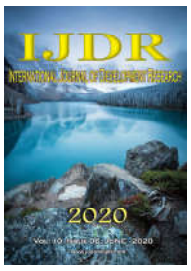
ISSN: 2230-9926

Available online at http://www.journalijdr.com

IJDR

International Journal of Development Research
Vol. 10, Issue, 06, pp. 37362-37368, June, 2020
https://doi.org/10.37118/ijdr.19190.06.2020



RESEARCH ARTICLE OPEN ACCESS

PREVALENCE AND FACTORS ASSOCIATED WITH METABOLIC SYNDROME IN CLIMACTERIC WOMEN

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ARTICLE INFO

Article History:
Received 17th March, 2020
Received in revised form
22nd April, 2020
Accepted 28th May, 2020
Published online 30th June, 2020

Key words:

Complementary therapies. Unified Health System. Students, Health Occupations. Integrative Medicine. Acupuncture Therapy.

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ABSTRACT

Objective: To estimate the prevalence of metabolic syndrome and its association with sociodemographic, behavioral, reproductive and clinical factors in climacteric women. ***Methods:*** Cross-sectional and analytical study with probabilistic cluster sampling. The study included 874 women, aged between 40 and 65 years, registered in 73 Family Health Strategy units in the city of Montes Claros, Minas Gerais, Brazil. Data were obtained through questionnaires, anthropometric evaluation and blood collection. For statistical analysis, the hierarchical Poisson regression model was adopted. ***Results:*** A significant association of metabolic syndrome was evidenced with the following variables at distal level: age group 46 to 51 years (PR=1.25; p=0.009) and 52 to 65 years (PR=1.39; p<0.001) and schooling/elementary school (PR=1.14; p=0.033). After adjusting sociodemographic factors, a positive association with metabolic syndrome was observed in women who reported moderate or severe climacteric symptoms (PR=1.12; p=0.028). At the proximal level, the presence of gout was positively associated with metabolic syndrome (PR=1.20; p=0.049). ***Conclusions:*** Older women with low level of schooling, moderate to severe climacteric symptoms and with gout disease showed a higher prevalence of metabolic syndrome in the climacteric.

Citation: ***Vivianne Margareth Chaves Pereira Reis, Josiane Santos Brant Rocha, Lucineia de Pinho, Maria Fernanda Santos Figueiredo Britoet al.*** **"**Prevalence and factors associated with metabolic syndrome in climacteric women*", International Journal of Development Research*, 10, 05, 37362-37368.

INTRODUCTION

Metabolic syndrome (MS) is characterized by a set of components such as hyperglycemia, arterial hypertension, high levels of triglycerides, low levels of high cholesterol and increased abdominal circumference (Vidigal, 2013). This syndrome is considered an important risk factor for the development of cardiovascular diseases (CVD) and type 2 diabetes mellitus, diseases that have been assuming increasing repercussions on women's health (Maharlouei *et al*., 2013). Symptoms of MS worsen in women aged between 40 and 65 years due to the transition of the climacteric phases (Meirelles, 2014), which covers pre, peri and postmenopausal (North American Menopause Society, 2013). Women in this life period are susceptible to physiological changes, such as the reduction in production of protective endogenous substances such as estrogen and progesterone (Fedacko *et al*., 2014). And consequently, the chances of developing obesity, dyslipidemia, glucose intolerance and hyperuricemia are driving elements of MS, for the development of cardiovascular diseases and diabetes (Fedacko *et al*., 2014; Karns, 2013). The appearance of MS may be associated with advancing age, sociodemographic, and behavioral factors, chronic non-communicable diseases, and lifestyle (Meirelles, 2014; Alshaikh, 2017; Wen *et al*., 2015). In the midst of involvements that negatively affect women's health in the climacteric, this study aimed to investigate the association between MS and sociodemographic, behavioral, reproductive and clinical factors in women.

