Prevalence of dyslipidemia in patients with type 2 diabetes in Jordan

Nazik M. Abdel-Aal, MD, MSc, Azmi T. Ahmad, MD, Erika S. Froelicher, MPH, PhD, Anwar MS Batieha, MD, PhD, Musdaq M. Hamza, MD, Kamel M. Ajlouni, FACP, FACE.

ABSTRACT

الأهداف: تقييم اختلاط الدهنيات عند مرضى السكري في المركز الوطني للسكري والغدد الصم والوراثة، ومعرفة أنواعها، اختلافاتها، وتأثير بعض العوامل المقترنة بالسكري من النوع الثاني عليها.

الطريقة: أُجريت هذه الدراسة في المركز الوطني للسكري والغدد الصم والوراثة – الجامعة الأردنية – عمان – الأردن، خلال الفترة مابين يونيو 2005م وحتى يوليو 2006م، شملت 702 مريضاً من المصابين بالنوع الثاني من السكري، والذين تزيد أعمارهم عن عشرين عاماً، وكانوا يتلقون علاجهم في المركز لستة أشهر على الأقل ضمن برنامج مُعد مسبقاً تُقاس بموجبه مؤشرات لضبط السكر، الدهون، التوتر الشرياني، والوزن.

النتائج: تبين أن نسبة ارتفاع الكولسترول الكلي 77.2%، انخفاض الكولسترول العالي الكثافة 83.9%، ارتفاع الكولسترول المنخفض الكثافة 91.5% ، وزيادة الدهنيات الثلاثية 83.1%، ووجد أن إصابة النساء بالإختلاطات الدهنية أكثر منها في الرجال، كما أن تعدد الإختلاطات 91.5%، ووجود خلل واحد 12.8%، وكسل الغدة الدرقية أهمية، كذلك استعمال معطلات مستقبلات بيتا أثر في زيادة هذه الإختلاطات.

خاتمة: إن شيوع إختلاطات الدهنيات عند مرضى السكري من النوع الثاني تدعونا جميعاً إلى العمل الجاد لتشخيصها مبكراً وعلاجها بكل اقتدار، بالإضافة إلى الحرص الشديد على تثقيف المريض والأخذ بيده لتغيير سلوكه وعاداته ذات العلاقة.

Objectives: To determine the frequency and patterns of dyslipidemia in patients with type 2 diabetes mellitus (DM) and to estimate the effects of sociodemographic and clinical variables on dyslipidemia.

Methods: The setting took place in the National Center for Diabetes, Endocrinology and Genetics (NCDEG) at the University of Jordan, Amman, Jordan. The NCDEG is the only referral center in the country; therefore, the patients represent the referred population in different parts of the country. A cross-sectional design was used. A total of 702 patients with DM from the NCDEG aged ≥20 years were consecutively enrolled between June 2005 and July 2006. Medical record abstraction of sociodemographic, clinical, and laboratory data was performed.

Results: The frequency of hypercholesterolemia was 77.2%, low high-density lipoprotein (HDL) was 83.9%, high low-density lipoprotein (LDL) was 91.5%, and hypertriglyceridemia was 83.1%. Females had greater abnormalities in lipid profiles. High LDL-cholesterol was the most common dyslipidemia in combination (91.5%) and in isolation (12.8%). Gender and hemoglobin A1C (HbA1c) predicted high total cholesterol; gender predicted high LDL-cholesterol; and use of beta-blockers predicted high triglycerides.

Conclusion: Over 90% of patients with type 2 DM had one or more types of dyslipidemia. The most common dyslipidemia in our study was high LDL-cholesterol and high triglycerides as reported in the literature. We recommend aggressive drug management, education, counseling, and behavioral interventions.

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From the National Center for Diabetes, Endocrinology and Genetics (Abdel-Aal, Ahmad, Hamza, Ajlouni, Froelicher), Jordan University, Amman, and the Department of Public Health (Batieha), College of Medicine, Jordan University of Science and Technology, Irbid, Jordan.

