ORIGINAL ARTICLES

Metabolic Syndrome and Insulin Resistance by HOMA-IR in Menopause

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Abstract

Background: Metabolic syndrome is an important cardiovascular risk factor, and its prevalence increases after menopause. However, it is still uncertain whether menopause is an independent risk factor for metabolic syndrome. One of the pathophysiological basis for metabolic syndrome is insulin resistance, which can be calculated by the Homeostatic Model Assessment-Insulin Resistance (HOMA-IR) method, and the association between insulin resistance and menopause is little known.

Objective: To evaluate the association between metabolic syndrome and insulin resistance in menopausal women.

Method: Descriptive study, which evaluated 150 women, aged 40 to 65, treated at a Gynecology Outpatient Clinic of a tertiary public hospital, from May to December of 2013. The sample was divided into two groups: Group I, comprising women in the premenopausal period and Group II, comprising women in the post-menopausal period. The presence of metabolic syndrome and its components were evaluated, as well as occurrence of insulin resistance in both groups. The association of menopausal status and the assessed variables was assessed using the Mann-Whitney, Chi-square and Fisher's exact tests. The significance level was set at 5%. The statistical analysis was performed using STATA 12.0.

Results: Metabolic syndrome and its components were more prevalent in postmenopausal women. Postmenopausal women also had a higher prevalence of insulin resistance, but no statistical association was observed between the findings.

Conclusion: The menopausal status was not significantly associated with metabolic syndrome and insulin resistance. Insulin resistance was considered an independent risk factor for the development of metabolic syndrome only in the postmenopausal group. (International Journal of Cardiovascular Sciences. 2018;31(3)201-208)

Keywords: Metabolic Syndrome; Insulin Resistance; Menopause; Climacteric; Cardiovascular Diseases.

Introduction

Approximately 40 million women were menopausal in the United States in 2010 and there was an estimate of 60 million menopausal women by 2020.[1] In Brazil, 28% of the women (24.3 million) are over 40 years of age, and in the city of São Luís, state of Maranhão, the estimated female population in 2010 was 538,138, of which 39% was in the age group between 40 and 59 years.[2]

A set of cardiovascular risk factors related to visceral obesity and Insulin Resistance (IR) defines Metabolic Syndrome (MS),[3] which is established in the presence of three or more of the following components: glucose intolerance with fasting glycemia ≥ 100 mg/dL; abdominal obesity or greater amount of visceral fat, with waist circumference > 90 cm in men and > 80 cm in women; triglycerides ≥ 150 mg/dL; high-density lipoprotein (HDL) cholesterol < 40 mg/dL for men and < 50 mg/dL for women; current antihypertensive therapy or blood pressure >130 x 85 mmHg.

IR represents a decrease in the ability of insulin to stimulate glucose use. Pancreatic β-cells increase insulin production and secretion as a compensatory mechanism, while glucose tolerance remains normal. This has been pointed out as a collective health problem, affecting several age groups, especially menopausal-aged women.[4]

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The Homeostasis Model Assessment-Insulin Resistance (HOMA-IR) index predicts the level of IR according to the glycemia and basal insulinemia. It has been widely used and represents one of the several alternatives for IR assessment, mainly because it is a simple, fast, easy to apply and low-cost method.[5]

The prevalence of MS and its association with IR in menopausal women is still poorly studied in our country. The identification of the main components of MS and their association with IR can be very useful in terms of public health, for instance, by allowing greater specificity for cardiovascular disease primary and secondary prevention actions.

The aim of this study was to evaluate the prevalence of MS, its components, and its association with IR in menopause.

Methods

This was a descriptive study, which evaluated 150 menopausal patients, aged 40 to 65 years, who agreed to participate in the study by signing the Free and Informed Consent form (FICF) at the Gynecology Outpatient Clinic of Hospital Universitário Materno Infantil of Universidade Federal do Maranhão, from May to December 2013. Patients who did not authorize their participation in the study; pregnant women; statin users; those who had undergone coronary angioplasty or myocardial revascularization, or those with a history of previous acute myocardial infarction; those who did not have information on the cause of menopause and the age at which it occurred; or cases of menopause caused by medical interventions (surgeries, radiotherapy or chemotherapy), were not included in the study. The patients were divided into two groups: Group I: premenopausal women and Group II: postmenopausal women.

