

Medication use and climacteric syndrome: a cross-sectional population-based study

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Abstract

Objective: The aim of this study was to evaluate medication use during the climacteric period and assess its association with sociodemographic factors, morbidities, and climacteric symptoms.

Methods: Secondary analysis of data from a previous exploratory cross-sectional population-based study, conducted with 749 women (45-60 y), with the help of home interviews. Associations between medication use and climacteric symptoms were analyzed, and their correlations with other variables were made. Univariate analysis was made using the χ^2 test, followed by Bonferroni correction (multiple comparison method). Values were adjusted for age using the polytomous logistic multivariate regression analysis. Using Poisson regression analysis, simple and multiple, we identified the main factors for medication use, with forward stepwise variable selection criteria (95% CI).

Results: The mean age was 52.5 years and menopause occurred at 46.5 years (mean). The overall prevalence of medication use was 68.8%. The use of exclusive medications for relieving climacteric symptoms was associated with the absence of diseases (prevalence ratio [PR] = 8.2; 95% CI = 3.5-18.9; $P < 0.001$) and menopause onset between 40 and 44 years (PR = 4.9; 95% CI = 2.0-11.9; $P < 0.001$). Polypharmacy was associated with the highest number of diseases (PR = 10.6; 95% CI = 4.6-24.2; $P < 0.001$) and somatic Menopause Rating Scale (MRS) score > 3 (PR = 1.4; 95% CI = 1.01-1.96; $P = 0.044$).

Conclusions: The prevalence of medication use among middle-aged women was high and was associated with the age of menopause onset, chronic diseases, and obesity/overweight status.

Key Words: Medication use – Menopause – Middle-aged women – Menopause Rating Scale – Multimorbidity – Polypharmacy.

In Western populations, menopause often influences the perception of aging. To achieve a longer and active life expectancy and to minimize the impacts of menopause and aging, many women at this stage of development seek medical care and explore their treatment options. At this stage, the therapeutic approach is often initiated for climacteric symptoms and chronic and degenerative diseases, which increase in incidence after 50 years of age.

These epidemiologic and demographic contexts have led to long-term pharmacological treatments and a higher occurrence of polypharmacy, characterized by the simultaneous use of multiple medications. Polypharmacy definitions were variable.¹ Owing to the age range of the studied population, we

categorized polypharmacy as daily use of three or more concomitant medications. It is universally known that polypharmacy is common among older populations (age > 65 y), which may present with a higher prevalence of chronic diseases and higher utilization of health services.² Although there is a clear need to use medications as one ages, there is a hypothesis that polypharmacy may start before advanced age, close to the climacteric transition, and have some harmful consequences. Polypharmacy can increase the risk of side effects and the potential probability of drug interactions, which can potentially intensify climacteric symptoms.

Polypharmacy, a worldwide issue that affects 15% to 22% of the population, is related to aging (medication use increases significantly among people 40-64 y of age), female sex, divorced or widowed status, low educational level, higher body mass index, and self-medication status.^{3,4} Some Brazilian population-based studies described a 25% to 35% prevalence of polypharmacy in the older population and a positive association with female sex, age 75 years or older, low education level, and living with a partner.^{5,6} No previous study assessed the prevalence of polypharmacy for a specific group of middle-aged women (45-59 y) in Brazil. This is a growing group which corresponds to 9% of the total population estimated in 2016 by the Brazilian Institute of Geography

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and Statistics (IBGE).⁷ In addition, few studies have evaluated the problem of polypharmacy and its association with climacteric symptoms in middle-aged women.^{2,8}

Preventive health measures for this group, such as control of the initial stage of chronic diseases, will increase the active life expectancy and enable a life free of significant disability. The feminization associated with the aging population requires a better assessment of middle-aged women. To determine the prevalence of medication use during the climacteric period and its association with sociodemographic factors, chronic diseases, and climacteric symptoms, a secondary analysis of a population-based study in a metropolitan region of Brazil was performed.

METHODS

Study area

A secondary analysis of a cross-sectional exploratory population-based study was performed between September 2012 and June 2013, in urban towns in the Metropolitan Region of Campinas (southeastern Brazil), with about 2,798,477 residents. Of them, 1,423,748 were female; of those, 257,434 were aged 45 to 60 years.⁹ This cross-sectional study followed the recommendations stated by the Strengthening the Reporting of Observational Studies in Epidemiology statement,^{10,11} whose methodology has been presented in previous studies.¹²⁻²⁰

Participant Selection

Inclusion criteria were native Brazilian middle-aged women (45-60 y) living in the study area. The inability to respond to the questionnaire for any reason, such as refusal, cognitive deficits, and/or scheduling incompatibility, was considered exclusion criteria.

Sample size

Sample size was calculated based on the prevalence of general climacteric symptoms, considered to be 70% in the city of Campinas.²¹ Hot flashes were used for reference. To estimate a desired maximal difference of 3.5% between the sample proportion and the entire population with an alpha error level of 0.05, the sample size was calculated to be 656 women. The final sample size was 749 women (excluding 71 who refused to participate).

