The first cut-off points for generalized and abdominal obesity in predicting lipid disorders in a nationally representative population in the Middle East: The National Survey of Risk Factors for Non-Communicable Diseases of Iran

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Abstract

Introduction: To determine the prevalence of dyslipidaemia and the optimal cut-off points of body mass index (BMI) and waist circumference (WC) at which abnormal lipid levels can be identified with maximum sensitivity and specificity in a nationwide population-based sample for the first time in the Middle East.
Material and methods: Using a probability proportional to size, multistage cluster sampling method, a sociodemographically representative sample of 3024 of the Iranian population aged 25-64 years living in urban and rural areas of all 30 provinces of the country was studied.
Results: The mean age of participants was 41.3 (0.07) years. The receiver operating curve (ROC) analysis showed that the optimal cut-off value of BMI to identify with maximum sensitivity and specificity the detection of lipid disorders was 25 kg/m^2 for males and 26-28 kg/m^2 for females. Considering WC, among males this optimal cut-off value was 88-89 cm for high total cholesterol (T. Chol), low HDL-C and high triglycerides (TG), whereas it was lower (86 cm) for predicting high LDL-C. Among females, this cut-off value was 83-84 cm for predicting high T. Chol, high LDL-C and high TG, but it was higher (90 cm) for low HDL-C. The most prevalent type of abnormal lipid level was low HDL-C.
Conclusions: The optimal cut-off points provided in the current study might serve as a public health action threshold in the Middle East population. The very high prevalence of high TG and low HDL-C suggest that current guidelines for screening lipid disorders that are based on total and LDL cholesterol should consider such ethnic differences.

Key words: ethnicity, cut-off points, anthropometric indexes, lipid disorders, Middle East, Iran.

Introduction

According to the World Health Organization (WHO), obesity ranks fifth and seventeenth in the list of the leading risk factors underlying the total burden of disease of the low-mortality and the high-mortality developing countries, respectively [1].

The lifestyle and body composition of populations are changing rapidly and usually occur at the first stages of the economic and social development of low- and middle-income countries [2]. Furthermore, genetic predisposition or early-life events may also contribute to the susceptibility of non-European populations to adverse body-fat patterning and the high prevalence of generalized and abdominal obesity in developing countries [3].

Overweight and obesity can lead to various metabolic abnormalities, insulin resistance, type 2 diabetes mellitus, lipid disorders, and cardiovascular disease.

Complex mechanisms are involved in lipid metabolism among obese individuals; these mechanisms may act at the level of the hypothalamus and/or on body composition through peripheral effects on adipose tissue. The increased health risks associated with obesity have been found to occur in Asians at lower body mass indices (BMIs); hence different cut-off values are suggested for BMI and waist circumference (WC) in various populations [4]. In addition, important ethnic differences are documented in serum lipid profile both in adults [5, 6] and children [7].

Although the Middle East has the highest dietary energy surplus of the developing countries and is facing an epidemic of obesity and diabetes [8], and while it is strongly recommended that ethnic group specific cut-points for anthropometric indices should be used for people of the same ethnic group, still reference standards for WC and BMI risk threshold values are not established in a nationally-representative population of this region.

The third Survey of Risk Factors of Non-Communicable Diseases (SURFNCD) was conducted in 2007 to assess the prevalence and profile of non-communicable disease related risk factors in the Iranian population.

This paper reports the results of this national survey in estimating the prevalence of dyslipidaemia and to determine the optimal cut-off points of BMI and WC at which abnormal lipid levels can be identified with maximum sensitivity and specificity. To the best of our knowledge, this is the first study of its kind conducted in a nationwide population-based sample, not only in the Middle East, but also in the Eastern Mediterranean region (EMR).