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Address correspondence and reprint request to: Prof. Kamel M. Ajlouni, The National Center for Diabetes, Endocrinology and Genetics, PO Box 13165, Amman 11942, Jordan. Tel. +962 (7) 77603603. Fax. +962 (6) 5356670. E-mail: ajlouni@ju.edu.jo

Type 2 diabetes mellitus (DM) is increasingly common worldwide reaching epidemic proportions.[1] Furthermore, cardiovascular diseases are the leading causes of death in many countries in the world including Jordan.[1,2] Patients with type 2 DM are at increased risk of accelerated atherosclerosis and premature death.[3,4] Dyslipidemias may contribute significantly to accelerated atherosclerosis. Because risk factors for coronary artery disease (CAD) are multiplicative, mild degrees of dyslipidemia may increase CAD risk considerably in the presence of other CAD risk factors.[5] Patients with DM have a 2-4 fold excess risk of CAD,[6] which is in part related to hyperglycemia. Other factors play an important role; the most common of these is dyslipidemia, a major risk factor for CAD.[7] Diabetes is considered a CAD equivalent by the East West study[8] and in the Organization to Assess Strategies for Ischemic Syndromes (OASIS) study.[9] In view of the high frequency of diabetes in Jordan, the high frequency of dyslipidemias that aggravate the complications of DM, and the lack of studies on these aspects in Jordan we initiated this study. The purposes of this paper are to report the frequency and patterns of dyslipidemia in patients with type 2 DM and to estimate the independent effects of sociodemographic and clinical variables on dyslipidemia.

Methods. A cross-sectional design was used. Since the National Center for Diabetes, Endocrinology and Genetics (NCDEG) inception in 1996, an examination on all patients, during each visit, was performed for blood pressure, body weight, ophthalmologic examination of the fundus and urine check for microalbuminuria. Total cholesterol, high-density lipoprotein-cholesterol (HDL-c), low-density lipoprotein-cholesterol (LDL-c) and triglycerides (TG) were checked in the first visit and at least every 6 months. Liver functions and renal functions were tested in the first visit and at least every year. All medical records of the patients who met the following inclusion criteria were eligible to be included in the study between June 2005 and July 2006: patients with a diagnosis of type 2 DM, receiving care at the NCDEG; age >20 years; and having 2 laboratory measurements of lipids one year apart. The exclusion criteria were patients with type 1 DM; pregnant women; and those without 2 lipid measurements approximately one year apart. These criteria yielded 702 patients. This sample size would be sufficient for 95% assurance in estimating lipid disorders, with a margin of error ≤3%, assuming the most conservative estimate of dyslipidemia of 50%. Operational definitions for study variables used the criteria for abnormal lipid levels based on the American Diabetes Association 2004.[10] Hypercholesterolemia refers to a total cholesterol (TC) level of ≥200 mg/dl, HDL-c was considered low when the level is <40 mg/dl in males, and <50 mg/dl in females; LDL-c was considered high when the level is ≥100 mg/dl; hypertriglyceridemia (TG) refers to a level ≥150 mg/dl; dyslipidemia is defined as the presence of one or more of the previous abnormalities in serum lipids, or normal level on treatment. Hypertension was defined as a diagnosis in the medical record; or current use of blood pressure lowering medications; or blood pressure values of >130 mm Hg systolic or >80 mm Hg diastolic on at least 2 occasions. Hypothyroidism was defined as a diagnosis in the medical record or use of thyroxin or a thyroid stimulating hormone (TSH) level >5mu/l. Coronary artery disease was defined as a previous diagnosis of CAD by angiography or electrocardiography. Diabetic retinopathy was defined as any degree of retinopathy detected by direct ophthalmoscopy carried out by an ophthalmologist in the NCDEG. Current smoking was defined as regular smoking of at least one cigarette per day for at least one month before enrollment. Laboratory measurement and cut-points were obtained at baseline and one year later. An automated spectrophotometer, Cobas Integra by Roche Diagnostics was used. Hemoglobin A1C (HbA1c) was assayed using high performance liquid chromatography; cut points for level of controls are ≤7 controlled; 7.1-8 fair; 8.1-10 poor; >10 uncontrolled. Microalbuminuria was measured using the dipstick method (Clinitek 00 made by Bayer Corporation-Elkhart IN 46515, USA). A value of >20 mg/L is considered positive. The laboratory standards used in NCDEG are the National Glyco Hemoglobin Standardization Program and the International Federation of Clinical Chemistry Methodologists. The medical records were reviewed for the use of selected medications: insulin, biguanides, sulphonylureas, thiazolidinediones, meglitinides, statins, fibrates, ezitemibes, beta-blockers and thiazide diuretics. Furthermore, the medications were coded as "used" or "not used," irrespective of dose.

