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Factors associated with the severity of menopausal symptoms in postmenopausal Brazilian women

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ABSTRACT

Purposes: To identify the socio-demographic and anthropometric profile and correlate them with the severity of menopausal symptoms in postmenopausal women.**Methods:** Cross-sectional study with 201 postmenopausal women attended in a Gynecology Outpatient Department in Rio de Janeiro city (RJ, Brazil). A questionnaire was applied for collection of demographic, socioeconomic, clinical and lifestyle variables. The Blatt-Kupperman Menopausal Index was used to evaluate the menopausal symptoms.**Results:** Women with moderate to severe symptoms (≥ 20) corresponded to 57.7% (116) of the sample. Obesity was not associated with the severity of menopausal symptoms ($p < 0.90$). Severe to moderate symptoms were inversely associated with age (PR 0.96; CI 95% 0.94–0.99; $p < 0.01$). Women within 6–10 years of menopause presented nearly 1.4 times higher prevalence of moderate to severe symptoms compared with those with more than 10 years of menopause. Unemployed women (PR 1.52; CI 95% 1.13–2.04; $p < 0.01$) and housewives (PR 1.53; CI 95% 1.12–2.09; $p < 0.01$) presented higher prevalence of menopausal symptoms compared with working women. Tobaccoism was associated with higher prevalence of moderate to severe symptoms ($p < 0.01$).**Conclusions:** Age constituted a protection factor for moderate to severe symptoms, whereas having within 6–10 years of menopause, smoking and being unemployed or a housewife were factors related to higher prevalence of moderate to severe menopausal symptoms.

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Fatores associados com a intensidade dos sintomas menopausais em mulheres brasileiras na pós-menopausa

RESUMO

Objetivo: Identificar o perfil sociodemográfico e antropométrico e associá-los com a intensidade dos sintomas menopausais em mulheres na pós-menopausa.

Palavras-chave:

Intensidade dos sintomas menopausais

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Fatores de risco
Sinais e sintomas
Sintomas menopausais

Métodos: Estudo transversal com 201 mulheres na pós-menopausa atendidas em um ambulatório de ginecologia no Rio de Janeiro/RJ. Foi aplicado um questionário para coleta das variáveis demográficas, socioeconômicas, clínicas e hábitos de vida. O Índice Menopausal de Blatt-Kupperman (IMBK) foi utilizado para avaliar os sintomas menopausais.

Resultados: Mulheres com sintomas moderados a grave (≥ 20) corresponderam a 57,7% (116) da amostra. A obesidade não foi associada com a intensidade de sintomas menopausais ($p < 0,90$). Os sintomas moderados a intensos associaram-se inversamente com a idade (RP 0,96; IC95% 0,94–0,99; $p < 0,01$). Mulheres com tempo de menopausa entre 6 e 10 anos apresentaram cerca de 1,4 vezes maior prevalência de sintomas moderados a intensos quando comparadas com aquelas com mais de 10 anos de menopausa. Mulheres desempregadas (RP 1,52; IC95% 1,13–2,04; $p < 0,01$) e donas de casa (RP 1,53; IC95% 1,12–2,09; $p < 0,01$) apresentaram maior prevalência de sintomas menopausais quando comparadas com mulheres trabalhando. O tabagismo foi associado a maior prevalência de sintomas moderados a intensos ($p < 0,01$).

Conclusões: A idade constituiu fator de proteção para sintomas moderados a intensos. Enquanto que ter entre 6 à 10 anos de tempo de menopausa, ser tabagista e ser desempregada ou dona de casa foram fatores associados a uma maior prevalência de sintomas menopausais moderados a intensos.

