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Metabolic Syndrome in Type 2 Diabetes Mellitus in Isfahan, Iran: Prevalence and Risk Factors

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ABSTRACT

Background: **Our goal was to estimate the prevalence and risk factors of metabolic syndrome (MetSyn) in people with type 2 diabetes mellitus (T2DM) using routinely collected data from a clinical information system at Isfahan Endocrinology and Metabolism Research Centre, Iran.**

Methods: **Consecutive diabetic patients (9889 total, 4164 male and 5725 female) from Isfahan Endocrinology and Metabolism Research Centre outpatient clinics, Iran, have been examined. The mean (SD) age of participants was 52.0 (10.9) years with a mean (standard deviation) duration of diabetes of 6.4 (6.4) years at initial registration. A modified National Cholesterol Education Program—Adult Treatment Panel III definition with body mass index instead of waist circumference was used for the MetSyn.**

Results: **The prevalence of MetSyn was 65.0% [95% confidence interval (CI) 64.0, 65.9], with higher rate in females than males (71.7 [95% CI: 70.5, 72.8] female and 55.8 [95% CI: 54.3, 57.3] male) and it was greater with older age. The age-adjusted prevalence rate of MetSyn was associated with female gender, duration of diabetes, fasting blood glucose, systolic and diastolic blood pressure, body mass index (BMI), smoking, proteinuria, insulin-treatment, triglyceride, cholesterol, HDL cholesterol, hypertension, and dyslipidemia. Using a stepwise binary logistic regression model, age, gender, fasting blood glucose, systolic and diastolic blood pressure, BMI, triglyceride, and cholesterol were significant predictors of MetSyn for T2DM patients.**

Conclusions: **These data suggest MetSyn in this population of Iranian type 2 diabetic patients is common, and with an estimated prevalence of 65%, MetSyn clearly poses a formidable health threat to Iranian diabetic patients. Lifestyle interventions in T2DM subjects are needed in Iran to halt the burden of macro- and micro-vascular complications in T2DM.**

INTRODUCTION

THE COMBINATION OF INSULIN RESISTANCE, dyslipidemia, hypertension, hyperinsulinemia, glucose intolerance, and obesity has been described as a "metabolic syndrome" (MetSyn) that is a strong determinant of type 2 diabetes mellitus (T2DM).[1] Patients with metabolic syndrome are at higher risk for many long-term complications, including micro- and macrovascular complications[2,3]. The relationship between MetSyn and diabetes and cardiovascular disease is well-established and consistent and has been examined in many different pop-

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ulations.[4–7] T2DM and cardiovascular disease have many risk factors in common, and many of these risk factors are highly correlated with one another.[4,8,9] MetSyn is very common; using the Third Report of the National Cholesterol Education Program Adult Treatment Panel (NCEP/ATP III) definition; the age-adjusted prevalence of the metabolic syndrome was 24% in men and 23.4% in women in U.S. adults.[10] About 44% of the U.S. population over 50 years of age meets the NCEP/ATP III criteria.[11] The NCEP/ATP III highlights the importance of treating patients with the metabolic syndrome to prevent cardiovascular disease.[1] Limited information is available about the prevalence of the metabolic syndrome in type 2 diabetic patients in developing nations and none in Iran. Accurate information regarding the prevalence of MetSyn and associated risk factors in people with diabetes is important for the prevention or delaying of its micro- and macro-vascular complications in these countries.

MetSyn is common in Iran, with about 34% of the Iranian population over 20 years of age meeting the NCEP/ATP III criteria.[12] Cardiovascular disease and T2DM are also common causes of morbidity and mortality and are serious problems in Iran, but to our knowledge there have been no previous studies of the prevalence or clustering of the risk factors of MetSyn in type 2 diabetic patients.

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

PATIENTS AND METHODS

Data source

Details of the recruitment and examination procedures of the Isfahan Endocrinology and Metabolism Research Center out-patient clinics have been published previously.[13,14] In brief, clinical data were collected for all patients at the first attendance and at review consultations (usually annually), using standard encounter forms. These included a retinal examination, lens, limbs, blood pressure, and construction of a problem list by the clinician, measurement of weight, height, fasting blood glucose, glycosylated hemoglobin (HbA_1), urine protein, triglyceride, cholesterol, and serum creatinine, and smoking history as part of a completed questionnaire on demography, family history, and smoking history by the patient. A registry clerk entered data from these forms into the computer after clinic hours.

Patients

Between 1992 and 2004, a total of 9889 patients with T2DM were registered in the system. These patients had mean (standard deviation [SD]) duration of diabetes of 6.4 (6.4) years and mean age of 52.0 (10.9) years at registration.

Risk factors of MetSyn 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 registration), duration of diabetes (the time between diagnosis and the baseline examination), body mass index (BMI) (weight/height^2 [Kg/m^2]), smoking status (never, current), hemoglobin A_1 (HbA_1, measured by ion-exchange chromatography; as an indicator of diabetic control), fasting blood glucose (glucose oxidase method; Clinical Chemistry Analyzer, 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, triglyceride, total cholesterol, HDL cholesterol (Clinical Chemistry Analyzer), LDL cholesterol (calculated by the Friedewald Equation, provided total triglycerides did not exceed 4.0 mmol/L.) and blood pressure (BP, systolic and diastolic) at registration. Diabetes treatment (insulin, oral agent, and diet alone) used in the analysis was that recorded at registration. The physician defined the type of diabetes using the problem list. Blood pressure was measured by standardized protocols, and hypertension was defined based on the criteria of the Seventh Report of the Joint National Com-

mittee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7).[15] According to this protocol, systolic and/or diastolic blood pressure ≥130/85 mmHg and/or the current use of antihypertensive medication in diabetes diagnosed as hypertension.

