Coronary heart disease in type 2 diabetes mellitus in Isfahan, Iran: prevalence and risk factors

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Objective — To estimate the prevalence and risk factors of CHD in people with type 2 diabetes mellitus.

Methods and results — A cross-sectional study of type 2 diabetic patients was conducted from 2001 to 2004. 1566 consecutive diabetic patients (524 men and 1042 women) from the Isfahan Endocrinology and Metabolism Research Centre outpatient clinics, Iran, have been examined. Part of the examination included an assessment of CHD including 12-lead resting electrocardiogram and a positive response to the angina pectoris section on the Rose questionnaire and self-reported medical history. The mean (SD) age of participants was 50.6 (12.3) years with a mean (SD) duration of diabetes of 7.6 (6.9) years. The prevalence of CHD was 28.0% [95% confidence interval (CI) 25.8, 30.2]. The prevalence of CHD increased with age ($P < 0.001$). It was associated with gender ($P < 0.01$), age at diagnosis of diabetes, duration of diabetes, systolic blood pressure ($P < 0.001$), low density lipoprotein cholesterol, body mass index and smoking ($P < 0.05$). The age- and gender-adjusted prevalence rate of CHD was 45% higher among insulin-treated patients, 49% higher among patients with BMI >30, and it was positively associated with increasing triglyceride levels and duration of diabetes. Using a stepwise binary logistic regression model, age, BMI, smoking, and insulin treatment were significant independent predictors of CHD. Gender, duration of diabetes, cholesterol and triglycerides had no significant independent association with CHD when other covariates were considered.

Conclusion — These findings indicate that there is a high prevalence of CHD among the Iranian type 2 diabetic patients, which underlines the need for more programmes of health promotion and lifestyle changes. *(Acta Cardiol 2006; 61(1): 13-20)*

Keywords: *coronary heart disease – complications – diabetes mellitus – risk factors – prevalence – Iran.*

Introduction

Patients with type 2 diabetes are at higher risk for several long-term complications, including early mortality, coronary heart disease (CHD) and cardiovascular disease. The relationship between diabetes complications and CHD is well established and consistent and has been examined in many different populations in developed nations[1-10]. Type 2 diabetes is reported to be associated with at least a twofold increased risk of CHD and the prognosis of clinical CHD is worse in diabetic patients than in non-diabetic patients[1-3, 11-16]. CHD risk factors have been reported to be increased in type 2 diabetes[4-7]. It has been reported that improving the traditional CHD risk factors reduces CHD events in patients with type 2 diabetes[8,9]. Epidemiological studies on the impact of CHD in type 2 diabetes in developing countries are scarce. Accurate information regarding the prevalence of CHD and associated risk factors in people with diabetes is important in the prevention or delaying of its development in these countries. It is essential for public health systems to know not only the prevalence of type 2 diabetes, but also the prevalence of long-term complications and the risk factors associated with the disease. CHD and type 2 diabetes mellitus are common causes of morbidity and mortality and are serious

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problems in Iran but to our knowledge, there have been no studies describing the prevalence or risk factors of CHD in diabetic patients.

The objective of this report was to estimate the prevalence of and risk factors of CHD in patients with type 2 diabetes using routinely collected data from a clinical information system for diabetes at the Isfahan Endocrinology and Metabolism Research Centre, Iran.

Patients and methods

Data source. We have conducted a cross-sectional study of 1567 consecutive patients with diabetes followed in the Isfahan Endocrinology and Metabolism Research Centre outpatient clinics. Details of the recruitment and examination procedures have been published previously[17,18]. In brief, clinical data are collected for all consecutive patients at the first attendance and at review consultations (usually annually) using a standard examination protocol. This includes an examination of the ocular fundus, lens, limbs, blood pressure and completion of a problem list by the clinician, measurement of fasting blood glucose, glycosylated haemoglobin (HbA_1), urine protein, triglycerides, cholesterol and serum creatinine, and reporting of smoking as part of a completed questionnaire on demography, family history, and smoking by the patient. A registry clerk enters data from these forms into the computer after the visit.

Patients. Between 1992 and 2004, a total of 9897 type 2 diabetes cases were registered in the system. However, during 2001 to 2004 a cross-sectional study was conducted using data only for 1566 (524 male and 1042 female) consecutive patients with type 2 diabetes. These patients underwent clinical evaluation including the symptom profiles and a 12-lead resting electrocardiogram. The patients had a mean (standard deviation (SD)) duration of diabetes of 7.6 (6.9) years and a mean age of 50.6 (12.3) years.

