

First Nationwide Study of the Prevalence of the Metabolic Syndrome and Optimal Cutoff Points of Waist Circumference in the Middle East

The National Survey of Risk Factors for Noncommunicable Diseases of Iran

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OBJECTIVE — The purpose of this study was to provide the first national estimate on the prevalence of the metabolic syndrome and its components and the first ethnic-specific cutoff point for waist circumference in the Eastern Mediterranean Region.

RESEARCH DESIGN AND METHODS — This national survey was conducted in 2007 on 3,024 Iranians aged 25–64 years living in urban and rural areas of all 30 provinces in Iran. The metabolic syndrome was defined by different criteria, namely the definition of the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III), the International Diabetes Federation (IDF) criteria, and the modified definition of the NCEP/ATP III (ATP III/American Heart Association [AHA]/National Heart, Lung, and Blood Institute [NHLBI]).

RESULTS — The age-standardized prevalence of the metabolic syndrome was about 34.7% (95% CI 33.1–36.2) based on the ATP III criteria, 37.4% (35.9–39.0%) based on the IDF definition, and 41.6% (40.1–43.2%) based on the ATP III/AHA/NHLBI criteria. By all definitions, the prevalence of the metabolic syndrome was higher in women, in urban areas, and in the 55- to 64-year age-group compared with the prevalence in men, in rural areas, and in other age-groups, respectively. The metabolic syndrome was estimated to affect >11 million Iranians. The optimal cutoff point of waist circumference for predicting at least two other components of the metabolic syndrome as defined by the IDF was 89 cm for men and 91 cm for women.

CONCLUSIONS — The high prevalence of the metabolic syndrome with its considerable burden on the middle-aged population mandates the implementation of national policies for its prevention, notably by tackling obesity. The waist circumference cutoff points obtained can be used in the region.

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Despite the rapidly growing prevalence of chronic noncommunicable diseases in developing countries, notably in Asians with an ethnic predisposition to insulin resistance and adverse body fat patterning seen in the metabolic

syndrome (1), limited data exist on national estimates of such disorders. In this context, the rapid epidemiological transition in Middle Eastern countries is a cause of concern. These nations have the highest dietary energy surplus of all develop-

ing countries (2) and one of the highest prevalence rates of overweight (3); the region is expected to show one of the world's greatest increases in the absolute burden of diabetes in the next two decades (4). Meanwhile there are no national data either on the distribution of the metabolic syndrome and its components or on the ethnic-specific optimal thresholds for waist circumference in this region. Our aim in this study was to estimate the national prevalence of the metabolic syndrome based on three sets of criteria and to determine the optimal cutoff point of waist circumference based on matching with other components of the metabolic syndrome in the Middle East.

RESEARCH DESIGN AND METHODS

— The third National Survey of Risk Factors of Non-Communicable Diseases (SURFNCD 2007) was a population-based nationwide health survey conducted in Iran using guidelines of the STEPwise approach to noncommunicable disease risk factor surveillance of the World Health Organization (WHO) (5) with some modifications (6). The sample size was calculated as 384 in each age and sex group and was increased to 500 because the cluster sampling method was used; 250 clusters, each with 20 individuals, were selected in each sex and age-group. We recruited individuals from the households in a cluster using a quota approach, but we avoided recruiting subjects from the same age-group in a single household.

The population aged >25 years was eligible for blood sampling and consisted of 4,000 individuals. Using a probability proportional to size multistage cluster random sampling method, a stratified representative sample of the population in the urban and rural areas of all 30 provinces of the country was studied. The Center for Disease Control and Manage-