A modified NCEP/ATP III[1] definition with body mass index (BMI) instead of waist circumference was used for the MetSyn by the presence of three or more of the following abnormalities: blood pressure ≥130/85 mmHg or a history of hypertension and current use of antihypertensive treatment; BMI≥25 Kg/m^2 (proposed by the Japan Society for the Study of Obesity[16]); serum triglyceride ≥150 mg/dL (≥1.7 mmol/L) and/or HDL cholesterol <40 mg/dL (<0.9 mmol/L) for men and <50 mg/dL (<1.0 mmol/L) for women and known diabetes mellitus. In some other studies BMI has been adopted instead of waist circumference for analysis of MetSyn.[17,18]

Proteinuria was defined as urine protein excretion over 500 mg/dL or albumin excretion over 300 mg/dL.

Tenets of the current version of the Declaration of Helsinki were followed, institutional ethical committee approval was granted, and each patient signed an informed consent.

Analysis

Statistical methods used included the Student's t-test, Chi-square test, and stepwise binary logistic regression model to test associations between baseline variables and MetSyn. Two types of statistical analyses are presented in this report: crude relative prevalence (RP) based on prevalence rates and adjusted RP determined by a forward stepwise binary logistic regression model using the SPSS for Windows computer package (SPSS Inc., Chicago, IL, USA), which simultaneously adjusts for other covariates. Independent variables entered into the model were those having a significant association with MetSyn ($P<.05$) in previous analyses. Standardized RP were calculated, for a continuous variable, as the RP of MetSyn associated with an increase of one standard deviation. For a categorical variable it was the risk of MetSyn associated with the presence of the risk factor relative to the risk 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 was examined in separate models. To save space and confusion, confidence intervals around the RP have been given, although significant *P* values (two-sided) ($P<.05$) have been reported. The 95% confidence intervals (CI) were estimated by confidence interval analysis software.[19]

RESULTS

Subject characteristics

Differences in distribution of several risk factors among 4164 men and 5725 women are shown in Table 1. Women had slightly shorter durations of diabetes, lower fasting blood glucose, and creatinine, were less likely to be smokers, had higher MetSyn, and were younger at registration and diagnosis of diabetes than men. Men had lower BMI, HbA_1 triglyceride, total cholesterol, HDL and LDL cholesterol, had lower hypertension and dyslipidemia than women. The prevalence of hypertension and dyslipidemia were significantly higher in women. The mean (SD) BMI was 26.1 (3.9) for men and 28.5 (4.8) for women. The prevalence of overweight (BMI ≥ 25) was 59.9% (95% CI: 58.4, 61.4%) in men, and 77.1% (95% CI: 76.0, 78.2%) in women. Only 1.6% (95% CI: 1.2, 2.0%) of men and 0.8% (95% CI: 0.5, 1.0%) of women were underweight (BMI<18.5).

Prevalence

As defined by the modified NCEP/ATP III criteria, of the 9889 patients, 6424 (2322 men and 4102 women) had MetSyn. Overall prevalence of MetSyn was 65% (95% CI: 64.0, 65.9%). Prevalence rates were higher in women (71.7%

TABLE 1. COMPARISON OF SELECTED CHARACTERISTICS BETWEEN 4164 MALES AND 5725 FEMALES

Variables	Men		Women		Difference (95% CI)
	No.	*Mean (SD)*	*No.*	*Mean (SD)*	
Age at registration (years)	4125	53.6 (10.9)	5647	50.9 (10.8)	2.7 (2.3, 3.1)***
Duration of diabetes (years)	4126	6.8 (6.7)	5655	6.1 (6.2)	0.6 (0.4, 0.9)***
Age at diagnosis (years)	4088	46.9 (10.9)	5577	44.8 (10.6)	2.1 (1.7, 2.5)***
BMI (Kg/m^2)	4041	26.1 (3.9)	5582	28.5 (4.8)	−2.4 (−2.6, −2.2)***
Systolic BP (mmHg)	3467	126.3 (20.7)	5020	126.9 (22.9)	−0.6 (−0.2, 0.04)
Diastolic BP (mmHg)	3323	77.5 (11.8)	4852	77.2 (12.3)	0.3 (−0.03, 0.08)
Fasting blood glucose (mg/dL)	3499	206.8 (76.2)	4935	203.1 (73.4)	3.7 (0.5, 6.9)*
HbA1 (%)	2273	10.1 (2.3)	3559	10.3 (2.3)	−0.2 (−0.3, −0.05)**
Creatinine (μM/L)	2325	1.1 (1.1)	3494	0.9 (0.8)	0.2 (0.1, 0.2)***
Triglyceride (mg/dL)	3333	225.2 (152.7)	4755	237.7 (154.2)	−12.5 (−19.3, −5.7)***
Cholesterol (mg/dL)	3359	216.1 (52.4)	4773	233.0 (54.2)	−16.9 (−19.2, −14.5)***
HDL Cholesterol (mg/dL)	784	42.9 (16.7)	1474	46.2 (15.6)	−3.2 (−4.6, −1.9)
LDL Cholesterol (mg/dL)	746	125.8 (40.6)	1428	141.7 (43.6)	−15.9 (−19.7, −12.2)***
		%		%	
Metabolic syndrome					
Absent	1842	44.2	1623	28.3	
Present	2322	55.8	4102	71.7	−15.9 (−17.8, −14.0)***
Smoking					
Never-smoker	2609	69.4	4974	97.1	
Current-smoker	1148	30.6	149	2.9	27.6 (26.1, 29.2)***
Proteinuria					
Absent	989	68.1	1610	69.0	
Present	464	31.9	722	31.0	0.9 (−2.1, 4.0)
Therapeutic regimen					
Diet	1017	24.8	1338	23.9	0.9 (−0.8, 2.7)
Oral agent	2617	63.9	3666	65.4	−1.5 (−3.4, 0.5)
Insulin	461	11.3	604	10.8	0.5 (−0.8, 1.8)
Hypertension					
Absent	2288	54.9	2667	46.6	
Present	1876	45.1	3058	53.4	−8.3 (−10.4, −6.4)***
Dyslipidemia					
Absent	1766	42.4	1990	34.8	
Present	2398	57.6	3735	65.2	−7.6 (−9.6, −5.7)***

Total of each variable may vary because of missing values. *$P < .05$, **$P < .01$, ***$P < .001$. Difference is the difference in the mean or percentage of the variable between males and females. Hypertension: systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg or use of oral antihypertensive medication. Dyslipidemia: triglyceride ≥150 mg/dL ≥1.7 mmol/L or HDL cholesterol <40 mg/dL (<0.9 mmol/L) in men or <50 mg/dL (<1.0 mmol/L) in women.

