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Original Article

Gender-dependent relationship between metabolic syndrome and HOMA-IR index in patients with impaired fasting glucose

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Abstract

Aim: This study aimed to assess whether metabolic syndrome (MetS) criteria varied by gender and whether the homeostatic model assessment of insulin resistance (HOMA-IR) index could be used as a new MetS predictor.

Materials and Methods: We performed a standard oral glucose tolerance test (OGTT) in 316 patients with impaired fasting glucose (IFG) and investigated the presence of impaired glucose tolerance (IGT), type 2 diabetes mellitus (T2DM), and MetS.

Results: We found that MetS was higher in females than males. The obesity rate was 57.0% and 36.8% for females and males, respectively. Of the patients who reached stage 3 obesity,13.4% were females and 0.9% were males. The HOMA-IR score was not an independent predictor for MetS. However, sensitivity was 91% and specificity was 100% for the cut-off value of HOMA-IR ≥ 2.38 in diabetic females with MetS. Abdominal obesity (91.2%), hyperglycemia (81.5%), hypertension (71.8%), hypertriglyceridemia (62.0%), and low high-density lipoprotein (HDL) (57.8%) were found in MetS patients.

Conclusion: Abdominal obesity and impaired glucose metabolism are powerful predictors demonstrating the presence of MetS. Females are at greater risk than males for obesity, T2DM, and MetS. Although the HOMA-IR score is not a new MetS predictor, it may be an effective indicator of the combination of MetS and diabetes in females.

Keywords: Diabetes mellitus; HOMA-IR; impaired fasting glucose; impaired glucose tolerance; metabolic syndrome; oral glucose tolerance test

INTRODUCTION

Metabolic syndrome (MetS) is a table containing metabolic disorders such as increased blood pressure, dyslipidemia, impaired fasting glucose (IFG), and central obesity (1-3). As the number of MetS components increases, the risk of type 2 diabetes mellitus (T2DM) also increases (4-6). Moreover, the combination of central obesity and the IFG component has been found to be more likely associated with T2DM risk compared to other MetS components. Hence, central obesity and IFG are powerful predictors for T2DM development (3,7-9).

Hyperinsulinemia and insulin resistance are significant pathological pathways for these metabolic disorders (10-12). Although insulin resistance is important for the development of T2DM and MetS, it is unknown whether the homeostatic model assessment of insulin resistance (HOMA-IR) index is a new criterion or predictor of MetS.

This study investigates the impaired glucose tolerance (IGT), T2DM, and MetS presence by performing an oral glucose tolerance test (OGTT) in patients with IFG. The body mass index (BMI), waist circumference, lipid profile, and the systolic and diastolic blood pressure of patients were compared. The relationships between these components of MetS and the IFG, impaired glucose tolerance (IGT), and T2DM groups were assessed. Moreover, the cut-off point, sensitivity, and specificity ratios of the HOMA-IR index were calculated for MetS. The HOMA-IR index was evaluated as a potential new MetS component or criteria. To the best of our knowledge, there have been no studies conducted on this subject so far. Therefore, our study is the first comparing HOMA-IR index with MetS criteria and examining the relationship between HOMA-IR index and MetS.

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MATERIALS and METHODS

Patient design

This sectional study included 316 patients who applied to the internal medicine outpatient clinic for any reason and displayed IFG after 8 h of fasting. These patients were called the next day, and 75 g OGTT was administered to them.

Demographic information, such as age, gender, waist circumference, and BMI were recorded. Total cholesterol, high-density lipoprotein (HDL), low density lipoprotein (LDL), triglycerides, fasting plasma insulin (FPI), and postprandial plasma insulin (PPI) were measured.

The University of Karabuk, Medicine Faculty Ethics Committee granted approval (77192459-050.99-E.1412, 2/26), and informed consent forms were signed by the patients.

Exclusion criteria included the following: patients under the age of 18; patients over the age of 65; patients who were pregnant; patients with chronic disease (including diabetes); patients taking drugs that could impair glucose metabolism, such as steroids; those who had serious infection, trauma, burn, and operations, which disturbed plasma glucose metabolism in the last 3 months; and alcohol or drug users.