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Table 1—Characteristics of participants by sex and living area

| | Men | | | Women | | |
|--------------------------------|--------------|---------------|---------------|--------------|---------------|---------------|
| | Total | Urban | Rural | Total | Urban | Rural |
| n | 1,431* | 942 | 489 | 1,535 | 1,003 | 532 |
| Age (years) | 41.5 ± 0.07 | 41.5 ± 0.1 | 41.6 ± 0.1 | 41.2 ± 0.07 | 41.0 ± 0.1 | 41.3 ± 0.8 |
| SBP (mmHg) | 124.7 ± 0.3 | 126.6 ± 0.4† | 122.4 ± 0.5† | 123.7 ± 0.5 | 123.5 ± 0.9† | 124.07 ± 0.4† |
| DBP (mmHg) | 80.0 ± 0.4‡ | 82.2 ± 0.7†‡ | 77.3 ± 0.4†‡ | 82.4 ± 0.4‡ | 82.1 ± 0.7†‡ | 82.7 ± 0.3†‡ |
| Weight (kg) | 74.3 ± 0.3 | 79.9 ± 0.4 | 71.1 ± 0.6 | 67.8 ± 0.3 | 70.6 ± 0.4 | 64.6 ± 0.3 |
| Height (cm) | 169.6 ± 0.2 | 171.0 ± 0.2 | 167.9 ± 0.3 | 156.4 ± 0.2 | 157.1 ± 0.3 | 155.5 ± 0.2 |
| BMI (kg/m ²) | 25.6 ± 0.1 | 26.3 ± 0.1† | 24.9 ± 0.2† | 27.8 ± 0.1 | 28.7 ± 0.2† | 26.8 ± 0.2† |
| Waist circumference (cm) | 89.8 ± 0.3 | 91.5 ± 0.4 | 87.7 ± 0.4 | 89.0 ± 0.3 | 90.4 ± 0.4 | 87.3 ± 0.4 |
| Total cholesterol (mmol/l) | 4.99 ± 5.2 | 5.05 ± 0.04 | 4.93 ± 0.03 | 5.24 ± 5.2 | 5.23 ± 0.03 | 5.25 ± 0.03 |
| LDL cholesterol (mmol/l) | 3.27 ± 0.02 | 3.28 ± 0.03 | 3.25 ± 0.02 | 3.45 ± 0.02 | 3.41 ± 0.03 | 3.50 ± 0.03 |
| HDL cholesterol (mmol/l) | 0.89 ± 0.01 | 0.85 ± 0.01 | 0.97 ± 0.01 | 1.03 ± 0.01 | 1.00 ± 0.01 | 1.06 ± 0.01 |
| Triglycerides (mmol/l) | 1.84 ± 0.03 | 2.00 ± 0.05 | 1.64 ± 0.03 | 1.66 ± 0.02 | 1.90 ± 0.03 | 1.50 ± 0.03 |
| Fasting blood glucose (mmol/l) | 5.22 ± 0.05‡ | 5.42 ± 0.08†‡ | 4.99 ± 0.03†‡ | 5.09 ± 0.04‡ | 5.11 ± 0.05†‡ | 5.08 ± 0.05†‡ |

Data are means ± SEM. *Number of participants who have nonmissing values for all variables; number of valid cases for each variable may slightly differ. † $P < 0.05$ for urban versus rural area. ‡ $P < 0.05$ for men versus women. DBP, diastolic blood pressure; SBP, systolic blood pressure.

ment approved the study, and informed written consent was obtained from participants.

Data collection

Strict training modules were designed and used to train interviewers and other staff. A vigorous quality assurance program was implemented to ensure the quality of data collection and laboratory examinations. After selecting the eligible individuals, all steps were done at the door. A team consisting of health care professionals recorded demographic and health information in a checklist and carried out the field examinations by standardized and calibrated instruments. Weight, height, and waist circumference were measured according to a standard protocol (5), and BMI was computed. Blood pressure was measured three times by using a digital sphygmomanometer (M7 Omron). The means of the second and third measurements were used in the analysis.