Material and methods

The third National SURFNCD 2007 was a population-based nationwide household survey conducted in Iran. We have previously published the protocol of the survey [9], and here we describe it in brief. Non-institutionalized Iranian citizens aged 25-64 years were eligible for the study in the case of giving informed consent and having no medical limitation on giving a blood sample. In each age group, only one member of the household was recruited. The sample size was calculated as 384 in each age and sex group, and was increased to 500 because of using the cluster sampling method. Hence 250 clusters, of 20 individuals each, were selected in each sex and age group (15-64 years divided into 10-year intervals). According to the study design, only the population aged above 25 years was eligible for blood sampling and consisted of 4000 individuals. A two-stage cluster sampling method was used to select the samples. The national data bank of zip codes was used in this national study to identify the clusters at random. Using a probability proportional to size (PPS) multistage cluster sampling method, a sociodemographically representative sample of the Iranian population aged 25-64 years living in urban and rural areas of all 30 provinces of the country was studied. Of 4000 target samples, 3864 valid interviews were conducted (96.6% response rate). All of them were invited for blood sampling, but about 3455 individuals got standard delivery and testing. Laboratory data of 3024 participants were complete and are reported in this paper. In all, the data of 75% of the desired number of participants and 79% of the recruited population were analyzed. The 20% of participants who dropped out in the laboratory phase were from different age and sex groups; the highest drop-out was from young men and the lowest from old women. The Center for Disease Management and Control of Iran, ethics committees and other relevant national regulatory organizations approved the study and informed written consent was obtained from all participants.

Strict training processes and vigorous quality assurance programmes were used to ensure the quality of data collection. The selected individuals were invited to the survey centres for interview and clinical examinations. A team consisting of expert healthcare professionals carried out the field examinations using standardized and calibrated instruments. Anthropometric measurement was conducted according to the standard protocol. Body mass index was calculated as weight divided by height squared (kg/m^2). Waist circumference was measured at the midpoint level of the mid-axillary line between the 12^{th} rib head and the superior anterior iliac spine. Body mass index and WC were documented as measures of generalized and abdominal obesity, respectively [10].

Participants were instructed to fast for 12 h before blood collection, and fasting compliance was determined by interview on the morning of the blood sampling. Trained laboratory technicians obtained fasting venous blood samples from the antecubital vein. The blood samples were transferred to a referral laboratory of each county using a cold box. The blood samples were centrifuged for 10 min at 1500 rpm immediately after clot formation to provide a serum sample and kept cool in a refrigerator at the temperature of 4 to 8°C for a maximum of 48 h. Blood sera were transferred to the National Reference Laboratory, a WHO-collaborating centre in Tehran, which was responsible for biochemical standardization of the process and coordination. Samples were kept frozen at –20°C if the distance between the centrifuging site and the referral laboratory was significant or the transfer time to Tehran was likely to last longer than 48 h.

We estimated total cholesterol (T. Chol) by cholesterol oxidase/p-aminophenazone (CHOD-PAP) method, and triglycerides (TG) by GPO-PAP (glycerolphosphate oxidase-peroxidase aminophenazone, Randox). High density lipoprotein cholesterol (HDL-C) was estimated by the precipitation method using phosphotungstate/magnesium precipitation of apolipoprotein B containing lipoproteins followed by estimation of cholesterol in the supernatant by enzymatic method. Low density lipoprotein-cholesterol (LDL-C) was calculated automatically with the Friedwald equation [11] by the AR1000 testing device. In 77 individuals with TG level higher than 400 mg/dl, we measured LDL-C by the enzymatic photometric method using standard kits (Pars Azmun, Iran). Uniform testing kits from the same batch number produced by an Iranian company, Pars Azmoun, were purchased and distributed throughout the provinces. Of all the samples, 10% were tested for a second time by the national reference laboratory as a quality assurance measure. The coefficient of variation was less than 5% for all samples.

Definition of abnormal lipid values

By using the guidelines of the Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III), the optimal serum level was considered as < 200 mg/dl for T. Chol, < 100 mg/dl for LDL-C, and < 150 mg/dl for TG in both genders, and low HDL-C was defined as < 40 mg/dl in men and < 50 mg/dl in women [12].

