



Role of Gender in the Prevalence of Metabolic Syndrome and Its Related Risk Factors in Shiraz Healthy Heart Center Population

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ABSTRACT

Background: Metabolic Syndrome (MetS) is defined as a group of cardiovascular risk factors and is an important health threat.

Objectives: This study aimed to determine the role of gender in the prevalence of MetS among Shiraz Healthy Heart Center population.

Patients and Methods: This study was performed on 350 adults aged 20 - 65 years from Shiraz Healthy Heart Center, Shiraz University of Medical Sciences. Individuals with obesity secondary to medication and genetic or endocrine disorders were excluded from the study. Weight and height were measured for calculating Body Mass Index (BMI). Waist circumference and blood pressure were measured, as well. Plasma glucose, serum High Density Lipoprotein-cholesterol (HDL-c), and Triglyceride (TG) were also analyzed. The presence of MetS was determined using Adult Treatment Panel-III (ATP-III) criteria.

Results: The results showed significant correlations between age and waist circumference, Fasting Blood Sugar (FBS), Systolic Blood Pressure (SBP), and Diastolic Blood Pressure (DBP). Moreover, statistically significant relationships were found between waist circumference and TG, SBP, DBP, and BMI. Significant correlations were also observed between FBS and TG, SBP, and DBP. Besides, there were strong correlations between TG and HDL-c, SBP, DBP, and BMI. Moreover, BMI, SBP, and DBP were significantly correlated. In addition, serum HDL-c was negatively associated with most of the variables. The prevalence of pre-diabetes, pre-hypertension, and hypertriglyceridemia was higher among males. On the other hand, the prevalence of hypertension, diabetes, high waist circumference, and MetS was significantly higher among the female participants.

Conclusions: A better understanding of the role of gender in the prevalence of MetS is important in developing prevention and treatment strategies.

► Implication for health policy/practice/research/medical education:

Early identification and active management of MetS, differentiating this abnormality and its related risk factors between genders, and assessing their correlations might be necessary to define better strategies for a good management of MetS. A better understanding of the mechanisms about gender differences in MetS might be important in practical interventions toward prevention and treatment of this syndrome. It is noteworthy to declare that the outcome of remedies targeting MetS may depend on age, gender, and some risk factors and their correlations.

1. Background

Metabolic syndrome or “X-syndrome” is a group of cardiovascular risk factors including central or abdominal obesity, dyslipidemia, Hypertension (HTN), and insulin

resistance (1-4), which are health threats (1). Individuals with MetS are susceptible to Cardiovascular Diseases (CVDs) and type 2 diabetes (5, 6). In addition to CVD and diabetes, those with MetS are at a higher risk for polycystic ovarian syndrome, fatty liver, cholesterolemia, gallstones, asthma, sleep disturbances, and some types of cancer. Components of MetS are a cluster of major, underlying, and emerging risk factors. Underlying risk factors for

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CVDs are central or abdominal obesity, sedentary life-style, and atherogenic diet. Besides, the major risk factors are HTN, high Low-Density Lipoprotein-cholesterol (LDL-cholesterol), low High-Density Lipoprotein-cholesterol (HDL-c), cigarette smoking, premature familial Coronary Heart Disease (CHD), and aging. The emerging risk factors encompass high Triglyceride (TG) levels, small LDL particles, insulin resistance, glucose intolerance, and pro-inflammatory and pro-thrombotic states (1). As to the components of MetS, abdominal obesity is highly correlated to MetS and is defined by increased waist circumference. Another component of MetS, atherogenic dyslipidemia, is demonstrated by high TG and low HDL levels. High blood pressure, which is highly correlated to obesity and is more prevalent in insulin-resistant patients, is also categorized in MetS. Insulin resistance is also a metabolic risk factor that is strongly associated with CVDs. Additionally, a pro-inflammatory state, which is defined as high C-Reactive Protein (CRP), is usually present in patients with MetS. The main cause of this state is obesity. Finally, a pro-thrombotic state is correlated to MetS associated with pro-inflammatory state (1). Metabolic disturbances due to MetS affect more than 30% of adults in Tehran, Iran (7). This estimated prevalence is higher than that in most developed countries, such as the United States (8). The estimated prevalence of MetS was almost 25% in individuals over the age of 20 years, and it affected almost 45% of those over 50 years in industrialized countries (9). Evidence has demonstrated that the prevalence of MetS has reached a threatening level and a defined target for secondary prevention in National Cholesterol Education Program (10). Because of the increasing trend in obesity (11), the prevalence of MetS is rising (11-14).

