Association of diabetes mellitus and dyslipidaemias in the Tehran population

K. Ghoddusi,[1] J. Ameli,[2] H. Kachuee,[2] V. Pourfarziani,[3] A. Saadat[4] and Q. Karami[5]

ترافق السكري مع اختلالات شحميات الدم لدى سكان طهران

كاظم قدوسي، جواد عاملي، حسين كجويي، وحيد بورفرزياني، عليرضا سعادت، غلامرضا كرمي

الخلاصة: استهدفت هذه الدراسة تقييم تأثير السكري على مرتسم شحميات الدم لدى سكان طهران وقد أجرى الباحثون قياسات لسكر الدم، والغليسريدات الثلاثية، والكوليستيرول الإجمالي، وكوليستيرول البروتينات الشحمية المنخفضة الكثافة وكوليستيرول البروتينات الشحمية الرفيعة الكثافة لدى 136 10 من الأشخاص الذين تتراوح أعمارهم بين 20 و69 عاماً، كما جمع الباحثون منهم معلومات عن السوابق الطبية والأنشطة البدنية والتدخين والبدانة. وكان معدل انتشار أيٍّ نمط من أنماط اختلال شحميات الدم في مجمل المجموعة 68.5٪، في حين كان معدل انتشار السكري 11٪ (10.6 لدى الرجال و11.3٪ لدى النساء). وكان معدل انتشار اختلال شحميات الدم بين السكريين 88.9٪ ولوحظ ترابُط قوي بين السكري وبين اختلال شحميات الدم (P <0.05). وفي تحليل التحوُّف كان السكري هو العامل الثاني بعد البدانة بين أهم العوامل المسبِّبة للاختلال الثانوي لشحميات الدم.

ABSTRACT The aim of this survey was to evaluate the role of diabetes in the lipid profiles of the Tehran population. Measurements were carried out on 10 136 people aged 20–69 years for blood sugar, triglycerides, total cholesterol, LDL cholesterol, and HDL cholesterol and data were collected on medical history, physical activity, smoking and obesity. The prevalence of any type of dyslipidaemia in the whole group was 68.5% and of diabetes mellitus was 11.0% (10.6% in men and 11.3% in women). The prevalence of dyslipidaemia in diabetics was 88.9%. There was strong association between diabetes mellitus and dyslipidaemia (***P*** < 0.05). In regression analysis, diabetes was the second most important factor after obesity in secondary dyslipidaemia.

Association de diabète sucré et de dyslipidémies dans la population de Téhéran

RÉSUMÉ Cette étude avait pour but d'évaluer le rôle du diabète dans les profils lipidiques de la population de Téhéran. Des mesures de la glycémie, des triglycérides, du cholestérol total, du cholestérol LDL et du cholestérol HDL ont été effectuées chez 10 136 sujets âgés de 20 à 69 ans et des données ont été recueillies sur les antécédents médicaux, l'exercice physique, le tabagisme et l'obésité. La prévalence de tous les types de dyslipidémie dans l'ensemble du groupe était de 68,5 % et celle du diabète sucré de 11,0 % (10,6 % chez les hommes et 11,3 % chez les femmes). La prévalence de la dyslipidémie chez les diabétiques était de 88,9 %. Il existait une forte association entre le diabète sucré et la dyslipidémie (p < 0,05). L'analyse de régression a démontré que le diabète était le deuxième facteur le plus important de dyslipidémie secondaire après l'obésité.

[1]Department of Endocrinology and Metabolism; [2]Department of Neurology; [3]Department of Nephrology; [4]Department of Haematology; [5]Department of Psychiatry, Baqyatallah University of Medical Science, Tehran, Islamic Republic of Iran (Correspondence to J. Ameli: javad_ameli@yahoo.com).
Received: 14/12/05; accepted: 09/03/06

Introduction

No other life-threatening disease is as prevalent or expensive to society and individuals as coronary artery disease (CAD). Atherosclerosis is responsible for almost all cases of CAD. Risk factor assessment is useful in adults to guide therapy and multivariate analysis can be used to help estimate the risk of coronary disease events [*1*]. Many of the important risk factors for cardiovascular disease are modifiable by specific preventive measures. In the INTERHEART study, 9 potentially modifiable factors accounted for over 90% of the attributable risk in the population [*2*]. In the same study, diabetes mellitus accounted for 10% of the population attributable risk of a first myocardial infarction.

