Does the Prevalence of Metabolic Syndrome in Pre- and Post-Menopausal Women Differ by the ATP III and IDF Criteria?

Pre- ve Post-Menopozal Kadınlar Arasında Metabolik Sendrom Prevalansı ATP III ve IDF Kriterlerine Göre Değişmekte midir?

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ABSTRACT Objective: The aims of this study were the estimation and comparison of cardiovascular risk factors and the prevalence of metabolic syndrome (MetS) among pre-menopausal (pre-M) and post-menopausal (post-M) women. **Material and Methods:** This study was conducted on 664 (pre-M: 378, post-M: 286) women, aged between 30-64 years. Body weight and waist circumferences (WC) were measured in all participants. Additionally, body mass index (BMI) and waist/hip ratio (WHR) were calculated, and lipid profiles were determined. **Results:** The mean ages of pre-M women and post-M women were found as 42.1 ± 4.50 and 56.2 ± 4.19 years, respectively (p< 0.001). Mean WC (p< 0.001), WHR (p< 0.001), systolic arterial pressure (SAP) (p< 0.001), and diastolic arterial pressure (DAP) (p< 0.001) levels were significantly higher in post-M women as compared to pre-M women. The mean fasting plasma glucose (FPG) (p= 0.005), low-density lipoprotein cholesterol (LDL-C) (p= 0.017), triglycerides (TG) (p= 0.017), and total cholesterol/high density lipoprotein cholesterol (TC/HDL-C) (p= 0.043) levels were significantly lower in pre-M women. However, TC level was significantly higher in post-M women (p< 0.001). We found a significant increase in the prevalence of the MetS among the post-menopausal women depending upon the International Diabetes Federation (IDF) and The National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria. **Conclusion:** Menopause is an important risk factor for metabolic syndrome. MetS was more prevalent among postmenopausal women compared to the premenopausal women depending upon both criteria.

Key Words: Metabolic syndrome X; osteoporosis, postmenopausal

ÖZET Amaç: Bu çalışma, pre-menopozal (pre-M) ve post-menopozal (post-M) kadınların kardiyovasküler risk faktörleri ve metabolik sendrom (MetS) sıklığı yönünden incelenmesi ve karşılaştırılması amacıyla planlanmıştır. **Gereç ve Yöntemler:** Bu çalışma yaşları 30-64 yaş arası değişen 664 (pre-M: 378, post-M: 286) kadın olguda gerçekleştirildi. Vücut ağırlığı ve bel çevresi (BÇ) bütün olgularda ölçüldü. Ayrıca beden kitle indeksi (BKİ) ve bel-kalça oranı (BKO) hesaplandı ve lipid profilleri belirlendi. **Bulgular:** Pre-M ve post-M kadın olguların ortalama yaşları sırasıyla, 42.1 ± 4.50 ve 56.2 ± 4.19 olarak belirlendi (p< 0.001). Ortalama BÇ (p<0.001), BKO (p< 0.001), sistolik kan basıncı (SKB) (p< 0.001), ve diyastolik kan basıncı (DKB) (p< 0.001) seviyeleri post-M kadınlarda pre-M kadınlara göre anlamlı düzeyde daha yüksekti. Ortalama açlık plazma glukozu (APG) (p= 0.005), düşük dansiteli lipoprotein kolesterol (LDL-C) (p= 0.017), trigliseridler (TG) (p= 0.017) ve total kolesterol/yüksek dansiteli lipoprotein kolesterol (TC/HDL-C) (p= 0.043) seviyeleri pre-M kadınlarda anlamlı derecede daha düşüktü. Bununla birlikte, TC seviyesi post-M kadınlarda anlamlı düzeyde daha yüksekti (p< 0.001). Post-menopozal kadınlar arasında Uluslararası Diyabet Federasyonu (IDF) ve Ulusal Kolesterol Eğitim Programı Erişkin Tedavi Paneli III (NCEP ATP III) kriterlerine göre değişken olarak anlamlı dercede bir artış gözlendi. **Sonuç:** Menopoz metabolik sendromda önemli bir risk faktörüdür. Metabolik sendrom postmenopozal kadınlarda premenopozal kadınlara kıyasla belirtilen iki kritere göre değişmek üzere daha sık gözlenmektedir.