METHODS

Population-based, cross-sectional and analytical study, whose population comprised 30,018 women, aged between 40 and 65 years, registered in 73 Family Health Strategy (FHS) units in the city of Montes Claros (Urban and rural area), Minas Gerais, Brazil, held between August 2014 and January 2015. In determining the sample size, the formula was used to estimate prevalence in cross-sectional studies (Luiz, 2000). An estimated prevalence of 50% of MS was considered, with a 95% confidence level and 5% margin of error. Correction was made for drawing purposes, adopting *deff* equal to 2.0 and an increase of 10% for the non-response rate. The calculations showed a sample size of at least 836 women. The technique used was the probability sampling by conglomerate in two stages. In the first stage, the probability proportional to size (PPS) method was used, and 20 FHS units were selected, and, in the second stage, by simple random sampling (SRS), 48 women were drawn in each unit selected. The 960 women selected were invited to participate in the study and then a date was scheduled to complete questionnaires, anthropometric evaluations and blood collection with those who met the inclusion criteria and accepted to participate in the study. We considered as inclusion criterion to be registered in the FHS and as exclusion criteria women who underwent angioplasty, were pregnant, postpartum women and bedridden patients. Data were collected at the premises of FHS units by a trained and calibrated team, composed of a physician, a pharmacist, five nursing and physical education students, and the responsible researcher. At the end of the sampling process, 874 women were included in the study. The dependent variable considered in this study was MS, according to the International Diabetes Federation (IDF) (Alberti *et al*., 2006), which recommends, as diagnosis, the presence of increased abdominal circumference (AC≥80 cm, cutoff point for South America) or body mass index (BMI) >30 kg/m^2 associated with two or more altered components, such as: systolic ≥130 mmHg or diastolic blood pressure (BP) ≥85 mmHg or drug treatment for hypertension; glucose ≥100mg/dL or previous diagnosis of type 2 diabetes; high density lipoprotein (HDL) <50 mg/dL or drug treatment for reduced HDL; triglycerides (TG) ≥150 mg/dL or drug treatment for elevated TG. For AC measurement, a measuring tape positioned around the lower curvature located below the ribs and above the navel at the end of the expiratory movement was used (Sociedade Brasileira de Cardiologia, 2005). The formula (BMI = weight (Kg) / height (cm²) was used to calculate BMI. The weight was measured with barefoot women, with the least amount of clothing possible, using the digital scale EKS 9800 FOCUS -- 180 kg. Height evaluation was performed with the women in anthropometric position, barefoot, using the stadiometer Sanny (World Health Organization, 1999. BP measurement was obtained with the women seated, after 5 minutes of rest, using calibrated digital aneroid sphygmomanometer, ONROM brand, positioned in the proximal region of the upper left limb, superior to the cubital fossa. Two measurements were performed, with an interval of one minute, establishing the mean. Systolic pressure occurred to the first heart sounds (phase I of *Korotkoff* sounds) and diastolic pressure occurred to its disappearance (phase V of *Korotkoff* sounds) (Sociedade Brasileira de Cardiologia, 2016). To analyze biochemical parameters such as fasting glycemia, HDLc fraction and TG, the individuals were submitted to fasting venous blood collection of at least 12 hours. Serum levels of TG and glucose were determined by the enzymatic colorimetric method. The HDLc level was obtained by selective precipitation of low-density lipoprotein (LDLc) and very low-density lipoprotein (VLDLc), followed by dosage by oxidase/peroxidase enzymatic cholesterol system with calorimetry and reading, using the random access analyzer Cobas Mira S (Sociedade Brasileira de Cardiologia, 2016). The independent variables were the sociodemographic, behavioral, reproductive and clinical factors obtained through self-reported questionnaires. The sociodemographic factors investigated were age (40 to 45 years, 46 to 51 years and 52 to 65 years), marital status (with partner and without partner), skin color (non-white and white), schooling (high school/college, middle school, elementary school), and formal employment (yes and no). Behavioral factors addressed physical activity (active/very active and sedentary/irregularly active), alcohol consumption (no and yes), smoking (no and yes), fruit consumption per day (consumes ≥ 3 fruits per day and consumes <3 fruits per day) and contraceptive use (no and yes). Regarding the classification of physical activity, the questionnaire International Physical Activity Questionnaire (IPAQ) was used in its short version, composed of six questions related to physical activities performed last week (Matsudo *et al*., 2001). The reproductive factors analyzed were climacteric phases (pre, peri and postmenopausal) and climacteric symptoms (absent/mild and moderate/severe), number of children (no child and ≥ 01 child) and age at first birth (≤18 years and >18 years). For the categorization of climacteric phases, women with regular menstrual cycle were classified as premenopausal; those with irregular menstrual cycle ranging from 2 to 11 months, as perimenopausal; and women with interrupted menstrual cycle for more than 12 months, as postmenopausal (North American Menopause Society, 2013). For the classification of symptomatology in the climacteric, the questionnaire of the Kupperman Index was adopted, whose

