Original Article

Metabolic Syndrome and Menopause: Cross-Sectional Study in Gynecology Clinic

José Albuquerque de Figueiredo Neto, Eduardo Durans Figuerêdo, José Bonifácio Barbosa, Fabrício de Flores Barbosa, Geny Rose Cardoso Costa, Vinícius José da Silva Nina, Rachel Vilela de Abreu Haickel Nina

Universidade Federal do Maranhão, Hospital Tarquínio Lopes Filho, São Luiz, MA - Brazil

Abstract

Background: In Brazil, there are few studies of the metabolic syndrome in the general population, and even fewer studies that establish a correlation between metabolic syndrome and climacteric.

Objective: To determine the prevalence of metabolic syndrome and its components among climacteric women.

Methods: Cross-sectional study with 323 climacteric women, divided into two groups: pre and post-menopausal. They were examined for the presence of metabolic syndrome, according to the criteria of National Cholesterol Education Program's (NCEP) and International Diabetes Federation (IDF). It was possible to notice the association between the variables under study and the metabolic syndrome by conducting a univariate analysis and a multivariate analysis. A p-value<0.05 was considered statistically significant.

Results: The prevalence of metabolic syndrome during the climacteric was 34.7% (NCEP) and 49.8% (IDF). The most frequent components of the metabolic syndrome were low HDL-cholesterol, hypertension, abdominal obesity, hypertriglyceridemia and diabetes in both criteria. The multivariate analysis showed that age was the most important risk factor for the development of metabolic syndrome (p<0.001), which was present in 44.4% (NCEP) and 61.5% (IDF) of postmenopausal women compared to 24% (NCEP) and 37% (IDF) of premenopausal women.

Conclusion: The prevalence of metabolic syndrome was higher in postmenopausal women than in premenopausal women. The main risk factor for the increase in this prevalence was age. Menopause, when it is analyzed alone, did not constitute a risk factor for metabolic syndrome. (Arq Bras Cardiol 2010; 95(3): 339-345)

Key words: Metabolic syndrome; menopause; prevalence; cardiovascular diseases.

Introduction

The epidemiology, case history and prognosis of cardiovascular diseases are different in men and women. Typically, women develop this type of disease ten years after men[1]. Among women aged 50 to 64, there is a considerable increase in cardiovascular risk[2]. This change in the cardiovascular risk profile coincides with the climacteric and it is characterized by the emergence or worsening of some risk factors: central obesity, systemic hypertension (SH) and dyslipidaemia. This set of factors, along with hyperglycemia or insulin resistance, comprises the concept of the metabolic syndrome (MS)[3,4].

The question about the role of menopause as a risk factor for MS was raised before the establishment of the syndrome concept as it is known today. Since the 70s, studies have shown a causal relationship between menopause and the risk factors that compose the metabolic syndrome, while others attribute the increase in risk only to the aging process[5-7].

Latin American studies with menopausal women have shown that age, sedentary lifestyle, time of menopause, obesity and hypertension increase the risk of developing MS[8,9].

The risk of coronary artery disease (CAD) attributed to MS seems to be particularly high among females, and it is estimated that half of all cardiovascular events in women is related to MS[10]. The relationship between menopause and MS is controversial. However, regardless of whether or not menopause is an independent risk factor for MS, any increase in prevalence will lead to undesirable results, including an increase in cardiovascular diseases[11].

In Brazil, especially in the north and northeast, studies on MS in the general population are scarce. Rarer still are those that associate MS with the climacteric. This lack of data, plus the importance of MS as a cardiovascular risk factor, encouraged us to conduct this study, which was intended to determine the prevalence of MS and its components in premenopausal and postmenopausal climacteric women, as well as the association between the menopausal status and MS.

Methods

Study design

Analytical and cross-sectional study conducted from February to September 2008 in the gynecology clinic of a tertiary public hospital, with the recruitment of 355 patients, 32 of whom refused to participate in the research.