(95% CI: 70.5, 72.8%)) than men (55.8% (95% CI: 54.3, 57.3%)). After age-adjustment, this difference remained statistically significant. There was a statistically significant increasing prevalence of MetSyn with increasing age, from 53.3% (95% CI: 50.7, 56.4%)) in the <40 year old age group to 61.6% (95% CI: 57.7, 65.5%)) in the 70 year old and over age group ($P<.001$). Of the 1066 patients who had insulin-treated, 615 had MetSyn, giving a prevalence of 57.7% (95% CI: 54.7, 60.7%)). This was lower than the prevalence rates seen for noninsulin-treated, 65.9% (95% CI: 64.9, 66.9%)).

Most of those with MetSyn had three components of the syndrome (36.2%), 25.3% had four and 3.5% had five components. Only 9.0% of the diabetic patients were free from any other components of the syndrome and 26.1% had one more component.

Risk factors

Table 2 shows the group means (SD) and proportions for those participants with and without MetSyn. As expected, those with MetSyn had higher systolic (131.9 vs 115.6 mmHg; $P<.001$)

TABLE 2. GROUP MEANS AND PROPORTIONS FOR SELECTED VARIABLES COMPARING 6424 PARTICIPANTS WITH AND 3465 WITHOUT METABOLIC SYNDROME (METSYN)

	MetSyn		*No MetSyn*		
Variables	*No.*	*Mean (SD)*	*No.*	*Mean (SD)*	*Difference 95% CI*
Age at registration (years)	6363	52.7 (10.4)	3416	50.9 (11.7)	1.8 (1.4, 2.3)***
Duration of diabetes (years)	6367	6.3 (6.4)	3422	6.6 (6.5)	−0.3 (−0.5, 0.05)
Age at diagnosis (years)	6301	46.4 (10.5)	3371	44.3 (11.2)	2.1 (1.7, 2.6)***
BMI (Kg/m^2)	6334	28.9 (4.2)	3297	24.9 (4.1)	4.0 (3.8, 4.2)***
Systolic BP (mmHg)	5777	131.9 (22.3)	2715	115.6 (16.9)	16.3 (15.3, 17.2)***
Diastolic BP (mmHg)	5621	79.7 (12.1)	2559	72.1 (10.2)	7.6 (7.1, 8.2)***
Fasting blood glucose (mg/dL)	5881	202.3 (71.9)	2560	210.2 (80.2)	−7.9 (−11.4, −4.5)**
HbA1 (%)	3965	10.2 (2.2)	1870	10.2 (2.4)	0.0 (−0.2, 0.07)
Creatinine (μM/L)	4247	1.0 (0.9)	1577	1.0 (1.0)	0.0 (−0.07, 0.04)
Triglyceride (mg/dL)	5769	262.6 (157.7)	2326	157.8 (112.4)	104.8 (97.8, 111.9)***
Cholesterol (mg/dL)	5771	232.7 (53.6)	2368	209.6 (51.8)	23.1 (20.6, 25.6)***
HDL Cholesterol (mg/dL)	1767	43.5 (15.9)	493	50.4 (15.3)	−6.9 (−8.4, −5.3)***
LDL Cholesterol (mg/dL)	1696	138.0 (43.8)	480	130.2 (40.5)	7.8 (3.4, 12.1)***
		%		%	
Gender					
Male	2322	36.1	1842	53.2	—
Female	4102	63.8	1623	46.8	17.0 (15.0, 19.0)***
Smoking					
Never smoker	5109	87.8	2480	80.9	—
Current smoker	713	12.2	586	19.1	−6.9 (−6.9 (−8.5, −5.2)***
Proteinuria					
Absent	1759	67.0	843	72.4	—
Present	865	33.0	321	27.6	5.4 (2.3, 8.5)**
Therapeutic regimen					
Diet	1525	24.2	830	24.4	−0.2 (−2.1, 1.5)
Oral agent	4174	66.1	2116	62.3	3.8 (1.8, 5.8)***
Insulin	615	9.7	451	13.3	−3.5 (−4.9, −2.2)***
Hypertension					
Absent	2064	32.1	2893	83.4	—
Present	4366	67.9	574	16.6	51.3 (49.7, 53.0)***
Dyslipidemia					
Absent	1100	17.1	2659	76.7	—
Present	5330	82.9	808	23.3	59.6 (57.9, 61.3)***

Note: Total of each variable may vary because of missing value. *P < .05, **P < .01, ***P < .001. Difference in the mean or percentage of the variables between MetSyn and no MetSyn. Hypertension: systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg or use of oral antihypertensive medication. Dyslipidemia: triglyceride ≥150 mg/dL (≥1.7 mmol/L) or HDL cholesterol <40 mg/dL (<.09 mmol/L) in men or <50 mg/dL (<1.0 mmol/L) in women.