score is obtained by the sum of the score of 11 climacteric symptoms, measured according to the intensity (Lickert scale ranging from 0 to 4). According to this index, women are classified according to absence of symptom and mild (less than or equal to 19), moderate (from 20 to 35) and severe symptom (higher than 35) (Kupperman, 1953). In this investigation, this variable was dichotomized in absence symptom/mild symptom and moderate/severe symptom. The clinical factors investigated were liver, gout and renal diseases, urinary incontinence, daytime sleepiness, sleep quality, and symptoms of depression. Information regarding liver, gout and kidney diseases was obtained through self-report, classifying women with the presence or absence of these diseases. Urinary incontinence indicators, daytime sleepiness, sleep quality and symptoms of depression were obtained using validated instruments. To evaluate urinary incontinence, the instrument International Consultation on Incontinence Questionnaire -- Short Form (ICIQ-SF) was applied, composed of four questions that assess the frequency, quantity, severity and impact of urinary incontinence. The women in the study were classified according to presence or absence of urinary incontinence (Tamanini, 2004). To evaluate daytime sleepiness, the Epworth Sleepiness Scale (ESE) was adopted, which analyzes the chance of sleeping in eight situations (scale from 0 to 3 points). The total score of this scale classified women according to absence of excessive daytime sleepiness (0 to 10 points) and presence of excessive daytime sleepiness (≥11 points) (Bertolazi *et al*., 2011). Sleep quality was evaluated using the Pittsburgh Sleep Quality Index (PSQI--BR) questionnaire, consisting of seven components whose scores range from 0 to 3 points. In the sum of the score, the participants were classified according to poor sleep quality (>5 points) and good sleep quality (≤5 points) (Bertolazi, 2011). To identify symptoms of depression, we used the Beck Depression Inventory (BDI), composed of 21 items, whose total score classified women according to: absence of symptom (0 to 11 points), mild symptom (12 to 19 points), moderate symptom (20 to 35 points), severe symptom (36 to 63 points)[18].

Data analysis

For the characterization of the sample, simple and relative frequency distributions were presented for all variables analyzed, and the prevalence of MS was estimated according to sociodemographic, behavioral, reproductive and clinical factors. Comparisons were made between the components of MS, using the Student's t test. These analyses were performed with correction by the design effect in order to incorporate the structure of the complex sampling design. For this, the interviewees were associated with a certain weight, which corresponded to the reverse of their probability of inclusion in the sample. The probability of inclusion was obtained by the product of the probability of inclusion in each of the two stages (Szwarcwald, 2008). The magnitude of the associations between the independent variables and the outcome was evaluated using the crude prevalence ratios, with their respective intervals of 95% confidence. Therefore, the Poisson regression model was adopted, with robust variance. The variables that presented descriptive level (p-value) ≤0.25 were selected for multiple analysis. In the multiple analysis, the Poisson regression model was also adopted to estimate the adjusted prevalence ratios (PR). A hierarchical model adapted to the model proposed by Rodrigues *et al*. (2013) was used to guide the composition of the variable blocks and their order of entry in the model. The distal level was composed of the variables of the sociodemographic block and the intermediate level was composed of behavioral and reproductive variables. The proximal level consisted of clinical variables. In this stage, only those variables that presented descriptive level $p<0.05$ remained in the final model; after adjustment for the variables of distal and intermediate levels. We used the statistical program SPSS, version 22 and the deviance test to evaluate the quality of the model adjustment.