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Introduction

Menopause is an event that marks the end of the reproductive phase of a woman. This condition is caused by the reduction of the ovarian function, with gradual decrease of female sexual hormones leading to menstrual cycle interruption. The period after the definite interruption of menstruation, in other words, after the absence of menstrual cycles for twelve consecutive months is characterized by post-menopause.¹ This period, for times, is accompanied by vasomotor, psychological and urogenital symptoms, besides metabolic and cardiovascular alterations, like osteoporosis, cardiovascular diseases and alterations in the distribution of physical fat.²⁻⁴

In Brazil, changes in morbidity and mortality patterns from infectious diseases to chronic non-communicable diseases, along with life expectancy increase, have brought an important impact to questions related to female aging.⁵ Nearly 28% of women (24.3 million) are aged 40 years and older in Brazil and, in the city of Rio de Janeiro the female population estimate of 2010 was 3.09 million women, of which 34.1% were in the age group 40–64 years.⁶ Menopause typically occurs between 45 and 55 years of age, and woman life expectancy is around 70 years. Therefore, the post-menopause period corresponds to around 1/3 of a woman's lifespan.⁷

The severity of menopausal symptoms compromise daily life activities and social life; thus, impairing quality of life and negatively impacting on public health.⁸ Menopausal symptoms may vary in frequency and severity.⁹ Therefore some studies have investigated factors that can be associated with the severity of these symptoms, such as age^{8,10} menopausal stage,¹¹⁻¹³ socioeconomic aspects,^{8,12} lifestyle,^{8,12,14,15} chronic conditions and comorbidities^{12,14,16-18}; but some findings are conflicting between studies.

Due to the conflicting evidences in the literature, further studies that investigate possible predictor factors to the severity of menopausal symptoms in postmenopausal

women are necessary. This information is important so that health professionals can intervene more appropriately and specifically.¹⁹ Thus, the objective of the present study was to identify the socio-demographic and anthropometric profile and associate it with the severity of menopausal symptoms in postmenopausal women attended in the Gynecology Outpatient Department (Oswaldo Cruz Foundation, FIOCRUZ, Rio de Janeiro, RJ, Brazil).

Methods

This is a cross-sectional study. The study was approved by the Research Ethics Committee of the National Institute of Women, Children and Adolescents Health Fernandes Figueira (IFF), Oswaldo Cruz Foundation (FIOCRUZ, RJ, Brazil) and performed in a reference Gynecology Outpatient Department in Rio de Janeiro city. The data collection period was August to December/2013. The study population was constituted by postmenopausal women attended by the subspecialties of urogynecology, general gynecology and reproductive endocrinology in the above-mentioned outpatient department.

Women aged between 45 and 65 years and without menstrual periods for 12 consecutive months or more (post-menopausal period) were included in the study. Women who were taking hormone replacement therapy (HRT) or had interrupted this treatment for less than 12 months, submitted to chemotherapy or radiotherapy due to cancer, to bilateral oophorectomy or presented decompensated hypothyroidism and/or Cushing's disease, or clinical history of premature menopause, i.e. menstrual cycle interruption earlier than 40 years of age¹⁷ were excluded from the study. Laboratorial tests (Thyroid-Stimulating Hormone, TSH; Free Thyroxine, free T4 and Follicle-Stimulating Hormone, FSH) were requested for all study participants, for eligibility purposes. Decompensated hypothyroidism was characterized

when TSH and free T4 test results were outside of the reference values (9–20 pmol/L for free T4 and 0.25–5 mcgUI/mL for TSH), using enzyme-linked fluorescence assay (ELFA, VIDAS® commercial kit, Biomérieux AS, Brazil). Women who presented FSH \leq 40 mUI/mL were excluded from the study, as recommended by the Ministry of Health.⁵ Tests were performed at the IFF/FIOCRUZ laboratory. All results were transferred to the patients' records.

All women in the waiting room with booked appointments to the studied subspecialties and who were eligible for the study were invited to participate in the study. After acceptance in the study, the women were directed to an individual room, local service where they were handed the Informed Consent form, in accordance with Resolution 466/2012 of the National Council of Health (Ministry of Health, Brazil), so that participants could show their agreement as for the participation in the study. In the same place, a closed-ended questionnaire for collection of demographic, socioeconomic, clinical and lifestyle variables (named clinical record), and the Blatt-Kupperman Menopausal Index for evaluation of menopausal symptoms were applied.