Blood samples

Blood samples from the participants were collected after overnight fasting of at least 8 h using standard phlebotomy procedures. The OGTT was performed by administering 75g of anhydrous glucose, and the plasma glucose concentration was measured again 2 h later. The plasma glucose was measured using the glucose oxidase peroxidative electrode method. Total cholesterol, HDL, LDL, and triglyceride levels were measured using the enzymatic method. FPI and PPI levels were determined by enzyme-linked immuno-sorbent assay kits. The HOMA-IR index was calculated from fasting glucose and insulin levels (13).

Definition of glycemic status

The glycemic status of the participants was defined according to the American Diabetes Association (ADA) recommendations. Normal fasting plasma glucose (FPG) was defined as <100 mg/dL, IFG was defined as 100–125 mg/dL, and IGT as 140–199 mg/dL. Diabetes was defined as an FPG ≥ 126 mg/dL or OGTT (2nd hour) ≥ 200 mg/dL (14).

Assessment of MetS components

The MetS components were identified according to the National Cholesterol Education Program-Adult Treatment Panel (NCEP-ATP) III (15)

The MetS diagnostic criteria of NCEP-ATP III are as follows:

MetS components	Male	Female
*Waist circumference	>102 cm	> 88cm
**Hypertriglyceridemia	≥ 150 mg/dL	≥ 150 mg/dL
**Low HDL	< 40 mg/dL	< 50 mg/dL
**Fasting blood glucose	≥ 100 mg/dL	≥ 100 mg/dL

HDL: High-density lipoprotein cholesterol
* Population and country specific definitions
** To use drugs for this criteria, a diagnosis of MetS includes three or more components from the above list

Statistical analysis

The continuous variables' mean ± standard deviation and categorical data were expressed as numbers and percentages. Normality analyses were performed with the Kolmogorov-Smirnov goodness-of-fit test for the cross-group analysis of continuous variables. One-way ANOVA test (post-hoc: Least Significant Difference) was used in the evaluation of the three groups that fitted the normal distribution of continuous variables. Cross-group comparisons of variables not eligible for normal distribution were performed with the Kruskal-Wallis test (post-hoc: Mann-Whitney U test). Chi-square testwas used in the comparison of categorical data. Receiver operating characteristic (ROC) analysis was also performed. The analyses were performed with the SPSS software program version 24.0 (IBM Corporation, Armonk, NY, USA). Lastly, the statistical significance level was $p<0.05$.

RESULTS

The average age of the participants in the IFG, IGT, and T2DM groups was 48.93±12.86, 54.16±9.34, and 52.95±12.45 years, respectively (p=0.003). In all groups, the females had higher BMI scores. The waist circumference, BMI, and HOMA-IR index of the patients were higher in the IGT and T2DM groups (p<0.001) (Table 1).

Table 1. Comparison of age, gender, and some clinical features between groups

	IFG (n=194)	IGT (n=83)	T2DM (n=39)	p
Age	48.93±12.86*	54.16±9.34*	52.95±12.45	0.003*
Gender (F/M)	120/74	59/24	23/16	0.270**
Waist circumference	98.0 (66-131)***	107.00 (70-141)	107.50 (85-145)	<0.001***
BMI	29.0 (16.6-76.9)***	31.2 (21.8-46.4)	31.2 (19.9-44.5)	<0.001***
HOMA-IR	1.89 (0.52-16.5)***	2.65 (0.92-12.2)	2.96 (0.78-7.56)	<0.001***

* One-way ANOVA test (Bonferroni corrected) ** Chi-square test *** Kruskal-Wallis test (post-hoc: Mann-Whitney U test)IFG: Impaired fasting glucose IGT: Impaired glucose tolerance T2DM: Type 2 diabetes mellitus HOMA-IR: Homeostatic model assessment of insulin resistance

Table 2. Comparison of age, BMI, waist circumference, HOMA-IR index, and other clinical characteristics by gender