Anahtar Kelimeler: Metabolik sendrom X; Osteoporoz, menopoz sonrası

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Metabolic syndrome (MetS) is a constellation of interrelated risk factors including hypertension, dyslipidemia [low levels of high-density lipoprotein cholesterol (HDL-C) and elevated triglycerides (TG) levels], obesity, insulin resistance and elevated blood glucose levels that increase the risk for cardiovascular disease and type 2 diabetes mellitus.[1]

World Health Organization (WHO) was the first to propose criteria for diagnosis of the metabolic syndrome,[2] followed by the European Group for the Study of Insulin Resistance (EGIR),[3] National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III),[4] American College of Endocrinology (ACE),[5] and International Diabetes Federation (IDF).[6] Although these organizations proposed to measure the same components, they suggested different combinations and different cut-off points. In WHO and EGIR definitions, the presence of insulin resistance was the starting point. In IDF definition, central obesity was the prerequisite of the metabolic syndrome. NCEP Adult Treatment Panel III has assigned the metabolic syndrome as a secondary target for intervention.[7]

Cardiovascular disease (CVD), and in particular coronary arterial heart disease (CAHD), is the leading cause of morbidity and mortality in women. The most effective means of decreasing the impact of CVD on women's health is by an active approach from childhood to proper principles of healthcare in order to modify the contribution of specific risk factors. The latter include obesity, abnormal plasma lipid profile, hypertension, diabetes mellitus, cigarette smoking, sedentary lifestyle, increased blood viscosity, augmented platelet aggregability, stress and autonomic imbalance.[8] The prevalence in postmenopausal women is reported to be higher than in premenopausal women.[9] Thus, postmenopausal status seems to play an important role in the prevalence of the metabolic syndrome. However, because it is difficult to separate the effects of natural aging from those of menopause, there are only a few studies on the effects of postmenopausal status on the metabolic syndrome, and, in particular, taking years since menopause into account. By analyzing the components of the MetS in pre- and postmenopausal women, higher concentrations of lipids, lipoproteins (except for HDL-C), blood, glucose and higher arterial blood pressure were observed among post-menopausal women.[10]

The objectives of this study were to estimate and comparise cardio-metabolic risk factors and the prevalence of MetS among pre- and post-menopausal women.

MATERIAL AND METHODS

This study was conducted on 664 [378 pre-menopausal (pre-M), 286 post-menopausal (post-M)] women, aged between 30-64 years, during 2007-2010. Subjects were randomly selected from the general population of Ankara, Turkey. The women were questioned on how long it had been since their last menstrual cycle. Menopause was defined as the absence of menses for 12 consecutive months. The participants were informed about the subject, purpose and rules of the research. Each participant signed a voluntary participation form and filled the questionnaires adhered to the Declaration of Helsinki (World Medical Association).

The individuals who did not voluntarily agreed to participate were not taken into the study as well as individuals who had chronic diseases (diabetes, cardiovascular diseases, hypertension, etc.).

ANTHROPOMETRIC MEASUREMENTS AND BLOOD CHEMISTRY

a) All measurements were taken by a trained dietician. During the measurement process, participants wore light clothes and were with bare feet. A portable scale was used to measure body weight to the nearest half-kilogram. Height was measured to the nearest 0.1 cm with a wall-mounted stadiometer. Waist circumference (WC) was measured above the iliac crest and below the lowest rib margin, at minimum respiration.[11] The waist and hip circumferences were measured with a flexible tape,

b) Measurement of blood pressure (BP), (SBP: Systolic blood pressure, DBP: Diastolic blood pressure) (BP, measured after 10 min resting at sitting