Trained laboratory technicians obtained fasting (10–12 h) venous blood samples and transferred them in cold boxes to a referral laboratory in each province that was at most 4 h away from the sampling site. In addition, for protecting blood glucose concentrations from glycolysis, the anticoagulant sodium fluoride was added to the collection vial. The blood samples were centrifuged, and sera were kept frozen at -20°C before being transferred to the National Reference Laboratory, a WHO-collaborating center in Tehran. We measured glucose with the glucose oxidase/ peroxidase-4-aminophenazone-phenol

method and triglycerides were measured using glycerol-3-phosphate oxidase-peroxidase aminophenazone (Randox). HDL cholesterol was determined after dextran sulfate-magnesium chloride precipitation of non-HDL cholesterol (7). Uniform testing kits from the same batch number (Pars Azmoun Company) were used to test the samples. Of all samples, 10% were rechecked by the National Reference Laboratory as a quality assurance measure. The coefficient of variation was $<5\%$ for all laboratory measurements.

Definitions and criteria for metabolic syndrome

We used the 2001 criteria of the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) (8), the 2005 criteria of the International Diabetes Federation (IDF) (9), and the definition of the NCEP ATP III modified in 2005 by the American Heart Association (AHA) and the National Heart, Lung, and Blood Institute (NHLBI) (10).

Statistical methods

Stata statistical software (release 9.1, StataCorp, College Station, TX) was used for analysis with complex sample survey modules and commands. Variables of provinces were the indicators of strata, and in each province there were a few clusters from which participants were recruited. Because the sampling was based on studying two individuals of each sex and a 10-year span within every randomly selected cluster, we used age and sex strata for poststratification and standardization for the Iranian population. Stan-

dardization was achieved by determining community size in the provinces and rural/urban areas represented by each participant in the study. These weights made the standardized results that can be generalized to the Iranian population aged 25 to 64 years according to the 2007 National Census. Continuous variables are described by mean ± SEM. For categorical data and abnormal levels of variables studied, the prevalence of abnormal cases with confidence intervals is reported.

The receiver operator characteristic curve for waist circumference to present at least two other components of the metabolic syndrome as defined by the IDF criteria (9) was plotted. The optimal cutoff values of waist circumference were calculated by plotting the true positive rate (sensitivity) against the false-positive rate ($1 - \text{specificity}$), when maximum accuracy (sensitivity plus specificity) was achieved. To be able to compare our results with those from other countries in the Eastern Mediterranean Region (EMR), the findings were also directly standardized with the WHO world standard population (11).

RESULTS— Of 4,000 target participants, 3,864 responded to interviews and 3,455 agreed to give blood samples. On the whole, data obtained from interviews and laboratory tests of 3,024 participants (i.e., 75% of the desired number and 79% of the recruited population) were complete and were included in the analysis. The 20% of participants who had dropped out in the laboratory phase were from different age-groups and sex groups;

however, the majority were young men and the minority were older women. Prevalence was estimated for nonmissing cases and standardized to the Iran population. In each stratum, the missing pattern seems random and is not confined to special places or attributes. Although some differences existed in various age-groups and sex groups, as poststratification was done with real weights, the final estimates are not biased by the imbalance of the groups. Participants were lost in the laboratory stage mainly because some standard transportation and sampling procedures were not followed; in addition, codes assigned to some patients were lost, and the patients could not be matched to their corresponding results.

We studied 3,024 individuals with a mean \pm SEM age of 41.3 ± 0.07 years, living in urban and rural areas of all 30 provinces of Iran. About two-thirds of the population were urban residents. Mean systolic and diastolic blood pressure and fasting plasma glucose (FPG) in urban residents were higher than those in rural residents (Table 1).

Overweight was documented in 34.2% of the population with a higher prevalence in women than in men (36.1% vs. 32.1%, respectively, $P = 0.001$). Overall, 25.1% of the population studied was obese, with a higher prevalence in women than in men (33.3% vs. 17.2%, respectively, $P < 0.0001$). In both sexes, overweight and obesity were more prevalent in urban areas than in rural areas (data not shown).