Groups	IFG	IGT	T2DM	p
Male	**(Average ± SD) (n=74)**	**(Average ± SD) (n=24)**	**(Average ± SD) (n=16)**	
Age	52.78±11.92	56.38±11.25	51.44±15.33	0.373*
BMI	27.95 (21.80-47.50)	28.50 (24.70-39.50)	29.95 (22.00-36.40)	0.295**
WC	101.00 (83.00-126.00)	**112.50 (96.00-128.00)**	107.50 (92.00-118.00)	**0.002****
HOMA-IR	1.85 (0.56-6.57)	2.25 (0.92-4.94)	**2.87 (0.78-4.63)**	**0.006****
Fasting glucose	111.89±7.18	113.95±5.07	**124.31±18.01**	**<0.001***
OGTT (fasting)	104.93±12.01	**115.83±12.09**	**137.12±17.28**	**<0.001***
OGTT (2nd hour)	99.06±22.34	**170.20±15.93**	**240.00±38.13**	**<0.001***
Insulin (fasting)	7.52±4.22	9.03±3.63	8.95±3.04	0.174*
Insulin (2nd hour)	31.71±22.49	42.16±36.99	34.73±18.12	0.788*
HDL	45.58±11.18	46.25±10.13	44.25±16.22	0.870*
LDL	12.46±40.73	132.12±32.17	132.97±45.58	0.314*
Total cholesterol	216.72±141.70	213.95±37.20	214.43±56.38	0.994*
Triglyceride	182.87±126.93	178.45±88.69	224.12±228.03	0.526*
SBP	121.23±19.18	**139.79±15.91**	**142.14±13.25**	**<0.001***
DBP	71.43±11.79	**83.12±9.41**	**82.50±12.97**	**<0.001***
Female	**(Average ± SD) (n=119)**	**(Average ± SD) (n=59)**	**(Average ± SD) (n=23)**	
Age	46.55±12.89	53.25±8.39	54.00±10.22	<0.003*
BMI	29.50 (16.60-76.90)	33.00 (21.80-46.40)	**34.20 (19.90-44.50)**	**<0.001****
WC	96.00 (66.00-131.00)	**104.00 (70.00-141.00)**	**107.50 (85.00-145.00)**	**<0.001****
HOMA-IR	1.94 (0.52-16.50)	2.76 (0.96-12.20)	**3.06 (2.31-7.56)**	**<0.001****
Fasting glucose	109.40±6.55	**113.74±6.90**	**116.13±6.72**	**<0.001***
OGTT (fasting)	104.16±9.70	**115.69±11.98**	**131.04±17.30**	**<0.001***
OGTT (2nd hour)	102.97±19.37	**163.83±18.12**	**243.56±31.77**	**<0.001***
Insulin (fasting)	9.55±8.83	12.20±6.96	**14.31±6.300**	**0.013***
Insulin (2nd hour)	37.50±23.80	59.25±35.05	**75.22±47.40**	**0.045***
HDL	53.73±12.94	51.80±11.33	50.04±8.99	0.326*
LDL	142.79±146.33	125.73±32.11	141.33±52.37	0.657*
Total cholesterol	207.76±47.70	211.16±37.04	214.52±55.90	0.773*
Triglyceride	129.69±60.94	**167.23±104.63**	**186.08±157.53**	**0.004***
SBP	121.08±15.39	**135.96±18.23**	**150.65±22.42**	**<0.001***
DBP	71.88±11.39	**81.49±12.49**	**88.69±16.73**	**<0.001***

*One-way ANOVA Test (post-hoc: Least Significant Difference)
** Kruskal-Wallis test (post-hoc: Mann-Whitney U test)
IFG: Impaired fasting glucose, IGT: Impaired glucose tolerance, T2DM: Type 2 diabetes mellitus, BMI: Body mass index, WC: Waist circumference, HOMA-IR: Homeostatic model assessment of insulin resistance, OGTT: Oral glucose tolerance test, HDL: High-density lipoprotein cholesterol, LDL: Low-density lipoprotein cholesterol, SBP: Systolic blood pressure, DBP: Diastolic blood pressure

Table 3. Comparison of MetS criteria between groups

		IFG	IGT	T2DM	Total	p
MetS						
No	n	120	21	6	147	
	%	62.8%	25.3%	15.4%	47.0%	
Yes	n	71	62	33	166	**<0.001***
	%	37.2%	**74.7%**	**84.6%**	53.0%	
Total	n	191	83	39	313	
	%	100.0%	100.0%	100.0%	100.0%	

*Chi-square test
MetS: Metabolic syndrome, IFG: Impaired fasting glucose, IGT: Impaired glucose tolerance, T2DM: Type2 diabetes mellitus

The average waist circumference was higher in the IFG and IGT groups in males (p=0.001 and p=0.015, respectively) compared to that in females. In the T2DM group, the average waist circumference was higher in females than that in males (p=0.091). The BMI and HOMA-IR indexes were higher in the IGT and T2DM groups for females compared to that in males (BMI p=0.002 and p=0.015, respectively; HOMA-IR p=0.021 and p<0.001, respectively) (Table2). Obesity was found in 36.8% of the males and 57.0% of the females. Furthermore, stage 3 obesity was found in 13.4% of females, whereas it was 0.9% in males (p<0.001) (Table 2).