The Blatt-Kupperman Menopausal Index is used to evaluate the severity of symptoms through eleven questions that include somatic and psychological symptoms. Each symptom is evaluated as absent (0), mild (1), moderate (2) and severe (3). For this study, the severity of symptoms was scored as <20 absent to mild and ≥ 20 moderate to severe.^{10,14,20,21}

As to physical activity, women were classified as active (very activate and active) and sedentary (irregularly active A, irregularly active B and sedentary) according to the International Physical Activity Questionnaire (IPAQ-c).^{22,23}

After filling out the clinical record, the weight (kg) was measured in a digital scale (model LD1050, Líder, Brazil), with INMETRO certification (N. 7.217.026-6). The height (cm) was measured using a wall-mounted stadiometer (Wiso, Brazil) respecting the Frankfurt plane position.²⁴ The body mass index (BMI) was calculated using the formula: $\frac{\text{Weight}}{\text{Height}^2}$ (kg/m²). Results were classified as eutrophic (BMI 18.5–24.9), overweight (BMI 25.0–29.9) and obese (BMI \geq 30.0).²⁵

The waist to hip ratio (WHR) was obtained by measuring the waist circumference (WC) (tape measure positioned at midway distance between the last floating rib and the iliac crest)²⁶ and the hip circumference (HC) (tape measure positioned at the largest gluteal area).²⁷ WC and HC were double-checked and the arithmetic mean was registered in the database. The used cutoff value was ≥ 0.80 for women, which indicated cardiovascular risk.²⁷

It was verified that 748 women attended in the outpatient gynecology department in the studied period were aged 45–65 years; 332 women reported having menstrual cycle, 53 were currently taking HRT, 46 reported having done chemotherapy/radiotherapy due to cancer, 24 had early menopause, 37 performed bilateral oophorectomy and 40 refused to participate in the study. A total of 216 women were recruited, and one woman was evaluated more than once because she was attended on different days and in different subspecialties. Twelve women had FSH \leq 40 mUI/mL, two did not show up for the laboratorial tests; consequently, fifteen women were excluded from the study for ineligibility.

Statistical analysis

When normality was not verified, results were expressed as median, minimum and maximum values. Chi-square test was used to determine statistical significance of associations between categorical variables. Fisher's exact test was applied if at least one expected frequency below five was observed. Mann-Whitney test was used to investigate statistically significant differences between averages. Variables that presented *p*-value lower than 0.20 were included in the Poisson regression model. The statistical significance level was 5%. The software programs used for analysis of data were SPSS, version 20 and R, version 3.0.2.

Results

During the study period, 748 women aged 45–65 years were attended in the gynecology outpatient department. Of this total, 28.9% (216) met the inclusion criteria and 93% (201) of them participated in the study. More than 57% (116) of women reported moderate to severe symptoms (≥ 20).

It was observed that the median age (57.0) of the group with more severe symptoms was lower than the median age of the group with absent or mild symptoms (59.0) ($p < 0.01$). Around 2/3 of the women who were within 6–10 years of menopause (68.5%) reported moderate to severe symptoms, whereas less than half of women with more than 10 years of menopause reported the same severity of symptoms (47.8%), [Table 1](#). There was no statistically significant difference between schooling and severity of menopausal symptoms. The same fact occurred for marital status, and income.

The prevalence of women with moderate to severe symptoms who smoked (79.2%) was higher when compared with those who were non-smokers (51.9%, $p < 0.01$, [Table 1](#)).

Most women participating in the study were obese (39.8%) and 56.2% of them reported moderate to severe symptoms. It was also verified that more than 60% of eutrophic women reported moderate to severe symptoms, presenting no statistically significant difference. High prevalence of cardiovascular risk was observed, given that more than 95% of women presented WHR ≥ 0.80 and a little less than 3/5 of them presented moderate to severe menopausal symptoms ($p = 0.15$).

The prevalence of different types of moderate to intense menopausal symptoms is in [Table 2](#). It was found that among these complaints arthralgia/myalgia was the most reported symptom among women studied with 62.7% prevalence, followed nervousness with 59.7% and hot flashes with 50.7%. And the least reported symptoms were dizziness (18.9%) and tinnitus (19.4%).