and diastolic blood pressure (79.7 vs 72.1 mmHg; $P<0.001$), BMI (28.9 vs 24.9; $P<.001$), triglyceride (262.6 vs 157.8 mg/dL; $P<.001$), cholesterol (232.7 vs 209.6 mg/dL; $P<.001$), LDL (138.0 vs 130.2; $P<.001$) and lower HDL cholesterol (43.5 vs 50.4 mg/dL; $P<0.001$) and fasting blood glucose (202.3 vs 210.2 mg/dL; $P<0.01$), and were older at registration (52.7 vs 50.9 year; $P<0.001$) and diagnosis of diabetes (46.4 vs 44.3 years old; $P<.001$). A lower proportion of those with MetSyn had used insulin (9.7% vs 13.3%; $P<.001$), but a higher proportion used oral agent (66.1% vs 62.3%; $P<.001$). A lower proportion of patients with MetSyn were current smokers (12.2% vs 19.1%; $P<.001$), but a higher proportion had proteinuria (33.0% vs 27.6%; $P<.01$), hypertension (67.9% vs 16.6%; $P<.001$), dyslipidemia (82.9% vs 23.3%; $P<.001$) and were female (63.8% vs 46.8%; $P<.001$).

To determine the influence of potential factors on MetSyn, univariate analysis was first performed (Table 3). Crude RP showed that

TABLE 3. PREVALLENCE RATES OF METABOLIC SYNDROME (METSYN) BY BASELINE VARIABLES

Variables	*At risk (No.)*	*Cases (No.)*	*Prevalence (%)*	*Crude relative prevalence (95%CI)*	*Age adjusted relative prevalence (95% CI)†*
Gender					
Male	4164	2322	55.8	1.00	1.00
Female	5725	4102	71.7	1.28 (1.24, 1.33)***	2.15 (1.97, 2.34)***
Age at registration (years)					
<40	1173	628	53.3	1.00	—
40–49	2885	1815	62.9	1.18 (1.11, 1.25)***	—
50–59	3015	2090	69.3	1.29 (1.22, 1.37)***	—
60–69	2105	1460	69.4	1.30 (1.22, 1.36)***	—
≥70	601	370	61.6	1.15 (1.06, 1.25)***	—
Age at diagnosis (years.)					
<30	505	262	51.9	1.00	—
30–59	8132	5340	65.7	1.27 (1.16, 1.38)***	—
≥60	1035	699	67.5	1.30 (1.18, 1.43)***	—
Duration of diabetes (years.)					
<5	5042	3305	65.5	1.00	1.00
5–7	1708	1148	67.2	1.03 (0.99, 1.07)	1.03 (0.91, 1.16)
8–11	1287	799	62.1	0.95 (0.90, 0.99)*	0.78 (0.69, 89)***
≥12	1752	1115	63.6	0.97 (0.93, 1.01)	0.77 (0.69, 0.87)***
Fasting blood glucose (mg/dL)					
≥110	464	283	61.0	1.00	1.00
110–129	745	539	72.3	1.19 (1.09, 1.29)***	1.75 (1.36, 2.24)***
130–149	980	724	73.9	1.21 (1.12, 1.31)***	1.86 (1.47, 2.36)***
150–169	958	689	71.9	1.18 (1.09, 1.28)***	1.70 (1.34, 2.15)***
≥170	5294	3646	68.9	1.13 (1.05, 1.02)***	1.46 (1.20, 1.78)***
HbA1 (%)					
≤9	2143	1443	67.3	1.00	1.00
9.1–11	1926	1337	69.4	1.03 (0.99, 1.07)	1.09 (0.95, 1.25)
11.1–13	1059	735	69.4	1.03 (0.98, 1.08)	1.08 (0.92, 1.27)
13.1–15	489	318	65.0	0.97 (0.90, 1.04)	0.88 (0.72, 1.09)
<15	218	132	60.6	0.90 (0.81, 1.00)	0.73 (0.55, 0.98)*
Systolic BP (mmHg)					
<130	4799	2510	52.3	1.00	1.00
130–149	2184	1906	87.3	1.67 (1.62, 1.72)***	6.77 (5.87, 7.80)***
150–169	1011	916	90.6	1.73 (1.68, 1.79)***	9.70 (7.76, 12.12)***
≥170	498	445	89.4	1.71 (1.64, 1.78)**	8.63 (6.42, 11.58)***
Diastolic BP (mmHg)					
<80	3300	1804	57.4	1.00	1.00
80–110	4213	3204	76.1	1.39 (1.34, 1.44)***	2.59 (2.34, 2.86)***
≥110	667	613	91.9	1.68 (1.62, 1.75)***	9.14 (6.86, 12.19)***
BMI (KG/m^2)					
<25	2902	804	27.7	1.00	1.0
35–34	6165	5037	81.7	2.95 (2.78, 3.13)***	13.61 (12.19, 15.20)***
≥35	564	493	87.4	3.16 (2.95, 3.37)***	23.73 (18.05, 31.19)***
Smoking					
Never smoker	7589	5109	67.3	1.00	1.00
Current smoker	1299	713	54.9	0.82 (0.77, 0.86)***	086 (0.75, 0.98)*
Proteinuria					
Absent	2602	1759	67.6	1.00	1.00
Present	1186	865	72.9	1.08 (1.03, 1.13)**	1.24 (1.06, 1.44)**
Creatinine (μM/I)					
≤1.5	5545	4038	72.8	1.00	1.00
>1.5	278	208	74.8	1.03 (0.96, 1.10)	1.05 (0.79, 1.39)
Therapeutic regimen					
Diet	2355	1525	64.8	1.00	1.00
Oral agent	6290	4174	66.4	1.02 (0.99, 1.06)	1.00 (0.90, 110)
Insulin	1066	615	57.7	0.89 (0.84, 0.95)***	0.68 (0.58, 0.79)***

TABLE 3. PREVALLENCE RATES OF METABOLIC SYNDROME (METSYN) BY BASELINE VARIABLES (CONT'D)

