Cardiovascular disease and risk factors in patients with type 2 diabetes mellitus in Mashhad, Islamic Republic of Iran

S. Bonakdaran,[1] S. Ebrahimzadeh[1] and S.H. Noghabi[1]

المرض القلبي الوعائي وعوامل الاختطار لدى المرضى بالسكريّ من النمط الثاني في مدينة مشهد في جمهورية إيران الإسلامية
شوكوفه بنكدران، سعيد ابراهيم زاده، سبيده حجازي نُقابي

الخلاصة: وتهدف هذه الدراسة التي أجريت في الأعوام 2006-2008 إلى تحديد معدل انتشار وعوامل اختطار المرض القلبي الوعائي بين المرضى الإيرانيين المصابين بالسكريّ من النمط الثاني. وقد سُجِّلَت السوابق المرضيّة والفحوص البدنية وأُجْرِيَت فحوصٌ مختبرية لسبع مئة واثنين وخمسين مريضاً راجعوا مركز بحوث الغدد الصماء والاستقلاب في مدينة مشهد. وقد بلغ معدل انتشار المرض القلبي الوعائي 20.1٪، وتَرَابَطَ المرض القلبي الوعائي تَرَبُطاً يُعْتَدُّ به إحصائياً بالعمر، ومدة السكريّ، وفرط ضغط الدم، واعتلال الشبكية السكريّ، والمتلازمة الاستقلابية، والقصور الكلويّ، وثلاثي الغليسريدات، وكوليسترول البروتين الشحمي الرفيع الكثافة، وحمض اليوريك، ونسبة ثلاثي الغليسريدات إلى البروتين الشحمي الرفيع الكثافة. وعند استخدام نموذج التحوّف اللوجستي تبيَّن أن العمر، والمتلازمة الاستقلابية، وكوليسترول البروتين الشحمي الرفيع الكثافة تمثِّل مُنْبِئَات مستقلة يُعْتَدُّ بها للمرض القلبي الوعائي. ويُبْرِزُ الانتشار الواسع للمرض القلبي الوعائي بين المرضى الإيرانيين بالسكريّ من النمط الثاني أهمية تحسين سُبُل اكتشاف وعلاج عوامل الاختطار الاَستقلابية للمرض القلبي الوعائي في هؤلاء المرضى.

ABSTRACT The aim of this study in 2006–08 was to determine the prevalence and risk factors of CVD in an Iranian population of patients with type 2 diabetes mellitus. History and physical examinations were recorded and laboratory tests were performed in 752 patients attending the Mashhad Endocrine and Metabolism Research Center. The prevalence of CVD was 20.1%. CVD was significantly associated with age, duration of diabetes, hypertension, diabetic retinopathy, metabolic syndrome, renal insufficiency, triglycerides, high-density lipoprotein (HDL) cholesterol, uric acid and triglycerides/HDL ratio. Using a logistic regression model, age, metabolic syndrome and HDL cholesterol were significant independent predictors of CVD. The high prevalence of CVD in Iranian patients with type 2 diabetes underscores the importance of better detection and treatment of metabolic risk factors of CVD in these patients.

Maladies cardio-vasculaires et facteurs de risque chez des patients atteints de diabète de type 2 à Mashhad (République islamique d'Iran)

RÉSUMÉ La présente étude visait à déterminer la prévalence et les facteurs de risque des maladies cardio-vasculaires dans une population iranienne de patients atteints de diabète de type 2 entre 2006 et 2008. Les antécédents et les examens cliniques de 752 patients consultant dans un centre de recherche sur l'endocrinologie et le métabolisme ont été consignés et des analyses en laboratoire ont été réalisées. La prévalence des maladies cardio-vasculaires était de 20,1 %. Les maladies cardio-vasculaires étaient significativement associées avec l'âge, la durée du diabète, l'hypertension, une rétinopathie diabétique, un syndrome métabolique, une insuffisance rénale, le taux de triglycérides, le taux de cholestérol des lipoprotéines de haute densité, l'acide urique et le rapport entre les triglycérides et les lipoprotéines de haute densité. L'analyse de régression logistique a révélé que l'âge, un syndrome métabolique et le taux de cholestérol des lipoprotéines de haute densité étaient des facteurs prédictifs indépendants importants pour les maladies cardio-vasculaires. La prévalence élevée des maladies cardio-vasculaires chez les patients iraniens souffrant de diabète de type 2 souligne l'importance d'un meilleur dépistage des facteurs de risque métaboliques de ces maladies chez les patients diabétiques et d'un meilleur traitement.