Statistical Package for Social Sciences (SPSS), versions 11.5 was used for data entry, analyses, checking for errors, logical inconsistencies, and extreme outliers. Detected errors were verified and corrected. Means and standard deviations, frequencies, chi-square tests, and t-test were calculated and the level of significant was set at $p<0.05$. Logistic regression models were fitted for the high TC, high LDL-c, and high TG, and reported as odds ratios (OR) with a 95% confidence intervals (CI). Also, the independent effects of selected baseline variables were estimated on dyslipidemias after one year adjusting for potential confounders. This study was approved by the NCDEG Ethics Committee.

Results. Of the 702 patients with DM, 50.7% (n=356) were men [mean age 58.5(± 9.5) years] and 49.3% (n=346) were women [mean age 56.9 (± 9.3) years]. The mean ±SD duration of diabetes was 9.1 ± 7.1

years (**Table 1**). Most of the patients were overweight/obese (90.9%), with the females having higher body mass index than males ($p<0.05$). Approximately 70% of the patients had hypertension, 39.8% had microalbuminuria, 25% had diabetic retinopathy, and 12.2% had hypothyroidism. **Table 2** compares the mean ±SD for lipid values by gender. Most of the patients used lipid lowering medications: statins 68.9%; fibrates 7.4%; and ezitemibe 3.3%. **Table 1** shows a fair level of control of DM in males (mean HbA1c=7.7%) and females (mean HbA1c=7.9%) with no significant difference. **Table 2** shows the most common dyslipidemias in combination (91.5%) and in isolation (12.8%) was high LDL-c. All 4 disorders were found in 13.5%. Whereas, the combination of high TG and low HDL-c was observed in 7%. **Table 3** depicts

Table 1 - Lipids levels and hemoglobin A1C (HbA1c) by gender.

Lipids	Males	Females	Total
	Mean ± SD	Mean ± SD	Mean ± SD
Total cholesterol	177.7 ± 36.0	196.7 ± 47.2	187.0 ± 41.4
HDL-c	41.3 ± 8.6	48.0 ± 12.5	45.0 ± 11.1
LDL-c	118.9 ± 31.4	127.6 ± 35.9	123.3 ± 33.5
Triglycerides	173.9 ± 88.2	193.1 ± 161.9	181.6 ± 109.3
HbA1c in %	7.7 ± 1.6	7.9 ± 1.7	7.8 ± 1.6

HDL - high-density lipoprotein-cholesterol,
LDL - low-density lipoprotein-cholesterol, HbA1c - hemoglobin A1C

Table 2 - Patterns of isolated and combined dyslipidemias.

Dyslipidemia	Isolated n (%)	Any combination [a] n (%)
High LDL-c	90 (12.8)	637 (91.5)
Low HDL-c	46 (6.6)	336 (47.9)
High triglycerides	24 (3.4)	580 (83.1)
High LDL-c + high TG	34 (4.8)	
High LDL-c + low HDL-c	63 (9.0)	
High TG + low HDL-c	49 (7.0)	
High total cholesterol + high LDL-c + low HDL-c + high TG	95 (13.5)	

[a] This column is not mutually exclusive. HDL - high-density lipoprotein-cholesterol, LDL - low-density lipoprotein-cholesterol, TG - triglycerides

Table 3 - Frequency of dyslipidemia by selected variables (n=702).