The reports of the National Health and Nutrition Examination Survey (NHANES) have shown that between 1960 and 2000 the prevalence of diagnosed diabetes increased from 1.8% to 5.0% [*3*]. In contrast, the proportion of people with hypercholesterolaemia (serum total cholesterol ≥ 240 mg/dL) declined substantially in the same period (from 34% to 17%).

Serum lipid abnormalities have been clearly shown to be risk factors for CAD; these include elevated low-density lipoprotein cholesterol (LDL-C), low high-density lipoprotein cholesterol (HDL-C), increased total-to-HDL-cholesterol ratio and hypertriglyceridaemia. The frequent coexistence of diabetes and hypercholesterolaemia further raises the risk for CAD and its associated morbidity [*4*].

In the Islamic Republic of Iran the age-adjusted mortality due to CAD increased by 20%–45% during 1971–91 [*5,6*]. Previous studies have reported the prevalence of cardiovascular risk factors among the Iranian population [*7,8*] and the aim of the present study was to evaluate the relationship between diabetes and hyperlipidaemia in the Tehran population. The data reported here are a part of more extensive study in which many confounding factors were evaluated, including hypothyroidism, physical activity, renal failure, nephrotic syndrome, smoking, obesity, lipogenic medications, and pregnancy. This paper focuses on the association of diabetes and dyslipidaemia.

Methods

Sample

In a cross-sectional, multi-stage, stratified cluster, random sampling technique, 10 136 people aged 20–69 years were selected from the Tehran population. The list of all households covered by the district's 3 health care centres (the official bodies responsible for the vaccination programmes and collection of health-related statistics in a district) was used to choose a random sample of households. In each household, all members aged 20–69 years were recruited. The district is located in the centre of Tehran and the age distribution of its population is representative of the overall population of Tehran.

Data collection

The participants were evaluated at the Tehran Lipid and Glucose Study clinic between September 2004 and March 2005 by trained physicians according to a standard protocol. After giving informed consent, personal, demographic, physical activity, smoking, and anthropometric information was obtained. Personal information included age, sex, past medical history and medications. The level of physical activity was defined according to the lipid research clinic criteria. Then subjects were divided into 3 groups: low, moderate and high physical activity. Smoking was defined as a person who continuously smoked at least 1 ciga-

rette per day. Smokers were divided into 5 groups of 1–5, 6–10, 11–15, 16–20 and > 20 cigarettes per day. Anthropometric data were obtained after empting the bladder and bowel. Weight was measured with the participant wearing underwear and without shoes. Height was determined with a wall measure in the standing position. Body mass index (BMI) was calculated by the equation: weight (kg)/height (m^2).

People were excluded if they had: a history of antilipidaemic medication or any other drugs interfering with lipid metabolism within the previous 3 months; significant hepatic, renal or thyroid dysfunction; acute or chronic inflammatory diseases; immobilization; recent surgical operations; myocardial infarction or cerebrovascular accident; or pregnancy.

Blood samples were drawn between 07:00 and 09:00 hours from all study participants after 12–14 hours of overnight fasting. Total cholesterol (TC), HDL-C, LDL-C, triglycerides (TG), fasting blood sugar (FBS), creatinine, thyroid-stimulating hormone (TSH), alkaline phosphatase, and bilirubin levels were assayed. Then, 2-hour postprandial plasma glucose was measured after 75 g oral glucose. Having 2 repeated creatinine levels > 2 mg/dL was defined as renal failure; 5 females and 8 males (total 13) had renal failure and all of them were dyslipidaemic. TSH level was assayed with an immunoradiometric assay method. TSH level > 10 μU/L was defined as hypothyroidism; 16 female and 8 males (total 24) had hypothyroidism. All of the hypothyroid males and 15 females were dyslipidaemic. Alkaline phosphatase was tested with enzymatic calorimetry; none of the subjects had abnormal levels. Bilirubin was checked if alkaline phosphatase was above the normal limit.