The age-standardized prevalence of the metabolic syndrome was 35.6% based on the ATP III criteria (8), 37.4% by the IDF definition (9), and 42.3% according to the ATP III/AHA/NHLBI criteria (10). By all definitions, the prevalence of the metabolic syndrome in women and in the 55- to 64-year age-group was higher than those in men and in other age-groups, respectively. The increase in the prevalence of metabolic syndrome with age had a higher slope in women than in men, with a 20% difference between men and women in the 25- to 34-year age-group by the ATP III criteria (8), increasing to $>75\%$ in the 55- to 64-year age-group. The estimated prevalence of the metabolic syndrome was consistently higher based on the IDF definition (9) compared with the ATP III (8) and ATP III/AHA/NHLBI (10) criteria (Table 2).

Regardless of the definition used (8–10), the prevalence of the metabolic syndrome in the urban population was 30–

100% higher than that in the rural population. The prevalence of the metabolic syndrome in the urban versus rural population by the ATP III definition, the IDF criteria (9), and the ATP III/AHA/NHLBI criteria (10) was 42.1% (range 39.6–44.5%) versus 28.1% (26.4–29.7%), 43.1% (40.7–45.5%) versus 30.9% (29.1–32.7%), and 49.5% (47.0–51.9%) versus 33.8% (32.1–35.6%), respectively ($P < 0.0001$ for all differences).

By all sets of criteria used (8–10), the most common component of the metabolic syndrome was low serum HDL cholesterol, found in 80% of the population. Half of the population had increased waist circumference, and more than one-third had high serum triglyceride levels and high blood pressure. FPG levels >110 mg/dl were found in 12% and levels >100 mg/dl in 16% of individuals (Table 3).

We estimated the burden of the metabolic syndrome for the Iranian population aged 25–64 years. According to the national census, in 2007 this population consisted of 15,900,331 men and 15,479,406 women. Based on the ATP III criteria (8), the metabolic syndrome affected 4,574,352 men (95% CI 4,301,254–4,847,450) and 6,621,786 women (6,260,567–6,983,008). The estimates based on the IDF definition (9) were 4,375,044 (4,301,254–4,847,450) for men and 7,412,998 (7,060,598–7,765,397) for women, and based on the ATP III/AHA/NHLBI criteria (10) they were 5,766,897 (5,477,624–6,056,171) for men and 7,514,809 (7,151,077–7,878,541) for women.

The optimal cutoff point of waist circumference for predicting at least two other components of the metabolic syndrome as defined by the IDF (9) was 88 cm for men and 91 cm for women (Fig. 1).

When standardized with the WHO world standard population (11), the estimates of metabolic syndrome in the EMR were 36.2% (95% CI 34.6–37.8) based on the ATP III criteria (8), 39.2% (37.6–40.9) based on the IDF criteria (9), and 44.6% (42.9–46.3) based on the ATP III/AHA/NHLBI criteria (10). By the same calculation, the regional estimates were 36.5% (34.7–38.2) for overweight, 24.3% (22.8–25.8) for generalized obesity, and 36.9% (35.4–38.4) for abdominal obesity based on the ATP III criteria (8), and 57.2% (55.6–58.8) based on the IDF (9) and ATP III/AHA/NHLBI criteria (10). Because the cluster effect was not considered in standardization, these CIs are slightly underestimated.

Table 2—Prevalence of metabolic syndrome based on different sets of criteria by age-group and sex