[1]*Endocrine Research Centre, Mashhad University of Medical Science, Mashhad, Islamic Republic of Iran (Correspondence to S. Bonakdaran: bonakdaransh@mums.ac.ir).*

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Introduction

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in type 2 diabetes mellitus (DM) [1]. DM is a risk equivalent for coronary heart disease (CHD) [2]. Silent ischaemia and asymptomatic CHD is more frequent in DM. Patients with type 2 DM have higher levels of atherogenic lipids [3], hypertension [4], obesity [5], insulin resistance [6], microalbuminuria [7], autonomic neuropathy [8], coagulation disorders [9] and other non-traditional risk factors that all contribute to increased risk of CVD in these patients. About 70% of mortality in DM is related to CHD [10], so early risk recognition and management of patients with DM is very important. The aim of this study was to determine the prevalence of CVD and risk factors that predict CVD in an Iranian population of patients with type 2 DM.

Methods

A cross-sectional study was carried out in Mashhad, Islamic Republic of Iran.

Sample

Between December 2006 and July 2008 a total of 1287 consecutive patients aged 40 years or older attending the Mashhad Endocrine and Metabolism Research Center with type 2 diabetes were enrolled. Among them 752 patients received total cardiovascular disease screening. Diagnosis of type 2 diabetes was based on World Health Organization (WHO) criteria

Clinical examinations

A complete history was taken for age, smoking status (former/current smoker or never smoker), duration of DM, family history of CVD and personal history of hypertension and hyperlipidaemia and treatments used. Clinical examinations included weight, height, blood pressure, fundoscopy and peripheral pulse assessment. A 12-lead resting electrocardiogram (ECG) was taken from all patients. Patients with baseline ECG changes suggestive of CHD, previous history of myocardial infarction, angina, coronary artery bypass graft, angioplasty, treatment for CVD, cerebrovascular accident, transient ischaemic attack, carotid surgery and peripheral vascular disease or absence of peripheral pulse were defined as symptomatic CVD. Patients without symptomatic CHD who were able to perform exercise were subjected to an exercise stress test. Other patients with contraindications or limitations for the exercise stress test underwent thallium scintigraphy.

On the basis of these factors the patients were divided into 2 groups: CVD (symptomatic or asymptomatic), i.e. patients with overt signs/symptoms of CVD or patients with a positive test in the exercise stress test or perfusion scan; and non-CVD, i.e. patients without signs/symptoms of CVD or with negative screening tests.

In patients without CVD, the CHD risk at 10 years was estimated using the UK Prospective Diabetes Study risk engine [11] and patients' risk score was then grouped as: < 10% (low risk), 10%–19% (moderate risk) and ≥ 20% (high risk) for CHD.

Hypertension was defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg in the resting position for at least for 30 minutes on 2 different occasions or history of hypertension and receiving antihypertensive drugs. The presence of retinopathy was evaluated by fundoscopic examination by an expert ophthalmologist. Obesity was defined as BMI > 30 kg/m^2. Abdominal obesity was waist circumference ≥ 102 cm in males and ≥ 88 cm in females. Metabolic syndrome was defined according to the Adult Treatment Panel III criteria as the presence of 3 or more of its 5 components (elevated blood pressure, elevated serum triglycerides, high waist circumference, high plasma glucose and low HDL) [12].

Laboratory tests

Total cholesterol, triglycerides (TG) and high-density lipoprotein (HDL) cholesterol were measured by the enzymatic method (ParsAzmon). Low-density lipoprotein (LDL) cholesterol was calculated according to the Friedwald formula [LDL= total cholesterol – (HDL + TG/5)]. Non-HDL cholesterol was calculated by the difference between total cholesterol and HDL. TG/HDL cholesterol ratio was calculated for assessment of the level of dense LDL, a relatively novel lipoprotein index that could serve as a good predictor of CHD [13,14]. The cut-offs for abnormal levels were: TG ≥ 150 mg/dL, total cholesterol ≥ 200 mg/dL, HDL cholesterol ≤ 40 mg/dL males or ≤ 50 mg/dL females, non-HDL cholesterol ≥ 130 mg/dL, LDL cholesterol ≥ 100 mg/dL, TG/HDL cholesterol ≥ 3.