Statistical analysis

Stata statistical software (Release 9.0, College Station, TX), which is used for the multistage sampling, clustering, and stratification design of national surveys, was used for statistical analyses and to generate population estimates. To extrapolate the results to the general population of Iran, by post-stratification weighting, data were standardized to the Iranian population of aged 25 to 64 years according to the 2007 National Census and by considering different age, gender, and urban/rural area strata. Descriptive data are presented as mean ± standard error (SE) and 95% confidence interval (95% CI). The differences of mean lipid values in terms of gender and living area were compared by *t*-test, and analyses of variance (ANOVA) were performed to determine differences among age groups; significant findings were further analyzed using post hoc tests. The receiver operator characteristic (ROC) curve for BMI and WC to predict the presence of abnormal lipid level was plotted. The BMI and WC cut-off values were calculated by plotting the true positive rate (sensitivity) against the false-positive rate (1-specificity) and finding the point of maximum sensitivity plus specificity. Confidence intervals of the maximum points were calculated by iteration and bootstrap sampling. The bias-corrected percentiles of 97.5 and 2.5 were considered as upper and lower limits of the 95% CI of the thresholds.

Results

This study recruited 3024 individuals with a mean age of 41.3 (0.07) years, living in urban and rural areas of all 30 provinces of Iran relatively proportional to their size. About two-thirds of the population were living in cities.

The characteristics of participants by gender, age group and living area are presented in Table I. It shows that in all age groups, the mean BMI was higher in females than in males, whereas the mean WC was not different in terms of gender. In both genders and in all age groups, the mean BMI and WC were higher in urban than in rural areas, and increased from 25 to 45 years of age, then levelled off. Similarly, in all age groups and in both genders, the mean serum TG and total and LDL cholesterol were higher in urban than in rural areas, the largest difference being documented for TG. In both genders, with increasing age from 25 to 45, the mean serum TG and total and LDL cholesterol increased and the mean HDL-C decreased; then they levelled off. The mean serum total, LDL and HDL cholesterol were higher in females than in males, whereas the mean serum TG was lower in females than in males.

Table I. Characteristics of participants by gender, age group and living area

Age groups [years]	Males		Females	
	Urban	Rural	Urban	Rural
	Mean (SE) 95% CI	Mean (SE) 95% CI	Mean (SE) 95% CI	Mean (SE) 95% CI
Body mass index [kg/m^2]				
25-34	24.97 (0.18) 24.60-25.34	23.23 (0.17) 22.88-23.58	27.20 (0.24) 26.72-27.68	25.45 (0.20) 25.05-25.85
35-44	26.84 (0.18) 26.49-27.20	25.10 (0.20) 24.70-25.50	29.07 (0.20) 28.66-29.48	27.32 (0.25) 26.94-27.70
45-54	27.97 (0.17) 27.63-28.31	26.22 (0.18) 29.83-30.56	30.19 (0.18) 29.83-30.56	28.45 (0.20) 28.04-28.86
55-64	27.15 (0.18) 26.79-27.51	25.40 (0.23) 24.95-25.85	29.37 (0.19) 28.98-29.76	27.63 (0.21) 27.21-28.04
Waist circumference [cm]				
25-34	85.93 (0.41) 85.12-86.75	82.18 (0.49) 81.22-83.14	85.31 (0.43) 84.46-86.16	81.56 (0.47) 80.63-82.49
35-44	91.61 (0.51) 90.61-92.61	87.86 (0.49) 86.90-88.82	90.99 (0.50) 89.99-91.98	87.24 (0.45) 86.35-88.12
45-54	97.14 (0.46) 96.21-98.05	93.38 (0.50) 92.39-94.36	96.51 (0.49) 95.53-97.49	92.75 (0.50) 91.76-93.72
55-64	97.11 (0.48) 96.16-98.06	93.36 (0.52) 92.34-94.38	96.49 (0.49) 95.52-97.47	92.74 (0.50) 91.76-93.72
Total cholesterol [mg/dl]				
25-34	183.7 (2) 179.7-187.6	185.3 (2) 181.3-189.2	188.6 (2.9) 182.9-194.3	190 (2) 186.1-194
35-44	198 (2.2) 193.8-202.3	188.1 (1.9) 184.3-191.9	202.8 (2.1) 198.5-207.0	194.2 (1.3) 191.7-196.8
45-54	211.3 (3.7) 204.0-218.5	201.9 (1.8) 198.5-205.4	217.2 (2.1) 213-221.4	224.4 (2.3) 219.9-228.9
55-64	199.4 (2.8) 193.8-205.0	194.6 (2.5) 189.7-199.6	226 (3) 220.1-232.0	224.3 (2.7) 219.1-229.6
LDL cholesterol [mg/dl]				
25-34	118.3 (1.5) 115.4-121.2	121.3 (1.5) 118.4-124.2	123.5 (2.5) 118.4-128.5	124.6 (1.8) 121-128.1
35-44	129.4 (1.5) 126.4-132.3	122.9 (1.6) 119.8-126	130 (1.7) 126.7-133.3	128.9 (1) 126.8-130.9
45-54	137.1 (4.6) 128-146.1	133.5 (1.5) 130.6-136.5	140.8 (2) 136.9-144.7	156.3 (2) 152.3-160.2
55-64	133 (2.4) 128.2-137.8	131 (2.2) 126.7-135.4	151.6 (2.6) 146.5-156.7	147.6 (2.5) 142.6-152.5
HDL cholesterol [mg/dl]				
25-34	33 (0.5) 32.1-33.9	38.6 (0.6) 37.4-39.9	41.7 (0.9) 39.9-43.5	41.8 (0.4) 41.0-42.6
35-44	31.7 (0.5) 30.7-32.7	34.2 (0.5) 33.3-35.2	36.2 (0.6) 35.1-37.4	43.1 (0.5) 42.1-44.1
45-54	33.7 (0.8) 32.1-35.3	33.2 (0.4) 32.4-34.0	36.5 (0.6) 35.3-37.7	38.2 (0.4) 37.4-39.0
55-64	33.6 (1.1) 31.5-35.7	38.1 (0.7) 36.8-39.4	38.2 (0.6) 37.1-39.3	39.8 (1.2) 37.4-42.2
Triglycerides [mg/dl]				
25-34	161.6 (6.7) 148.3-174.8	126.2 (4.6) 117.1-135.3	117 (4.6) 107.9-126.0	118.1 (3.5) 111.2-125.1
35-44	185.7 (8.8) 168.3-203.1	155.4 (3.9) 147.8-163.1	181.1 (4.5) 172.2-190.0	111.7 (2.9) 106.0-117.5
45-54	204.4 (15.3) 174.3-234.6	177.3 (4.3) 168.7-185.9	200.6 (5.2) 190.2-210.9	150 (5.6) 138.9-161
55-64	164.8 (6.4) 152.3-177.3	127.8 (6.3) 115.5-140.1	181.7 (7.9) 166.1-197.3	185.2 (9.9) 165.8-204.7