Variables	Hypercholesterolemia	Low HDL	High LDL	Hypertriglyceridemia
	n (%)	n (%)	n (%)	n (%)
Gender				
Men	256 (72.7)	290 (81.5)	316 (89.0)	291 (82.2)
Women	278 (81.8)	299 (86.4)	321 (94.1)	289 (84.0)
P-value	0.01	0.07	0.02	0.52
Age group (years)				
<50	89 (67.9)	110 (82.1)	115 (87.1)	107 (80.5)
50-59	186 (79.5)	204 (85.4)	221 (93.6)	202 (85.2)
≥60	259 (79.2)	275 (83.6)	301 (91.8)	271 (82.6)
p-value	**0.02**	0.70	0.10	0.48
Body mass index				
<25	36 (67.9)	42 (79.2)	48 (90.6)	40 (75.5)
25 – 29.9	152 (76.4)	165 (82.1)	184 (92.0)	166 (83.0)
≥30	244 (76.5)	285 (87.4)	293 (91.3)	274 (84.8)
p-value	0.34	0.13	0.93	0.24
Duration of DM				
≤5 years	199 (76.2)	226 (84.6)	243 (91.7)	219 (82.6)
6- -10	141 (75.8)	160 (85.1)	171 (91.4)	159 (84.6)
≥11	190 (79.8)	198 (82.5)	216 (91.1)	197 (82.8)
p-value	0.53	0.72	0.98	0.84
Smoking				
Yes	57 (76.0)	65 (85.5)	68 (90.7)	63 (84.0)
No	152 (77.9)	162 (82.2)	178 (91.8)	158 (80.8)
p-value	0.82	0.73	0.92	0.73
Hypertension				
Yes	386 (80.1)	423 (86.2)	450 (92.6)	414 (85.0)
No	148 (70.8)	165 (78.6)	186 (89.0)	166 (79.0)
p-value	**0.01**	**0.01**	0.08	**0.04**
HbA1c (%)				
≤7	75.6 (183)	109 (44.1)	223 (90.7)	205 (83.3)
7.1- 9	250 (78.4)	163 (50.8)	292 (91.5)	264 (82.5)
>9	98 (77.2)	61 (47.7)	119 (93.7)	108 (84.4)
p-value	0.74	0.29	0.60	0.89

Table 4 - Summary of logistic regression analyses for hypercholesterolemia, high LDL, and hypertriglyceridemia.

Dyslipidemia	Odds ratio	95% Confidence interval	*P*-value
*Hypercholesterolemia**			
Gender	3.6	1.6, 7.8	0.00
HbA1c	1.3	1.1, 1.6	0.01
High LDL-c‡			
Gender	2.4	1.2, 4.6	0.01
*Hypertriglyceridemia***			
Use of beta-blockers	2.2	1.2, 3.5	0.01

Non significant variables were eliminated from the 3 models: *age, duration of diabetes, body mass index (BMI), hypertension, use of beta-blockers, use of lipid lowering agents, hypothyroidism were removed from the model; ‡age, duration of diabetes, BMI, HbA1c, hypertension, hypothyroidism, use of beta-blockers, use of lipid lowering agents were removed from the model; **age, gender, duration of diabetes, BMI, HbA1c, hypertension, hypothyroidism, use of lipid lowering agents were removed from the model.

the frequencies for dyslipidemias by gender, age and clinical variables. Females had statistically significantly higher frequencies of high TC and high LDL-c than males. Older patients tended to have a higher frequency of high TC's than younger patients ($p<0.02$). High TC, low HDL, and high TG were statistically significantly more common in patients with hypertension. **Table 4**, reports the statistically significant OR with 95% CI, obtained from a logistic regression analysis of gender and HbA1c on hypercholesterolemia. Whereas age, duration of diabetes, body mass index, hypertension, the use of beta-blockers, the use of lipid-lowering drugs, and hypothyroidism did not predict hypercholesterolemia; and were removed from the model. Females were more likely to have high TC than males [OR=3.6, 95%CI (1.6, 7.8)]. For each 1% increase in HbA1c there was a 1.3 fold [95% CI (1.1, 1.6)] rise in the risk of high TC. Age, gender, duration of diabetes, BMI, hypertension, the use of beta-blockers, the use of lipid-lowering drugs, and HbA1c were not significantly predictive of low HDL-c and thus were removed from the model. Gender [females versus males OR=2.4, 95% CI (1.2, 4.6)] was significantly and independently predictive of elevated LDL levels. Whereas, age, duration of diabetes, BMI, HbA1c, hypertension, the use of lipid-lowering drugs, and hypothyroidism were not significantly related to high LDL and were thus removed from the model (**Table** 4). Use of beta-blockers was significantly and independently predictive of hypertriglyceridemia [OR=2.2, 95% CI (1.2, 3.5)]. Whereas, age, gender, duration of diabetes, body mass index, HbA1c, hypertension, the use of lipid-lowering drugs, and hypothyroidism were not significantly related to high TG; and were removed from the model.