After the multivariate analysis, it could be observed that the moderate to severe menopausal symptoms were inversely associated with age (PR 0.96; CI 95% 0.94–0.99; $p < 0.01$). Women who were within 6–10 years of menopause presented nearly 1.4 times higher prevalence of moderate to severe symptoms when compared with those with more than 10 years after menopause ($p < 0.03$). Unemployed women (PR 1.52; CI 95% 1.13–2.04; $p < 0.01$) and housewives (PR 1.53;

Table 1 – Patient characteristics and prevalence of moderate or severe menopausal symptoms in postmenopausal women attended in a Gynecology Outpatient Department from August to December/2013 (n = 201).

| Variables | % | n | Prevalence of moderate to severe symptoms % | n = 116 | p-Value |
|------------------------------|---------------|-----|---|---------|---------|
| Age ^{a,b} | 57.00 [45–65] | | 57.00 [45–65] | | <0.01 |
| Marital status | | | | | 0.67 |
| Single | 15.4 | 31 | 54.8 | 17 | |
| Divorced | 11.9 | 24 | 54.2 | 13 | |
| Widow | 11.4 | 23 | 69.6 | 16 | |
| Married | 61.2 | 123 | 56.9 | 70 | |
| Schooling years ^a | | | 8.00 [0–17] | | 0.18 |
| 0–5 | 34.8 | 70 | 67.1 | 47 | 0.23 |
| 6–9 ^a | 29.9 | 60 | 50 | 30 | |
| 10–11 ^a | 29.9 | 60 | 55 | 33 | |
| 12–17 | 5.5 | 11 | 54.5 | 6 | |
| Occupation ^a | | | | | <0.01 |
| Unemployed ^a | 13.4 | 27 | 81.5 | 22 | |
| Retired | 19.9 | 40 | 50 | 20 | |
| Housewife ^a | 13.9 | 28 | 71.4 | 20 | |
| Working | 52.7 | 106 | 50.9 | 54 | |
| Per capita income | | | | | 0.17 |
| 0–1 | 61.8 | 123 | 62.6 | 77 | |
| 1–2 | 27.6 | 55 | 52.7 | 29 | |
| ≥2 | 10.6 | 21 | 42.9 | 9 | |
| BMI | | | | | 0.90 |
| Eutrophic | 22.9 | 46 | 60.9 | 28 | |
| Overweight | 37.3 | 75 | 57.3 | 43 | |
| Obese | 39.8 | 80 | 56.2 | 45 | |
| WHR ≥ 0.80 ^a | 97.0 | 195 | 57.9 | 113 | 0.15 |
| Pregnancies ^a | 3.0 [0–21] | | 3.00 [0–8] | | 0.02 |
| Menopause time ^b | | | 7.00 [1–25] | | 0.31 |
| 1–5 years ^a | 39.8 | 80 | 58.8 | 47 | 0.07 |
| 6–10 years ^a | 26.9 | 54 | 68.5 | 37 | |
| >10 years | 33.3 | 67 | 47.8 | 32 | |
| Smoking ^a | | | | | 0.04 |
| Yes ^a | 11.9 | 24 | 79.2 | 19 | |
| No | 52.7 | 106 | 51.9 | 55 | |
| Ex | 35.3 | 71 | 59.2 | 42 | |
| Alcohol consumption | | | | | 0.75 |
| Yes | 28.4 | 57 | 59.6 | 34 | |
| No | 71.6 | 144 | 56.9 | 82 | |
| Physical activity | | | | | 0.25 |
| Active | 43.3 | 87 | 52.9 | 46 | |
| Sedentary | 56.7 | 114 | 61.4 | 70 | |

Source: Study data, 2014.

MS, metabolic syndrome; BMI, body mass index; WHR, waist to hip ratio.

Data are expressed as median [min–max] or percentages %.

^a p-Value found in univariate regression analyses was <0.20.

^b Mann-Whitney test; Chi-square test was used to check statistical significance of associations between categorical variables.

CI 95% 1.12–2.09; $p < 0.01$) presented higher prevalence of menopausal symptoms compared with working women. And finally, the prevalence of women who smoke presenting moderate to severe symptoms was 1.45 times higher than in non-smokers (PR 1.45; CI 95% 1.10–1.90; $p < 0.01$), Table 3.