A creatinine level above 2 mg/dL for at least 2 months was considered as chronic renal failure. Dyslipidaemia was defined by the presence of high TC (≥ 240 mg/dL), high LDL-C (≥ 160 mg/dL), low HDL-C (< 35 mg/dL) or high TG (> 400 mg/dL) according to the Adult Treatment Panel (ATP) II criteria. Dyslipidaemia was defined as primary if none of the known contributing factors (low physical activity, nephrotic syndrome, hypothyroidism, obesity, smoking, diabetes mellitus and use of dyslipidaemia-inducing medications) was present. Diabetes was defined as FBS ≥ 126 mg/dL or 2-hour postprandial plasma glucose ≥ 200 mg/dL, according to American Diabetes Association criteria

Analysis

The analysis was done with *SPSS*, version 10.05 software package and using the *t*-test, chi-squared test and logistic regression. Logistic regression was used to calculate the odds ratio (OR) and 95% confidence interval (CI) for physical activity, renal failure, hypothyroidism, BMI, smoking and diabetes mellitus. *P*-values < 0.05 were considered significant.

Results

A total of 9632 adults (4013 men and 5619 women) matched the inclusion and exclusion criteria. There were 1059 people with diabetes (425 men and 643 women), giving a prevalence of diabetes in our population of 11.0%. The prevalence of diabetes was 10.6% in men and 11.3% in women

The prevalence of any type of dyslipidaemia in the total study population was 68.5% (n = 6598). This was slightly higher in men (72.3%, n = 2901) than women (65.8%, n = 3697). The prevalence of dyslipidaemia in diabetics was 88.9% (n = 941), which was significantly higher than in the general population ($P < 0.05$). The prevalence of dyslipidaemia was lower in diabetic men (86.0%, n = 365) than diabetic

women (90.9%, *n* = 576). The prevalence of primary dyslipidaemia was 35.4% (39.8% of men and 31.9% of women). High TC was the most common dyslipidaemia in women (26.9%) and low HDL-C (31.4%) was the most common in men. The mean levels of serum TG, TC and LDL-C in diabetic people were significantly higher than in nondiabetic people (Tables 1 and 2). Not surprisingly, HDL-C also was higher in diabetics than nondiabetics ($P < 0.05$).

High TC was the most common dyslipidaemia in diabetic women (52.8%) and high LDL-C was the most common in diabetic men (37.4%).

Table 3 shows the number of patients with and without dyslipidaemia by diabetes mellitus, hypothyroidism, renal failure, smoking and obesity. Table 4 shows the variables that were significant when the individual odds were evaluated with logistic regression analysis. Obesity (BMI > 30 kg/m^2) had the greatest association with lipid profile (OR = 2.71; 95% CI: 1.97–3.75). Diabetes mellitus was strongly associated with dyslipidaemia (OR = 2.38; 95% CI: 1.42–3.98). Smoking (OR = 1.85; 95% CI: 1.29–2.66) and age (OR = 1.07; 95% CI: 1.06–1.08) were also significantly associated. Because of the low frequency of nephropathy and hypothyroidism, their roles in dyslipidaemia were not significant. Table 5 shows more details of the relationship of lipid profiles with age and sex.

In the general population, the prevalence of low physical activity was 62.6% (*n* = 6029), moderate activity 13% (*n* = 1253) and vigorous physical activity 24.4% (*n* = 2351). Although dyslipidaemia was prevalent in all 3 groups, the prevalence decreased with increasing physical activity: 68% in the low physical activity group, 66% in the moderate physical activity group and 62% in the vigorous physical activity group.

Table 1 **Prevalence of dyslipidaemias in the study population and diabetic group**

Lipid	General population						Diabetics			
	Total (*n* = 9632)		Men (*n* = 4013)		Women (*n* = 5619)		Total (*n* = 1059)		Men (*n* = 425)		Women (*n* = 643)	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Dyslipidaemia (any type)	6598	68.5	2901	72.3	3697	65.8	941	88.8	365	85.9	576	89.6
High triglycerides (≥ 400 mg/dL)	401	4.2	211	5.3	190	3.4	122	11.5	52	12.2	70	10.8
High total cholesterol (≥ 240 mg/dL)	2308	24.0	794	19.8	1514	26.9	486	45.9	146	34.3	340	52.8
High LDL-cholesterol (≥ 160 mg/dL)	2138	22.2	1263	31.5	733	13.0	264	24.9	159	37.4	105	16.3
Low HDL-cholesterol C (< 35 mg/dL)	1994	20.7	776	19.3	1364	24.3	361	34.1	114	26.8	247	38.4

n = ***total number of participants; LDL = low-density lipoprotein; HDL = high-density lipoprotein.***