Discussion. Our study of 702 patients showed a different pattern and a surprisingly high frequency of dyslipidemia (high LDL-c of 91.5%, low HDL-c of 83.9%, high TG of 83.1% and high TC of 77.2%) compared with reports from Kuwait,[11] Yemen,[12] Ethiopia,[13] India,[14] and Nepal;[15] but similar to Malaysia.[16] The variation in the patterns of dyslipidemia reported by different studies may be the result of differing cut points, different populations and different surveillance methods across these studies. Apart from genetic differences, cultural factors, dietary and exercise pattern and therapeutic approaches may determine the patterns of dyslipidemia in patients with DM. Females had higher TC's, TG's, and LDL-c than males. This gender difference is similar to the LDL-c in the U.K. Prospective Diabetes Study study;[17] and for TG in an Ethiopian study. Moreover, females in our study had lower HDL-c levels consistent with studies from Kuwait and Malaysia. However, this observation has not been consistent. The findings from our study are based on patients with DM and show a much higher frequency of high TC (77.2% versus 41.5) and high TG (83.1% verses 38.6) compared to a prior population-based study in Jordan.[18] In our study, gender was a major factor in determining the TC and LDL-c levels. The pattern of dyslipidemia in our study differed from the "typical" diabetic dyslipidemia (namely high TG and low HDL-c with no difference in the levels of TC or LDL-c) as reported in many studies.[19-21] Although the so called 'typical' diabetic dyslipidemia was present in our patients, it was not the most common form of dyslipidemia encountered. Our data showed that high LDL-c was the most frequent lipid abnormality. A number of studies have reported no or little difference in LDL-c level between diabetics and non diabetics.[10,22] This observation has been disputed by others showing significant frequencies of high LDL's in diabetics compared to non-diabetics.[11,13,14,17,23] The low HDL-c observed in the present study is consistent with the findings of other studies.[24] Patients with DM had a higher frequency of low HDL-c compared to the general population. We noticed that more than 80% of patients had low HDL-c, which adds to their CV risk, since HDL-cholesterol is a powerful predictor of CVD in patients with diabetes.[25] Decreased HDL-c in patients with DM is an end result of insulin resistance, which eventually leads to increased catabolism of HDL in the presence of normal levels of activity of the cholesteryl ester transfer protein (CETP) and hepatic lipase. Low levels of HDL-c may as well result from decreased production secondary to impaired catabolism of VLDL-c and decreased lipoprotein lipase (LPL) activity. Our study also showed a high frequency of high

TG (80%). Elevated TG is an established CV risk factor and has recently been shown also to be independent of other covariates.[26] Of note is that a study conducted by Hokanson et al showed that the CV risk of high TG differs by gender; with a 1.3 fold increase in males and a 1.8 fold increase in females.[27] Glycemic control as measured by HbA1c was a significant determinant of TC; this finding confirms earlier results by others.[28-30] It should be noted that our estimates of frequencies of dyslipidemia in type 2 DM may not be representative of Jordan, but represents those who attended the NCDEG and are likely to have more severe diabetes and a higher frequency of complications, therefore estimates reported in our study are likely to be overestimating the Jordanian population. Alternatively, potential survival bias may underestimate the true population prevalence. Prospective and longitudinal studies in patients with type 2 diabetes starting at the time of diagnose is needed.

In conclusion, dyslipidemia is very common among type 2 diabetics, combination of abnormalities in lipids is more common than single abnormalities. Prospective studies are needed.

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References

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