Considering blood pressure as one of the components of MetS, high Systolic Blood Pressure (SBP) in women is associated with cardiovascular risk (15). Gender differences in CHD and CVD mortality can be partially explained by higher prevalence of HTN in females (16). Puberty in men, compared to women, with later onset can be another reason for lower blood pressure in men (17). Additionally, a progressive increase in the prevalence of HTN can be found with higher adipose tissue or waist circumference as another component of MetS (18). Body Mass Index (BMI) is considered an independent risk factor for HTN in women (18), rooting from steroid hormones and weight in women (19). Studies have found that changes in weight and adipose tissue contents can affect insulin resistance. Elevated blood glucose level, a component of MetS in women, was also found to cause higher vulnerability to diabetes incidence in spite of normal glucose metabolism (20, 21). Serum concentrations of HDL-c and TG are other risk factors of MetS. Furthermore, lower TG and higher HDL-c levels are predominantly seen in pre-menopausal women due to the effects of estrogen (22, 23).

2. Objectives

Understanding differences between genders regarding MetS components might result in better strategies for MetS identification and management. Currently, limited studies have been performed on the prevalence of MetS in different

genders in Iran, especially Shiraz (capital of Fars province). Therefore, this study aims to determine the role of gender in the prevalence of MetS and its related risk factors in the individuals referred to Healthy Heart Center of Shiraz University of Medical Sciences, Shiraz, Iran.

3. Patients and Methods

In this cross-sectional, experimental study, 350 subjects were selected from Healthy Heart Center of Shiraz, Iran by systematic random sampling. This program is under the supervision of Shiraz University of Medical Sciences that predominantly works on screening programs. People are referred to this center from various organizations, institutes, and public community from different ethnic or occupational groups of Shiraz metropolitan city. The study protocol was approved by the Research Council of the Heart Research Center at the University. All the participants completed written informed consents and a socio-demographic questionnaire containing information about age, occupation, and marital status.

The individuals aging 20 - 65 years were included in the study, while those with obesity secondary to medication and genetic or endocrine disorders were excluded.

BMI was computed for each participant as body weight divided by height squared. Weight was measured using digital scales to the nearest 100 grams while the participants were barefooted and lightly clothed. Height was also recorded by a tape measure in standing position with the shoulders straight from head to heel with bare feet. Waist circumference was measured at the narrowest level between the lower rib and iliac crest and recorded to the approximately 0.1 centimeter. All the measurements were done by the same person to minimize possible error. The individuals with BMI over 30 kg/m² and between 25 and 29.9 kg/m² were considered as obese and overweight, respectively (4).

Blood pressure was measured twice using a standard mercury sphygmomanometer with the participant seated with 30 second intervals between the measurements. The average blood pressure between the two measurements was recorded.

Adult Treatment Panel-III (ATPIII) criteria were used for determining the presence of MetS (1). The participants with three or more of the following criteria were considered to have MetS (Table 1):

For laboratory measurements, blood samples were taken from the participants after an overnight fasting (12-hour). Fasting Blood sugar (FBS) was analyzed using the calorimetric method with glucose oxidase. Enzymatic reagents were used for measuring serum TG. Finally, serum HDL-c was recorded after precipitation of apolipoprotein-B containing lipoproteins with phosphotangestic acid.

The SPSS statistical software, version 16 (SPSS Inc., Chicago, IL) was used for statistical analyses. The correlations between dependent and independent variables were defined and assessed. Then, these observations were evaluated at α -level of 0.05. Multivariate analysis of the variables was also applied.

The correlations between the variables were measured using 2-tailed Pearson's correlation. Mean and standard deviation

Table 1. Criteria for Metabolic Syndrome

	Criteria	Male	Female
1	Waist circumference	> 102 cm	> 88 cm
2	HDL-c	< 60 mg/dL	< 40 mg/dL
3	Serum triglyceride	≥ 150mg/dL	
4	Blood pressure	≥ 130/85 mmHg	
5	Fasting blood sugar	≥ 110mg/dL	

of the variables were calculated according to gender. Co-evaluation of the variables was also done using MANOVA.

In qualitative analysis of the variables, the prevalence of the abnormalities according to different genders was compared by chi-square test at the significant level of 0.05. In case valid P values were not obtained in chi-square test, Fisher's exact test was used.

4. Results

Mean and standard deviation of the variables according

to gender have been presented in Table 2. Accordingly, most of the variables had significant correlations at the level of 0.05. The results of t-test demonstrated strongly significant differences between the two genders regarding MetS variables (Table 2).

Descriptive data regarding the variables' grand means based on the 95% confidence intervals have been shown in Table 3. The estimated marginal means of the study parameters have been presented in Table 4.