Risk factors of CHD were assessed using the following data from the patient's registration consultation: gender, age at diagnosis (the age at the time the diagnosis was first recorded by a physician on the participant's chart), age (the age at the time of the examination), duration of diabetes (the time between diagnosis and the examination), body mass index (BMI) (weight/height^2 [kg/m^2]), smoking status (never, current), haemoglobin A_1 (HbA_1) (measured by ion-exchange chromatography; as an indicator of diabetic control), fasting blood glucose (measured by glucose oxidaze method; Clinical Chemistry Analyser Liasys, Italy), proteinuria (measured by precipitation with 3% sulfosalicylic acid and determination of turbidity by measuring absorbance at a wavelength of 550 nm with a spectrophotometer), serum creatinine, total cholesterol, triglycerides, high-density lipoprotein (HDL) cholesterol (measured using standardised procedures), low-density lipoprotein (LDL) cholesterol (calculated by the Friedewald Equation[19] provided total triglycerides did not exceed 400 mg/dl), blood pressure (systolic and diastolic) and diabetes treatment (insulin, and non-insulin). The physician defined the type of diabetes using the problem list and according to the diagnostic criteria set out by the World Health Organization (WHO) in 1985 until 1998[20]. From then on the new diagnostic criteria of the WHO [21] were applied.

The diagnosis of retinopathy was first based on indirect ophthalmoscopy through dilated pupils. Then the diagnosis of retinopathy was confirmed (or not) through fundus photography. The term of "any retinopathy" refers to both nonproliferative and proliferative retinopathy.

Coronary heart disease was defined as the presence of a past history of CHD (previous myocardial infarction, confirmed angina, coronary bypass grafting) and/or abnormal 12-lead resting electrocardiogram and/or a positive response to the angina pectoris section on the Rose questionnaire[22].

Proteinuria was defined as urine protein excretion > 500 mg/dl or albumin excretion > 300 mg/dl.

Ethical approval was obtained from the local research ethics committee. The study complied with the declaration of Helsinki.

Analysis. Statistical methods used included the Student's t test, chi square test, and stepwise binary logistic regression. Two types of statistical analyses are presented in this report: Crude relative prevalence (RP) was based on prevalence rates and adjusted RP was determined by a forward stepwise binary logistic regression analysis using the SPSS for Windows computer package which simultaneously adjusts for other covariates. Independent variables entered into the model were those having a significant association with CHD ($P < 0.05$) in a previous analysis. Standardized RP rates were calculated, for a continuous variable, as the RP of CHD associated with an increase of one standard deviation. For a categorical variable it was the prevalence of CHD associated with the presence of the risk factor relative to the prevalence when it was absent. Likelihood ratio tests were selected for testing the significance of the coefficients. The likelihood ratio test made at each step determined if the last variable that entered the regression added significantly to the variables already selected. The forward stepwise procedures with 0.05 entry and removal criteria resulted in a ranking of the variables according to their relative importance. Adjustment for age and gender was examined in separate models. To save space and confusion, confidence intervals have been given, although significant P values ($P < 0.05$) have been reported.

Results

Subject characteristics. Differences in distribution of several risk factors among 524 men and 1042 women are shown in table 1. Women had lower duration of diabetes, lower height and weight, creatinine and uric acid, were more likely to have never smoked than men. Men had lower BMI, cholesterol and LDL, and were older than women.

Prevalence. Of the 1566 patients, 439 (169 men and 270 women) had CHD. The overall prevalence of CHD was 28.0% (95% CI: 25.8, 30.2). There was a statistically increasing prevalence of CHD with increasing age, from 8.6% (95% CI: 5.4, 12.9) in the < 40 year age group to 41.5% (95% CI: 29.4, 54.4) in the ≥ 70 year age group ($P < 0.001$). The prevalence of CHD increased with duration of diabetes, and was present in 22.9% (95% CI: 19.7, 26.1) of patients with diabetes duration less than 5 years and in 37.3% (95% CI: 32.4, 42.3) of those with diabetes duration ≥ 12 years. Prevalence rates were higher in men (32.3% (95% CI: 28.2, 36.3) than in women (25.9% (95% CI: 23.2, 28.5). After age-adjustment this difference was not statistically significant. Of the 487 patients who were insulin-treated, 141 had CHD, giving a prevalence of 29.0% (95% CI: 24.9, 33.0). This was greater than the prevalence rates observed in non-insulin-treated patients, 27.6% (95% CI: 25.0, 30.3), but the difference was not statistically significant.