The sociodemographic variables were: age (in full years), ethnicity, family income, schooling, marital status and occupation. Personal history data were also obtained (such as: date of last menstrual period, and time of menopause); comorbidities (Systemic Arterial Hypertension – (SAH), Diabetes Mellitus – (DM) and Cerebrovascular Accident – (CVA); daily use of medications and family history of coronary artery disease before age 60; and Information on social and life habits (regular physical activity, and the reporting of smoking status and alcohol intake).

The anthropometric variables were collected through a physical examination, including weight, height and Waist Circumference (WC). The WC measurement was made at the midpoint between the iliac crest and the lowest rib, using a simple fiberglass measuring tape with a latch (manufacturer: Sanny), in the orthostatic position, without clothes covering the chest and at the end of expiration.[6]

Blood pressure (BP) was obtained using the mean of two measurements, obtained through the standardized auscultatory method. Patients were classified according to the VI Brazilian Hypertension Guideline (VI Diretriz Brasileira de Hipertensão).[7] Participants who had a previous diagnosis of hypertension and/or used antihypertensive drugs were considered hypertensive, and those with a previous diagnosis of diabetes mellitus or undergoing treatment with hypoglycemic agents were considered diabetic, according to the consensus of the Brazilian Society of Endocrinology.[8]

The presence of MS was defined according to the criterion of Albert et al., which requires the presence of three or more of the following components: WC > 80 cm; systolic BP > 130 mmHg and/or diastolic BP > 85 mmHg or undergoing pharmacological treatment for arterial hypertension; fasting triglyceride levels > 150 mg/dL or undergoing pharmacological treatment for hypertriglyceridemia; HDL-cholesterol levels < 50 mg/dL or pharmacological treatment; fasting glycemia > 100 mg/dL or pharmacological treatment for hyperglycemia.

The biochemical tests were: fasting glucose, total cholesterol, HDL-cholesterol, triglycerides, urea, creatinine and glycated hemoglobin by the colorimetric method. All examinations were analyzed in the laboratory of Hospital Universitário Materno Infantil of Universidade Federal do Maranhão.

HOMA-IR was also calculated using the formula (insulin mUI/L x blood glucose mmol/L/22.5) to evaluate the insulin resistance (IR) of the participants. As reference values, HOMA-IR > 4.65 was used if Body Mass Index (BMI) was >28.9 kg/m^2 and HOMA-IR > 3.60 if BMI > 27.5 kg/m^2, according to Stern et al.[10]

The collection of anthropometric measures and blood samples after a 12-hour fasting was performed at the same time and according to this sequence.

Statistical analysis

Statistical analysis was performed using Fisher's exact test, Mann-Whitney and chi-square tests. A statistically

significant value of $p < 0.05$ was considered, using the STATA® software, version 12.0

This study is part of a larger project, entitled "Endothelial Dysfunction and Cardiovascular Risk Assessment in Menopausal Women", which was approved by the Research Ethics Committee (REC) of Hospital Universitário da Universidade Federal do Maranhão, under Opinion n. 182/11, according to Resolution 196/96 and its complementary regulations of the National Health Council (CNS/MS).

Results

A total of 150 women were evaluated, 75 in the premenopausal Group I and 75 in the postmenopausal Group II, aged 40 to 59 years, and mean age of 49.6 (± 6.7 years). Metabolic syndrome (MS) was diagnosed in 57 women (38%), of which 24 (32%) were premenopausal and 33 (44%) were postmenopausal women. There was no statistical difference between menopause and MS. When studying the association between MS components and menopausal status, higher mean values of blood pressure (BP), triglycerides, fasting glucose and waist circumference were found, as well as lower values of HDL-cholesterol in group II. The menopausal status was an independent risk factor only for the increase in BP and fasting glycemia (Table 1).