| Age | ATP III (8) | | | IDF (9) | | | ATP III/AHA/NHLBI (10) | | |
|-------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------------|------------------|------------------|
| | Total | Men | Women | Total | Men | Women | Total | Men | Women |
| 25–34 years | 19.0 (16.4–21.7) | 17.5 (14.6–20.4) | 20.5 (16.5–24.5) | 21.5 (19.3–23.8) | 16.9 (14.6–19.1) | 26.2 (22.2–30.2) | 24.9 (22.2–27.7) | 22.6 (19.5–25.8) | 27.2 (22.9–31.5) |
| 35–44 years | 35.8 (33.2–38.3) | 31.0 (27.9–34.0) | 41.2 (37.1–45.3) | 37.8 (35.0–40.5) | 29.3 (25.3–33.3) | 47.3 (48.6–50.9) | 43.3 (40.8–45.8) | 39.3 (35.7–43.0) | 47.7 (44.0–51.4) |
| 45–54 years | 50.1 (48.2–53.8) | 37.0 (33.3–40.8) | 66.6 (62.0–71.2) | 51.4 (48.5–54.3) | 33.4 (29.7–37.2) | 71.4 (67.3–75.6) | 57.6 (54.7–60.5) | 45.0 (41.2–48.7) | 71.7 (67.6–75.9) |
| 55–64 years | 57.6 (53.8–61.4) | 41.5 (35.7–47.2) | 72.9 (68.2–77.7) | 59.5 (56.0–62.9) | 43.3 (38.2–48.4) | 74.8 (70.1–79.5) | 64.4 (60.8–68.1) | 52.8 (47.4–58.2) | 75.5 (70.8–80.2) |
| Total | 35.6 (34.1–37.1) | 28.8 (27.0–30.5) | 42.8 (40.4–45.1) | 37.4 (35.9–39.0) | 27.5 (25.7–29.3) | 47.9 (45.6–50.2) | 42.3 (40.7–43.8) | 36.3 (34.4–38.1) | 48.5 (46.2–50.9) |

Data are % (95% CI).

Table 3—Prevalence of the metabolic syndrome components based on different sets of criteria

| | High FPG | High triglycerides | Low HDL cholesterol | High blood pressure | Increased waist circumference |
|---------------------------------|------------------|--------------------|---------------------|---------------------|-------------------------------|
| ATP III (8) | | | | | |
| Total | 12.4 (11.4–13.4) | 37.8 (36.0–39.5) | 79.9 (78.2–81.6) | 41.9 (40.1–43.5) | 36.0 (34.7–37.4) |
| Men | 13.3 (12.0–14.7) | 40.1 (37.9–42.2) | 75.9 (73.9–77.9) | 39.6 (37.4–41.9) | 16.5 (14.9–18.0) |
| Women | 11.4 (9.9–12.9) | 35.4 (33.0–37.7) | 84.1 (81.8–86.3) | 44.1 (41.9–46.3) | 56.5 (54.3–58.6) |
| IDF (9)*–ATP III/AHA/NHLBI (10) | | | | | |
| Total | 15.7 (14.5–16.9) | 37.8 (36.0–39.5) | 79.9 (78.2–81.6) | 41.9 (40.1–43.5) | 54.9 (53.5–56.3) |
| Men | 17.2 (15.7–18.6) | 40.1 (37.9–42.2) | 75.9 (73.9–77.9) | 39.6 (37.4–41.9) | 38.6 (36.6–40.7) |
| Women | 14.2 (12.5–15.9) | 35.4 (33.0–37.7) | 84.1 (81.8–86.3) | 44.1 (41.9–46.3) | 71.9 (69.9–73.9) |

Data are % (95% CI). *All components are similar in the IDF (9) and ATP III/AHA/NHLBI (10) definitions except the increased waist circumference that is the core component of the IDF criteria.

CONCLUSIONS— In this first nationally representative study of the burden of the metabolic syndrome in the Middle East, we found alarming prevalence rates of the syndrome and its components as defined by different sets of

criteria. This finding may be accounted for by the rapid epidemiological, demographic, and nutritional transition in the Iranian community. In addition, although the optimal cutoff points of waist circumference for predicting other components of the metabolic syndrome in the Iranian population were similar in both sexes, in men they were lower and in women they were higher than the Europid cutoff points currently recommended for use with the Middle Eastern populations (9). Our study of the burden of the metabolic syndrome, which in turn influences the risk of chronic diseases, provides up-to-date evidence-based data that can be used to orient the health systems of Middle Eastern countries toward prevention and early control of modifiable factors related to clustering of risk factors in this region.