Ethical aspects: The risks and benefits of the study were clarified to the participants. Those who agreed to participate in the research voluntarily signed the informed consent form. Care was taken to preserve the identity of the participants. This study was submitted to the Ethics Committee, obeying the ethical precepts of resolution 466/2012, being approved with number 817,166.

RESULTS

The study included 874 women with a mean age of 51.03 (±7.2 years), considering the loss of 86 (8.95%) non-respondents. Figure 1 shows the prevalence of MS and its components, in which the most frequent components were altered AC, low HDL and elevated BP, while the component with the lowest prevalence was altered glycemia. A prevalence of 61.6% (95% CI:55.5% -- 67.4%) was estimated for MS. A higher percentage of women with 2 to 4 components of MS was found. We also noted that cases of women with none and with six components of MS were rare (Figure 2). The sample consisted mainly of women with the following characteristics: age between 52 and 65 years, having a partner, having non-white skin color, having only elementary and middle school, and not having formal employment. Most of them were sedentary or irregularly active, did not drink alcohol, did not smoke, consumed less than three fruits per day, used contraceptives, were in the postmenopausal phase, had absence or mild climacteric symptoms, had one or more children and were older than 18 years at the time of their first delivery. We observed a high proportion of women who reported absence of liver, gout and renal diseases, urinary incontinence, and symptoms of depression. However, a negative health profile was exposed by the predominance of poor sleep quality. Furthermore, a high prevalence of MS was observed in all categories of sociodemographic, behavioral, reproductive and clinical factors (Table 1).

Significant changes were found in the MS components of women with the presence of MS compared with women with absence of MS (Table 2). In the bivariate analysis, we observed that MS is positively associated, at the level of $p\leq0.250$, with women aged between 46 and 51 years and 52 to 65 years, without partner, white, with lower education, without a formal employment, in the postmenopausal phase, with moderate and severe climacteric symptoms, with presence of liver, gout and kidney diseases, urinary incontinence, poor sleep quality and severe symptoms of depression. On the other hand, protective factors for MS were the use of contraceptives, being in the perimenopausal phase and age at first birth older than 18 years (Table 3). Behavioral factors (physical activity, alcohol consumption, smoking and fruit consumption), and reproductive factors (number of children) did not present significant associations at level $p\leq0.250$ with MS. A significant association of metabolic syndrome was evidenced with the following variables at distal level: age group 46 to 51

Table 1. Characterization of the sample, according to sociodemographic, behavioral, reproductive, clinical factors of climacteric women in Montes Claros-MG, Brazil, 2014/2015