Variables	*At risk (No.)*	*Cases (No.)*	*Prevalence (%)*	*Crude relative prevalence (95%CI)*	*Age adjusted relative prevalence (95% CI)†*
Triglyceride (mg/dl)					
<150	4303	2466	57.3	1.00	1.00
150–449	3349	2915	87.0	1.52 (1.48, 1.56)***	5.07 (4.50, 5.70)***
≥450	443	388	87.6	1.53 (1.46, 1.60)***	5.41 (4.05, 7.23)***
Cholesterol (mg/dL)					
<200	2542	1494	58.8	1.00	1.00
200–219	1492	1048	70.2	1.20 (1.14, 1.25)***	1.65 (1.43, 1.89)***
≥220	4105	3229	78.7	1.34 (1.29, 1.39)***	2.56 (2.29, 2.85)***
LDL Cholesterol (mg/dL)					
≤100	446	339	76.0	1.00	1.00
>100	1730	1357	78.4	1.03 (0.97, 1.09)	1.17 (0.92, 1.50)
HDL Cholesterol (mg/dL)					
>40	1317	934	70.9	1.00	1.00
≤40	943	833	88.3	1.25 (1.19, 1.30)***	3.03 (2.40, 3.83)***
Hypertension					
Absent	4957	2064	41.6	1.00	1.00
Present	4940	4366	88.4	2.12 (2.05, 2.20)***	12.38 (11.06, 13.85)***
Dyslipidemia					
Absent	3759	1100	29.3	1.00	1.00
Present	6138	5330	86.8	2.97 (2.82, 3.12)***	16.96 (15.27, 18.84)***

Total number at risk is not the same for each variable because of missing values. †Relative prevalence (with 95% CI) calculated by binary logistic regression. $*P < .05$, $**P < 0.01$, $***P < .001$. Hypertension: systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥85 mmHg or use of oral antihypertensive medication. Dyslipidemia: triglyceride ≥1.7 mmol/L or HDL cholesterol <0.9 in men or <1.0 mmol/L in women.

those who had MetSyn were more likely to be female, older at registration and diagnosis of diabetes, with higher fasting blood glucose, systolic and diastolic blood pressure, BMI, cholesterol, triglyceride, proteinuria, hypertension, dyslipidemia, and lower HDL, were never smokers, and were not insulin-treated. After gender- and age-adjustment the smoking was statistically significant. For all variables there was a fairly consistent 'dose response' across the range of values; for example, the risk of MetSyn was higher in older age groups, amongst patients with proteinuria, non-smokers, hypertension, dyslipidemia, higher fasting blood glucose, systolic and diastolic blood pressure, BMI, cholesterol, triglyceride, and lower HDL. The insulin-treated type 2 diabetic patients were less likely to have MetSyn than non-insulin-treated patients in this univariate analysis. The age-adjusted logistic regression coefficient showed that the prevalence rate of MetSyn was more than two times higher among females, 46% higher among patients with fasting blood glucose ≥170 mg/dL, 23.7 times higher among patients with BMI ≥35, 17.0 times higher among patients with dyslipidemia, 12.4 times higher among patients with hypertension, 3 times higher among patients with HDL ≤40 mg/dL, 2.56 times higher among patients with cholesterol ≥220 mg/dL, 5.4 times higher among patients with triglyceride ≥450 mg/dL, 24% higher among patients with proteinuria, 9.1 times higher among patients with diastolic blood pressure ≥110 mmHg, 8.6 times higher among patients with systolic blood pressure ≥170 mmHg and 32% lower among insulin-treated patients, 14% lower among never-smokers and 23% lower among patients with duration of diabetes ≥12 years.

To determine the independent predictors of the prevalence of MetSyn a forward stepwise

binary logistic regression was performed to test 11 predictor variables: age, fasting blood glucose, systolic and diastolic blood pressure, BMI, triglyceride, total cholesterol, duration of diabetes (included as continuous variables), gender, smoking (current, never) and treatment (insulin, and non-insulin). The dependent variable was the MetSyn (present, absent). Some 1849 subjects were excluded from these analyses because of missing risk factors information, leaving 8040 patients to analyse. Table 4 shows the association of these variables in order of their entry into the regression equation in each group. Older age (RP 1.01 (95% CI: 1.005, 1.02)), female (RP 1.46 (95% CI: 1.25, 1.70)), higher fasting blood glucose (RP 1.00 (95% CI: 0.998, 1.000)), systolic (RP 1.58 (95% CI: 1.41, 1.67)) and diastolic blood pressure (RP 1.16 (95% CI: 1.06, 1.26)), BMI (RP 1.44 (95% CI: 1.40, 1.47)), triglyceride (RP 1.011 (95% CI: 1.010, 1.012)) and cholesterol (RP 1.002 (95% CI: 1.000, 1.003)) significantly increased the prevalence of MetSyn. Duration of diabetes, smoking, and treatment regimen had no significant independent association with MetSyn when other covariates were considered.