The results of Fisher's test showed a significant difference

Table 2. Pearson's Correlations between the Study Variables

Variable	Test	Age	Waist	FBS	TG	HDL	SBP	DBP	BMI
Age	Pearson correlation	1	0.153 ^a	0.168 ^a	0.034	0.081	0.400 ^a	0.201 ^a	0.072
	P value		0.004	0.002 ^a	0.523	0.128	< 0.001	0.000	0.178
Waist	Pearson correlation		1	0.081	0.190 ^a	-0.005	0.226	0.186 ^a	0.781 ^a
	P value			0.127	< 0.001	0.932	< 0.001	< 0.001	< 0.001
FBS	Pearson correlation			1	0.180 ^a	-0.044	0.241 ^a	0.183 ^a	0.060
	P value				0.001	0.404	< 0.001	0.001	0.258
TG	Pearson correlation				1	-0.394 ^a	0.167 ^a	0.155 ^a	0.129 ^a
	P value					< 0.001	0.002	0.004	0.015
HDL	Pearson correlation					1	-0.041	-0.044	-0.003
	P value						0.440	0.415	0.955
SBP	Pearson correlation						1	0.633 ^a	0.137 ^a
	P value							< 0.001	0.010
DBP	Pearson correlation							1	0.135 ^a
	P value								0.011
BMI	Pearson correlation								1
	P value								

^a Correlation is significant at 0.01 level (2-tailed). Correlation is significant at 0.05 level (2-tailed).

Abbreviations: FBS, fasting blood sugar; TG, triglyceride; HDL, high density lipoprotein; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index

Table 3. Mean, Standard Deviation, and Multivariate Analysis of the Study Variables

Variable	Gender	N	Mean ± SD	T2Hostelling	Multivariate (Significance Level)
Waist	Male	133	94.84 ± 10.98		
	Female	217	98.18 ± 12.15		
TG	Male	133	193.38 ± 87.93		
	Female	217	172.22 ± 82.41		
HDL	Male	133	47.93 ± 8.98		
	Female	217	55.85 ± 10.90	13.55	P < 0.001
SBP	Male	133	126 ± 15.70		
	Female	217	121 ± 18.55		
DBP	Male	133	78.66 ± 11.37		
	Female	217	73.95 ± 11.34		
BMI	Male	133	26.59 ± 3.82		
	Female	217	28.67 ± 5.26		
FBS	Male	133	111.21 ± 30.73		
	Female	217	110.99 ± 34.40	0.003 ⁺	0.960

Abbreviations: FBS, fasting blood sugar; TG, triglyceride; HDL, high density lipoprotein; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; NS, not significant

⁺ Independent sample t-test

Table 4. Estimated Marginal Means (Grand Mean) of the Study Variables

Variables	Mean	95% Confidence Interval	
		Lower bound	Upper bound
Waist circumference	96.52	95.25	97.79
FBS	111.12	107.53	114.71
TG	182.91	173.74	192.09
HDL	51.89	50.79	53.00
SBP	123.87	121.97	125.77
DBP	76.31	75.08	77.54
BMI	27.63	27.12	28.151

Abbreviations: FBS, fasting blood sugar; TG, triglyceride; HDL, high density lipoprotein; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index

between the two genders concerning various stages of HTN. However, no significant difference was seen between males and females concerning FBS in the normal range (Table 5). Nevertheless, Pearson's chi-square test revealed a significant difference between males and females regarding high FBS levels ($P = 0.031$).

The study results revealed a significant difference between males and females with respect to high waist circumference (more than the normal levels). Additionally, the prevalence of this abnormality was 3 folds higher among females compared to males (78.7 vs. 21.8%; $P < 0.001$).

The study findings indicated no significant differences between the two genders with regard to serum TG concentration in normal ranges. However, in the abnormal ranges of serum TG, this difference was clearly significant by Pearson's chi-square test ($P = 0.017$) (Table 5).

The prevalence of various risk factors was not significantly different between the males and females with 1, 2, and 3 risk factors. Also, no significant difference was observed between the male and female participants with 4 risk factors. Although this rate was two times higher in females compared to males (12.4 vs. 6.8%), due to the small sample size, this difference was not statistically significant. The prevalence of MetS was also assessed in both genders with 3 or more risk factors (Table 6).

In this study, SBP was evaluated and the results showed a significant difference between males and females concerning the prevalence of prehypertension ($P = 0.021$) (Table 6).

This study also analyzed the prevalence of various classifications of FBS in both genders. According to the results, the prevalence of pre-diabetes was not different between males and females. Also, the prevalence of diabetes was 8.3% and 10% in males and females, respectively and the difference was not statistically significant (Table 5).