All patients were diabetics on treatment and fasting blood sugar (FBS) was measured routinely by the glucose oxidase method (Human GmbH).

Glycated haemoglobin (HbA1C) was assessed by column chromatography (Biosource), using a cut-off of > 7% for abnormal levels.

Urine albumin in spot urine was measured by immunoturbidometry assay (ParsAzmon). Urine creatinine was measured by enzymatic colorimetric assay normal cut off > 20–25 mg/kg in males and 15–20 mg/kg in females). Uric acid was measured by enzymatic method and hyperuricaemia was defined as the serum levels > 7.0 mg/dL in men and > 5.5 mg/dL in women. Blood urea nitrogen was assessed by colorimetric method with normal range between 5–20 mg/dL. Albumin excretion was determined by calculation of the albumin to creatinine ratio in spot urine test on a fresh early morning sample, and microalbuminuria was defined as a ratio 30–300 mg/g and

macroalbuminuria as the ratio > 300 mg/g in 2 out of 3 measurements. Creatinine clearance was detected using the Crockcroft–Gault formula. Normal renal function was defined by creatinine clearance > 90 mL/min/1.73 m^2 and renal insufficiency by creatinine clearance < 60 mL/min/1.73 m^2.

Data analysis

Statistical analyses were performed by *SPSS*, version 16. Data was expressed as mean and standard deviation (SD). Non-normal variables were compared by Mann–Whitney U-test. Other variables were tested by either one-way ANOVA or Student *t*-test. Categorical variables were compared by the chi-squared test. Variables with a statistically significant difference between the CVD and non-CVD groups were evaluated by multiple logistic regression with forward stepwise analysis to identify independent risk factors for CVD. *P*-values <0.05 were considered significant.

Results

A total of 752 patients (355 males and 397 females) with type 2 DM were analysed. Their mean duration of DM was 7.9 (SD 6.4) years. The clinical and biochemical characteristics of the study group are shown in Table 1. Overall 151 (20.1%) of our patients had CVD. The mean CHD risk score in patients without CVD was 19.9% (SD 13.2%).

The prevalence of CVD risk factors in the total sample is shown in Table 2. Hypertension or history of hypertension was observed in 51.6% of our patients and blood pressure under optimal control (< 130/80 mmHg) was only detected in 21.0% of the sample. Obesity was found in 25.7% and abdominal obesity in 45.8%. A high proportion of our patients (73.5%) had metabolic syndrome. Diabetic retinopathy was found in 14.3%. Three-quarters (75.0%) had HbA1C > 7%. Lipid abnormalities

Table 1 Characteristics of the patients with type 2 diabetes mellitus (*n* = 752)

Variable	Mean	SD
Demographic and clinical data		
Age (years)	52.7	10.5
Duration of DM (years)	7.9	6.4
BMI (kg/cm^2)	28.0	4.1
Waist circumference (cm)	106.8	12.3
Systolic blood pressure (mmHg)	141.6	18.7
Diastolic blood pressure (mmHg)	83.2	10.4
Laboratory data		
FBS (mg/dL)	92.4	68.7
HbA1C (%)	8.4	1.8
Total cholesterol (mg/dL)	212.7	42.4
LDL cholesterol (mg/dL)	130.3	31.5
HDL cholesterol (mg/dL)	42.3	8.6
TG (mg/dL)	211.0	124.8
TG/HDL ratio	5.3	3.6
Blood urea nitrogen (mg/dL)	17.9	9.8
Creatinine(mg/dL)	0.97	0.50
Uric acid (mg/dL)	4.7	1.3
Urine albumin/creatinine ratio (mg/g)	34.7	122.7
Glomerular filtration rate (mL/min)	105.8	38.4

BMI = body mass index; FBS = fasting blood sugar; HbA1C = glycated haemoglobin; LDL = low-density lipoprotein; HDL = high-density lipoprotein; TG = triglycerides; SD = standard deviation.

