level of LDL.

Cardiovascular diseases are the leading cause of death in many countries in the world including Jordan. Coronary heart disease is the most common single cause of death in the United States[1]. Hypercholesterolemia (HC) is a well-established major risk factor for coronary heart disease[2-5]. The increased risk of coronary artery disease in subjects with diabetes mellitus can be partially explained by the lipoprotein abnormalities associated with diabetes mellitus.

Hypertriglyceridemia and low levels of high-density lipoprotein are the most common lipid abnormality[6]. In insulin dependent diabetes mellitus (IDDM), these abnormalities can usually be reversed with glycemic control. In contrast, in non insulin dependent diabetes mellitus (NIDDM), although lipid values improve, abnormalities commonly persist even after optimal glycemic control has been achieved. Screening for dyslipidemia is recommended in subjects with diabetes mellitus. A goal of low-density lipoprotein cholesterol of less than 130 mg/dL and triglycerides lower than 200 mg/dL should be sought[7]. In the United States, only 43% of the population aged 20-74 years were found to have cholesterol levels within the desirable range (<200mg/dl (5.2 mmol/L)) with 57% having either borderline high (30%) or high (27%) cholesterol levels[8]. More recent data from the National Health and Nutrition Examination Surveys show a decline in the mean cholesterol level for adults 20-74 years from 5.69 mmol/L in 1960 to 1962 to 5-30 mmol/L in 1988 to 1991 with 51% of US adults having cholesterol values above the desirable level[9]. In

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Sweden, 24% of adult males and 12% of adult females had HC, defined as a cholesterol level of >6.5 mmol/l (250mg/dl) while 14% of males and 3% of females had HT, defined as a triglyceride level of >2. 3 mmol/L (210 mg/dL)[10].

Data on cholesterol and triglyceride levels in Middle Eastern communities are scarce. In Saudi Arabia, Mitwali conducted a survey among apparently healthy males in Riyadh City and reported a mean cholesterol level[11] and Al Nuaim conducted another study about hyperlipidemia among Saudi diabetic patients[12].

METHODS

During 2 consecutive years between October 1996 and October 1998, we prospectively studied the lipid profile in 395 non insulin dependent diabetic patients (NIDDM) seen in endocrinology and general medicine clinics. The following data from the history was recorded; age, sex, education, smoking, alcohol drinking habits, duration of diabetes, history of other diseases as hypertension, ischaemic heart disease, renal or thyroid disease, family history of hyperlipidemia and ischaemic heart disease. Height and weight were measured and recorded in order to calculate the body mass index. The following laboratory tests were done; serum total cholesterol, low density lipoprotein, high density lipoprotein, triglyceride, serum urea, serum creatinine, thyroid function test, serum total protein, albumin, and urine analysis for albumin.

The inclusion criteria for the patient to be enrolled in the study were: 1). The age of the patient should be 30 years and above. 2). The patient should have no family history of hyperlipidemia. 3). The duration of diabetes should be more than 5 years. 4). The body mass index should be less than 30 in both sexes. 5). The patient should have normal serum total protein and albumin, normal kidney function test and normal thyroid function test.

Body mass index was calculated according to the formula: Body mass index (BMI) = weight (kg)/ height (m)^2. Obesity is defined as a body mass index of > 30 kg/m^2. Control of diabetes was defined as: good control if fasting blood sugar < 140 mg% and HbA1C < 7%, fair control if fasting blood sugar 141-200 mg% and HbA1C >9%.

According to the above inclusion criteria 395 non-insulin dependent diabetes mellitus patients were

enrolled in the study and according to the results of fasting blood sugar and HbA1C were subdivided into three groups; good control of diabetes 105 patients, fair control 162 patients and poor control 128 patients. The group of fair control of blood sugar was excluded from the study in order to compare between the good and poor groups to study the effect of blood sugar control on plasma lipid in non-insulin dependent diabetes mellitus.

In order to have two groups of patients for comparison we also studied 160 patients as a control group fulfilling the above criteria except that they did not have diabetes. These were volunteers who came to the endocrinology or general medicine clinic for non-specific complaints or those who came with their relatives.

Biochemical analysis for the lipid profile: blood samples were taken in sterile evacuated tubes without additives, serum was separated from cellular components by allowing the tube to stand for one hour then centrifuged for 15 minutes at 1500 revolution per minute (RPM). Testing for cholesterol and triglyceride were carried by the enzymatic calorimetric method using BM-Twin TG/CHO. Trig. GPO-PAP/cholesterol CHOD-PAP and BM-Hitachi system 704 autoanalyzer. Testing of LDL calculation was done by using Friedewald equation.