Table 2 **Mean serum lipid levels in the general study population and the diabetic group**

Lipid (mg/dL)	General population (*n* = 9632) Mean (SE)	Diabetics (*n* = 1059) Mean (SE)
Total cholesterol	226.0 (0.5)	244.0 (2.0)
Triglycerides	196.0 (6.0)	264.5 (6.0)
LDL-cholesterol	148.3 (0.5)	155.0 (1.5)
HDL-cholesterol	40.7 (0.1)	41.1 (0.5)

n ***= total number of participants; SE = standard error; LDL = low-density lipoprotein; HDL = high-density lipoprotein.***

Discussion

The prevalence of diabetes in our sample of the Tehran population was 11.0%, which is higher than previous reports in Brazil [*9*], the Netherlands [*10*] and Germany [*11*]. In Australia, the AusDiab study reported that 7.4% of the population aged 25 years or over had diabetes mellitus, 90% of whom had type 2 diabetes [*12*]. The prevalence of diabetes increases progressively with age. The prevalence of type 2 diabetes has more than doubled in Australia since 1981, and the total number of cases has increased threefold. A high prevalence of diabetes in the Tehran population could be attributed to industrialization in the Islamic Republic of Iran, leading to modification of lifestyles, unhealthy diets, decreased physical activity and an increased prevalence of obesity. In addition, increased attention of patients and physicians and widespread screening to identify undiagnosed cases could be other reasons for the high prevalence of diabetes.

Among the diabetics in our study, the frequency of hypercholesterolaemia was 45.9%, high LDL-C was 24.9%, low HDL-C was 34.1% and hypertriglyceridaemia was 11.5%. All of these rates were significantly higher than in the general population. This suggests an important influence of diabetes on the lipid profile of our diabetic population. Lipid abnormalities are common in patients with diabetes mellitus, and undoubtedly contribute to the increased risk of cardiovascular disease. The lipid pattern in patients with type 1 diabetes is largely related to glycaemic control. Several studies have shown that type 2 diabetes, poor glycaemic control and insulin resistance are associated with hypertriglyceridaemia, high

Table 3 **Number of patients with and without dyslipidaemia by diabetes mellitus, hypothyroidism, renal failure, smoking and obesity**

Patient group	Dyslipidaemia No.	No dyslipidaemia No.
Diabetes		
Yes	941	118
No	5657	2916
Hypothyroidism		
Yes	23	1
No	6575	3033
Renal failure		
Yes	13	0
No	6585	3034
Current smoking		
Yes	538	547
No	6060	2487
Obesity		
Yes	978	1979
No	5620	1055

Table 4 **Factors significantly associated with secondary dyslipidaemia**

Variable	Odds ratio	95% CI
Diabetes	2.38	1.42–3.98
Obesity	2.71	1.97–3.75
Current smoking	1.85	1.29–2.66
Age (years)	1.07	1.06–1.08

CI = confidence interval

Table 5 **Serum lipids by age and sex**

Lipid/age (years)	Males				Females			
	Percentile				Percentile			
	75th	50th	25th	Mean	75th	50th	25th	Mean
Total cholesterol (mg/dL)								
20–29	200	177	153	180	201	177	155	181
30–39	229	202	175	204	225	198	173	201
40–49	238	212	184	213	239	212	187	215
50–59	237	213	186	214	275	243	212	246
60–69	242	213	186	216	275	244	216	247
Triglycerides (mg/dL)								
20–29	170	114	81	144	130	91	68	110
30–39	229	161	112	191	180	121	86	145
40–49	253	176	122	214	220	156	111	180
50–59	234	169	122	195	255	184	134	215
60–69	219	149	106	180	251	177	129	205
LDL-cholesterol (mg/dL)								
20–29	129	110	90	112	131	109	92	113
30–39	153	129	107	130	149	126	104	128
40–49	159	135	111	137	157	134	113	137
50–59	158	137	116	138	183	156	132	159
60–69	164	139	116	142	185	159	133	161
HDL-cholesterol (mg/dL)								
20–29	46	39	32	39	53	46	39	46
30–39	42	35	32	38	53	42	39	45
40–49	42	35	32	38	49	42	35	43
50–59	42	39	32	38	53	46	39	46
60–69	46	39	32	40	53	46	39	46

LDL = low-density lipoprotein; HDL = high-density lipoprotein.