Population

Climacteric women (aged 40 to 65) with symptoms, with an intact uterus and no hormonal therapy. They were divided into two groups: postmenopausal women and premenopausal women.

The sample size calculation, considering the MS prevalence of 30%, confidence interval of 5%, absolute accuracy of 3%, was of 323 patients.

Definitions

Climacteric - Period of the woman's life between the end of the reproductive phase and the onset of senescence (40-65 years)[12].

Symptomatic climacteric - It is characterized by: vasomotor instability, irregular menstrual bleeding, psychological symptoms and genitourinary atrophy[13].

Menopause - Last spontaneous menstruation[12].

Premenopause - Period during which climacteric women still have menstrual cycles, whether such cycles are regular or not[13].

Perimenopause or menopausal transition - Period that extends from two years before the last menstruation and until one year later. Women have irregular menstrual cycles and endocrine changes[13].

Postmenopause - Period that starts one year after the last menstruation**.** It is subdivided into early (up to five years after the last menstruation) or late (more than five years after the last menstruation)[13].

Metabolic syndrome - Disorder represented by a set of cardiovascular risk factors related to central adiposity, insulin resistance, hypertension, low HDL-cholesterol (HDL-c) and hypertriglyceridemia, diagnosed according to the criteria of the National Cholesterol Education Program's Adult Treatment Panel III - NCEP-ATP III-2005[3] and the International Diabetes Federation - IDF-2005[4] (Table 1),

According to NCEP-ATP III, MS represents the combination of three of the following variables: diabetes, systemic hypertension, abdominal obesity, hypertriglyceridemia, low HDL-c[3]. According to the IDF, the diagnosis is made by the presence of abdominal obesity (AC≥80 cm) plus two criteria among those presented in Table 1[4].

Data collection

A registration form was filled out. This form contained: age, group (pre or postmenopausal), race, occupation, personal and family history, smoking, alcoholism, medicines, blood pressure, abdominal circumference (AC), hip circumference

Table 1 - Components of metabolic syndrome in women

	NCEP-ATP III(2005)[3]	IDF (2005)[4]
Abdominal circumference	≥ 88 cm	≥ 80 cm
Triglycerides	≥ 150 mg/dl	≥150 mg/dl
HDL-cholesterol	< 50 mg/dl	< 50 mg/dl
Blood pressure	SBP ≥ 130 mmHg or DBP ≥ 85 mmHg or use of antihypertensive drug	SBP ≥ 130 mmHg or DBP ≥ 85 mmHg or use of antihypertensive drug
Fasting blood glucose	≥ 100 mg/dl or use of hypoglycemic drug	≥ 100 mg/dl or use of hypoglycemic drug
Diagnosis of MS	three criteria	AC + two criteria

(HC), BMI, triglycerides, HDL-C, fasting blood glucose.

For "age", four categories were adopted: ages 40 to 45; 46 to 50; 51 to 55 and 56 to 65. For "occupation," three categories were adopted: non-manual; manual and out of the economically active population (EAP). The data were entered into MS-Excel™ (Microsoft, Charlotte, NC, USA) and then exported to Stata™ 10.0 (StataCorp, College Station, TX, USA) for statistical analysis.

Statistical analysis

The data were presented as mean, standard deviation, percentages, odds ratios and confidence intervals.

The relationship between the menopausal status and MS was observed in a simple logistic regression model, with the odds ratio and its confidence interval being estimated at 95%. We also conducted a bivariate analysis of age group, race and occupation in relation to MS. In a multiple logistic regression model, we calculated the odds ratio of the menopausal status in relation to MS, adjusted for age group, race and occupation. The analyses were carried out separately for NCEP and IDF criteria. A p value higher than 0.05 was considered statistically significant.

Ethical aspects

The data were collected after the institution's Research Ethics Committee gave its approval, and the patients signed an Informed Consent Form.

Results

The average age of the population studied was 49.7 years. The prevalence of MS by NCEP criteria was 34.7% (112 cases), while by the IDF, it was 49.85% (161 cases).