DISCUSSION

In this cross-sectional study of 9889 T2DM clinic attenders, we found an overall prevalence of MetSyn of 65% (6424 patients) (71.7% of the women and 55.8% of the men). To the best of our knowledge, no other prevalence rates for MetSyn among Iranian type 2 diabetic patients have been reported. The age-adjusted prevalence of MetSyn in an urban general population in Tehran aged over 20 years, as defined by NCEP/ATP III criteria, was 33.7%.[12] The prevalence of the MetSyn in this T2DM population is more than double the prevalence in the general populations[10,12,20–26] and similar to the study on T2DM from other diabetic population.[27–29] Therefore, T2DM patients should be screened for MetSyn. Prevalence rates in various studies from around the world show considerable variation. The differences in diagnostic criteria for this syndrome are partially responsible for variations in the reported prevalence among different studies.[20,21] One study from Brazil on known T2DM, based on WHO criteria, found 85% of diabetic patients had MetSyn.[27] Two other studies[28,29] have assessed the prevalence of the MetSyn based on WHO criteria. They found the same prevalence of the MetSyn in type 2 diabetic patients, although they were conducted in different populations. One study from China, which has a low prevalence of coronary heart disease (CHD) in the general population, found a prevalence of MetSyn of 75.1% among the subjects with T2DM, based on WHO Criteria.[28] In another study from Finland, which has a high prevalence of CHD in the general population, the MetSyn, defined by modified WHO criteria, was present in 91.5% of type 2 diabetic men and in 82.7% of women.[29] In studies using other criteria, the prevalence of the MetSyn varies according to the population studied.[20,22,30] In the Bruneck Study of insulin resistance in metabolic disorders, the prevalence of insulin resistance was 83.9% in subjects with T2DM.[20] In a study performed in the United Kingdom[30] 129 individuals with new-onset diabetes were characterized as to the presence or absence of the MetSyn according to the NCEP/ATP III criteria. Seventy-two percent of patients with diabetes had the MetSyn. Patients with the MetSyn were more obese than those without it. Albeit epidemiological studies have shown that among the general population the prevalence and characteristics of MetSyn vary between different race/ethnic groups.[10,12,23–26] Our results, as well as those of the Brazilian, Chinese, Italian, British, and Scandinavian

Table 4. Risk Factors Related to Prevalence of Metabolic Syndrome for Patients with T2DM (Stepwise Binary Logistic Regression Model)

Variables	*Odds ratio (95% CI)*
Age at registration (years)	1.01 (1.005, 1.021)***
Gender	
Male	1.00
Female	1.46 (1.25, 1.70)***
Fasting blood glucose (mg/dL)	1.00 (0.998, 1.00)*
Systolic BP (mmHg)	1.58 (1.49, 1.67)***
Diastolic BP (mmHg)	1.16 (1.06, 1.26)**
Body mass index	1.44 (1.40, 1.47)***
Triglyceride (mg/dL)	1.011 (1.010, 1.012)***
Cholesterol (mg/dL)	1.002 (1.000, 1.004)***

*$P < .05$, **$P < .01$, ***$P < .001$.

studies,[20,27–30] suggest that the prevalence of the MetSyn in T2DM patients seems to be independent of ethnic factors. Our clinic-based figure is lower than the values reported by the Brazilian, Chinese, Italian, British and Scandinavian studies.[20,27–29] Lower rates in our study could have been due to a different definition of MetSyn; differences in medical care access and therapy, or other factors. However, it seems that the prevalence of MetSyn among Isfahani diabetic patients was high.

Using the NCEP/ATP III cut off points for triglyceride and HDL-cholesterol, we reported that 62.0% of the study patients had dyslipidemia. Different features of the MetSyn were common in diabetic patients, especially in women. Obesity, hypertension, and dyslipidemia were all significantly more common among women. Over half of the men and women had hypertension and dyslipidemia, which is in accordance with the other studies.[29,31]

The higher MetSyn prevalence found in women was probably related to higher dyslipidemia, obesity, and high blood pressure rates in women than in men. In Iran, women generally have less physical activity, and overweight and obesity are more common among them,[32]

Consistent with prior studies in diabetic and non-diabetic populations,[10,12,33] the present study found similarly increasing prevalence of MetSyn with increasing age in a diabetic population. This increasing trend can be attributed to a similar age-related trend in each of the components of MetSyn. In addition, age-related increase in insulin resistance has been shown in young, middle aged, and elderly healthy normal weight adults.[6]

In this study, those with the MetSyn had higher levels of systolic and diastolic blood pressure, which is part of the definition of the syndrome. Other features of the syndrome, such as an abnormal lipid profile and high BMI, are also likely to contribute. In this diabetic population, the prevalence of hypertension was 49.9%. Some findings show that about half of the patients with hypertension can have insulin resistance and hyperinsulinemia.[34] Boyko et al.[35] reported a significant correlation between blood pressure and fasting insulin, independent of overall adiposity, in Japanese-Americans. A meta-analysis review showed a significant correlation between fasting serum insulin level and systolic and diastolic blood pressure,[36] further supporting the role of hyperinsulinemia in the pathogenesis of essential hypertension. Therefore, identifying individuals with T2DM and the MetSyn can be helpful in defining those who need aggressive treatment for the risk of micro- and macro-vascular complications.

Reports on the US population aged 20 years and older[10,25] showed that approximately one-fourth meet the NCEP/ATP III MetSyn criteria. Using the World Health Organization (WHO) diagnostic criteria for the MetSyn, the reported prevalence in the US population was 25.1%.[33] However, applying the WHO definition requires an abnormal oral glucose tolerance test (OGTT) (i.e., diabetes or impaired glucose tolerance) or the presence of insulin resistance (in normoglycemic subjects), plus two additional abnormalities: obesity, dyslipidemia, hypertension, or microalbuminuria. In contrast, the NCEP/ATP III definition can be easily applied without OGTT or actual insulin resistance measurement.

The Isfahan clinical information system for diabetes provides one of the largest clinic-based data sets of its kind in developing countries. Although this study had several findings relevant to the better understanding of the prevalence of and risk factors of MetSyn in T2DM, it has some limitations. Albeit we have not carried out any special studies of the validity or reliability of data for this analysis, a clerk was employed to check consistency and, where possible, to ensure completeness of data. Previous studies show that these patients are a representative sample of known diabetic patients of Isfahan.[37,38] Our experience with other parts of the data set gives us some confidence that data quality is sufficient for this type of study and that our results provide useful additional evidence on the prevalence of and risk factors for MetSyn in type 2 diabetic patients. As a cross-sectional study, the present analysis is limited in its ability to elucidate causal relationships between risk factors and MetSyn. The study was performed according to the modified NCEP/ATP III criteria.[1] We used BMI instead of waist circumference due to unavailability of data regarding waist circumference in

our database. The central pattern of distribution, with its higher weighting of waist circumference, is associated with more insulin resistance than is the peripheral pattern of distribution.[39,40] Some data show that waist circumstance predicts diabetes marginally better than BMI.[41,42] Nevertheless, most physicians routinely assessed BMI, whereas the value of waist measurements in clinical practice has not been thoroughly examined and may require modification for different ethnic groups. A number of studies have also shown that BMI is as effective as waist circumference for predicting the development of T2DM and other metabolic disturbances.[41–45] In addition, the Japan Society for the study of Obesity has reported that BMI can estimate visceral fat measured by computed tomography as robustly as waist circumference and that obesity-related complications increase for a BMI of 25.[16] Nevertheless, this study provides new data from Iran, a developing country that has been under-represented in past studies