Table 2 Prevalence of cardiovascular risk factors in patients with type 2 diabetes mellitus (DM)

Risk factor	% of patients (*n* = 752)
Demographic and clinical data	
Age > 60 years	13.7
Male sex	47.2
Duration of DM > 10 years	27.7
Family history of CVD	32.5
Obesity	25.7
Abdominal obesity	45.8
Hypertension	51.6
Metabolic syndrome	73.5
Renal insufficiency	8.8
Retinopathy	14.3
Smoking	15.9
Laboratory data	
High HbA1C	75.0
High total cholesterol	95.2
Low HDL cholesterol	86.9
High non-HDL cholesterol	85.4
High TG	63.1
High TG/HDL ratio	65.8
Microalbuminuria	21.5
Macroalbuminuria	1.6

HDL = high-density lipoprotein; LDL = low-density lipoprotein; BMI = body mass index; TG = triglycerides; HbA1C = glycated haemoglobin.

Table 3 Comparison of risk factors in type 2 diabetes mellitus (DM) patients with and without cardiovascular disease (CVD)

Risk factor	With CVD (*n* = 151)	Without CVD (*n* = 601)	*P*-value
Demographic and clinical data			
Male/female sex ratio	1.05	0.99	0.75
	Mean (SD)	**Mean (SD)**	
Age (years)	58.2 (10.3)	51.3 (10.7)	< 0.001
Duration of DM (years)	10.5 (3.4)	7.3 (2.7)	< 0.001
	% of patients	**% of patients**	
Obesity	19.6	27.2	0.08
Hypertension	78.1	44.9	< 0.001
Metabolic syndrome	80.1	71.9	0.04
Renal insufficiency	15.8	7.0	< 0.001
Retinopathy	20.7	12.8	0.01
Smoking	20.5	14.9	0.13
Laboratory data	**Mean (SD)**	**Mean (SD)**	
FBS (mg/dL)	184.5 (60.3)	194.3 (70.5)	0.23
HbA1C (%)	8.42 (1.89)	8.30 (1.82)	0.73
Total cholesterol (mg/dL)	216.8 (50.5)	211.7 (40.1)	0.24
LDL cholesterol (mg/dL)	132.1 (37.6)	129.9 (29.7)	0.64
HDL cholesterol (mg/dL)	42.0 (8.3)	43.5 (9.4)	0.04
Non-HDL cholesterol (mg/dL)	173.2 (47.9)	169.5 (38.9)	0.37
TG (mg/dL)	226.7 (132.0)	207.0 (122.7)	0.02
TG/HDL ratio	5.52 (3.14)	5.28 (3.75)	0.04
Uric acid (mg/dL)	5.00 (1.35)	4.70 (1.29)	0.02
Creatinine (mg/dL)	1.05 (0.55)	0.95 (0.49)	< 0.001
Albumin/creatinine ratio (mg/g of creatinine)	45.3 (138.3)	32.1 (105.3)	0.22

FBS = fasting blood sugar; HbA1C = glycated haemoglobin; LDL = low-density lipoprotein; HDL = high-density lipoprotein; TG = triglycerides; SD = standard deviation.

were prevalent in a large number of our patients; 95.2% had high total cholesterol and 86.9% had low HDL cholesterol. The prevalence of microalbuminuria (21.5%), macroalbuminuria (1.6%) and renal insufficiency (36.7%) were high.

Table 3 shows the prevalence of risk factors in patients with and without CVD. The CVD group were significantly older [58.2 (SD 10.3) versus 51.3 (SD 10.7) years] and had a longer duration of DM [10.5 (SD 3.4) versus 7.3 (2.7) years] ($P < 0.001$) than the non-CVD group. The prevalence of hypertension was 78.1% in the CVD group and 44.9% in the non-CVD group ($P < 0.001$). The prevalence of metabolic syndrome (80.1% versus 71.9%) ($P = 0.04$) and of diabetic retinopathy (20.7% versus 12.8%) were also significantly higher in the CVD group ($P = 0.01$). Concerning the laboratory data, there were statistically significant differences between the CVD and non-CVD sub-groups in the mean levels of blood urea nitrogen, creatinine, triglycerides, HDL cholesterol, TG/HDL ratio, uric acid and glomerular filtration rate (Table 3).

Of patients with 5 components of metabolic syndrome, 25.6% had CVD compared with 12.2% of patients with 1 component of metabolic syndrome ($P = 0.003$).