Risk factors. Table 2 shows the group means (SD) and proportions for the participants with and without CHD by gender. In both sexes those with CHD had longer duration of diabetes, body mass index (BMI), weight, and had lower HDL and were diagnosed with diabetes at older ages and were older. A higher proportion of men with CHD were current smokers and had higher uric acid and HbA_1 levels. Women with CHD had higher systolic blood pressures and cholesterol levels.

To determine the influence of potential factors on CHD, univariate analysis was first performed (table 3). Crude RP showed that those who had CHD were more likely to be male, older, older at diagnosis of diabetes, had longer duration of diabetes, higher systolic blood

Table 1. – *Group means and proportions for selected variables between 524 men and 1042 women.*

Variables	*Men*		*Women*		*Difference*
	No.	*Mean (SD)*	*No.*	*Mean (SD)*	*95% CI@*
Age (y)	524	52.6 (13.7)	1042	49.6 (11.4)	3.0 (1.8, 4.3)***
Duration of diabetes (y)	522	8.9 (8.3)	1032	7.0 (5.9)	1.9 (1.2, 2.6)***
Age at diagnosis of diabetes (y)	522	43.8 (14.0)	1031	42.5 (11.7)	1.3 (–0.9, 2.5)
BMI (kg/m^2)	510	25.2 (4.0)	1016	27.6 (4.6)	–2.4 (–2.8, –1.9)***
Height (cm)	515	167.5 (8.5)	1017	154.1 (6.6)	13.4 (12.7, 14.3)***
Weight (kg)	518	71.1 (13.8)	1042	65.6 (11.9)	5.5 (4.2, 6.8)***
Systolic BP (mm Hg)	505	127.6 (21.7)	1028	127.8 (23.2)	–0.2 (–0.3, 0.2)
Diastolic BP (mm Hg)	502	77.6 (11.9)	1019	77.9 (12.5)	–0.3 (–0.2, 0.1)
Fasting blood glucose (mg/dl)	483	200.5 (72.0)	987	201.9 (69.4)	–1.4 (–9.1, 6.2)
HbA_1 (%)	380	10.3 (2.2)	803	10.6 (2.4)	–0.3 (–0.6, –0.4)*
Triglycerides (mg/dl)	469	218.3 (142.1)	966	239.0 (162.1)	–20.7 (–37.9, –3.5)*
Total cholesterol (mg/dl)	474	216.2 (55.4)	963	231.3 (55.6)	–15.1 (–21.3, –9.0)***
HDL-cholesterol (mg/dl)	143	42.4 (106)	375	45.2 (17.6)	–9.1 (–6.0, 0.2)
LDL-cholesterol (mg/dl)	138	123.9 (37.4)	368	138.9 (41.4)	–15.2 (–22.5, –7.4)***
Creatinine (m/l)	339	1.3 (1.6)	707	1.0 (1.1)	0.3 (0.1, 0.4)**
Uric acid (mg/dl)	212	5.5 (1.7)	386	4.8 (1.8)	0.7 (0.4, 1.0)***
		No. (%)		No. (%)	
Smoking					
Never-smoker		331 (69.2)		931 (96.4)	-
Current smoker		147 (30.8)		35 (3.6)	27.1 (22.8, 31.4)***
Proteinuria					
Absent		274 (71.0)		592 (70.7)	-
Present		112 (29.0)		245 (29.3)	–0.3 (–5.7, 5.2)
Therapeutic regimen					
Non-insulin		370 (70.6)		712 (68.3)	-
Insulin		154 (29.4)		331 (31.7)	–2.3 (–7.2, 2.5)
Residential area					
Urban		497 (94.8)		994 (95.4)	-
Rural		27 (5.2)		48 (4.6)	0.6 (–1.7, 2.8)
Any retinopathy					
No		174 (47.0)		412 (51.5)	-
Yes		196 (53.0)		388 (48.5)	4.5 (–1.7, 10.6)

Note: total of each variable may vary because of missing values. CI = confidence interval. *P < 0.05, **P < 0.01, ***P < 0.001. @ The difference in the mean or percentage of the variables between men and women.