All differences significant (p < 0.05) in terms of gender except for waist circumference
All differences significant (p < 0.05) for urban vs. rural area except for total and LDL cholesterol
All differences significant (p < 0.05) between age groups

Table II. Prevalence of abnormal* levels of anthropometric and lipid profile by gender and living area

		BMI > 25	High WC	High T. chol	High LDL-C	Low HDL-C	High TG
		% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)
Male							
	Urban	39[a] (37-42)	39.6[c] (37.1-42.1)	42.4 (38.7-46.2)	78.1 (75.2-80.9)	81.4[e] (78.8-83.8)	47.9[g] (44.6-51.2)
	Rural	32[a] (28-35)	32[c] (28.8-35.2)	40.8 (38.2-43.3)	79.3 (76.9-81.6)	69.5[e] (66.3-72.7)	30.8[g] (28.3-33.3)
Female							
	Urban	34[b] (30-37)	34.4[d] (30.9-38)	49.7 (45.8-53.5)	79.1 (75.4-82.9)	85.2[f] (81.5-89)	39.8[h] (36.4-43.1)
	Rural	29[b] (27-31)	29.6[d] (27.3-31.8)	40.8 (38.3-43.3)	83.8 (81.5-86)	82.7[f] (80.7-84.8)	30.3[h] (27.3-33.3)

**based on ATPIII criteria [12]*
All differences significant ($p < 0.05$) in terms of gender except for LDL-C
[a,b,c,d,e,f,g,h]$p < 0.05$ for urban vs. rural area

Table III. Receiver operator characteristic (ROC) analysis for body mass index to predict the presence of undesirable lipid level according to gender