position, was expressed as the average of three consecutive measurements taken from each arm),

c) Measurement of fasting plasma glucose (FPG), (subjects not receiving insulin and/or oral hypoglycemic agents) and

d) Measurement of fasting plasma lipids concentrations of triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), total cholesterol (TC), and calculated low-density lipoprotein cholesterol (LDL-C). Early-morning venous blood samples were obtained from each participant for biochemical screening tests, following a twelve-hour overnight fasting. Professional staff performed venipuncture by using vacutainers to obtain 15 ml of whole blood. Blood was centrifuged for plasma separation at the government hospitals where the actual biochemical analyses were performed. The LDL-C was calculated by Friedewald and colleagues' formula; LDL-C= TC-(HDL-C + (TG/5).[12]

DEFINITION OF THE METABOLIC SYNDROME

MetS was defined analogous with the National Cholesterol Education Program: Adult Treatment Panel III criteria.[4] This definition requires the presence of at least three or more of the five components of the following categorically defined risk factors below:

- Abdominal obesity; waist circumference greater than 88 cm
- High triglycerides (150 mg/dL or greater),
- Low HDL cholesterol (less than 50 mg/dL in women),
- Hypertension (130/85 mmHg or greater),
- Hyperglycemia (110 mg/dL or greater).

The IDF definition[6] requires central obesity as a mandatory component for diagnosis of MetS. Using the IDF criteria requires abdominal obesity + any two of the other four components below:

- Abdominal obesity; waist circumference greater than 80 cm in women,
- High triglycerides (150 mg/dL or greater),
- Low HDL cholesterol (less than 50 mg/dL in women),
- Hypertension (130/85 mmHg or greater),
- Hyperglycemia (100 mg/dL or greater).

DATA ANALYSIS

The data analysis was carried out using SPSS version 13.0 software (SPSS Inc., Chicago, IL, USA). The results were expressed as mean + standard deviation (SD) or as percentages. Tables and figures were drawn, and analysis was done using independent sample t test, and the Chi square test, where found appropriate. A significance level of 0.05 was used in all statistical analyses done in this study.

RESULTS

The mean ages of 378 pre-M women and 268 post-M women were found as 42.1 ± 4.50 and 56.2 ± 4.19 years, respectively ($p< 0.001$). The body mass index (BMI) and WC of the individuals are shown in Table 1. According to BMI classification, 31.5% of the pre-menopausal women and 27.3% of the post-menopausal women were in "normal weight" category. The obesity prevalence and the WC measurements were higher in post-menopausal women (35.3%, 70.3%, respectively).

Table 2 shows age adjusted mean ± SD for BMI, WC, waist/hip ratio (WHR), systolic (SAP) and diastolic arterial blood pressure (DAP). Mean WC ($p< 0.001$), WHR ($p< 0.001$), SAP ($p< 0.001$), and DAP ($p< 0.001$) were significantly higher in post-M women as compared to pre-M women. Sur-

TABLE 1: BMI and WC classifications of the study group.

	Pre-menopausal %	Post-menopausal %	p
BMI (kg/m^2)			0.105
Underweight	5.0 (19/378)	4.5 (13/286)	
Normal	31.5 (119/378)	27.3 (78/286)	
Overweight	34.4 (130/378)	32.9 (94/286)	
Obese	29.1 (110/378)	35.3 (100/286)	
WC (cm)			<0.001
<80 cm	30.2 (114/378)	16.4 (47/286)	
80-88 cm	18.0 (68/378)	13.3 (38/286)	
>88 cm	51.9 (196/378)	70.3 (201/286)	

BMI: Body mass index, WC: Waist circumference.

TABLE 2: Clinical characteristics of the study group.