Discussion

It was verified that age was a protection factor for moderate to severe symptoms. In the study of De Lorenzi and collaborators, it was noticed that the obtained score decreased

Table 2 – Prevalence of moderate or severe menopausal symptoms in postmenopausal women attended in a Gynecology Outpatient Department from August to December/2013 (n = 201).

| Symptoms | Moderate to severe % (n) |
|-----------------------------|--------------------------|
| Arthralgias/myalgias | 62.7% (126) |
| Nervousness | 59.7% (120) |
| Hot flushes | 50.7% (102) |
| Insomnia/sleep disturbances | 47.3% (95) |
| Depressive mood/melancholia | 30.3% (61) |
| Paresthesia | 30.3% (61) |
| Weakness (fatigue) | 43.3% (87) |
| Cephalaea | 27.9% (56) |
| Palpitations | 26.4% (53) |
| Tinnitus | 19.4% (39) |
| Dizziness | 18.9% (38) |

Source: Study data, 2014.

Table 3 – Factors associated with moderate to severe menopausal symptoms (BKMI ≥ 20) in postmenopausal women attended in a Gynecology Outpatient Department from August to December/2013. Data were submitted to multiple regression analysis.^a

| Variables | PR adjusted (CI 95%) | p-Value ^a |
|------------------------|----------------------|----------------------|
| Age | 0.9 (0.94–0.99) | 0.01 |
| Menopause time | | |
| 1–5 years | 1.1 (0.80–1.54) | 0.55 |
| 6–10 years | 1.4 (1.04–1.89) | 0.03 |
| >10 years | 1.00 | – |
| Number of pregnancies | 1.0 (0.99–1.09) | 0.10 |
| Schooling | | |
| 0–5 years | 1.00 | – |
| 6–9 years | 0.8 (0.58–1.07) | 0.12 |
| 10–11 years | 0.8 (0.66–1.11) | 0.24 |
| 12–17 years | 0.9 (0.51–1.48) | 0.60 |
| Occupation | | |
| Unemployed | 1.5 (1.13–2.04) | 0.01 |
| Retired | 1.1 (0.78–1.57) | 0.56 |
| Housewife | 1.5 (1.12–2.09) | 0.01 |
| Working | 1.00 | – |
| Per capita income | | |
| 0–1 minimum wage | 1.00 | – |
| 1–2 minimum wages | 1.00 (0.75–1.33) | 0.99 |
| ≥ 2 minimum wages | 0.9 (0.54–1.52) | 0.70 |
| Smoking | | |
| Yes | 1.6 (1.10–1.90) | 0.01 |
| No | 1.00 | – |
| Ex | 1.1 (0.84–1.40) | 0.52 |
| Waist to hip ratio | 4.8 (0.87–26.35) | 0.07 |

Source: Study data, 2014.

PR, prevalence ratio; CI 95%, confidence interval at 95%.

^a Adjusted for age, menopause time, number of pregnancies, schooling, occupation, per capita income, tobaccoism and WHR.

as age increased, but significant statistical relation was not demonstrated.⁸ Differently from this finding, another study demonstrated that women aged 60 years and older had around 0.38 times less chance of presenting moderate to severe climacteric symptoms, reinforcing that older women reported fewer menopausal symptoms compared with younger women.¹⁰ It is possible to infer that most women aged 56 years and older at the present study were more than 10 years past menopause, perhaps explaining the fact that in this study younger women reported higher severity of symptoms.

It was observed that the prevalence of women with moderate to severe symptoms within 6–10 years of menopause was 1.4 times higher than among those with more than 10 years past menopause. In another study, significant statistical difference was not observed regarding time after menopause and moderate to severe symptoms, but there is methodological difference between data collection of the studies.¹⁴ In a study developed in Brazil, it was noticed that menopausal symptoms tended to reduce with time after menopause, except for arthralgia, myalgia and insomnia, perhaps for being associated with aging.¹⁸ In this study it was found that the arthralgia/myalgia was the most prevalent complaint among moderate to severe symptoms, which may be an explanation for the peak of symptoms to be between 6 and 10 years of menopause time. Postmenopause is divided into early postmenopause and late postmenopause, considering early postmenopause as the first five years after the onset of menopause.²⁸ The time of onset of menopause can directly influence the severity of menopausal symptoms, since after some years of menopause, hormonal stability occurs, leading to reduction or absence of symptoms that previously impaired quality of life.²⁹