Out of the 323 women, 154 (47.68%) were premenopausal and 169 (52.32%) were postmenopausal. MS was more prevalent among postmenopausal women than among premenopausal women by both criteria. According to the NCEP criteria, 44.4% of postmenopausal women had MS, compared to 24% of premenopausal women - OR=2.52 (CI = 1.56 to 4.07), p<0.001. And by the IDF, MS was present in 61.5% of postmenopausal

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women and in 37% of premenopausal women - OR = 2.72 (CI = 1.74 to 4.27), p<0.001.

With respect to age, the older the patient was, the more frequent the MS became, with a statistically significant relationship between age and occurrence of MS by both criteria (p<0.001).

When the NCEP concept was used, there was no statistically significant relationship (p=0.228) between race and the occurrence of MS, despite its greater frequency among black people (42.9%), followed by white people (37.9 %) and mixed race people (31%). This relationship was not observed when the IDF concept was used (p=0.323), although the MS was more prevalent among black women (59.2%), followed by mixed race (49.2%) and white (46%).

With respect to occupations, it was observed that the MS was prevalent among women outside the economically active population (EAP) in both diagnosis protocols. By the NCEP criteria, MS was present in 42.2% of women outside the EAP, in 29.8% of those with non-manual occupations and in 29.7% of women with manual occupations (p=0.071). There was also no statistical relationship between the occupation categories and the prevalence of MS by the IDF criteria (p=0.110).

The prevalence of MS, distributed according to age, menopausal status, race and occupation, is shown in Table 2 (NCEP) and Table 3 (IDF).

When the components of MS were examined separately, low HDL-C was prevalent among 79.6% of the patients (n=257), followed by systemic hypertension in 65% of

Table 2 - Prevalence of metabolic syndrome according to NCEP, by menopausal status, age, race and occupation in climacteric women

	n	% MS[1]	OR	CI 95%	P value
Menopausal status					< 0,001*
Premenopause	154	24	1	-	
Postmenopause	169	44.4	2.52	1.56 – 4.07	
Age group					< 0.001*
Ages 40 to 45	99	14.1	1	-	
Ages 46 to 50	71	39.4	3.95	1.88 – 8.28	
Ages 51 to 55	102	35.3	3.31	1.65 – 6.64	
Ages 56 to 65	51	66.7	12.1	5.39 – 27.34	
Race					0.2*
White	87	37.9	1	-	
Black	49	42.9	1.23	0.6 – 2.5	
Mixed-race	187	31.0	0.74	0.43 – 1.25	
Occupation					0.071*
Non-manual	94	29.8	1	-	
Manual	101	29.7	0.99	0.54 – 1.84	
Outside the EAP[2]	128	42.2	1.72	0.98 – 3.02	

1 -%MS - Prevalence of metabolic syndrome according to the definition of the National Cholesterol Education Program - Adult Treatment Panel III. 2 - Economically Active Population. n - number of individuals. (*) Chi-square test.

Table 3 - Prevalence of metabolic syndrome according to IDF, by menopausal status, age, race and occupation in climacteric women

	n	% MS[1]	OR	CI 95%	P value
Menopausal status					< 0,001*
Premenopause	154	37.0	1	-	
Postmenopause	169	61.5	2.72	1.74 – 4.27	
Age group					< 0.001*
Ages 40 to 45	99	33.3	1	-	
Ages 46 to 50	71	43.7	1.55	0.83 – 2.9	
Ages 51 to 55	102	53.9	2.34	1.32 – 4.14	
Ages 56 to 65	51	82.4	9.33	4.1 – 21.46	
Race					0.323*
White	87	46.0	1	-	
Black	49	59.2	1.7	0.84 – 3.46	
Mixed-race	187	49.2	1.14	0.68 – 1.89	
Occupation					0.110*
Non-manual	94	45.7	1	-	
Manual	101	44.6	0.95	0.54 – 1.67	
Outside the EAP[2]	128	57.0	1.57	0.92 – 2.69	

1 -% SM - Prevalence of metabolic syndrome according to the definition of the International Diabetes Federation. 2 - Economically Active Population. n - number of individuals. (*) Chi-square test.

patients (n=210), hypertriglyceridemia in 12.4% (n=40) and hyperglycemia in 11.8% (n = 38).