	Pre-menopausal (n= 378)	Post-menopausal (n= 286)	p
	mean ± SD	mean ± SD	
Age (years)	42.1 ± 4.50	56.2 ± 4.19	<0.001
Weight (kg)	70.9 ± 15.5	70.0 ± 16.45	0.378
BMI (kg/m2)	27.3 ± 5.58	28.0 ± 6.27	0.116
WC (cm)	88.2 ± 14.60	93.3 ± 13.77	<0.001
Waist/hip	0.73 ± 0.10	0.87 ± 0.11	<0.001
SAP (mm Hg)	124.8 ± 19.17	136.1 ± 20.71	<0.001
DAP (mm Hg)	79.7 ± 11.17	94.4 ± 10.95	<0.001

BMI: Body mass index, WC: Waist circumference, SAP: Systolic arterial pressure, DAP: Diastolic arterial pressure. Values are expressed as mean ± standard deviation.

prisingly, there were no significant differences as regards to BMI and weight among the groups. They are two very important parameters in MetS; because of the physiopathology of the disease and because the weight is a fundamental parameter to make the diagnosis, depending on the criterion being used.

The biochemical characteristics of the groups were shown in Table 3. The mean FPG (p= 0.005), LDL-C, (p= 0.017), TG (p= 0.017), and TC/HDL-C (p= 0.043) levels were significantly lower in pre- M women. However, TC was significantly higher in post-M women (p< 0.001). No significant difference was appreciated as regards to the HDL-C level (p= 0.062).

Table 4 shows the prevalence of metabolic syndrome according to the IDF and ATPIII Index. The prevalence of MetS was higher in the IDF criteria as compared to ATPIII in both pre-M and post-M women (34.4% and 54.5%, respectively). Additionally, a significant increase was presented in the prevalence of MetS among the post-menopausal group concerning both criteria. This increase was independent of the criterion used.

Abdominal obesity and low HDL-C were the criteria of MetS with the highest prevalence in both groups (Figure 1 and 2). According to the IDF criteria, the ratio of participants with high FPG levels (post-M: 41.3%, pre-M: 25.9%) and WC (post-M: 83.6%, pre-M: 69.8%) measurements were higher than the participants concerning the ATPIII criteria [(post-M: 25.2%, pre-M: 17.7%) and (post-M: 70.3%, pre-M: 51.9%), respectively (p< 0.001)].

DISCUSSION

Obesity is very common in postmenopausal women. Studies have shown that about 50% of postmenopausal women are obese.[10] The increase in body fat (BF) in postmenopausal women, especially the increase in abdominal adipose tissue, results in the increasing risk of cardiovascular diseases (CVDs). In the present study, both of the study groups were accepted as "overweight" (BMI: 27.3 ± 5.58 and, 28.0 ± 6.27 kg/m^2, in pre-M and post-M women, respectively). Mean WC and WHR ratios were significantly higher in post-M women as compared to pre-M women (p< 0.001). In addition, obesity prevalence and the WC measurements were higher in post-menopausal women. There were no significant differences for BMI or weight between the groups.

The main risk factors of CVD may be classified into no modifiable and modifiable ones. The

TABLE 3: Biochemical characteristics of the study group.

	Pre-menopausal (n= 378)	Post-menopausal (n= 286)	
	mean ± SD	mean ± SD	p
FPG (mg/dL)	100.0 ± 37.3	109.0 ± 44.84	0.005
TC (mg/dL)	200.1 ± 42.80	216.4 ± 42.82	<0.001
LDL-C (mg/dL)	124.2 ± 39.94	132.0 ± 43.94	0.017
HDL-C (mg/dL)	44.5 ± 10.00	46.1 ± 12.43	0.062
TG (mg/dL)	157.0 ± 71.75	172.5 ± 95.43	0.017
TG/HDL-C	3.8 ± 2.27	4.1 ± 3.31	0.098
TC/HDL-C	4.7 ± 1.64	4.9 ± 1.6	0.043

FPG: Fasting Plasma Glucose, TC: Total cholesterol, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, TG: Triglycerides. Values are expressed as mean ± standard deviation.

TABLE 4: The prevalence of pre-menopausal and post-menopausal women with metabolic syndrome diagnosis according to each criterion.