After stratification of the patients according to CHD risk scores (< 10%, 10%–20% and ≥ 20%) in the patients without CHD (Table 4), the following variables were significantly different between risk groups: age, sex, duration of DM, hypertension, metabolic syndrome, retinopathy, microalbuminuria, HbA1C, total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, TG/HDL ratio, uric acid, non-HDL cholesterol, blood urea nitrogen, creatinine and glomerular filtration rate ($P < 0.05$). Smoking, waist circumference and FBS level were not significantly different between the groups.

The results of stepwise multiple logistic regression showed that the independent risk factors for CVD were age, total cholesterol level, HDL cholesterol level and presence of metabolic syndrome, with an actual number of 322 patients having all these risk factors (Table 5).

Discussion

The prevalence of CHD in a large sample of the Iranian population (the

Table 4 Comparison of significant risk factors in diabetic patients according to coronary heart disease (CHD) risk group

Variable	Low risk (< 10)	Moderate risk (10–19.99)	High risk (≥ 20)	*P*-value
Demographic and clinical data	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	
Age (years)	44.1 (7.7)	51.2 (7.6)	59.3 (8.6)	< 0.001
Duration of diabetes (years)	5.4 (4.5)	7.5 (6.5)	10.3 (7.1)	< 0.001
BMI (kg/m^2)	28.6 (4.3)	28.1 (4.4)	27.5 (3.8)	< 0.001
	%	**%**	**%**	
Sex (% male)	31.3	47.8	56.8	< 0.001
Hypertension (%)	31.6	44.7	70.4	< 0.001
Metabolic syndrome (%)	65.8	71.4	80.5	0.001
Retinopathy (%)	6.1	13.7	21.6	< 0.001
Renal insufficiency (GFR < 60) (%)	0.5	2.6	16.8	< 0.001
Smoking (%)	10.0	18.0	18.8	0.08
Laboratory data	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	
FBS (mg/dL)	187.2 (66.4)	198.9 (69.8)	200.2 (70.2)	0.06
HbA1C (%)	7.8 (1.6)	8.6 (1.7)	8.8 (1.9)	< 0.001
Total cholesterol (mg/dL)	203.2 (35.4)	216.6 (41.0)	217.7 (45.3)	< 0.001
LDL cholesterol (mg/dL)	122.7 (26.4)	133.8 (30.9)	134.4 (34.8)	< 0.001
HDL cholesterol (mg/dL)	43.9 (7.7)	42.3 (8.6)	41.3 (9.0)	< 0.001
Non-HDL cholesterol (mg/dL)	163.5 (63.0)	174.7 (38.5)	177.7 (42.5)	< 0.001
TG (mg/dL)	194.8 (121.4)	205.2 (119.9)	220.2 (129.2)	0.007
Uric acid	4.5 (1.2)	4.7 (1.2)	4.9 (1.4)	0.004
Creatinine	0.83 (0.17)	0.92 (0.42)	1.10 (0.56)	< 0.001
Urine albumin to creatinine ratio (mg/gr)	18.4 (24.9)	20.2 (25.2)	49.6 (161.4)	< 0.001
TG/HDL	4.6 (3.1)	5.3 (4.1)	5.7 (3.6)	< 0.001

GFR = glomerular filtration rate; FBS = fasting blood sugar; HbA1C = glycated haemoglobin; LDL = low-density lipoprotein; HDL = high-density lipoprotein; TG = triglycerides; SD = standard deviation.

Tehran Lipid and Glucose Study) was reported to be 21.8% (22.3% in women and 18.8% in men) [12]. The main target of the present study was to determine the prevalence of CVD and various risk factors in an Iranian population with type 2 DM. Other studies in the Islamic Republic of Iran indicated that there is a high prevalence of CHD in patients with type 2 DM and glucose intolerance state [15–17] but the prevalence of CVD in Iranian type 2 DM patients has not yet been evaluated. The prevalence of CVD was 20.1% in our patients. The Framingham study showed an even higher prevalence just of CHD (39.1% in males and 27.2% in females) [18]. Studies in other countries have reported a prevalence of CHD up to 55% among adult type 2 DM patients [19,20]. The prevalence of CVD in our type 2 DM patients was slightly lower than in another study from the Islamic Republic of Iran study reporting a prevalence of CVD of 28% in type 2 diabetic patients [15].