It was also noticed that the prevalence of unemployed women or housewives with moderate to severe symptoms was nearly 50% higher than that observed in women who worked at the time of the study. Such a fact was not verified in a study that aimed at indicating factors associated with menopausal symptoms.⁸ A higher prevalence of neuropsychiatric symptoms during postmenopause suggests that this finding can be explained by the negative perception of aging and feeling of inutility, which is a difficult condition for women.³⁰ The interpretation of the results that correlate occupation and severity of menopausal symptoms is difficult in this case, as this is a cross-sectional design, in which there is possibility of reverse causality, characterizing a limitation of the present study.

Regarding lifestyle, women who smoke presented higher prevalence of moderate to severe symptoms, corroborating previous studies, such as that of Pérez et al., who verified that women who smoked presented 1.92 more chances to report more severe symptoms compared with women who did not smoke.³¹ Smoking has been previously associated with menopausal symptoms.^{32–34} Studies show low estrogen levels, specifically estradiol and estrone in women who smoke compared with non-smokers.³⁵ Nicotine interferes with the estrogen binding globulin and accelerates the follicular atresia process, anticipating the onset of menopause, besides aggravating the mentioned symptoms.⁸

In the present study associations between physical activity and severity of menopausal symptoms were not observed,

however several studies demonstrate that regular physical activity has a protective effect, reducing the occurrence of postmenopausal symptoms.^{8,15,36}

In the multivariate analysis, a borderline p -value ($p < 0.07$) was found for the association between $WHR \geq 0.80$ and prevalence of moderate to severe symptoms. In the study of Paolillo et al., a statistically significant association was observed ($p < 0.05$) between $WHR > 0.80$ and higher scores for somatic and urogenital symptoms.⁴

Regarding BMI, significant statistical associations were not observed with severity of menopausal symptoms. Several studies have investigated this correlation, showing conflicting results. In 2005, De Lorenzi et al. observed no statistically significant difference between obesity and severity of menopausal symptoms.⁸ Another study in 2007 confirmed this finding.¹⁶ In 2010, Fernandez-Alonso using different cutoff points to diagnose obesity, demonstrated that obese women presented 3.35 times more chances to present moderate to severe symptoms compared with non-obese women ($p < 0.01$).¹⁴ A recent Brazilian study demonstrated that obese women reported more symptoms than non-obese women. It was also particularly observed that obese women reported more severe vasomotor symptoms, which are hypoestrogenism-related symptoms.¹⁸ Theoretically, women with higher BMI, had less severe vasomotor symptoms due to the increased estrogen levels via peripheral conversion of androstenedione.¹⁸ Nevertheless, some studies have shown that actions of adipose tissue, such as thermal isolation, produce higher body temperatures and result in increased vasomotor symptoms, being a possible explanation for association between severe climacteric symptoms and higher BMI.^{14,18}

The obtained results evidenced a high prevalence of women with some type of postmenopausal symptom and more than half with moderate to severe symptoms. Our findings suggest that age constituted a protection factor, having within 6–10 years of menopause, being smoker and unemployed or housewife are factors associated with severity of menopausal symptoms. Associations between severity of symptoms and physical activity were not observed, indicating a possible limitation in the measurement of this variable in the present study, as evaluation of practice of physical exercises would be necessary.

The questionnaire used to evaluate the menopausal symptoms was not submitted to a formal validation process in Brazil, representing another limitation of the study. In addition, due to the cross-sectional study design, it was difficult to establish causal relations. However, this questionnaire was chosen because of its broad clinical applicability and for being the questionnaire recommended by the Brazilian Federation of Gynecology and Obstetrics (FEBRASGO), in addition to already be used in the clinic for routine medical records. Another limitation of the study, refers to the recruitment of patients have been just the gynecology outpatient clinic, as this article was part of the results of the dissertation of an author, with the search field the gynecology outpatient clinic.

Further studies are of great importance to verify possible predicting factors of menopausal symptoms, in order to allow the increase of preventive actions and therapeutic approaches, both medical or not, to provide women with the

best quality of life in such important phase which is the post menopause and the entire climacteric period.

Conflicts of interest

The authors declare no conflicts of interest.

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