	Pre-menopausal %	Post-menopausal %	p
IDF	34.4 (130/378)	54.5 (156/286)	<0.001
ATP III	30.2 (114/378)	47.6 (136/286)	<0.001

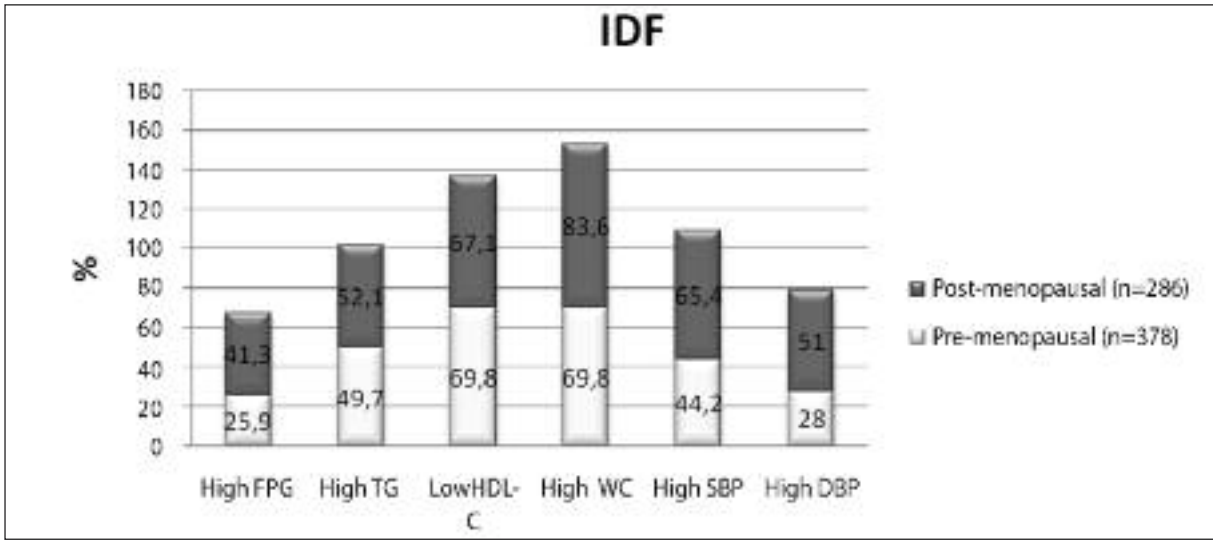

FIGURE 1: The prevalence of the various components of metabolic syndrome and contribution per gender to IDF criteria.
FPG: Fasting Plasma Glucose, TG: Triglycerides, HDL-C: High-density lipoprotein cholesterol, WC: Waist circumference, SBP: Systolic blood pressure, DBP: Diastolic blood pressure.