Variables		Frequency (n=874)		Prevalence MS
Sociodemographic factors		n	%[a]	%[a]
Age	40 to 45 years	236	27.9	49.2
	46 to 51 years	241	26.8	61.1
	52 to 65 years	397	45.3	69.6
Marital Status	With a partner	560	63.1	60.7
	Without partner	314	36.9	63.1
Skin color[b]	Non-white	714	82.8	60.7
	White	154	17.2	66.7
Schooling[b]	High school/College	281	31.8	56.8
	Elementary School	231	26.6	57.0
	Middle School	358	41.6	68.3
Formal employment[b]	Yes	347	40.4	55.9
	No	520	59.6	65.7
Behavioral Factors				
Physical Activity	Active/Very active	114	12.7	61.9
	Sedentary/Irregularly active	760	87.3	61.6
Alcoholism[b]	No	646	78.8	62.6
	Yes	163	21.2	56.5
Smoking[b]	No	719	89.5	61.3
	Yes	80	10.5	62.8
Fruit consumption[b]	≥3 fruits per day	291	35.1	59.9
	<3 fruits a day	532	64.9	62.6
	No	300	37.2	66.5
Contraceptive use[b]	Yes	524	62.8	58.9
Reproductive Factors				
Climacteric Phases[b]	Premenopausal	214	24.4	61.1
	Perimenopausal	185	21.3	50.4
	Postmenopausal	473	54.3	66.4
Climacteric Symptoms	Absent/mild	541	62.3	58.6
	Moderate/Severe	333	37.7	66.5
Number of Children[b]	No children	69	8.4	66.6
	≥01 child	750	91.6	61.2
Age at 1st birth[b]	≤18 years	218	27.3	68.0
	>18 years	605	72.7	59.3
Clinical Factors				
Liver disease[b]	Absent	792	91.6	60.8
	Present	74	8.4	68.0
Gout Disease[b]	Absent	822	95.4	61.2
	Present	38	4.6	74.8
Kidney Disease[b]	Absent	700	85.4	60.3
	Present	119	14.6	69.2
Urinary incontinence[b]	Absent	676	77.5	60.3
	Present	195	22.5	66.2
Sleep quality[b]	Good	327	37.0	58.3
	Poor	542	63.0	63.3
Symptom of Depression[b]	Absent	528	60.6	62.6
	Mild	220	25.3	61.4
	Moderate	110	12.7	56.4
	Severe	11	1.4	91.4

[a] Corrected by the design effect *(deff)*
[b] Totals vary due to loss of information.

Table 2. Descriptive measures of the components in the total sample and according to the presence and absence of Metabolic syndrome (MS) among climacteric women in Montes Claros-MG, Brazil, 2014/2015

Components of MS	Total Sample	Absence of MS	Presence of MS	p-value
	Mean[a] (SD)	Mean[a] (SD)	Mean[a] (SD)	
AC (cm)	93.04 (13.79)	85.13 (14.03)	97.53 (11.23)	<0.001
BMI (kg/m²)	28.81 (5.73)	26.58 (5.51)	29.89 (5.79)	<0.001
TG (mg/dL)	157.84 (75.57)	127.64 (54.40)	176.14 (81.03)	<0.001
HDL (mg/dL)	41.09 (10.26)	46.33 (11.79)	37.84 (7.469)	<0.001
Glycemia (mg/dL)	89.06 (32.16)	79.98 (21.09)	93.23 (36.69)	<0.001
SBP (mmHg)	127.08 (17.72)	119.87 (16.58)	128.62 (17.49)	<0.001
DBP (mmHg)	83.05 (12.45)	78.80 (10.25)	84.00 (11.66)	<0.001

MS: metabolic syndrome; AC: abdominal circumference; BMI: body mass index; TG: triglycerides; HDL: high density lipoprotein; SBP: Systolic blood pressure; DBP: diastolic blood pressure; SD: standard deviation. [a] Corrected by the design effect *(deff)*

Table 3. Gross and adjusted prevalence ratio (PR for metabolic syndrome (MS) according to sociodemographic, behavioral, reproductive and clinical factors of climacteric women in Montes Claros-MG, Brazil, 2014-2015