Table 2. – *Group means and proportions for selected variables between men and women with and without coronary heart disease (CHD).*

Variables	*Male*		*Female*	
	With CHD Mean (SD)	*Without CHD Mean (SD)*	*With CHD Mean (SD)*	*Without CHD Mean (SD)*
Age (y)	57.7 (9.1)	50.2 (14.9)***	53.7 (8.8)	48.2 (11.8)***
Duration of diabetes (y)	10.2 (8.0)	8.2 (8.5)*	8.2 (6.5)	6.6 (5.7)***
Age at diagnosis of diabetes (y)	47.5 (10.1)	42.0 (15.2)***	45.5 (10.2)	41.5 (12.0)***
BMI (kg/m^2)	25.9 (3.7)	24.9 (4.2)**	28.5 (4.5)	27.2 (4.6)***
Height (cm)	168.1 (6.9)	167.2 (9.2)	153.4 (6.0)	154.3 (6.8)
Weight (kg)	73.3 (12.0)	70.0 (14.5)*	66.9 (11.1)	65.1 (12.1)*
Systolic BP (mm Hg)	130.2 (21.9)	126.4 (21.6)	132.7 (22.7)	126.1 (23.1)***
Diastolic BP (mm Hg)	77.5 (12.3)	77.6 (11.8)	78.7 (11.7)	77.6 (12.8)
Fasting blood glucose (mg/dl)	201.8 (71.3)	199.8 (72.4)	200.8 (73.0)	202.3 (68.1)
HbA_1 (%)	10.6 (2.2)	10.1 (2.2)*	10.5 (2.4)	10.6 (2.4)
Triglycerides (mg/dl)	232.3 (135.2)	211.6 (145.0)	255.8 (153.7)	233.0 (164.7)
Total cholesterol (mg/dl)	220.1 (52.8)	214.3 (56.5)	238.0 (52.0)	228.9 (56.7)*
HDL- cholesterol (mg/dl)	39.4 (8.6)	43.6 (11.1)*	44.0 (15.2)	48.5 (22.4)*
LDL- cholesterol (mg/dl)	132.2 (38.0)	120.4 (36.8)	147.4 (43.7)	135.5 (40.0)*
Creatinine (m/l)	1.4 (1.7)	1.2 (1.5)	0.9 (0.3)	1.1 (1.3)
Uric acid (mg/dl)	5.9 (1.9)	5.3 (1.5)*	4.6 (1.2)	4.8 (1.9)
	No. (%)	No. (%)	No. (%)	No. (%)
Smoking				
Never-smoker	96 (63.6)	235 (71.9)*	238 (96.0)	693 (96.5)
Current smoker	55 (36.4)	92 (28.1)	10 (4.0)	25 (3.5)
Proteinuria				
Absent	78 (67.2)	196 (72.6)	134 (66.3)	458 (72.1)
Present	38 (32.8)	74 (27.4)	68 (33.7)	177 (27.9)
Therapeutic regimen				
Non-insulin	120 (71.0)	250 (70.4)	178 (65.9)	534 (69.1)
Insulin	49 (29.0)	105 (29.6)	92 (34.1)	239 (30.9)
Residential area				
Urban	163 (96.4)	334 (94.1)	262 (97.0)	732 (94.8)
Rural	6 (3.6)	21 (5.9)	8 (3.0)	40 (5.2)
Any retinopathy				
No	56 (57.1)	132 (48.5)	99 (52.1)	321 (52.6)
Yes	42 (42.9)	140 (51.5)	91 (47.9)	289 (47.4)

*P < 0.05, **P < 0.01, ***P < 0.001.

pressure, BMI, triglycerides, LDL and were current smokers. The age- and gender-adjusted prevalence rate of CHD was 45% higher among insulin-treated patients, 49% higher among patients with BMI > 30, 50% higher among patients with duration of diabetes ≥ 12 years and it was higher with increasing triglyceride levels. For all variables there was a fairly consistent 'dose response' across the range of values, for example, the prevalence of CHD was higher in older age groups, amongst patients with longer duration of diabetes, higher BMI, and triglycerides.

To determine the independent predictors of the prevalence of CHD a forward stepwise binary logistic regression was performed to test 8 predictor variables: age, duration of diabetes, cholesterol, triglycerides, BMI (included as continuous variables), gender, smoking (current and never) and treatment (insulin and non-insulin). The dependent variable was the CHD (present, absent). 292 subjects were excluded from these analyses because of missing risk factor information, leaving 1274 patients to analyse. Older age (RP 1.05 (95% CI: 1.04, 1.07), higher BMI (RP 1.05 (95% CI: 1.02, 1.08), smoking (RP 1.53 (95% CI: 1.06, 2.20) and insulin treatment (RP 1.57 (95% CI: 1.18, 2.07) significantly increased the prevalence of CHD. Gender, duration of diabetes, cholesterol and triglycerides had no significant independent association with CHD when other covariates were considered.