Table 5 Stepwise multiple logistic regression analysis of factors associated with cardiovascular disease in patients with type 2 diabetes mellitus (*n* = 752)

Risk factor[a]	OR (95% CI)	*P*-value
Age	0.93 (0.89–0.98)	0.006
Metabolic syndrome	2.50 (1.01–6.16)	0.04
Total cholesterol	0.98 (0.97–0.99)	0.012
HDL cholesterol	1.09 (1.04–1.14)	< 0.001

[a]*Included factors: age, duration of diabetes, hypertension, retinopathy, glomerular filtration rate, triglyceride, high-density lipoprotein (HDL) cholesterol, uric acid, albuminuria, triglycerides/HDL cholesterol ratio.*
OR = odds ratio; CI = confidence interval.

Although optimal glycaemic control (HbA1C < 7%) must be a target for prevention of micro- and macrovascular complications in patients with type 2 DM, 75.0% of our patients had HbA1C > 7%. Poor glycaemic control was much higher in our patients compared with other studies [21,22]. Jurado et al. in the North Catalonia Diabetes Study, for example, showed that 56.9%

of their patients had good control of diabetes (HbA1C < 7%) [21]. In the present study, no significant difference was found in FBS and HbA1C levels between CVD and non-CVD groups.

Good blood pressure control in DM is associated with reduced risk of CVD [23]. Hypertension or history of hypertension was recorded in 51.6% of our patients and blood pressure under optimal control was only found in 21.0% of the sample. This finding is in agreement with Jurado et al.'s study, which found only 19.7% of patients had blood pressure under control [21]. Similar to other studies we found a significant association between high blood pressure and CVD.

Dyslipidaemia is a known major risk factor for CVD in DM [23]. Lipid abnormalities were found in a large number of our patients. Total cholesterol, TG levels and TG/HDL ratio were significantly higher and HDL cholesterol levels significantly lower in patients with CVD compared with the non-CVD group. This result is similar to another study that reported a dyslipidaemia prevalence of 77.7% in type 2 DM [21].

Almost three-quarters of our patients (73.5%) had metabolic syndrome, which is similar to other studies. In Ireland a small study of type 1 and 2 DM patients attending for annual review showed that 61.0% patients had metabolic syndrome, more patients with type 2 (69.5%) than type 1 DM (22.2%) [24]. A study in Australian reported that the overall prevalence of metabolic syndrome was 72.3% in a large sample of subjects with type 2 DM [24,25]. The prevalence of metabolic syndrome was significantly higher in the CVD group (80.1% versus 71.9%). All the components of metabolic syndrome are considered to be independent risk factors for CVD [26]. We showed a significant difference in the number of components of metabolic syndrome in CVD versus non-CVD groups and metabolic syndrome was also an independent risk factor for CVD. Considering this result, control of metabolic syndrome components seems to be important for prevention of CVD in patients with type 2 DM.

Microalbuminuria and nephropathy are associated with increased risk of CVD in clinical studies [27,28]. In our patients the prevalence of microalbuminuria (21.5%), macroalbuminuria (1.6%) and renal insufficiency (36.7%) were high. The association of microalbuminuria with CVD was not significant but the urine albumin to creatinine ratio differed significantly between CHD risk groups. Albuminuria was significantly higher in the high risk group (risk score > 20%) compared with the moderate (risk score 10%–20%) and low risk (risk score < 10%) groups. Different studies have documented a significant association between chronic kidney disease and increased risk of CVD [29,30]. In our study the prevalence of CVD was higher in patients with low GFR and a significant difference was found in the prevalence of renal insufficiency between patients with and without CVD. This result is consistent with other studies demonstrating that GFR is a prognostic factor for CVD in DM [29,31]. Previous studies evaluating the role of uric acid in atherosclerosis have shown conflicting results [32,33]. In the present study the association between CVD and uric acid was significant but uric acid was not an independent risk factor for CVD. This association is consistent with a meta-analysis of uric acid and CHD [34].

A positive association was found between the presence of retinopathy and CVD in our study. Poor glycaemic control and high blood pressure contribute to retinopathy as a sign of microvascular disease and CVD as a sign of macrovascular disease in DM. In other studies, retinopathy is correlated with the presence of CVD [35].

The results showed that the prevalence of CVD and insufficient control of CVD risk factors among our patients was high. These findings are in agreement with other studies in different regions [21,22]. More aggressive interventions are crucial for patients with DM, including better patient education and more aggressive control of glycaemia, hypertension, hyperlipidaemia and metabolic syndrome.

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