Variables		PR (95%CI)	p-value	PR (95%CI)	Value
		Crude		Adjusted (n=855)	p
Sociodemographic					
Age	40 to 45 years	1.00		1.00	
	46 to 51 years	1.28 (1.08-1.52)	0.005	1.25 (1.06-1.49)	0.009
	52 to 65 years	1.48 (1.27-1.72)	<0.001	1.39 (1.19-1.60)	<0.001
Marital Status	With a partner	1.00			
	Without partner	1.07 (0.96-1.20)	0.206	NS	
Skin color	Non-white	1.00	0.172		
	White	1.09 (0.96-1.25)		NS	
Schooling level	High school/College	1.00		1.00	
	Middle School	1.03 (0.88-1.20)	0.752	0.94 (0.80-1.10)	0.441
	Elementary School	1.27 (1.12-1.45)	<0.001	1.14 (1.01-1.30)	0.033
Formal Employment	Yes	1.00			
	No	1.18 (1.05-1.32)	0.004	NS	
Behavioral/Reproductive					
Contraceptive use	No	1.00	0.064		
	Yes	0.90 (0.81-1.00)		NS	
Climacteric Phases	Premenopausal	1.00			
	Perimenopausal	0.88 (0.73-1.05)	0.157	NS	
	Postmenopausal	1.14 (1.00–1.30)	0.047	NS	
Climacteric Symptoms	Absent/mild	1.00		1.00	
	Moderate/Severe	1.17 (1.05-1.30)	0.003	1.12 (1.01-1.25)	0.028
Age at 1st birth	≤18 years	1.00			
	>18 years	0.89 (0.80-1.00)	0.057	NS	
Clinical					
Liver disease	Absent	1.00			
	Present	1.13 (0.95-1.33)	0.164	NS	
Gout Disease	Absent	1.00		1.00	
	Present	1.26 (1.05-1.52)	0.014	1.20 (1.01-1.44)	0.049
Chronic Kidney Disease	Absent	1.00			
	Present	1.13 (0.98-1.29)	0.096	NS	
Urinary incontinence	Absent	1.00			
	Present	1.10 (0.98-1.24)	0.104	NS	
Sleep quality	Good	1.00			
	Poor	1.08 (0.96-1.21)	0.189	NS	
Symptom of Depression	Absent	1.00			
	Mild	0.98 (0.86-1.11)	0.743	NS	
	Moderate	0.91 (0.76-1.09)	0.314	NS	
	Severe	*1.47 (1.21-1.80)	<0.001	NS	

PR: prevalence ratio; NS: nonsignificant; 95%CI: confidence interval.

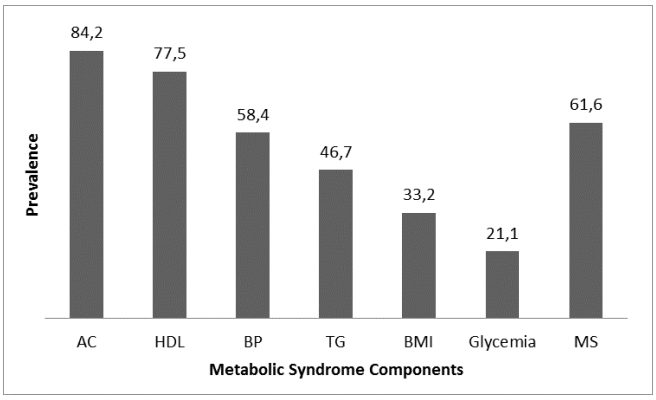

FIG. 1. Prevalence of components of MS and its components in climacteric women, Montes Claros-MG, Brazil, 2014/2015. AC – abdominal circumference; HDL – high-density lipoprotein; BP – blood pressure; TG – triglycerides; BMI – body mass index; Glycemia; MS – metabolic syndrome.

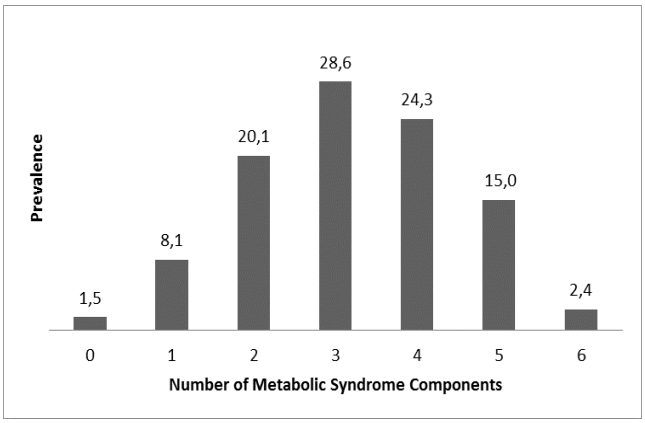

Fig. 2. Prevalence (%) of the number of components of Metabolic Syndrome in climacteric women, Montes Claros-MG, Brazil, 2014/2015