Abdominal obesity was prevalent among 40.9% (n=132) of the individuals, by the NCEP criteria (AC≥88 cm), and among 81.1% (n = 262), according to the IDF concept (AC≥80 cm).

The prevalence of all components studied was higher among postmenopausal women than among premenopausal women, where only abdominal obesity and systemic hypertension were statistically significant (AC-IDF p=0.049) (AC-NCEP p <0.001) (systemic hypertension, p=0.001) (Table 4).

The number of components among patients with MS was also analyzed. According to the NCEP concept, 73.2% of women with MS had three, 19.6% had four, and 7.1% had all five MS components. When the IDF criterion was used, 77.6%, 15.5% and 6.8% of the women with MS had, respectively, three, four and five components.

With respect to the menopausal status, the number of components among the patients with SM increased among postmenopausal women, by both diagnosis criteria.

There was a statistically significant relationship between the increase in age and the prevalence of MS, by the NCEP concept (p<0.001) and by the IDF concept (p=0.005). By the NCEP criteria, there was a 15-fold increase in the risk of MS among women aged 56 to 65 (OR=14.87; CI 4.24 to 52.13) compared to those between 40 and 45 years old. There was also a significant increase (7.5 times) in the risk of MS when the same age groups were compared according to the IDF concept. (OR=7.5 CI 2.18 to 26.07)

Table 4 - Prevalence of metabolic syndrome components in relation to menopausal status in climacteric women

	Premenopause		Postmenopause				Total
	n	%	n	%	OR	p	n
AC IDF[1]							
≥ 80 cm	118	76.6	144	85.2	1.76	0.049*	262
HDL cholesterol							
< 50 mg/dl	117	76.0	140	82.8	1.53	0.126*	257
Blood pressure							
≥ 130 or ≥ 85 mmHg	86	55.8	124	73.4	2.18	0.001*	210
AC NCEP[2]							
≥ 88 cm	46	29.9	86	50.9	2.43	<0.001*	132
Triglyceridemia							
≥ 150 mg/dl	14	9.1	26	15.4	1.82	0.086*	40
Glycemia							
≥ 100 mg/dl	14	9.1	24	14.2	1.66	0.155*	38

1 - Abdominal circumference by the criterion of the International Diabetes Federation. 2 - Abdominal circumference by the criterion of the National Cholesterol Education Program - Adult Treatment Panel III. n - number of individuals. (*) Chi-square test.

With regard to menopausal status, race and occupation, the multivariate analysis revealed no statistically significant relationship between these variables and the occurrence of MS (Table 5 - NCEP) (Table 6 - IDF).

Discussion

The MS concept has been around for several decades, but it was only after the standardization of diagnostic criteria that it was possible to compare prevalence between populations. Differences in genetic profile, eating habits, level of physical

Table 5 - Multivariate analysis of MS NCEP[1] adjusted for age, menopausal status, race and occupation in climacteric women

	OR	CI 95%	P value
Age			<0.001
Ages 40 to 45	1	-	
Ages 46 to 50	4.04	1.84 – 8.92	
Ages 51 to 55	4.17	1.34 – 12.95	
Ages 56 to 65	14.87	4.24 – 52.13	
Menopausal status			0.549
Premenopause	1	-	
Postmenopause	0.75	0.29 – 1.92	
Race			0.347
White	1	-	
Black	1.12	0.52 – 2.4	
Mixed-race	0.72	0.41 – 1.29	
Occupation			0.534
Non-manual	1	-	-
Manual	1.14	0.59 – 2.22	
Outside the EAP[2]	1.41	0.76 – 2.6	

1 - MS NCEP - Metabolic syndrome according to the definition of the National Cholesterol Education Program - Adult Treatment Panel III. 2 - Economically Active Population.