In the stratified analysis of serum TG levels based on different TG levels (borderline high, high, and very high), significant differences were seen between the males and females with high serum TG levels ($P = 0.022$) (Table 6). However, no significant difference was observed between those with very high serum TG levels due to the very small sample size.

Finally, the results of Pearson's chi-square test demonstrated a significant difference between the two genders regarding different levels of BMI (overweight and obesity) ($P = 0.002$) (Table 6). This difference was confirmed by likelihood standardized statistics and linear by linear association.

5. Discussion

MetS and its related risk factors have become worldwide threats due to their links to different chronic diseases (9). Findings of the present study indicated significant correlations between age and waist circumference, FBS, SBP, and DBP. Furthermore, statistically significant relationships were found between waist circumference and TG, SBP, DBP, and BMI. Also, significant correlations were demonstrated between FBS and TG, SBP, DBP. There were high correlations between TG and HDL-c, SBP, DBP, and BMI. Additionally, significant correlations exist between BMI and systolic and diastolic blood pressure.

Positive correlations were found between waist circumference and systolic and diastolic blood pressure. In a study by Yalcin et al. correlations between adiposity and blood pressure was detected (18) which supported our results regarding the correlations between waist circumference and blood pressure. The results of the present study considering the significant correlations between age and MetS risk factors are supported by Arthur et.al study (24). A negative correlation was found

Table 5. The Prevalence of Study Variables According to Different Genders

Variables		Gender		P value
		Male	Female	
High waist circumference	Yes	21.8% (29)	78.8% (171)	0.001
	No	78.2% (104)	21.2% (46)	
High FBS	Yes	67.7% (90)	55.8% (124)	0.031
	No	32.3% (43)	44.2% (96)	
High TG	Yes	62.4% (83)	49.3% (107)	0.017
	No	37.6% (50)	50.7% (110)	
HTN	Yes	45.1% (60)	32.7% (71)	0.015
	No	54.9% (73)	67.3% (146)	

Abbreviations: NS, not significant; FBS, fasting blood sugar; TG, triglyceride; HTN, hypertension

Table 6. Distribution of Metabolic Syndrome Risk Factors between the Two Genders

Risk Factors		Gender		P value
		Male	Female	
Normal	No risk factors	10(7.5%)	17 (7.8%)	0.481
Different risk factors	Yes, 1- Risk factor	34 (25.6%)	46 (21.1%)	
	Yes, 2- Risk factors	45 (33.8%)	68 (31.2%)	
	Yes, 3- Risk factors	35 (26.3%)	60 (27.5%)	
	Yes, 4- Risk factors	9 (6.8%)	27 (12.4%)	
Total risk factors	Yes	45 (33.1%)	87 (39.9%)	0.200
	No	89 (66.9%)	131 (60.1%)	
SBP	Normal	45 (34.6%)	112 (50.9%)	0.021
	Pre-hypertension	64 (49.2%)	76 (34.5%)	
	Stage-1 hypertension	55 (11.5%)	25 (11.4%)	
	Stage-2 hypertension	6 (4.6%)	7 (3.2%)	
FBS	Normal	38 (28.6%)	88 (39.8%)	0.057
	Pre-diabetic	84 (63.2%)	111 (50.2%)	
	Diabetic	11 (8.3%)	22 (10.0%)	
TG	Normal	50 (37.6%)	112 (50.7%)	0.022
	Borderline high	27 (20.3%)	48 (21.7%)	
	High	55 (41.4%)	61 (27.6%)	
	Very high	1 (0.8%)	0 (0.0%)	
BMI	Underweight	2 (1.5%)	4 (1.9%)	0.002
	Normal weight	47 (35.3%)	51 (23.7%)	
	Overweight	59 (44.4%)	79 (36.7%)	
	Obesity	25 (18.8%)	81 (37.7%)	

Abbreviations: SBP, systolic blood pressure; FBS, fasting blood sugar; TG: triglyceride; BMI, body mass index

between serum TG and HDL-cholesterol in the current study and this finding was seen in previous studies as well (23, 25). Biologically, the balance between HDL-c and TG is mediated through an enzyme called cholesterol ester transfer protein (CETP). Additionally, transfer of TG from TG-rich lipoproteins to HDL-c is done using this enzyme in exchange for cholesteryl esters, and that's why a negative correlation between these two variables can be found according to CETP activity (26). HDL-c and TG are considered important risk factors for CVD (27, 28) and these correlations can be important. Moreover, BMI and waist circumference are considered the markers of adiposity. The present study finding according to correlations between blood pressure and body mass index was supported by previous studies related to the fact that BMI and adiposity are strong independent determinants for blood pressure and the effects of central obesity (android obesity) on blood pressure (18). However, in another study, despite an increasing trend in abdominal obesity, decreasing trends were seen in HDL-c levels (29). The results of our study related to negative correlations between HDL-c and abdominal obesity according to body mass index and waist circumference are consistent with what was mentioned in that study (29).