Discussion

In this cross-sectional study of 1566 type 2 diabetes clinic attenders we found an overall prevalence of CHD of 28.0% (439 patients) (32.3% of the men and 25.9% of the women). To the best of our knowledge, no other prevalence rates for CHD among Iranian type 2 diabetic patients have been reported. The prevalence of CHD in an urban general population in Isfahan aged 35-79 years was 19.4%[23]. This prevalence seems surprisingly high for patients with type 2 diabetes from a developing country like Iran. These data are con-

Table 3. – *Prevalence rates of coronary heart disease by selected characteristics.*

Variables	At risk (No.)	Cases (No.)	Prevalence (%)	Crude relative prevalence (95% CI)	Age-, gender-adjusted relative prevalence (95% CI)†
Gender					
Female	1043	270	25.9	1.00	-
Male	524	169	32.3	1.19 (1.00, 1.40)**	-
Age (y)					
< 40	243	21	8.6	1.00	-
40-49	414	94	22.7	2.33 (1.48, 3.64)***	-
50-59	507	162	32.0	3.00 (1.98, 4.69)***	-
60-69	342	137	40.1	3.60 (2.33, 5.55)***	-
≥ 70	65	27	41.5	3.69 (2.20, 6.20)***	-
Age at diagnosis (year)					
< 30	188	20	10.6	1.00	-
30-59	1253	375	29.9	2.40 (1.56, 3.67)***	-
≥ 60	116	42	36.2	2.76 (1.69, 4.52)***	-
Duration of diabetes (year)					
< 5	672	154	22.9	1.00	1.00
5-7	267	73	27.3	1.15 (0.90, 1.48)	1.17 (0.84, 1.64)
8-11	252	73	29.0	1.20 (0.94, 1.54)	1.27 (0.91, 1.77)
≥ 12	367	137	37.3	1.49 (1.19, 1.78)***	1.50 (1.12, 2.00)**
Systolic blood pressure (mm Hg)					
< 140	1053	263	25.0	1.00	1.00
140-159	266	93	35.0	1.30 (1.06, 1.59)***	1.26 (0.93, 1.69)
≥ 160	218	77	35.3	1.31 (1.05, 1.63)***	1.17 (0.84, 1.62)
Diastolic blood pressure (mm Hg)					
< 70	212	57	26.9	1.00	1.00
70-89	972	281	28.9	1.06 (0.82, 1.36)	1.01 (0.72, 1.44)
≥ 90	332	91	27.4	1.02 (0.76, 1.36)	0.77 (0.52, 1.16)
Fasting blood glucose (mg/dl)					
< 126	185	62	33.5	1.00	1.00
126-179	440	119	27.0	0.85 (0.65, 1.11)	0.70 (0.47, 1.02)
≥ 180	849	235	27.7	0.86 (0.68, 1.10)	0.80 (0.56, 1.14)
HbA_1 (%)					
< 7.5	59	15	25.4	1.00	1.00
7.5-9.4	412	121	29.4	1.12 (0.69, 1.81)	1.30 (0.67, 2.52)
≥ 9.5	715	189	26.4	1.03 (0.65, 1.65)	1.24 (0.65, 2.38)
Cholesterol (mg/dl)					
< 200	441	122	27.7	1.00	1.00
200-219	274	63	23.0	0.86 (0.66, 1.13)	0.73 (0.51, 1.05)
≥ 220	726	222	30.6	1.08 (0.89, 1.31)	1.07 (0.80, 1.39)
HDL-cholesterol (mg/dl)					
≥ 40	299	92	30.8	1.00	1.00
< 40	222	58	26.1	0.85 (0.63, 1.14)	0.86 (0.58, 1.28)
LDL-cholesterol (mg/dl)					
< 100	106	20	18.9	1.00	1.00
≥ 100	403	128	31.8	1.68 (1.11, 2.56)**	1.63 (0.94, 2.82)
Triglycerides (mg/dl)					
< 150	453	97	21.4	1.00	1.00
150-449	869	269	31.0	1.34 (1.09, 1.65)***	1.49 (1.13, 1.96)**
≥ 450	117	39	33.3	1.42 (1.02, 1.96)***	1.91 (1.21, 3.02)**
BMI (kg/m^2)					
< 25	526	129	24.5	1.00	1.00
25-29.99	643	185	28.8	1.17 (0.97, 1.42)	1.15 (0.87, 1.51)
≥ 30	361	118	32.7	1.33 (1.08, 1.65)*	1.49 (1.09, 2.05)*
Smoking					
Never-smoker	1267	336	26.5	1.00	1.00
Current smoker	182	65	35.7	1.45 (1.10, 1.92)**	1.34 (0.93, 1.94)
Proteinuria					
Absent	869	213	24.5	1.00	1.00
Present	357	106	29.7	1.20 (0.99, 1.45)	1.15 (0.87, 1.53)