Table 6 - Multivariate analysis of MS IDF[1] adjusted for age, menopausal status, race and occupation in climacteric women

	OR	CI 95%	P value
Age			0.005
Ages 40 to 45	1	-	
Ages 46 to 50	1.47	0.74 – 2.94	
Ages 51 to 55	1.98	0.7 – 5.56	
Ages 56 to 65	7.53	2.18 – 26.07	
Menopausal status			0.758
Premenopause	1	-	
Postmenopause	1.15	0.47 – 2.85	
Race			0.476
White	1	-	
Black	1.57	0.75 – 3.32	
Mixed-race	1.11	0.64 – 1.91	
Occupation			0.706
Non-manual	1	-	
Manual	1.07	0.58 – 1.95	
Outside the EAP[2]	1.26	0.71 – 2.25	

1 - MS IDF - Metabolic syndrome according to the definition of the International Diabetes Federation. 2 - Economically Active Population.

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activity, age, gender, and lifestyle influence the prevalence of MS and its components[11].

The prevalence of MS in women varies a lot. According to the characteristics of the population studied and the diagnostic criteria adopted, the prevalence ranges from 10.7% among Korean women above 30 years-old by the NCEP criteria[14,15], to 74% in post-menopausal women with coronary artery disease in Birmingham (USA) by the IDF[16].

The overall prevalence of MS by NCEP, in this study, was 34.7%. Such data are consistent with those found by Ford et al[17] in 4,441 American women over 40 (33%). Deibert et al[18] conducted a study that followed climacteric women for 12 months in Germany and they found a prevalence of 36.1% of MS (NCEP).

In this study, by the NCEP concept, the prevalence of metabolic syndrome among postmenopausal women (44.4%) was higher than among pre-menopausal women (24%). This finding is consistent with a multicenter study conducted in 2007 with 3,965 climacteric women in Latin America[9], which found MS in 42.9% of postmenopausal women and 28.1% of premenopausal women. Deibert et al[18] found prevalence of 36.1% among post-menopausal women and 22.7% among premenopausal women. Studies of menopausal women in Canada[19], Ecuador[8] and South Korea[20] found prevalence of 31%, 41.5% and 54.6% respectively.

By the IDF criteria, there was higher prevalence of MS among postmenopausal women (61.5%) compared to premenopausal women (37%). Among menopausal Chinese women, Ding et al[21] found 37.3% of MS (IDF). Socio-cultural influences, eating habits, sedentary lifestyle and different levels of urbanization among the populations also change the prevalence of MS, which may explain this difference.

As to the age group, this study found an increasing prevalence of MS. According to NCEP criteria, 14.1% of the 40 to 45 age group and 66.7% of the 56 to 64 age group. By the IDF concept, 33.3% and 82.4% of the same age groups. This finding was statistically significant in both the univariate analysis and multivariate analysis. In Brazil, epidemiological data referring to MS in the general population are scarce and rarer still with regard MS among climacteric women. A study conducted in the semiarid region of Bahia State with 138 women found 18.2% of MS (NCEP-2001) among women under the age of 45 and 56.9% among those that were 45 years or older[22]. A study conducted in the city of Vitória, State of Espírito Santo, which evaluated 887 women, found prevalence of MS (NCEP-2001) of 33.6% in women aged 45 to 54 and 53.4% among those aged 55 to 64[23]. A study conducted in Seychelles found prevalence of 46% and 68% among women in the 45 to 54 and 55 to 64 age groups[24].

The genetic aspect may contribute to the high prevalence found in this study, because the Negroid features are widely distributed in the population studied (73.1% black women/mixed-race women). The same occurs in the populations studied in Bahia[22] (84.3%) and Espírito Santo[23] (66.8%). It is important to highlight the high frequency of metabolic-syndrome components among African descendants, such as systemic hypertension at an earlier stage and more prevalent, obesity and type 2 DM, particularly in black women[22].