In our study the level of fasting plasma cholesterol was considered normal if < 200mg/dl (5.2mmol/L) and elevated if > 230mg/dl (6mmol/L). For triglyceride it was taken as normal if level was 130-180 mg% (1.43-1.98 mmol/L) and elevated if more than 200mg/dl (2.2mmol/L). For low density lipoprotein (LDL) the normal level should be < 130 mg% and elevated if more than 160 mg%. High-density lipoprotein (HDL) was considered to be reduced if its level was <35mg/dI. Combined hyperlipidemia (CHLD) was defined as high cholesterol and high triglyceride together.

Ethical considerations: An informed consent was obtained from every participant. The study was approved by the Research Ethics Committee of the Royal Medical Services. Identifying information was kept under strict confidentiality.

Chi-Square test was used for statistical analysis.

RESULTS

The patients enrolled in the study were 393, subdivided into two groups; diabetics 233 patients

Table 1. **Shows the characteristics of each group of patients and comparison between those with NIDDM and the control group (non diabetics)**

	Diabetics poor control of diabetes	(NIDDM) good control of diabetes	Non diabetics (Control group)	Total. No. of patients (diabetics and (non diabetics)
No. of patients	128	105	160	393
Age(mean)	48	44	38	43
Gender				
Men	37(29%)	71(68%)	90(56%)	198(50.4%)
Women	91(71%)	34(32%)	70(44%)	195(49.6%)
Education				
Illiterate	63(49%)	16(15%)	24(15%)	103(26%)
1-12 years	51(40%)	32(31%)	104(65%)	187(48%)
13+	14(11%)	57(54%)	32(20%)	103(26%)
Smoking	38(3%)	9(0.9%)	13(0.8%)	60(15%)
Alcohol drinking	21(1.6%)	7(0.7%)	14(0.9%)	42(11%)
Hypertension	23(18%)	21(20%)	10(0.6%)	54(14%)
Ischaemic heart disease	40(31%)	27(26%)	6(0.4%)	73(19%)

Table 2. **Shows the distribution of plasma lipids in diabetics (NIDDM) and a comparison with non diabetics (control group)**

	Diabetics poor control	(NIDDM) good control	Total (good + poor control)	Non diabetic (control group)
Total No.	128	105	233	160
Hypertriglyceridemia	49 (38%)	37 (35%)	86 (37%)	35 (22%)
Hypercholesterolemia	44 (34%)	34 (32%)	78 (34%)	33 (21%)
High LDL	27 (21%)	15 (14%)	42 (18%)	19 (12%)
Low HDL	31 (24%)	24 (23%)	55 (24%)	17 (10%)
Combined hyperlipidemia	26 (20%)	18 (17%)	44 (19%)	11 (7%)

(divided into two groups according to the control of blood sugar, good control 105, poor control 128) and non diabetics 160 patients as a control group for comparison.

Our results were based on the sample of 393 individuals (2 groups; diabetics and non diabetics), 30 years and older (mean age 43 years), from patients followed at endocrinology and general medicine clinics. There were 195 (49.6%) women and 198 (50.4%) men. Twenty six percent of the sample were illiterate, 15% were current smokers, 49.5% were obese, 11% had alcohol drinking habit, 14% had hypertension and 19% had ischaemic heart disease. The mean ages were 46 years for diabetics and 38 for non-diabetics. Table 1 show the characteristics of each group.

The prevalence of hypercholesterolemia was significantly higher among diabetic individuals (78 patients (34%)) than among non-diabetic (33 patients (21%)). Hypercholesterolemia was found in 34% of patients with poor control of diabetes and in 32% in patients with good control. The prevalence of hypertriglyceridemia was also higher among diabetics (86 patients (37%)) than among non-diabetics (35 patients (22%)). There was no significant difference between hypertriglyceridemia in group of poor control of diabetes (38%) and those with good control of diabetes (35%). Combined hyperlipidemia (CHLD) was higher among obese than non-obese subjects and among diabetics than non-diabetics (19% and 7%, respectively). CHLD (HC and HT together) was found in 17% of patients with good diabetic control and in 20% of patients with poor diabetic control. Illiterate people had the highest rate of CHLD compared to other educational groups. High density lipoprotein (HDL) was found to be significantly reduced among diabetics (55 patients (24%)) than non-diabetics (17 patients (10%)). HDL

was found to be reduced in 23% of patients with good control diabetes and in 24% of patients with poor control group. Low density lipoprotein (LDL) was higher in diabetics (42 patients (18%)) than non diabetics (19 patients (12%)) and was found to be high in 21% of patients with poor control of diabetes and in 14% of patients with good control of diabetes. Table 2 shows the distribution of serum lipid in the two groups (diabetics and non-diabetics), summarising the above results.