Table 3. – *Prevalence rates of coronary heart disease by selected characteristics.*

Variables	At risk (No.)	Cases (No.)	Prevalence (%)	Crude relative prevalence (95% CI)	Age-, gender-adjusted relative prevalence (95% CI)†
Creatinine (μm/l)					
< 1.5	979	279	28.5	1.00	1.00
≥ 1.5	70	19	27.1	0.96 (0.64, 1.45)	0.85 (0.48, 1.49)
Uric acid (mg/dl)					
< 7	539	151	28.0	1.00	1.00
≥ 7	62	19	30.6	1.09 (0.74, 1.63)	1.06 (0.59, 1.92)
Any retinopathy					
No	588	133	22.6	1.00	1.00
Yes	585	156	26.7	1.18 (0.96, 1.44)	1.12 (0.85, 1.47)
Residential area					
Rural	76	15	19.7	1.00	1.00
Urban	1491	425	28.5	1.35 (0.84, 2.15)	1.53 (0.83, 2.80)
Therapeutic regimen					
Non-insulin	1085	300	27.6	1.00	1.00
Insulin	487	141	29.0	1.04 (0.87, 1.24)	1.45 (1.12, 1.86)**

Total number of person-years and at risk is not the same for each variable because of missing values. *P < 0.5, **P < 0.01, ***P < 0.001.
†Relative prevalence (with 95% CI) calculated by binary logistic regression analysis.

sistent with the high prevalence of CHD in the diabetic population[1-3]. Prevalence rates in various studies from around the world show considerable variation. Estimates of prevalence of CHD will depend upon the definition of the CHD used and the composition of the community examined by age and social class, making comparisons between studies of limited value. However, the estimates of the prevalence of CHD varied widely in other studies too as a result of variations in study design, detection methods, or the examination of patients at different stages in the natural history of diabetes and the study of selected populations of diabetic individuals. One study from Spain among known type 2 diabetes, found 33% of diabetic patients had macroaniopathy, with 30% having an abnormal ECG and 12.4% CHD[24]. Another study from China, which has a low prevalence of CHD in the general population, found the prevalence of large vessel disease of 17.9% among the subjects with type 2 diabetes[25]. In the WHO Multinational Study of Vascular Disease in Diabetes (MSVDD) the prevalence of macrovascular complications was 33.5% in subjects with type 2 diabetes mellitus[26]. In the United Kingdom Prospective Diabetes Study (UKPDS) 33% of the newly diagnosed type 2 diabetic patients had either an abnormal ECG or retinopathy at the diagnosis[27]. In Finland, which has a high prevalence of CHD in the general population, newly diagnosed diabetic patients had an 18% prevalence of myocardial infarction in both sexes, and if angina and abnormal ECG were included, 32% of the men and 42% of the women had CHD, which was higher than in the control population[28]. Our clinic-based prevalence is higher than the values reported in China[25] but lower than the study in Finland and the UKPDS. Our figure is also lower than the prevalence rates of CHD in type 2 diabetic patients found in Spain[24]. The low rates of macrovascular disease found in China is a likely contributor to the low rates of arterial disease in the Chinese subjects with diabetes, and resembles the Tokyo and Hong Kong centres of the WHO MSVDD[25,26]. Slightly lower rates in our study could have been due to a different definition of CHD, and differences in medical care access and therapy might be one reason. However, it seems that the prevalence of CHD among Isfahanian patients with diabetes was high.

The reasons for the excess risk of CHD associated with diabetes are not fully understood. One possibility is the direct effects of glycaemia on the heart. However, the UKPDS showed significant reduction of microvascular disease, but did not show a decrease in CHD morbidity and mortality with glucose control[29]. Miettinen et al.[30] showed that the 1-year case fatality rate for first myocardial infarction was 45% in diabetic men and 39% in diabetic women. These case fatality rates were significantly higher than the rates in non-diabetic men and women (38% and 25%, respectively).