	Cut-off value	Se#	Upper limit*	Lower limit*	ROC value^	ROC se	Sensitivity	Specificity
Male								
High T. chol	25	1.109	23.5	27.5	0.637	0.014	64.7	52.8
High LDL-C	25	1.564	22.5	28	0.629	0.019	58.2	58.2
Low HDL-C	24.5	0.958	24.5	31.5	0.587	0.017	62.7	54.0
High TG	25	0.829	23.5	28	0.671	0.014	70.4	55.9
Female								
High T. chol	28	0.67	28	30	0.613	0.014	56.4	63.0
High LDL-C	28	1.859	28	28.5	0.611	0.021	50.6	71.7
Low HDL-C	26	1.423	23	28	0.611	0.02	64.5	51.7
High TG	27.5	0.846	26.5	29.5	0.673	0.014	68.9	58.8

**boot strap bias corrected 95% confidence interval, #bootstrap standard error of threshold, ^ area under ROC curve*
High T. chol: total cholesterol ≥ 200 mg/dl, high LDL-C: LDL-C ≥ 100 mg/dl, low HDL-C: HDL-C < 40 mg/dl in men and < 50 mg/dl in women, high TG: triglycerides ≥ 150 mg/dl

Apart from total and LDL cholesterol, the prevalence of all risk factors was significantly different between urban and rural residents. Abdominal obesity and overweight were more prevalent in urban males followed by urban females, rural males and rural females. The prevalence of high total and LDL cholesterol was not significantly different in urban vs. rural areas; the prevalence of low HDL-C was higher in urban females, and urban males had the highest prevalence of hypertriglyceridaemia (Table II).

The ROC analysis showed that the optimal cut-off value of BMI to identify with maximum sensitivity and specificity the detection of lipid disorders was 25 for males and 26-28 for females (Table III). Considering WC, among males the optimal cut-off value was 88-89 for high T. Chol, low HDL-C and high TG, whereas it was lower (86) for predicting high LDL-C. Among females, this cut-off value was 83-84 for predicting high T. Chol, high LDL-C and high TG, but it was higher (90) for low HDL-C (Table IV).

Discussion

This survey was the first nationwide study on serum lipid profile and determination of the optimal cut-off values for BMI and WC in predicting abnormal lipid levels in a Middle Eastern population. We found a considerably high prevalence of lipid disorders that is consistent with the high prevalence of overweight and abdominal obesity in the population studied.

Table IV. Receiver operator characteristic (ROC) analysis for waist circumference to predict the presence of undesirable lipid level according to gender

	Cut-off value	Se#	Upper limit*	Lower limit*	ROC value^	ROC se	Sensitivity	Specificity
Male								
High T. chol	88	2.111	88	94	0.637	0.014	70.9	49.6
High LDL-C	86	3.956	79	95	0.629	0.019	69.2	50.9
Low HDL-C	89	5.137	81	102	0.587	0.017	58.5	54.7
High TG	89	2.759	83	95	0.671	0.014	70.1	55.2
Female								
High T. chol	84	1.393	84	95	0.613	0.014	79.5	40.2
High LDL-C	83	0.434	–	–	0.611	0.021	75.0	45.2
Low HDL-C	90	3.029	81	94	0.611	0.02	57.6	61.0
High TG	84	2.853	81	91	0.673	0.014	86.4	37.0

**boot strap bias corrected 95% CI, #bootstrap standard error of threshold, ^area under ROC curve*
High T. chol: total cholesterol ≥ 200 mg/dl, high LDL-C: LDL-C ≥ 100 mg/dl, low HDL-C: HDL-C < 40 mg/dl in men and < 50 mg/dl in women, high TG: triglycerides ≥ 150 mg/dl

It is well documented that the clustering of cardio-metabolic risk factors increases the risk of mortality at population level [13]. Population-based studies on lipid profile in the Middle East are very limited, and to the best of our knowledge none of them has been conducted at national level; this limitation makes comparisons difficult. In a community-based cross-sectional study conducted in one city in Oman, among 1421 adults studied, 34.5% had high T. Chol [14]. A cross-sectional survey among 2120 Bahrainis aged 40-69 years selected from the national population register showed that dyslipidaemia was prevalent in hypertensive and diabetic individuals [15]. Over 50% of the adult Kuwaiti population are reported to have hyperlipidaemia. The commonest lipid abnormality seen in Kuwaiti diabetic patients is hypertriglyceridaemia, with low HDL levels and variable LDL levels [16]. In a study among 871 individuals in a city in Iraq, 57.8% of participants had high LDL-C, 56.8% had high non-HDL-C, 49.9% had low HDL-C and 41.6% had high TG levels [17]. In a non-random sample of the population studied in an urban area of Karachi, 16% of men and 24% of women had high T. Chol levels [18].