years (PR=1.25; p=0.009) and 52 to 65 years (PR=1.39; p<0.001) and schooling/elementary school (PR=1.14; p=0.033). At the intermediate level, after adjusting sociodemographic factors, the presence of moderate or severe climacteric symptoms presented a positive association with MS (PR=1.12; p=0.028). At the proximal level, after adjusting the variables of distal and intermediate levels, only the presence of gout was positively associated with MS (PR=1.20; p=0.049) (Table 3).

DISCUSSION

In this study, the sociodemographic, behavioral, reproductive and clinical factors associated with MS in climacteric women were investigated. Among them, the variables age, schooling, presence of climacteric symptoms and gout were associated with MS, and a high prevalence of MS was found in the investigated population. As to the association observed between the variable age and MS, it is noteworthy that adverse physiological changes affecting older women, such as estrogen reduction and basal metabolism, have been an explanation for the appearance of MS in this age group. With advancing age, especially in the postmenopausal phase, these changes exert an important influence on the components of MS, such as increased body weight, abdominal circumference and insulin resistance.

Decreased estrogen in the body favors estradiol reduction and leptin elevation, hormones that regulate obesity, appetite, insulin resistance (Yu, 2016) and lipid absorption from blood circulation (Misso, 2003). Due to abdominal obesity, other components of MS are altered, such as triglycerides and HDL (Lobo, 2014). Also, the insulin resistance is considered an important marker for the elevation of blood glucose levels (Udo, 2014). Advancing age also influences increased blood pressure through oxidative stress, a condition that favors the loss of nitric oxide, a vasodilator substance released in the endothelium, these changes in the arterial wall act as markers of hypertension (Bahia, 2004). This event may also be related to hemodynamic changes in hypertension such as increased cardiac output or peripheral vascular resistance, which occurs with advancing age (Picon, 2012). Low schooling was another factor associated with MS, as reported in previous studies (Schmitt, 2013; Yokokawa, 2016; Ngo, 2014). The low level of education of most of this sample may explain this association. The level of education is related to the accumulation of knowledge about health care (Ravenell, 2016). In this sense, people with a higher educational level tend to have a more critical perception about general health, capable of increasing healthier and more careful habits (Tran *et al*., 2017). The presence of climacteric symptoms also showed a positive association with MS in this study, corroborating the findings of other studies (32.33). Estrogen reduction is known for having an effect on climacteric symptoms, such as mood and anxiety change (Chedraui, 2014). We believe the presence of these symptoms may be related to obesity and to MS (Chedraui, 2014). Therefore, it is possible that the estrogen reduction in the menopausal period and the obese profile of the women in the sample may have contributed to the climacteric symptoms and its association with MS, since 74.0% of the women in this study were overweight or obese (data not presented). Among the clinical variables analyzed, gout was the only disease that was associated with MS, corroborating the finding of a previous study (Joo, 2014). Gout disease is an inflammatory arthropathy triggered by the accumulation of uric acid in the blood, which may cause hypertension, diabetes, high cholesterol, increased body fat (Fedacko *et al*., 2014; Choi, 2016). Our hypothesis is that the presence of uric acid in the body may simply be a consequence of oxidative stress or hyperinsulinemia, and there is evidence that uric acid may play a causal role in MS (Fedacko, 2014). On the other hand, MS was pointed out as an imbalance factor for the absorption and excretion of uric acid in the organism causing the gout disease (Zurlo, 2016). However, with the cross-sectional design of this study, we did not evaluate the causal effect among the variables, but the association was confirmed. The presence of gout disease was analyzed through self-report and not by clinical examinations, which may have caused an underestimation of the results, thus characterizing a limitation of this investigation.

Conclusion

The results of this study found a higher prevalence of MS in older women, those with low level of education, with moderate to severe climacteric symptoms and with gout disease.

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