In summary, MetSyn appears to be quite common in Isfahani T2DM. With an estimated prevalence of 65%, MetSyn clearly poses a formidable health threat to Iranian diabetic patients, who need more programmes of health promotion and lifestyle changes. Lifestyle interventions in T2DM subjects are needed in Iran to halt the burden of macro- and microvascular complications in T2DM.

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REFERENCES

1. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults: Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *J Am Med Assoc* 2001;285:2486–2497.
2. Isomaa B, Henricsson M, Almgren P, Tuomi T, Taskinen MR, Groop L. The metabolic syndrome influences the risk of chronic complications in patients with type II diabetes. *Diabetologia* 2001;44:1148–1154.
3. Isomaa B, Almgren P, Tuomi T, Forsen B, Lahti K, Nissen M, Taskinen MR, Groop L. Cardiovascular morbidity and mortality associated with the metabolic syndrome. *Diabetes Care* 2001;24:683–689.
4. Stern MP. Diabetes and cardiovascular disease: the common soil hypothesis. *Diabetes 1995;*44:369–381.
5. Reaven GM. Role of insulin resistance in human disease. *Diabetes* 1988;37:1595–1607.
6. DeFronzo RA, Ferrannini E. Insulin resistance: a multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. *Diabetes Care* 1991;14:173–194.
7. Ferrannini E, Haffner SM, Mitchell BD, Stern MP. Hyperinsulinaemia: the key feature of a cardiovascular and metabolic syndrome. *Diabetologia* 1991;34:416–422.
8. Hamman RF. Genetic and environmental determinants of non-insulin-dependent diabetes mellitus (NIDDM). *Diabetes Metab Rev* 1992;8:287–338.
9. Castelli WP. Epidemiology of coronary heart disease: the Framingham Study. *Am J Med* 1984;76:4–12.
10. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the Third National Health and Nutrition Examination Survey. *JAMA* 2002;287:356–359.
11. Alexander CM, Landsman PB, Teutsch SM, Haffner SM. Third National Health and Nutrition Examination Survey (NHANES III); National Cholesterol Education Program (NCEP). NCEP-defined metabolic syndrome, diabetes, and prevalence of coronary heart disease among NHANES III participants age 50 years and older. *Diabetes* 2003;52:1210–1214.
12. Azizi F, Salehi P, Etemadi A, Zahedi-Asl S. Prevalence of metabolic syndrome in an urban population: Tehran Lipid and Glucose Study. *Diabetes Res Clin Pract* 2003;61:29–37.
13. Janghorbani M, Amini M, Ghanbari H, Safaiee H. Incidence of and risk factors for diabetic retinopathy in Isfahan, Iran. *Ophthalmic Epidemiology* 2003;10:81–95.
14. Janghorbani M, Amini M. Cataract in type 2 diabetes mellitus in Isfahan, Iran: Incidence and risk factors. *Ophthalmic Epidemiology* 2004;11:347–358.
15. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ; Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. National Heart, Lung, and Blood Institute; National High Blood Pressure Education Program Coordinating Committee. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension* 2003;42:1206–1256.
16. Examination Committee of Criteria for 'Obesity Disease' in Japan; Japan Society for the Study of Obesity. New criteria for 'obesity disease' in Japan. *Circ J* 2002;66:987–992.