The need for early and precise diagnosis of risk factors has been emphasized in some ethnic groups, notably among Asians [19]. Important ethnic differences in weight and lipid disorders are shown in studies among immigrant populations. A recent study in Sweden revealed that immigrant women from Iran and Turkey are heavier than women born in Sweden and have a higher prevalence of abdominal obesity, with an unfavourable lipid profile, which may predispose them to a higher incidence of diabetes and atherosclerotic cardiovascular disease [5]. Another recent study among 30 migrants from Pakistan to the UK, 30 British-born British Pakistani women, and 25 British- born women of European origin demonstrated that British-born British Pakistani women had healthier levels of anthropometric indices and lipid profile, i.e. a lower waist to hip ratio, lower mean TG levels, and higher mean HDL levels than migrant British Pakistani women. These findings confirm the gene-environment interaction in the development of chronic diseases and their risk factors [20].

In the current study, we found that a BMI cut-off of 25 in men and 28 among women was appropriate for predicting abnormal lipid profile, which is consistent with the WHO cut-off points recommended for the Caucasian population [4], and there is no need to define ethnic-specific cut-off points for BMI in the Middle East, as previously provided for some other populations in East Asia and/or other parts of the EMR. A study in China [21] and a study in Thailand [22] suggested that a BMI cut-off of 23 might be appropriate for use in identification of high risk of obesity-related metabolic disorders. An optimal cut-off value of 23.6 for BMI in males and 22.1 in females is suggested for the Taiwanese population [23].

A study in Tunisia, as a country in the EMR, found that the optimum BMI cut-off points for predicting cardiovascular risk factors were 24 kg/m^2 in men and 27 kg/m^2 in women [24].

Considering WC, among males, the optimal cut-off values (86-89) were lower than those recommended by ATPIII (11) and IDF [25], and in females, the optimal cut-off values (83-84, and 90 for low HDL-C) were lower than the ATPIII definition [12] but higher than IDF criteria [25]. This finding underscores the necessity of providing an ethnically specific cut-off point for WC in the Middle East population.

Other studies in Asian countries found different cut-off points; the appropriate WC cut-off point for central obesity for men and women is determined to be 90 and 85 cm in Korea [24], 80.5 and 71.5 cm in Taiwan [21], 81.5-84 and 76-80.5 cm in Thailand [22], and 85 and 79 cm in Tunisia [24]. The study conducted in Iraq found higher cut-off points, i.e. 97 cm in men and 99 cm in women [27].

Study strengths and limitations

The main strength of this study is its novelty in providing information about lipid disorders and optimal cut-off values for predicting dyslipidaemia for the first time in a large nationwide population-based sample in the Middle East. The other strength is using the standard WHO STEPwise protocol, taking quality assurance and quality control into account. However, this study is not without its limitations. The cross-sectional nature of these data also does not allow us to infer causality, and the findings need to be confirmed in longitudinal studies. Including diabetic patients and individuals using drugs affecting the serum lipid profile might have affected our results. Because of large differences between the ethnic and socio-cultural background of the EMR population with Western and African populations, we compared our findings only with studies conducted in Asia and in the EMR. In addition, the limited number of national studies and different definitions used for abnormal lipid levels make the comparisons difficult.

In conclusion, our findings strongly recommend that regarding ethnic differences in the pattern of fat deposition, ethnic group specific cut-off points for WC should be provided for epidemiological studies. The optimal cut-off points provided in the current study might serve as a public health action threshold in the Middle East population.

Our finding on the very high prevalence of low HDL-C in our population suggests that the current guidelines for screening lipid disorders that are based on total and LDL cholesterol should consider such ethnic differences.

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