Univariate analysis (table 3) shows an expected pattern of association for many variables with CHD. In multivariate analysis fewer remain independently associated. In this study, men had a slightly higher prevalence of CHD. After adjusting for other confounders, gender was not a significant independent predictor.

Duration of diabetes was associated with the prevalence of CHD in type 2 diabetes. When adjusting for other risk factors by multivariate analysis, duration of diabetes was not a significant risk factor for CHD. But there was statistically significant interaction between age and duration of diabetes and effects of both variables were not independent. Our findings are consistent with results from two large American and one British cohort. The British regional heart study, the health professionals follow-up study and the nurses' health

study in the United States found that risk of CHD increased with increasing duration of diabetes[14-16].

Consistent with previous studies in a non-diabetic population[31], the present study found a similarly increasing prevalence of CHD with increasing age in a diabetic population.

In univariate analysis, we found that the prevalence of CHD seems to be higher in insulin-treated type 2 diabetic patients than in non-insulin treated patients. After adjustment for other covariates in the multivariate analysis, the type of treatment was significant. A higher prevalence of CHD among insulin-treated patients could be attributable to their longer duration of diabetes, younger age at onset and poorer metabolic control than in non-insulin-treated type 2 diabetes.

Cigarette smoking and obesity, two well-known risk factors for CHD in the general population, have also been shown to be risk factors for CHD in patients with diabetes. In this study, smoking (classified into two simple categories of never, and current smokers) and obesity was associated with the prevalence of CHD after correcting for other covariates.

Our diagnosis of CHD was based on a single examination. Nevertheless, four qualified cardiologists made observations over the years, and problems of observer error need to be considered. It seems reasonable to assume that observer error is independent of such variables as age, gender, duration of diabetes and type of treatment of the patient. If this is so, misclassification resulting from observer error will tend to reduce rather than increase the significance of differences between groups of patients. If therefore a significant difference is found between two otherwise comparable groups of patients, it is reasonable to infer that it is not due to observer error but must reflect a true difference. Nevertheless, this study provides new data from Iran, a developing country, which has been under-represented in past studies.

In summary, CHD appears to be quite common in type 2 diabetes mellitus in Isfahan. With an estimated prevalence of 28%, CHD clearly poses a formidable health threat to Iranian diabetic patients, which underlines the need for more programmes of health promotion and lifestyle changes.

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References

1. Kannel WB, McGee DL. Diabetes and glucose tolerance as risk factors for cardiovascular disease: the Framingham Study. *Diabetes Care* **1979**; 2: 120-6.
2. Stamler J, Vaccaro O, Neaton JD, Wentworth D. Diabetes, other risk factors, and 12-yr cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. *Diabetes Care* 1993; **16**: 434-44.
3. Wingard DL, Barrett-Connor E. Heart disease and diabetes. In: *National Diabetes Data Group. Diabetes in America*. 2nd ed. Washington, DC: Government Printing Office; 1995: 429-48 (NIH publication no. 95-1468).
4. Laakso M. Lipids and lipoproteins as risk factors for coronary heart disease in non-insulin-dependent diabetes mellitus. *Ann Med* 1996; **28**: 341-5.
5. Garg A. Treatment of diabetic dyslipidemia. *Am J Cardiol* 1998; **81**: 47B-51B.
6. Kreisberg RA. Diabetic dyslipidemia. *Am J Cardiol* 1998; **82**: 67U-73U; 85U-86U.
7. Haffner SM. Management of dyslipidemia in adults with diabetes. *Diabetes Care* 1998; **21**: 160-78.
8. Haffner SM, Alexander CM, Cook TJ, Boccuzzi SJ, Musliner TA, Pedersen TR, Kjekshus J, Pyörälä K. Reduced coronary events in simvastatin-treated subjects with coronary heart disease and diabetes or impaired fasting glucose: subgroup analyses in the Scandinavian Simvastatin Survival Study (4S). *Arch Int Med* 1999; **159**: 2661-7.
9. UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. *BMJ* 1998; **317**: 703-13.
10. Wannamethee SG, Shaper AG, Lennon L. Cardiovascular disease incidence and mortality in older men with diabetes and in men with coronary heart disease. *Heart* 2004; **90**: 1398-403.
11. Haffner SM, Lehto S, Ronnemaa T, Pyorala K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. *N Engl J Med* 1998; **339**: 229-34.
12. Mukamal KJ, Nesto RW, Cohen MC, Muller JE, Maclure M, Sherwood JB, Mittleman MA. Impact of diabetes on long-term survival after acute myocardial infarction: comparability of risk with prior myocardial infarction. *Diabetes Care* 2001; **24**: 1422-7.
13. Malmberg K, Yusuf S, Gerstein HC, Brown J, Zhao F, Hunt D, Piegas L, Calvin J, Keltai M, Budaj A. Impact of diabetes on long-term prognosis in patients with unstable angina and non-Q-wave myocardial infarction: result of the OASIS (organization to assess strategies for ischemic syndromes) registry. *Circulation* 2000; **102**: 1014-9.
14. Cho E, Rimm EB, Stampfer MJ, Willett WC, Hu FB. The impact of diabetes mellitus and prior myocardial infarction on mortality from all causes and from coronary heart disease in men. *J Am Coll Cardiol* 2002; **40**: 954-60.
15. Becker A, Bos G, de Vegt F, Kostense PJ, Dekker JM, Nijpels G, Heine RJ, Bouter LM, Stehouwer CD. Cardiovascular events in type 2 diabetes: comparison with nondiabetic individuals without and with prior cardiovascular disease: 10-year follow-up of the Hoorn Study. *Eur Heart J* 2003; **24**: 1406-13.
16. Hu FB, Stampfer MJ, Solomon CG, Liu S, Willett WC, Speizer FE, Nathan DM, Manson JE. The impact of diabetes mellitus on mortality from all causes and coronary