In males, HOMA-IR index and fasting blood glucose were significantly higher in the T2DM group than in the IFG group (p<0.05), whereas 0 and 2nd hour blood glucose in the OGTT, systolic blood pressure (SBP), and diastolic blood pressure (DBP) were significantly higher in T2DM and IGT groups than in the IFG group (p<0.001). In females, age, BMI, HOMA-IR index, fasting insulin, and 2nd hour insulin were significantly higher in the T2DM group than in the IFG group (p<0.05). Moreover, waist circumference, fasting glucose, 0 and 2nd hour blood glucose in the OGTT, triglycerides, SBP, and DBP were significantly higher in the T2DM and IGT groups than in the IFG group (p<0.001) (Table 2). The presence of MetS in the IGT and T2DM groups were higher than in the IFG group (74.7%, 84.6%, 91.2%, and 37.2%, respectively) (p<0.001) (Table 3).

In the MetS group, waist circumference, BMI, FPG, fasting and 2nd hour glucose in OGTT, HDL, triglycerides, SBP, and DBP were higher than in the non-MetS group (p<0.001). However, there was no significant difference in terms of HOMA-IR index. Although FPG differed in the MetS group, the FPI in the two groups was similar. For this reason, no significant difference was found between the two groups in terms of the HOMA-IR index (Table 4).

Table 4. Comparison of socio-demographic and clinical findings of participants per the presence of MetS

	MetS (-) (n=145)	MetS (+) (n=167)	p
Age	49.13 ± 12.98*	52.76 ± 10.95*	0.007*
Gender (Female/Male)	94/55	109/59	0.815**
Waist circumference	97.00 (66.00-130.00)***	108.00 (83.00-145.00)***	**<0.001*** **
BMI	28.00 (16.60-76.90)***	31.60 (19.90-47.60)***	**<0.001*** **
HOMA-IR	2.02 (0.56-15.10)***	2.41 (0.52-16.50)***	0.057***
Fasting glucose	109.80 ± 9.59*	116.29 ± 17.16*	**<0.001***
OGTT (fasting)	106.04 ± 13.99*	115.68 ± 15.16*	**<0.001***
OGTT (2nd hour)	114.29 ± 39.84*	155.09 ± 56.70*	**<0.001***
Insulin (fasting)	9.49 ± 7.05	10.15 ± 7.13	0.414*
Insulin (2nd hour)	33.35 ± 23.43*	51.69 ± 34.26*	**0.042***
HDL	54.78 ± 13.02*	46.19 ± 10.37*	<0.001*
LDL	127.78 ± 39.22	137.45 ± 125.19	0.372*
Total cholesterol	214.00 ± 104.47	214.48 ± 55.35	0.665*
Triglyceride	121.66 ± 56.57*	198.01 ± 135.13*	**<0.001***
SBP	119.01 ± 14.86*	136.74 ± 20.18*	**<0.001***
DBP	70.32 ± 10.02*	81.13 ± 13.88*	**<0.001***

*T-test **Chi-square test ***Mann-Whitney U test
MetS: Metabolic syndrome, BMI: Body mass index, HOMA-IR: Homeostatic model assessment of insulin resistance, OGTT: Oral glucose tolerance test, HDL: High-density lipoprotein, LDL: Low density lipoprotein, SBP: Systolic blood pressure, DBP: Diastolic blood pressure

Table 5. AUC values of HOMA-IR index by group and gender

AUC*					
Test Result Variable(s): HOMA-IR					
Group	AUC	Std. Error[b]	p	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
IFG					
Female	0.438	0.057	0.267	0.327	0.549
Male	0.498	0.070	0.972	0.360	0.635
IGT					
Female	0.628	0.085	0.128	0.460	0.795
Male	0.288	0.163	0.188	0.000	0.607
T2DM					
Female	**0.909**	0.061	**0.175**	0.789	1.000
Male	0.236	0.124	0.100	0.000	0.479

*ROC curve analysis test
AUC: Area Under the Curve, IFG: Impaired fasting glucose, IGT: Impaired glucose tolerance, T2DM: Type 2 diabetes mellitus, HOMA-IR: Homeostatic model assessment of insulin resistance

In terms of ROC analysis, the HOMA-IR index had a meaningful area under the curve (AUC) only in female diabetic patients, but this was not statistically significant (Table 5).