Limited experience exists regarding the prevalence of the metabolic syndrome in the EMR. In a study in Tunisia, this prevalence was 45.5% based on the IDF criteria (9) and 24.3% according to the ATP III definition (8), with significantly higher prevalence in women than in men. The two most common components were increased waist circumference and low HDL cholesterol (12). A survey in Turkey reported a prevalence of 33.9% for metabolic syndrome (8), with a higher prevalence in women (39.6%) than in men (28%) (13). Another study in Turkey reported a prevalence of 10.09 and 27.33% for the metabolic syndrome in men and women, respectively (14).

It is well documented that Asians have an ethnic predisposition to adverse body fat distribution and metabolic syndrome (1); hence, optimal cutoff points for waist circumference have been established for South Asians (9); by using this cutoff, the prevalence of the metabolic syndrome in this population is estimated

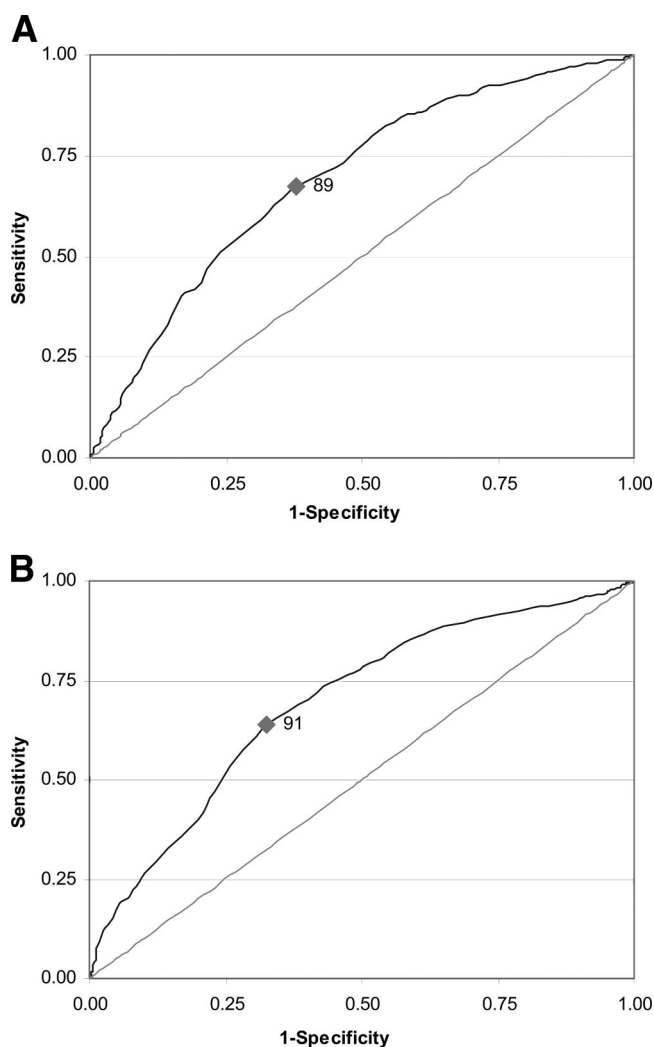


Figure 1—A: Men: receiver operator characteristic (ROC) curves for waist circumference to predict the presence of at least two risk factors of the metabolic syndrome, as defined by the IDF for men. Area under ROC curve = 0.69. B: Women: the ROC curves for waist circumference to predict the presence of at least two risk factors of the metabolic syndrome, as defined by the IDF for women. Area under ROC curve = 0.69.

to be 10–30% (15). None of the Middle Eastern studies have been conducted at the national level, and many target specific populations; hence, their findings cannot be generalized to the region. A study of female Saudi subjects found the prevalence of metabolic syndrome to be 16.1 and 13.6% according to the IDF (9) and ATP III (8) definitions, respectively (16). In a population in Northern Jordan, the prevalence of the metabolic syndrome (8) was reported to be 36.3%, with a significantly higher prevalence in women than in men. The most common abnormality was low HDL cholesterol in men (62.7%) and increased waist circumference in women (69.1%) (17). The prevalence of the metabolic syndrome (8) was reported to be 21.0% in one city in Oman, with low HDL cholesterol (75.4%) and increased waist circumference as the two most common components (18).