heart disease in women: 20 years follow-up. *Arch Intern Med* 2001; **161**: 1717-23.
17. Janghorbani M, Amini M, Ghanbari H, Safaiee H. Incidence of and risk factors for diabetic retinopathy in Isfahan, Iran. *Ophthalmic Epidemiol* 2003; **10**: 81-95.
18. Janghorbani M, Amini M. Cataract in type 2 diabetes mellitus in Isfahan, Iran: Incidence and risk factors. *Ophthalmic Epidemiol* 2004; **11**: 347-58.
19. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem* 1972; **18**: 499-502.
20. World Health Organization. Diabetes mellitus: report of a WHO study group. Technical report series 727. WHO, Geneva 1985.
21. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med* 1998; **15**: 539-53.
22. Rose GA, Blackburn H, Gillium RF, Prineas RJ. Cardiovascular survey methods. 2nd ed. Geneva, Switzerland: World Health Organization, 1982.
23. Sarraf-Zadegan N, Sayed-Tabatabaei FA, Bashardoost N, Maleki A, Totonchi M, Habibi HR, Sotodehmaram E, Tafazoli F, Karimi A. The prevalence of coronary artery disease in an urban population in Isfahan, Iran. *Acta Cardiol* 1999; **54**: 257-63.
24. Arteagoitia JM, Larranaga MI, Rodriguez JL, Fernandez I, Pinies JA. Incidence, prevalence and coronary heart disease risk level in known Type 2 diabetes: a sentinel practice network study in the Basque Country, Spain. *Diabetologia* 2003; **46**: 899-909.
25. Chi ZS, Lee ET, Lu M, Keen H, Bennett PH. Vascular disease prevalence in diabetic patients in China: standardised comparison with the 14 centres in the WHO Multinational Study of Vascular Disease in Diabetes. *Diabetologia* 2001; **44** (Suppl 2): S82-6.
26. Diabetes Drafting Group. Prevalence of small vessel and large vessel disease in diabetic patients from 14 centres. The World Health Organisation Multinational Study of Vascular Disease in Diabetics. *Diabetologia* 1985; **28** (Suppl): 615-40.
27. UK Prospective Diabetes Study 6. Complications in newly diagnosed type 2 diabetic patients and their association with different clinical and biochemical risk factors. *Diabetes Res* 1990; **13**: 1-11.
28. Uusitupa M, Siitonen O, Pyorala K, Aro A, Hersio K, Penttila I, Voutilainen E. The relationship of cardiovascular risk factors to the prevalence of coronary heart disease in newly diagnosed type 2 (non-insulin-dependent) diabetes. *Diabetologia* 1985; **28**: 653-9.
29. UK Prospective Diabetes Study 6. Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* 1998; **352**: 837-53.
30. Miettinen H, Lehto S, Salomaa V, Mahonen M, Niemela M, Haffner S, Pyorala K, Tuomilehto J, for the FINMONICA Myocardial Infarction Register Study Group. Impact of diabetes on mortality after the first myocardial infarction. *Diabetes Care* 1998; **21**: 69-75.
31. American Heart Association 1993 Heart and Stroke Facts Statistics. Dallas, Tex: National Center; 1992. AHA publication 55-0502 (COM).