When evaluating the prevalence of IR calculated by the HOMA-IR Index, 28 participants had insulin resistance. In Group I, ten women (13.3%) had IR, while in Group II,

Table 1 – Distribution of metabolic syndrome components, according to the menopausal status, in women treated at a gynecology outpatient clinic. São Luís (MA), Brazil, 2015

Variables	General		Menopausal status				p value
			Premenopausal		Postmenopausal		
	n	%	n	%	n	%	
Arterial hypertension							**0.001***
No	100	66.67	60	80.00	40	53.33	
Yes	50	33.33	15	20.00	35	46.67	
Triglycerides							**0.212**
Normal	45	30.00	26	34.67	19	25.33	
High	105	70.00	49	65.33	56	74.67	
HDL cholesterol							**0.400**
Normal	93	62.00	49	65.33	44	58.67	
Low	57	38.00	26	34.67	31	41.33	
Fasting glucose							**0.031***
Normal	89	59.33	51	68.00	38	50.67	
Altered	61	40.67	24	32.00	37	49.33	
Waist circumference							**0.597**
No risk	47	31.33	25	33.33	22	29.33	
Risk	103	68.67	50	66.67	53	70.67	
Metabolic syndrome							**0.130**
Absent	93	62.00	51	68.00	42	56.00	
Present	57	38.00	24	32.00	33	44.00	

**p < 0.05, chi-square test.*

18 participants (24%) had IR, as shown in table 2. In this analysis, the menopausal status was once again not a direct predictor for the IR presence.

The study also assessed whether IR alone may be considered an independent risk factor for the development of MS and its components in both groups of assessed women. IR was statistically different from the increase in triglycerides and fasting glucose in the premenopausal group.

The study showed the association between the presence of IR and MS in both groups. The IR, calculated by the HOMA-IR index, differed from the statistically significant result in the presence of MS, only in the postmenopausal group, as shown in table 4.

Discussion

The prevalence of MS in women of different populations varies considerably. Differences in genetic profile, eating habits, physical activity level, age and lifestyle influence the prevalence of MS.[11] It is postulated that, among the several risk factors for the syndrome development, menopause is a direct predictor.[12] In our study, the prevalence of MS was 24% in premenopausal women and 44% in the postmenopausal group, with no statistically significant association. Figueiredo Neto et al.,[13] in a study carried out in the State of Maranhão, Brazil, using the National Cholesterol Education Program's (NCEP) criteria, found a prevalence of 24% in premenopausal women and 44.4% in postmenopausal ones, also without a statistically significant association. As for the study carried out by Ali et al.,[14] in Tunisia, with 2,680 women between 2004 and 2005, using NCEP criteria, they found a prevalence of 25.6% and 45.7% in the pre- and postmenopausal groups, respectively, with the menopausal status being an independent risk factor for the development of MS.

In our study, we evaluated the prevalence of MS components and the possible association with menopausal status. Among them, the most frequent in both groups was the increase in triglycerides, with a prevalence of 65.3% and 74.6% in the pre- and postmenopausal groups, respectively. After that, the increase in the waist circumference was the most often observed, with a frequency of 66.6% in the premenopausal period and 70.6% in the postmenopausal one. However, neither showed a statistical association with menopausal status. Cho et al.,[15] in a study carried out in South Korea, with 1,003 women, identified the increase in WC and the reduction in HDL-cholesterol as the most prevalent components of premenopausal MS, reaching 46.1% and 22.5%; respectively. In the postmenopausal period, the increase in WC was the most common (78.9%), followed by an increase in BP (40.6%).[15] Arthur et al.,[16] in a study carried out with African women, using the International Diabetes Federation (IDF) criteria, identified as the most prevalent factors in the premenopausal group the increase in WC (79%) and in BP (49.7%). Jouyandesh et al.,[17] based on the National Cholesterol Education Program – The Adult Treatment Panel III (NCEP-ATP III), studying 118 postmenopausal women from January 2011 to January 2012 at a clinic for menopause follow-up, found as the most prevalent components, once again, an increase in WC (64.3%) and BP (47.9%).[17] However, the authors suggest that the frequencies observed in the prevalence of MS components may vary among populations due to environmental, nutritional, economic and genetic diversity, characteristic of women in each area.