In female patients with T2DM, the HOMA-IR cut-off point indicating MetS was ≥ 2.38. The sensitivity was 91.0%, the specificity was 100%, and the area under the ROC curve was expressed as AUC ± standard error (AUC±SE), and it was 0.91±0.061 (p=0.175) (Table 6) (Figure 1).

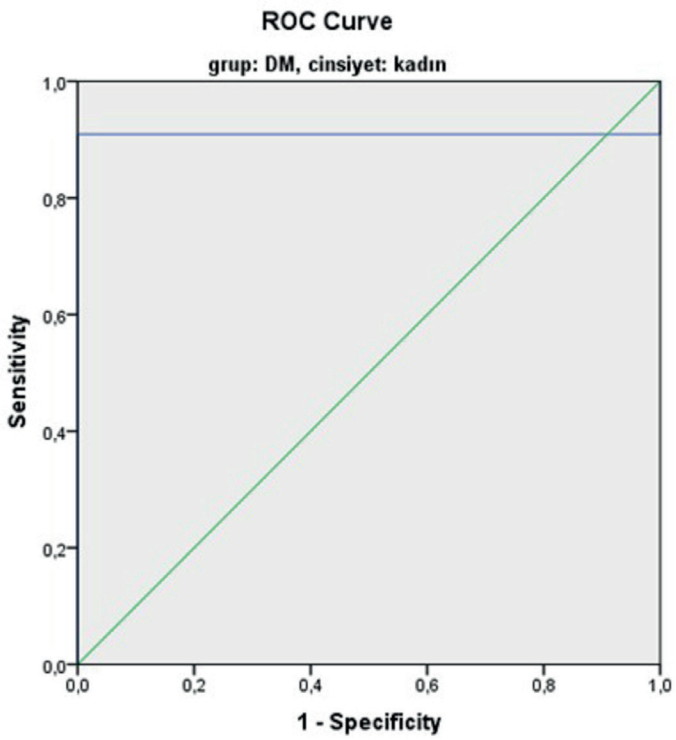

Figure 1. Cut-off value and ROC curve results of HOMA-IR for MetS in females with diabetes

Table 6. AUC and cut-off values of HOMA-IR as an indicator of MetS in diabetic female

	Diagnostic test					ROC curve		
	Cut-off	Sensitivity	Specificity	PPV	NPV	AUC	95% CI	p
HOMA-IR	≥ 2.38	91.00	100.00	87.00	13.00	**0.91**	0.789-1.000	0.175**

*PPV: Positive predictive value, NPV: Negative predictive value, CI: Confidence interval
**Receiver Operating Characteristic (ROC) curve analysis test, AUC: Area Under the Curve, HOMA-IR: Homeostatic model assessment of insulin resistance

DISCUSSION

In this study, we found that the presence of MetS was higher in females. Furthermore, 57.0% of the females and 36.8% of the males were obese. Moreover,13.4% of females reached stage 3 obesity, whereas only 0.9% of males reached this stage. We determined the HOMA-IR score was not an independent predictor for MetS. However, it displayed powerful sensitivity and specificity in diabetic females with MetS.

The combination of central obesity and IFG has been found to be more likely associated with MetS risk than with other components (91.2% and 81.5%, respectively). Whereas waist circumference is a gender-dependent parameter, it is expected to be lower in females. However, the waist circumference of females with T2DM was similar to those of males.

In a previous study, 1,757 non-diabetic participants were followed for 5 years in terms of metabolic parameters. It

was found that there was a synergic relationship between metabolic syndrome components and HOMA-IR. If there are at least three metabolic syndrome components, there may be a significant increase in HOMA-IR. It has been observed that the degree of increase in HOMA-IR was higher, especially in combination with abdominal obesity (16). The International Diabetes Federation declares abdominal obesity as a compulsory criterion of metabolic syndrome (17).