In the present study HDL-c and other variables (including waist circumference, SBP, DBP, TG, BMI, and FBS) were negatively correlated. The results of the current study are supported by a study in adults, regarding a decrease in HDL-c correlated with an increase in abdominal obesity (29).

By multivariate analysis, almost all of the variables were significantly correlated. A higher prevalence of hypertension was seen in male participants and this was significantly different between genders. This result can be partially explained by a higher prevalence of overweight

in males. This finding was supported by another study that men were more likely to develop hypertension in adulthood. Some investigators believe that a higher prevalence of hypertension is reported in females due to their steroidal hormone impacts on blood pressure (19). However, those findings were not supported in the current study.

According to the FBS measurements, more females had diabetes. However, prevalence of pre-diabetes as "impaired fasting glucose" was more among males. Findings of previous studies indicated that changes in weight and adipose tissue can affect insulin resistance and blood sugar in women, as a component of MetS. Therefore, this makes them more susceptible to diabetes (21). Findings of the current study might be partially explained by higher prevalence of obesity and high waist circumference in female participants suffering from diabetes.

In this study significant higher waist circumferences were found among females compared with males. In contrast to the present study results, previous research by Miyatake and his colleagues showed a higher abdominal obesity in males based upon waist circumference (30), which might be due to the differences between the sample size, age, and other related risk factors.

A higher prevalence of hypertriglyceridemia was found among males compared with females, which was statistically different. In another study, lower triglyceride levels in premenopausal women due to the effects of estrogen is in line with the results of the present study in this regard (23).

After analyzing numerous risk factors, more male participants had one or two risk factors in comparison with the females. On the other hand, more women had three or four risk factors in comparison with men, which means that the female participants had a higher prevalence of

MetS (presence of 3 or more risk factors) according to the findings of this study. A higher prevalence of MetS among women compared with men is supported by some other researches (21, 31). Furthermore, in some other studies such as one by Santos et.al, almost the same prevalence in both genders was reported (32). In the current study higher prevalence of MetS in the females can be partially described by the higher prevalence of obesity and higher waist circumference in this group. The results of this study were supported by previous studies that demonstrated the effects of obesity on MetS prevalence (33, 34). In general, findings of this study indicated that there are gender differences in the prevalence of metabolic syndrome and its related risk factors.

The limitations of the current study might be the smaller sample size of the males and lack of sufficient data regarding dietary information from study subjects. In addition, female predominance in the participants compared with males in this study might affect the results interpretation.

Strength of this study is the assessment of MetS and its related risk factors based on different genders in a multicenter study population. Moreover, we evaluated all correlations and multivariate analysis of the MetS risk factors that was done almost for the first time in Shiraz population. Further strength of the study is that the participants mostly come from different ethnic and occupational groups from various areas.

In conclusion, women in this study were found to have higher risk for MetS. Significant correlation between abdominal obesity and MetS is implicated especially in women (While it is noteworthy to state that as a normal physiologic phenomenon, higher waist circumferences are reported in postmenopausal women due to estrogen changes). Early identification and active management of MetS and differentiating this abnormality and its related risk factors between genders and assessing their correlations might be necessary to define better strategies for an appropriate management of MetS. A better understanding of the mechanisms about gender differences in MetS might be important in practical interventions toward prevention and treatment of this syndrome. It is noteworthy to express that the outcome of remedies targeting MetS may depend on age, gender and some risk factors of patients and their correlations.

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Authors' Contribution

Study concept and design: Mohammad Hasan Eftekhari, Zahra Sohrabi, Nader Parsa; Acquisition of data: Zahra Sohrabi; Analysis and interpretation of data: Nader Parsa, Zahra Sohrabi; Drafting of the manuscript: Nader Parsa, Zahra Sohrabi, Mohammad Hasan Eftekhari; Critical revision of the manuscript for important intellectual content: Nader Parsa, Zahra Sohrabi, Mohammad Hasan Eftekhari; Statistical analysis: Nader Parsa, Zahra Sohrabi; Administrative, technical, and material support: Mohammad Javad Zibaei Nezhad, Nader Parsa; Study

supervision: Mohammad Hasan Eftekhari, Zahra Sohrabi, Nader Parsa

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