Table 2 – Prevalence of overall insulin resistance and according to the menopausal state in women treated in a Gynecology Outpatient Clinic. São Luís (MA), Brazil, 2015

Insulin resistance	General		Menopausal status				p value
			Premenopausal		Postmenopausal		
	n	%	n	%	n	%	
Absent	122	81.33	65	86.67	57	76.00	0.094
Present	28	18.67	10	13.33	18	24.00	

** $p < 0.05$, chi-square test.*

Table 3 – Statistically significant difference between HOMA-IR and metabolic syndrome and its components, according to menopausal status in women treated in a Gynecology Outpatient Clinic. São Luís (MA), Brazil, 2015

Variables	Premenopausal		Postmenopausal	
	HOMA-IR	p value*	HOMA-IR	p value*
	Mean ± Standard deviation		Mean ± Standard deviation	
Metabolic syndrome				
Absent	2.17 ± 1.15	0.1294	2.62 ± 1.77	0.0025*
Gift	3.16 ± 2.45		4.64 ± 3.27	
HDL cholesterol				
Normal	2.33 ± 1.32	0.7426	2.72 ± 1.76	0.0114*
Low	2.78 ± 2.30		4.39 ± 3.40	
Blood Pressure				
Normal	2.17 ±1.10	0.1751	3.04 ± 2.02	0.2470
Altered	3.20 ± 2.54		3.76 ± 3.15	
Waist circumference				
Normal	2.01 ± 1.28	0.0835	2.89 ± 2.45	0.0871
Cardiovascular risk	2.73 ± 1.87		3.63 ± 2.76	
Triglycerides				
Normal	1.65 ± 1.00	0.0001*	2.89 ± 2.28	0.2073
High	2.93 ± 1.86		3.59 ± 2.79	
Fasting glucose				
Normal	1.92 ± 1.02	< 0.0001*	2.73 ± 1.76	0.0531
Altered	3.69 ± 2.25		4.12 ± 3.24	

** p < 0.05, chi-square test.*

Furthermore, when we evaluated the association between the MS components and the menopausal status, we observed that the occurrence of menopause was considered an independent risk factor for the increase of both BP and blood glucose levels. Kim et al.[18], when studying 3,219 Korean women, found a statistically significant association only between the following syndrome components: WC, BP and triglycerides. Linet al.,[19] in a study developed in the northern region of Taiwan, with 597 women, based on NCEP criteria, demonstrated that menopause is a direct predictor for the development of four of the five MS components, including: WC, BP, triglycerides and HDL-cholesterol. Again, the authors believe that the divergent associations found in their study are consequences of the genetic, socioenvironmental and sociocultural differences of the studied populations.

It is known that MS has IR among its pathophysiological bases,[20] but for some time, the influence of menopause has been discussed on the onset of insulin resistance. To date, literature data are unclear regarding whether menopause is associated with increased IR, but evidence indicates that the role of aging and body fat redistribution (central adiposity) in IR increase in postmenopausal women is well established.[21] This study evaluated the presence of IR through the HOMA-IR index in pre- and postmenopausal women, as well as the association between the MS components with the HOMA-IR value, observing a

Table 4 – Association between insulin resistance and metabolic syndrome in premenopausal and postmenopausal women treated in a Gynecological Outpatient Clinic. São Luís (MA), Brazil, 2015.

Insulin Resistance	Premenopausal				p value*	Postmenopausal				p value
	Metabolic syndrome					Metabolic syndrome				
	Absent		Present			Absent		Present		
	n	%	n	%		n	%	n	%	
Absent	46	90.20	19	79.17	0.190	39	92.86	18	54.55	< 0.001†
Present	5	9.80	5	20.83		3	7.14	15	45.55	

** chi-square test; † p < 0.05 Fisher's exact test.*

prevalence of IR in 13.3% premenopausal and 24% postmenopausal women, with no statistically significant association. Lejsková et al.,[22] studying 909 pre- and postmenopausal women in the Czech Republic, found a slight increase in HOMA-IR values after menopause, but no significant association with menopausal status. These findings are corroborated by the study by Toth et al.,[23] which evaluated the association between menopausal status and insulin sensitivity through the direct and more reliable method to evaluate IR – the glycemic clamp – and demonstrated that menopause is not an independent risk factor for the development of IR.

The presence of IR was associated with the development of MS in the pre- and post-menopause, and it was observed that IR behaved as a direct predictor of MS only in the group of women who had already undergone the menopausal transition. This observation is consistent with what was found in the Czech study carried out by Lejsková et al.[22]. However, in a European study, the association occurred only in those women who already had a high HOMA-IR index in the reproductive period. These findings indicate that the menopausal transition alone did not result in an IR increase, and that the IR only determined MS in postmenopausal women.