DISCUSSION

The present study provides the first data on the distribution of cholesterol, triglyceride, LDL and HDL levels in diabetics in Jordan. It is based on a sample from two groups of patients, representing diabetics subdivided into two groups according to blood sugar control and the non-diabetics (control group) for comparison. On initial analysis of our data, the most important finding is the high prevalence in our non diabetics population of HC (21%), HT (22%), CHLD (7%), high LDL in (12%) and reduced HDL in 10%. Comparison of our data with those from other Arab Countries is hampered by the scarcity of such data, the different methods of presentation, the type of study population and the cut off points used. In diabetics (NIDDM), plasma cholesterol and triglyceride is markedly elevated (34% and 37% respectively), combined hyperlipidemia (CHLD) in 19%, elevated LDL in 18% and reduced HDL in 24%. A recent study of diabetic individuals in Saudi Arabia reported a prevalence of CHLD of 15%, a figure lower than the 19% observed among diabetic subjects in our study[10]. In the present study we observed much higher levels of cholesterol and triglycerides in men. We have no explanation for the high level of serum lipids in our non-diabetic population. Food consumption patterns, lifestyle and physical inactivity should be thoroughly investigated in this population and could be largely responsible for our findings. In general, our findings showed a pattern of lipid distribution consistent with that reported from the United States[9] and Europe[13].

It is interesting to note that diabetes mellitus is a strong predictor of HC and HT. Elevated triglycerides and lowered HDL cholesterol, have been consistently observed in patients with non insulin-dependent diabetes mellitus (NIDDM)[11,14]. Elevated LDL cholesterol was observed in some studies[15] but not in others[10]. According to our results, serum cholesterol, triglyceride, and LDL were significantly higher among diabetics than

non diabetics and HDL was significantly reduced among diabetics than non diabetics. There were no significant difference between serum level of cholesterol, triglyceride and HDL among patients with poor control of diabetes and those with good control of diabetes. LDL was significantly elevated in patients with poor control of diabetes than those with good control. Table 3 shows the quantitative changes of serum lipid and lipoproteins in NIDDM.

Table 3. **Quantitative changes of serum lipid and lipoproteins in NIDDM.**

Lipid or lipoprotein	Poor control of diabetes	Good control of diabetes
Serum cholesterol	Increased	Increased
Serum triglyceride	Increased	Increased
LDL	Increased	Normal
HDL	Reduced	Reduced

Dyslipidemia is an important factor contributing to cardiovascular disease and accelerated atherosclerosis in NIDDM and its control should be considered in those patients[2,7,16]. Our data on hyperlipidemia in diabetics is the first from Jordan and is based on the study of patients seen in out-patient department. Further studies among additional diabetic populations, especially those in remote underdeveloped areas and Bedouin's are needed. Based on available data, we conclude that hyperlipidemia is an important public health problem in Jordan, comparable to that in Europe and the United States. Health education campaigns with the purpose of changing the lifestyle of the society, eg. dietary habits, smoking, weight reduction, increased physical activity, better control of diabetes and lipid-lowering drugs may be needed.

Lipid disturbances in uncomplicated diabetes mellitus may be due to hypoinsulinaemia, hyperinsulinaemia, and hyperglycaemia. The evaluation of lipid risk factors for ischaemic heart disease in diabetes mellitus is possible only after its full controlling. The normalization of glycaemia or insulin therapy is the best methods of treatment of lipid disturbances in diabetes mellitus[17]. Hypertension, dyslipidemia, insulin resistance, and hyperinsulinemia which are the acknowledged risk factors for coronary artery disease are all more common in persons with non-insulin-dependent diabetes than in nondiabetic persons. The interrelationships of these risk factors are becoming increasingly recognized[18,19]. In diabetic women a significantly higher incidence of combined hyperlipidaemias was recorded, as compared with men

and the mean total cholesterol and triglyceride levels were also significantly higher in women with type 2 diabetes[20].

CONCLUSION

In conclusion our results indicate that non diabetics (control group), hypercholesterolemia and HT are highly prevalent with a pattern consistent with that of the United States and other developed countries. Dietary habits and lifestyle of the people have to be investigated and may provide an explanation for our findings.

In diabetics (NIDDM), hypercholesterolemia (HC), and hypertriglyceridemia (HT) are markedly elevated and good control of blood sugar does not significantly affect their plasma levels. HDL is markedly reduced among diabetics than non diabetics, and not significantly affected by the control of blood sugar. LDL also is higher among diabetics than non diabetics but good control of blood sugar significantly reduces the LDL plasma level.

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