LDL-C and low HDL-C concentrations [*13–15*]. In our study the mean HDL-C level in diabetics was slightly higher than in the general population (41.1% versus 40.7%). This is an unusual and new finding and we have no explanation for it. The low prevalence of hypertriglyceridaemia in our diabetic population could be due to our diagnostic criteria (ATP II) which defined hypertriglyceridaemia as TG level > 400 mg/dL. If we had chosen the ATP III criteria (TG > 200 mg/dL), hypertriglyceridaemia would probably become the most common metabolic disorder in diabetics.

This study revealed that hyperlipidaemia is a major problem in the Tehran population and secondary causes may have a role in its occurrence. Many of our participants had more than one CAD risk factor. However, logistic regression and odds ratios demonstrated that after obesity, diabetes was the most important factor associated with secondary dyslipidaemia in this population. We know that about half of diabetics are unaware of their disease. Therefore, screening programmes for diabetes and lipid profile testing of diabetics is recommended.

Acknowledgements

We express appreciation to the participants of Tehran Lipid and Glucose Study unit, the Health Department of Shahid Beheshti University of Medical Sciences and Mrs S. Sadeghi.

References

1. Ridker PM. Evaluating novel cardiovascular risk factors: can we better predict heart attacks? ***Annals of internal medicine***, 1990, 130(11):933–7.
2. Yusuf S et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case–control study. ***Lancet***, 2004, 364:937–52.
3. Gregg EW et al. Secular trends in cardiovascular disease risk factors according to body mass index in US adults. ***Journal of the American Medical Association***, 2005, 293(15):1868–74 (Erratum in: ***JAMA***, 2005, 294(2):182).
4. Grundy SM et al. Primary prevention of coronary heart disease: guidance from Framingham. A statement for healthcare professionals from the AHA Task Force on Risk Reduction. American Heart Association. ***Circulation***, 1998, 97(18):1876–87.
5. Alwan A, ed. ***Prevention and control of cardiovascular diseases.*** Alexandria, World Health Organization Regional Office for the Eastern Mediterranean, 1995:24 (WHO EMRO Technical Publications Series, 22).
6. Zali M, Kazem M, Masjedi MR. [***Health and disease in Iran***]. Tehran, Deputy of Research, Ministry of Health, 1993 (Bulletin No. 10) [in Farsi].
7. Azizi F et al. Cardiovascular risk factors in an Iranian urban population: Tehran lipid and glucose study (phase 1). ***Sozial- und Präventivmedizin***, 2002, 47(6):408–26.
8. Sheikholeslam R et al. Non communicable disease risk factors in Iran. ***Asia Pacific journal of clinical nutrition***, 2004, 13(Suppl.):S100.
9. Castanho VS et al. Sex differences in risk factors for coronary heart disease: a study in a Brazilian population. ***BMC public health***, 2001, 1(1):3.
10. Ubink-Veltmaat LJ et al. Prevalence, incidence and mortality of type 2 diabetes mellitus revisited: a prospective population-based study in The Netherlands (ZODIAC-1). ***European journal of epidemiology***, 2003, 18(8):793–800.
11. Clemens A, Reimann JF, Seigel EG. Optimierte Diabetestherapie beim Typ-2-Diabetiker [Optimized diabetes therapy in type 2 diabetics]. ***Medizinische Klinik (Munich, Germany: 1983)***, 2003, 98(9):484–92.
12. Dunstan DW et al. The rising prevalence of diabetes and impaired glucose tolerance: the Australian Diabetes, Obesity and Lifestyle Study. ***Diabetes care***, 2002, 25(5):829–34.
13. Pérez A et al. Prevalence and phenotypic distribution of dyslipidemia in type 1 diabetes mellitus: effect of glycemic control. ***Archives of internal medicine***, 2000, 160(18):2756–62.
14. Battisti WP, Palmisano J, Keane WE. Dyslipidemia in patients with type 2 diabetes. Relationships between lipids, kidney disease and cardiovascular disease. ***Clinical chemistry and laboratory medicine***, 2003, 41(9):1174–81.
15. Stalder M, Pometta D, Suenram A. Relationship between plasma insulin levels and high density lipoprotein cholesterol levels in healthy men. ***Diabetologia***, 1981, 21(6):544–8.