This thesis is reinforced by the finding of Manco et al.[24] study, carried out in several European countries, with 523 participants, which analyzed IR in men and women of different ages. They observed that IR proportionally increases in both genders from middle age on, suggesting that menopause does not significantly affect IR.[24]

Among the components of the MS, the association with IR occurs in the premenopausal period only with elevated triglyceride levels and with altered glycemic levels. In the postmenopausal period, IR is an independent risk factor only for the reduction of HDL-cholesterol. No similar data were found in the recent articles on MS and IR for the studied population.

This study had as limitation a non-probabilistic sample with a relatively small number of assessed individuals, and further studies with larger sample sizes are necessary.

Conclusion

In the analyzed sample, menopause was not considered a risk factor for the development of metabolic syndrome, as well as for insulin resistance. However, the menopausal status was shown to be an independent risk predictor for fasting blood glucose and blood pressure components.

Insulin resistance was considered a risk factor for the development of metabolic syndrome only in the postmenopausal period.

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Author contributions

Conception and design of the research: Fonseca EJNC, Figueredo Neto JA. Acquisition of data: : Fonseca EJNC, Silva BL, Figueredo Neto JA, Rocha TPO, Melo JB, Andrade MVG, Sousa SMB, Lopes EJ, Lopes EJ. Analysis and interpretation of the data: Fonseca EJNC, Serra CB, Figueredo Neto JA. Statistical analysis: Fonseca EJNC, Nogueira IAL, Figueredo Neto JA. Obtaining financing: Fonseca EJNC, Nogueira IAL, Figueredo Neto JA, Melo JB. Writing of the manuscript: Fonseca EJNC, Figueredo Neto JA. Critical revision of the manuscript for intellectual content: Fonseca EJNC, Nogueira IAL, Figueredo Neto JA, Rocha TPO.

Potential Conflict of Interest

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

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Study Association

This article is part of the thesis of master submitted by Érika Joseth Nogueira da Cruz Fonseca, from Universidade Federal do Maranhão.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Hospital Universitário da Universidade Federal do Maranhão under the protocol number 005900/2011-00. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

References

1. Gold EB, Crawford SL, Avis NE, Crandall CJ, Matthews KA, Waetjen LE, et al. Factors related to age at natural menopause: longitudinal analyses from SWAN. Am J Epidemiol. 2013;178(1):70-83. doi: 10.1093/aje/kws421.
2. Instituto Brasileiro de Geografia e Estatística (IBGE). Síntese de indicadores sociais: uma análise das condições de vida da população brasileira. [Internet]. 2010. [Acesso em 2015 jul 16]. Disponível em: http:www.ibge.gov.br/home/estatistica/populacao/condicoesde vida/indicadoresminimos/sinteseindicsociais2010/SIS_2010.pdf.3
3. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Clement JI, Donato KA, 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(16):1640-5. doi: 10.1161/CIRCULATIONAHA.109.192644.
4. Gobato AO, Vasques AC, Zambon MP, Barros Filho AA, Hessel G. Metabolic syndrome and insulin resistance in obese adolescents. Rev Paul Pediatr. 2014;32(1):55-62. doi: http://dx.doi.org/10.1590/S0103-05822014000100010.
5. Vasques AC, Rosado LH, Alfenas RC, Geleneze B. Critical analysis on the use of the homeostasis hodel assessment (HOMA) indexes in the evaluation of the insulin resistance and the pancreatic beta cells functional capacity. Arq Bras Endocrinol Metab. 2008;52(1):32-9. doi: http://dx.doi.org/10.1590/S0004-27302008000100006.
6. Lainscak M, Haehling S, Anker SD. Natriuretic peptides and other biomarkers in chronic heart failure: from BNP, NT-pró BNP, and MR-pro ANP to routine biochemical markers. Int J Cardiol. 2009;132(3):303-11. doi: 10.1016/j.ijcard.2008.11.149.
7. Sociedade Brasileira de Cardiologia; Sociedade Brasileira de Hipertensão; Sociedade Brasileira de Nefrologia. [VI Brazilian Guidelines on Hypertension]. Arq Bras Cardiol. 2010;95(1 Suppl):1-51. PMID: 21085756. Erratum in: Arq Bras Cardiol. 2010;95(4):553.
8. Sociedade Brasileira de Diabetes.. Diagnóstico e classificação do Diabetes Mellitus do tipo 2. Consenso Brasileiro sobre Diabetes. [Acesso em 2015 jan 10]. Disponível em: http://www.c:/bvs/editavles/pdf/consensoSBD.doc.
9. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia. 1985;28(7):412-9. PMID: 3899825.
10. Stern SE, Williams K, Ferrannini E, DeFronzo RA, Bogardus C, Stern MP. Identification of individuals with insulin resistance using routine clinical measurements. Diabetes. 2005;54(2):333-9. PMID: 15677489.
11. Allal-Elasmi M, Taieb SH, Hsairi M, Zayani Y, Omar S, Sanhaji H, et al. The metabolic syndrome: prevalence, main characteristics and association with socio-economic status in adults living in Great Tunis. Diabetes Metab. 2010;36(3):204-8. doi: 10.1016/j.diabet.2009.11.009.
12. Mendes KG. Estado menopáusico e síndrome metabólica em mulheres no climatério atendidas em um ambulatório no Sul do Brasil [Dissertação]. Porto Alegre: Universidade Federal do Rio Grande do Sul; 2012.
13. Figueiredo Neto JA, Figueiredo ED, Barbosa JB, Barbosa Fde F, Costa GR, Nina VJ, et al. Metabolic syndrome and menopause: cross-sectional study in gynecology clinic. Arq Bras Cardiol. 2010;95(3):339-45. doi: http://dx.doi.org/10.1590/S0066-782X2010005000094.
14. Ali SB, Belfki-Benali H, Aounallah-Skhiri H, Traissac P, Maire B, Delpeuch F, et al. Menopause and metabolic syndrome in Tunisian women. BioMed Research International. 2014; Article ID 457131, 7 pages. doi: https://dx.doi.org/10.1155/2014/457131.
15. Cho GJ, Lee JH, Park HT, Shin JH, Hong SC, Kim T, et al. Postmenopausal status according to years since menopause as an independent risk factor for the metabolic syndrome. Menopause. 2008;15(3):524-9. doi: 10.1097/gme.0b013e3181559860.
16. Arthur FK, Adu-Frimpong M, Osei-Yeboah J, Mensah FO, Owusu L. The prevalence of metabolic syndrome and its predominant components among pre-and postmenopausal Ghanaian women. BMC Res Notes. 2013 Nov 8;6:446. doi: 10.1186/1756-0500-6-446.
17. Jouyandeh Z, Nayebzadeh F, Qorbani M, Asadi M. Metabolic syndrome and menopause. J Diabetes Metab Disord. 2013;12(1):1. doi: 10.1186/2251-6581-12-1