The sex difference in the prevalence of the metabolic syndrome in this study is in line with that in previous studies in the EMR (12–15,18) and local studies in Iran (19,20). The prevalence of the metabolic syndrome (8) in one of the studies in Iran was reported to be 33.7%, with a higher prevalence in women (42%) than in men (24%) (19); the corresponding figure in the other study was 23.3%, with a higher prevalence in women (35.1%) than in men (10.7%), respectively (20). The metabolic syndrome was documented in about 75% of women aged 55–64 years; this finding is alarming and confirms the theory that more attention should be paid to prevention and control of this disorder, which poses serious health threats.

In all of the aforementioned population-based studies in the Middle East (17–20) as well as in this one, low HDL cholesterol followed by abdominal obesity has been the most common component of the metabolic syndrome. The high prevalence of low HDL cholesterol, even in many individuals without obesity and hypertriglyceridemia, supports an ethnic predisposition to this type of dyslipidemia. The findings in a recent study of the strong association between migration of Iranians to Sweden and the prevalence of hypertension and smoking but not dyslipidemia (21) provide further confirmatory evidence of the ethnic predisposition to low HDL cholesterol. This ethnic predisposition should be examined in future genetic studies.

The IDF consensus strongly recommends that ethnic group-specific cut points for waist circumference should be

used; for the Eastern Mediterranean and Middle Eastern populations, it is recommended that the European cutoff points of waist circumference be used until more specific data become available (9). In a survey in Tunisia, a cutoff point of 85 cm was documented for waist circumference in both sexes (22). A study in a city of Iraq showed waist circumference cutoff points of 97 cm in men and 99 cm in women (23). In a study in Tehran, the cutoff points for waist circumference were 80–93 cm for men and 79–96 cm for women (24). The optimal cutoff points obtained from the current study (i.e., 89 cm for men and 91 cm for women) are different from the Europid cutoff points that are currently recommended for use with Middle Eastern populations (9,10).

Our finding of greater waist circumference values in the Iranian community than in Western populations may be partly due to ethnic differences in body fat patterning and the genetic tendency of Asians to abdominal obesity (1); in addition, high carbohydrate intake and sedentary lifestyle in the Iranian community might be contributing factors (20,25). However, a recent study comparing elderly Iranians inside Iran with those settled as migrants in Sweden showed the prevalence of general obesity to be higher in Iranian women in Sweden (42%) than in Iran (34%), but abdominal obesity was found in nearly 80% of women in both groups (21). This finding suggests that the role of ethnicity on increased waist circumference might be more important than lifestyle factors, a concept that needs to be confirmed by birth cohorts and other longitudinal studies.

Study limitations and strengths

The main limitation of this study for determining the optimal cutoff point for waist circumference is its cross-sectional nature; longitudinal studies are required to confirm our findings. Furthermore, the sensitivity and specificity of this cutoff point were not high; however, it would be useful as a screening tool. The strength of this study is its nationally representative sample with valid weights for standardization that enable us to infer with some confidence the distribution and epidemiology of the metabolic syndrome and its components in Iran and even in the region.

In summary, the high prevalence of the metabolic syndrome and its considerable effect on the middle-aged population

mandate the implementation of national policies for its prevention and control in the Middle Eastern countries, which face the world's greatest increment in the absolute burden of diabetes in the next two decades. The cutoff points provided by this survey can be used as optimal cutoff points in the region.

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