In Turkey, a study was published in 2002 to adjudicate the prevalence of obesity and diabetes. In all, 24,788 volunteers were included (55.3% females) in the study. The prevalence of obesity, diabetes, IGT, and central obesity was found to be 22%, 7.2%, 6.7%, and 34%, respectively. These parameters were significantly and remarkably higher in females than males (18). The first study was followed by a second, which was published in 2013. In this study, 26,499 volunteers were included (63% females) in the study. The average BMI in females was 29.2, and it was 27.4 in males. The prevalence of diabetes, prediabetes, overweight condition, obesity, and central obesity was 16.5%, 30.8%, 37%, 36%, and 54%, respectively (19). According to these two studies, the prevalence of diabetes, IGT, and obesity increased by 90%, 106%, and 40%, respectively.

There were 16,213 participants included in a prevalence study we conducted in 2019. In this study, we found that both diabetes and obesity were higher in females than in males. Moreover, we found that obesity became an increasing health threat in childhood (20). This situation may be explained by children being raised by mothers with unhealthy eating habits.

Females in Muslim societies are generally responsible for housework and childcare. This explains why they spend most of their time inside the house. Therefore, females continue living a partially isolated and sedentary lifestyle. Moreover, in Muslim countries, the hijab is traditionally worn by some Muslim females and Islamic styles of dress in general prevail. The garment has different legal and cultural status in various countries. Females cover themselves, so it is not possible for them to perceive their own body shape. These living conditions may explain the fact that females are at higher risk for obesity, insulin resistance, glucose metabolism disorders, MetS, and diabetes.

In Iran, which is a Muslim country like Turkey, 31,050 adults were included in a recent prevalence study; result revealed that 22.7% of them were obese and that 59.3% were overweight. The obesity rate was 29.8% in females and 15.3% in males (21). In 2019, a prevalence study was conducted in Saudi Arabia. A total of 1,419 individuals (752 females and 667 males) were included in the study, with the overall prevalence of overweight and obesity being 35.1% and 34.8%, respectively, in males, and 30.1% and 35.6%, respectively, in females. Whereas the majority of females under the age of 30 have normal weight, they experience a significant expansion in overweight condition and obesity after 30 (22). This situation can be explained by the fact that Muslim women spend more time at home and live a sedentary isolated life after marriage.

The prevalence of MetS and its components is increasing globally similar to obesity. In a study, MetS components and risk factors as well as their development and changes over time (from 2001 to 2013) in Iranian adults were examined. A total of 6,504 adults were observed for 12 years. There was a significant increase in waist circumference, BMI, SBP, DBP, and fasting blood glucose and a substantial decrease in total cholesterol, triglycerides, and physical activity levels. Moreover, the age, gender, marital status, education levels, and changes in the MetS components in the local area were seen to be significantly related. In this study, although there was a tendency for increases in MetS criteria, there was a decrease in total cholesterol and triglycerides due to the widespread use of lipid-regulating drugs, a more effective hyperlipidemia treatment (23). Similarly, in the current study, there was no significant difference between the groups in terms of lipid profile.

MetS, obesity, and T2DM are health problems that have been evaluated as the diseases of our age, and they affect large segments of society and cause serious morbidity and mortality globally. In particular, females appear to be at greater risk from these conditions. As the number of MetS criteria increases, the prevalance of obesity and T2DM also increases. Insulin resistance is a crucial factor in the etiopathogenesis of these diseases. Therefore, HOMA index can also be a useful identifier indicating the associations between MetS, obesity, and T2DM.

LIMITATIONS

In this study, 202 of 316 patients were female, and only 23 had T2DM. Therefore, having a small group of female diabetic patients was a limiting factor of this study. The HOMAIR score had high sensitivity and specificity for females with MetS and diabetes, but there is a need for studies with larger samples to verify this relationship.

CONCLUSION

The components of abdominal obesity and impaired glucose metabolism are powerful predictors that indicate the presence of MetS. Females are at a greater risk for obesity, T2DM, and MetS than males. Although the HOMA-IR index is not a new MetS predictor, it may be a good indicator of the combined presence of MetS and diabetes in females.

Conflict of interest : The authors declare that they have no competing interest.