18. Kim HM, Park J, Ryu SY, Kim J. The Effect of menopause on the metabolic syndrome among Korean women: the Korean National Health and Nutrition Examination Survey, 2001. Diabetes Care. 2007;30(3):701-6. doi: 10.2337/dc06-1400.

19. Lin WY, Yang WS, Lee LT, Chen CS, Liu CS, Lin CC, et al. Insulin resistance, obesity and metabolic syndrome among non-diabetic pre and post-menopausal women in North Taiwan. Int J Obes (Lond). 2006;30(6):912-7. doi: 10.1038/sj.ijo.0803240.

20. Meirelles RM. Menopause and metabolic syndrome. Arq Bras Endocrinol Metab. 2014;58(2):91-6. doi: http://dx.doi.org/10.1590/0004-2730000002909.

21. Jou HJ, Huang HT. Metabolic syndrome: menopausal women and the health care challenge. Taiwan J Obstet Gynecol. 2009;48(3):205-9. doi: 10.1016/S1028-4559(09)60291-6. Erratum in: Taiwan J Obstet Gynecol. 2009;48(4):453.

22. Lejsková M, Alusík S, Suchánek M, Zecová S, Pitha J. Menopause: cluestering of metabolic syndomecomponentes and population changes in insulin resistance. Climateric. 2011;14(1):83-91. doi: 10.3109/13697131003692745.

23. Toth MC, Sites CK, Eltabbakh GH, Poehlman ET. Effect of menopausal status on insulin-stimulated glucose disposal. Diabetes Care. 2000;23(6):801-6. PMID: 10841000.

24. Manco M, Nolfe G, Calvani M, Natali A, Nolan J, Ferrannini E, et al; European Group for the Study of Insulin Resistance. Menopause, insulin resistance and risk factor for cardiovascular disease. Menopause. 2006;13(5):809-817. doi: 10.1097/01.gme.0000233492.38638.74.