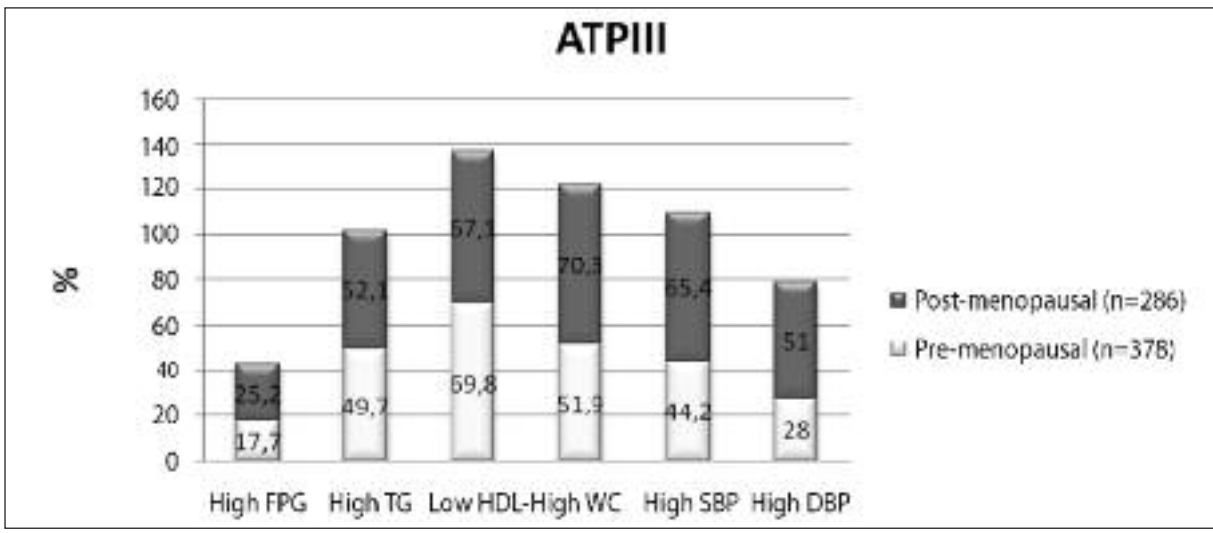

FIGURE 2: The prevalence of the various components of metabolic syndrome and contribution per gender to ATPIII criteria.
FPG: Fasting Plasma Glucose, TG: Triglycerides, HDL-C: High-density lipoprotein cholesterol, WC: Waist circumference, SBP: Systolic blood pressure, DBP: Diastolic blood pressure.

first ones are as follows: age, gender and CVD genetics. The latter ones include hypertension (HT), dyslipidaemia, obesity, intolerance to glucose, tobacco usage, sedentarism and diabetes mellitus (DM). It is interesting to note that the first four modifiable risk factors are components of the MetS. MetS is a complex interrelation of the risk factors of CVD and DM which include hyperglycaemia, hypertension, central obesity, increase of TG levels and diminution of HDL-C levels.[11,12] Among women, the development of CVD shows an increase after 45-54 years of age (menopause age), appearing 10 years later than men.[13] The results of this study demonstrated that postmenopausal women presented, in a significant way, higher levels of arterial pressure, glycaemia, total cholesterol, LDL-C, TG and TC/HDL-C relation in comparison with premenopausal women. In addition to this, they presented a higher prevalence of MetS.

The impact of hypertension as a CVD risk is stronger than it is in men.[9,14] More than one- third of the postmenopausal women in developed countries are at moderate to high risk as judged by elevated blood pressure and the prevalence of hypertension increases with age.[15] There are different mechanisms attributable to hypertension in menopausal women, including but not limited to the activation of the renin-angiotensin-aldosterone system (RAAS), of the sympathetic nervous system (SNS) and the synthesis of endothelins. The increase of the endothelin, which is inhibited by the oestrogens, constitutes a third factor implicated in the genesis of hypertension in menopause. To conclude, the hypoestrogenaemia of menopause would play a direct and indirect role in the biochemical and mechanic changes that contribute to the development of hypertension.[16,17] In the present study, arterial blood pressure was significantly higher in post-M women ($p< 0.001$).

A number of observations suggest that estrogen deficiency after menopause is a risk factor for CVD: the age- adjusted risk of CVD in women with premature menopause is higher than it is in premenopausal women. Estrogens also increase plasma lipids and triglycerides. The intrahepatic lipid-related mechanisms of estrogen actions involve enhanced catabolism and clearance of LDL-C by increasing the number of LDL receptors in hepatocytes; decreasing hepatic HDL receptors and attenuation of HDL catabolism. The decrease in endogenous estrogen as a result of menopause may independently affect lipoprotein concentration, but may not alter the effect on plasma lipids of some common genetic polymorphisms that regulate lipoprotein metabolism.[18,19]

Olszanecka et al. have found that post-menopausal women do not differ from premenopausal ones in respect to mean arterial pressure (normotensive 85.2 ± 5.6 vs 84.4 ± 4.9 mm Hg; hypertensive 99.5 ± 5.9 vs 98.8 ± 5.3 mm Hg).[20] Menopause had no effects on glucose metabolism. Total cholesterol and LDL-C levels were significantly higher in postmenopausal women. Similar to what we have found in our study, the plasma lipid levels of post-M women were significantly higher compared to pre-M women ($p < 0.05$).