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REFERENCES

1. Alberti K, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the international diabetes federation task force on epidemiology and prevention; national heart, lung, and blood institute; American heart association; world heart federation; international atherosclerosis society; and international association for the study of obesity. Circulation 2009;120:1640-5.
2. National CEPN. 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) final report. Circulation 2002;106:3143.
3. Kurotani K, Miyamoto T, Kochi T, et al. Metabolic syndrome components and diabetes incidence according to the presence or absence of impaired fasting glucose: The Japan Epidemiology Collaboration on Occupational Health Study. J Epidemiol 2017;27:408-12.
4. Nakanishi N, Takatorige T, Fukuda H, et al. Components of the metabolic syndrome as predictors of cardiovascular disease and type 2 diabetes in middle-aged Japanese men. Diabetes Res Clin Pract 2004;64:59-70.
5. Sattar N, Gaw A, Scherbakova O et al. 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;108:414-9.
6. Wilson PW, D'Agostino RB, Parise H et al. Metabolic syndrome as a precursor of cardiovascular disease and type 2 diabetes mellitus. Circulation 2005;112:3066-72.
7. Wannamethee SG, Shaper AG, Lennon L, et al. Metabolic syndrome vs Framingham Risk Score for prediction of coronary heart disease, stroke, and type 2 diabetes mellitus. Arch Intern Med 2005;165:2644-50.
8. Heianza Y, Arase Y, Fujihara K, et al. Screening for pre-diabetes to predict future diabetes using various cut-off points for HbA1c and impaired fasting glucose: the Toranomon Hospital Health Management Center Study 4 (TOPICS 4). Diabet Med 2012;29:279-85.
9. Levitzky YS, Pencina MJ, D'Agostino RB, et al. Impact of impaired fasting glucose on cardiovascular disease: the Framingham Heart Study. J Am Coll Cardiol 2008;51:264-70.
10. Reaven GM. Role of insulin resistance in human disease. Diabetes 1988;37:1595-607.
11. Smiley T, Oh P, Shane LG. The relationship of insulin resistance measured by reliable indexes to coronary artery disease risk factors and outcomes--a systematic review. Can J Cardiol 2001;17:797-805.
12. von Bibra H, Saha S, Hapfelmeier A, et al. Impact of the triglyceride/high-density lipoprotein cholesterol ratio and the hypertriglyceremic-waist phenotype to predict the metabolic syndrome and insulin resistance. Horm Metab Res 2017;49:542-9.
13. Wallace TM, Levy JC, Matthews DR. Use and abuse of HOMA modeling. Diabetes Care 2004;27:1487-95.
14. Association AD. Standards of medical care in diabetes—2013. Diabetes Care 2013;36:11-66.
15. Expert Panel on Detection E. 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). JAMA. 2001;285:2486.
16. Bonora BM, Marescotti M, Marcuzzo G, et al. Synergistic interactions among metabolic syndrome components and homeostasis model assessment of insulin resistance in a middle-aged general population over time. Metab Syndr Relat Disord 2015;13:171-8.
17. Alberti KGM, Zimmet P, Shaw J. The metabolic syndrome—a new worldwide definition. Lancet 2005;366:1059-62.
18. Satman I, Yilmaz T, Sengul, A et al. Population-based study of diabetes and risk characteristics in Turkey: results of the turkish diabetes epidemiology study (TURDEP). Diabetes Care 2002;25:1551-6.
19. Satman I, Omer B, Tutuncu Y, et al. Twelve-year trends in the prevalence and risk factors of diabetes and prediabetes in Turkish adults. Eur J Epidemiol 2013;28:169-80.
20. Sevencan NÖ, Özkan AE. 3-Year Obesity and Diabetes Prevalence of a University Hospital: Retrospective Analysis of Adult and Childhood Data. Türk Diyab Obez 2019;3:31-6.
21. Djalalinia S, Moghaddam SS, Sheidaei A, et al. Patterns of Obesity and Overweight in the Iranian Population: Findings of STEPs 2016. Front Endocrinol (Lausanne) 2020;11.
22. Al-Raddadi R, Bahijri SM, Jambi HA, et al. The prevalence of obesity and overweight, associated demographic and lifestyle factors, and health status in the adult population of Jeddah, Saudi Arabia. Ther Adv Chronic Dis. 2019;10:2040622319878997.
23. Khosravi-Boroujeni H, Sarrafzadegan N, Sadeghi M, et al. Determinants of Changes in Metabolic Syndrome Components in a 12-Year Cohort of Iranian Adults. Metab Syndr Relat Disord 2019;17:120-7.