When the components of MS are examined separately, the change most frequently found was abdominal obesity by the IDF criteria (AC $\geq$ 80 cm), with frequency of 81.1%. As the IDF criterion for abdominal obesity is more stringent than the NCEP criterion (AC $\geq$ 88 cm), and as climacteric women showed a statistically significant increase in AC, this component became the most frequent one, followed by low HDL-c (79.6%), systemic hypertension (65%), abdominal obesity (NCEP) (40.9%), hypertriglyceridemia (12.4%) and fasting hyperglycemia (11.8%). When all the components of MS were analyzed in relation to menopausal status, the same order of frequency was maintained, and all changes were more common in the postmenopausal group. Oliveira et al[22] found the same frequency order, in the following percentages: 84.1%, 53.6%, 47.1%, 18.1% and 16.7%. In the city of Vitoria, State of Espírito Santo, there was an inversion only in the first two components. The other ones followed the same order[23].

In a study conducted in the city of Porto Alegre, 5.1% of women had an aggregate of four to five risk factors for cardiovascular disease, and 4.5% had a combination of high blood pressure and diabetes, which are two of the MS components[25].

Oh et al[15] studied 449 South Korean women and the most frequent components were: Low HDL-c, systemic hypertension, hypertriglyceridemia, hyperglycemia and abdominal obesity. According to the authors, the genetic characteristics of the Korean population are responsible for this lower prevalence of abdominal obesity.

The studies that are aimed at demonstrating the correlation between menopause and cardiovascular risk factors, including MS, are contradictory. A higher prevalence of each factor and the MS among menopausal women than among women of childbearing age is the most common result. In the 1980s and 1990s, Staessen et al. demonstrated that menopausal women and older women had higher BP than premenopausal and younger women[26,27]. In 1987, Villecco et al[28] found a "temporary increase in BP, related to ovarian failure." Hjortland et al[29] monitored 1,686 climacteric women and found no significant difference in weight, BP and blood glucose in postmenopausal women.

A recent review in California that linked surgical menopause with cardiovascular risk failed to allow the desired meta-analysis due to the heterogeneity of the results found, also due to methodological errors of the studies[30].

These conflicting results may be attributed to several factors: different study designs, population studied, age, time since menopause, spontaneous or surgical menopause, diagnostic criteria of MS and even serious methodological errors. In a study conducted at the University of Bristol, for example, the "menopausal" status was assigned to every woman over 50, arguing that "this is the average age of menopause for British women[31]."

Before so many confounding factors, it becomes difficult to draw any definitive conclusion from these studies. There is widespread belief that women lose the "cardiovascular advantage" after menopause, and this increases cardiovascular morbidity and mortality[32]. The decline in ovarian function is considered the cause of this phenomenon[9,33,34].

Statistics available do not provide support for a definitive conclusion about the role of menopause as an independent risk factor for the increase in the prevalence of MS. In this study, there was a higher prevalence of MS among menopausal women when both diagnostic criteria were considered, but this difference was not statistically significant after the adjustment for age, which differs from most studies. The age-group stratification was statistically significant in the univariate analysis and multivariate analysis. 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 age increase.

Casiglia et al[35], in a study with 9,364 Italian men and women found results that were similar to the ones of this study: higher prevalence of MS components among post-menopausal women, but this difference disappeared after adjustment for age. In the study conclusion, the authors mentioned that "the cardiovascular effects usually attributed to menopause seem to be merely a consequence of the older age of menopausal women[35]."

The issue involving the role of menopause as a risk factor for the onset of MS and its effects remains controversial. A limitation of this study was the small population studied, although the results are consistent with many other studies[8,9,19,22,23]. Due to the ethnic and cultural heterogeneity of the population of this region, other studies are needed to confirm the results found and, then, take actions to prevent MS in climacteric women.

Conclusion

MS was more prevalent among postmenopausal women than among premenopausal women by both criteria. Menopause is not an independent risk factor for metabolic syndrome. Age is the main independent risk factor for the occurrence of MS.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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