In our study, waist circumference seemed to be the most important factor in the pathogenesis of hypertension in middle-aged women. In addition, the effects of age should be taken into account in postmenopausal women. The effects of age were found to be insignificant in a prospective study on a British cohort of women, which investigated the relationship between menopause stage and CV risk factors.[21]

According to the NCEP ATPIII criteria, the prevalence of metabolic syndrome among postmenopausal women (47.6%) was higher than in premenopausal women (30.2%) in our study. This finding is consistent with a multicenter study on 3.965 climacteric women in Latin America, which found MetS in the 42.9% of postmenopausal women and in 28.1% of premenopausal women.[22] Deibert et al.[23] found the prevalence of MetS as 36.1% among postmenopausal women and as 22.7% among premenopausal women. In our study, there was also a higher prevalence of MetS among postmenopausal women (54.5%) compared to premenopausal women (34.4%) concerning the IDF criteria. Figueiredo et al. has found the prevalence of metabolic syndrome among postmenopausal women (44.4%) higher than the pre-menopausal women (24%) with regard to the NCEP ATPIII criteria.[24] Therefore, our results allow us to conclude that, in the study population, the increase in the prevalence of metabolic syndrome among postmenopausal women was caused mainly by the increase of age in postmenopausal women (61.5%) compared to premenopausal women (37%) concerning the IDF criteria. Among menopausal Chinese women, Ding et al.[25] found the prevalence of MetS as 37.3% (with regard to IDF). Socio-cultural influences, eating habits, sedentary lifestyle and different levels of urbanization among the populations also change the prevalence of MetS, which may explain this difference.

Dhanaraj et al. found that the higher percentage of MetS was observed in the modified NCEP-ATP III criteria.[26] In comparison to men, presence

of MetS was higher in women with regard to the modified WHO, NCEP-ATP III, modified NCEP-ATP III, and IDF criteria. The predictive ability to diagnose MetS was the highest with modified the NCEP-ATP III and the lowest with the IDF criteria.

The overall prevalence of MetS was 24% according to the NCEP-ATP III criteria and 33% according to the IDF criteria. When IDF criteria is used, 37% of participants older than 51 years have MetS, although this value is 28% when NCEP-ATP III criteria is used. Obese women have an increased probability of MetS when adjusted for age, education level, menopause status, and/or alcohol use (IDF criteria: estimated odds ratio [OR], 2.68; 95% CI, 1.44-4.97; NCEP-ATP III criteria: estimated OR, 3.42; 95% CI, 1.71-6.84).[27] Previous studies carried out in healthy populations showed a higher prevalence of MetS by the criterion when compared with the NCEP-ATP III criterion.[28]

MetS summarizes the existence of a series of diseases, which altogether, increase the vascular risk more than the addition of its individual risks. Patients with MetS present two times greater risk of CVD and five times greater risk of diabetes type 2 for the next 5-10 years in comparison with people without MetS.[29] Evaluation of endothelial dysfunction in metabolic syndrome patients can provide important data for potential cardiovascular events in the future.[30]

Finally, independently from the diagnosis criterion used, the importance of early detection of MetS in post-menopausal women should be noted in order to modify the life style and prevent a greater risk of CVD and DM.

CONCLUSION

MetS was more prevalent among postmenopausal women than among premenopausal women concerning both of the criteria. Menopause is an important risk factor for metabolic syndrome. The effects of menopause on serum lipids may modulate CVD risk profile in postmenopausal females.

LIMITATIONS

The nature of a pilot study imposes numerous limitations, first of which is the small sample size and limited geographic region from which the participants were recruited. Therefore, we are looking forward to repeat of this study with a larger sample size in a more diverse geographic region.

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