17. Ridker PM, Buring JE, Cook NR, Rifai N. C-reactive protein, the metabolic syndrome, and risk of incident cardiovascular events: an 8–year follow-up of 14719 initially healthy American women. *Circulation* 2003 107:391–397.
18. Sattar N, Gaw A, Scherbakova O, Ford I, O'Reilly DS, Haffner SM, Isles C, Macfarlane PW, Packard CJ, Cobbe SM, Shepherd J. Metabolic syndrome with and without C-reactive protein as a predictor of coronary heart disease and diabetes in the West of Scotland Coronary Prevention Study. *Circulation* 2003; 108:414–419.
19. Gardner MJ, Altman DG. Statistics with confidence. London: British Medical Association 1989.
20. Bonora E, Kiechl S, Willeit J, Oberhollenzer F, Egger G, Targher G, Alberiche M, Bonadonna RC, Muggeo M. Prevalence of insulin resistance in metabolic disorders: the Bruneck Study. *Diabetes* 1998;47:1643–1649.
21. Rantala AO, Kauma H, Lilja M, Savolainen MJ, Reunanen A, Kesaniemi YA. Prevalence of the metabolic syndrome in drug-treated hypertensive patients and control subjects. *J Intern Med* 1999;245:163–174.
22. Lee WY, Park JS, Noh SY, Rhee EJ, Kim SW, Zimmet PZ. Prevalence of the metabolic syndrome among 40,698 Korean metropolitan subjects. *Diab Res Clin Pract* 2004;65:143–149.
23. Jaber LA, Brown MB, Hammad A, Zhu Q, Herman WH. The prevalence of the metabolic syndrome among Arab Americans. *Diabetes Care* 2004;27: 234–238.
24. Meigs JB, D'Agostino RB Sr., Wilson PW, Cupples LA, Nathan DM, Singer ED. Risk variable clustering in the insulin resistance syndrome. The Framingham Offspring Study. *Diabetes* 1997;46:1594–1600.
25. Park Y-W, Zhu S, Palaniappan L, Heshka S, Carnethon M, Heymsfield SB. The metabolic syndrome: prevalence and associated risk factor findings in the US population from the Third National Health and Nutrition Examination Survey. *Arch Intern Med* 2003;163:427–436.
26. Florez H, Silva E, Fernandez V, Ryder E, Sulbaran T, Campos G, Calmon G, Clavel E, Castillo-Florez S, Goldberg R. Prevalence and risk factors associated with the metabolic syndrome and dyslipidemia in White, Black, Amerindian and Mixed Hispanics in Zulia State, Venezuela. *Diabetes Res Clin Pract* 2005;69:63–77.
27. Costa LA, Canani LH, Lisboa HR, Tres GS, Gross JL. Aggregation of features of the metabolic syndrome is associated with increased prevalence of chronic complications in Type 2 diabetes. *Diabet Med* 2004; 21:252–255.
28. Lee YJ, Tsai JC. ACE gene insertion/deletion polymorphism associated with 1998 World Health Organization definition of metabolic syndrome in Chinese type 2 diabetic patients. *Diabetes Care* 2002;25:1002–1008.
29. Ilanne-Parikka P, Eriksson JG, Lindstrom J, Hamalainen H, Keinanen-Kiukaanniemi S, Laakso M, Louheranta A, Mannelin M, Rastas M, Salminen V, Aunola S, Sundvall J, Valle T, Lahtela J, Uusitupa M, Tuomilehto J; Finnish Diabetes Prevention Study Group. Prevalence of the metabolic syndrome and its components: findings from a Finnish general population sample and the Diabetes Prevention Study cohort. *Diabetes Care* 2004;27:2135–2140.
30. Valiante S, Barchetta I, Calabria M Prevalence of GAD antibodies in diabetic patients with or without the metabolic syndrome. Program and abstracts of the 65th Scientific Sessions of the American Diabetes association; June 10–14, 2005; San Diego, California. Abstract 1273–P.
31. Reaven GM, Lithell H, Landsberg L. Hypertension and associated metabolic abnormalities—the role of insulin resistance and the sympathoadrenal system. *N Engl J Med* 1996;334:374–381.
32. Mirmiran P, Mohammadi F, Allahverdian S, Azizi F. Measurement of total energy requirement in adults: prospective Tehran Lipid and Glucose Study. Pajouhandeh. *J. Shaheed Beheshti Univ Med Sci* 2001;6: 157–166 (in Farsi).
33. Ford ES, Giles WH. A comparison of the prevalence of the metabolic syndrome using two proposed definitions. *Diabetes Care* 2003;26:575–581.
34. Balkau B, Charles MA, Drivsholm T, Borc-Johansen K, Wareham N, Yudkin JS, et al. European Group for the Study of Insulin Resistance (EGIR): Frequency of the WHO metabolic syndrome in European cohorts, and an alternative definition of an insulin resistance syndrome. *Diabetes Metab* 2002;28:364–376.
35. Boyko EJ, Leonetti DL, Bergstrom RW, Newell-Morris L, Fujimoto WY. Visceral adiposity, fasting plasma insulin, and blood pressure in Japanese-Americans. *Diabetes Care* 1989;18:174–181.
36. Denker PS, Pollock VE. Fasting serum insulin levels in essential hypertension: a meta-analysis. *Arch Intern Med* 1992;152:1649–1651.
37. Amini M, Bashardost N, Kazemi M, Shahparian M, Afshinnia F, Kabirzadeh M. Risk factors of diabetes mellitus among Isfahan city population aged over 40. *Res Med Sci J* 1998;2: 3–7 (in Farsi).
38. Amini M, Amin-Al-roaia A, Rezvanian H, Kachooiee A, Safaiee H, Horri N, Afshinnia F, Sattar G. Evaluation of glycaemic status in patients with known diabetes mellitus type I & II in Isfahan city during 1997. *Res Med Sci J* 1998;2: 8–12 (in Farsi).
39. Kissebah AH, Vydelingum N, Murray R, Evans DJ, Hartz AJ, Kalkhoff RK, Adams PW. Relation of body fat distribution to metabolic complications of obesity. *J Clin Endocrinol Metab* 1982;54:254–260.
40. Krotkiewski M, Bjorntorp Psjostrom L, Smith U. Impact of obesity on metabolism in men and women. Importance of regional adipose tissue distribution. *J Clin Invest* 1983;72:1150–1162.
41. Wei M, Gaskill SP, Haffner SM, Stern MP. Waist circumstance as the best predictor of non-insulin dependent diabetes mellitus (NIDDM) compare to body mass index, waist/hip ratio and other anthropometric measurements in Mexican Americans. A 7-year prospective study. *Obs Res* 1997;5:16–23.

42. Stevens J, Couper D, Pankow J, Folsom AR, Duncan BB, Nieto FJ, Jones D, Tyroler HA. Sensitivity and specificity of anthropometrics for the prediction of diabetes in a biracial cohort. *Obes Res* 2001;9:696–705.
43. Sattar N, Tan CE, Han TS, Forster L, Lean ME, Shepherd J, Packard CJ. Associations of indices of adiposity with atherogenic lipoprotein subfractions. *Int J Obes Relat Metab Disord* 1998;22:432–439.
44. Rexrode KM, Buring JE, Manson JE. Abdominal and total adiposity and risk of coronary heart disease in men. *Int J Obes Relat Metab Disord* 2001;25:1047–1056.
45. Han TS, Williams K, Sattar N, Hunt KJ, Lean ME, Haffner SM. Analysis of obesity and hyperinsulinemia in the development of metabolic syndrome: San Antonio Heart Study. *Obes Res* 2002;10:923–931.

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