Participant selection and design (cross-sectional study)

The survey was restricted to the urban population due to logistical difficulties and the additional cost to study the rural area. According to a list of census tracts provided by the IBGE, 92 urban census tracts were selected, using a simple random sampling approach. The 92 sectors were randomly divided into 2 blocks by sector and the number of women aged 45 to 60 years was determined. Ten women from each sector were selected for interviews. Trained research assistants guided by maps drove to the selected households and invited the selected woman to participate in the study. All interviews were made on the spot. When first contact with interviewees was not successful, appointments were made. The refusals

were mostly due to lack of availability. All participants signed an Informed Consent Form before the interview.

Techniques suitable for all stages of the survey were used to train the interviewers, who completed 20-hour trainings, consisting of a combination of theoretical and practical classes. A guide was created based on the ethical aspects of research with human beings, the study objectives and methodology, interview techniques, and administrative matters. Practical classes included a demonstration in which they watched a previously prepared interview. This feature was idealized to enable interviewers to gain familiarity with the conversation approach, instruments that were used to select the volunteers, and the data collection. The questions included in the questionnaire were discussed in detail during the training.

The whole process of training was completed and supervised by the researchers of the Reproductive Health Research Center of Campinas (CEMICAMP) and the PhD student responsible for the research project. Each item of the questions and their technical meanings were discussed. Based on the performance and the quality of the interviews in class and homework assignments, it was decided who was prepared to collect data for the survey. After this training, a test to assess progress was applied. Their fieldwork was supervised by the principal investigators and by CEMICAMP researchers who act in partnership with UNICAMP. The supervisors were senior researchers who had already gained considerable experience from other population-based studies with similar methodology conducted in the past. The observation and supervision continued during the practical work until the process was completed.

The study protocol was approved by the National Commission for Research Ethics (protocol number 030/2011/ amendment number 779/2011) and by the ethics committee of the Department of Obstetrics and Gynecology, Faculty of Medical Sciences, State University of Campinas, UNICAMP (CAAE 0697.0.146.000-11).

Definitions

Medication was categorized into four groups according to use: without medication, exclusive medication for climacteric symptoms (hormone therapy, vaginal hormone therapy, alternative therapy), nonexclusive medication for climacteric symptoms (medication for hypertension, diabetes, dyslipidemia, osteoporosis, arthritis/arthrosis, asthma, depression, anxiety), and use of both (exclusive and nonexclusive medication for climacteric symptoms). To minimize a possible memory bias, the strategy used was the adoption of standardized procedures by the interviewers during the data collection, such as prescription requests, packaging, or package inserts.

Polypharmacy was defined as daily and simultaneous intake of three or more medications. Chronic diseases were categorized into 0, 1, 2, or 3 or more; having three or more chronic diseases was categorized as multimorbidity.

The intensity of climacteric symptoms was dichotomized according to the median of the total Menopause Rating Scale

(MRS) score; scores >8 indicated severe climacteric symptoms. The intensity of the somatic symptoms was dichotomized according to the median partial score of MRS for this domain; scores >3 indicated severe somatic symptoms. The intensity of the psychological symptoms was dichotomized according to the median of the partial MRS score for this domain and considered severe for scores >2 . The intensity of the urogenital symptoms was dichotomized according to the median partial MRS score for this domain and considered severe at values >1 . The MRS is a questionnaire used to evaluate menopausal symptoms and has already been validated and translated into Portuguese.²² The scale consists of 11 questions covering psychological, somatic, and urogenital symptoms. Each question has five possible answers and is scored incrementally by severity. The total score can range from 0 (no symptoms) to 44 (maximal symptoms).

Data collection and Questionnaire

The data collection began on 09/10/2012 and ended on 06/06/2013.

The dependent variable was medication use for the treatment of climacteric symptoms and/or for controlling preexisting chronic diseases.

The independent variables were sociodemographic characteristics, including age (45-49, 50-54, and 55-60 y), schooling (years of attendance at educational institutions categorized into up to 4 y and more than 4 y), having a partner (with or without), menopause status (premenopausal if experiencing regular menstrual cycles; perimenopausal if having irregular menstrual cycles or amenorrhea for less than 1 y; and postmenopausal if amenorrhea lasted for more than 1 y), and body mass index (kg/m^2) of less than or more than 25. Lifestyle habits considered included smoking (yes/no), alcohol intake (yes/no), and physical activity (more than 3 times/wk, yes/no). For health problems and self-reported health status, the following parameters were evaluated: hypertension (yes/no), diabetes mellitus (yes/no), dyslipidemia (yes/no), myocardial infarction (yes/no), stroke (yes/no), deep venous thrombosis or pulmonary embolus (yes/no), asthma or bronchitis (yes/no), chronic rheumatic diseases (yes/no), osteoporosis (yes/no), depression (yes/no), anxiety (yes/no), cancer (yes/no), and tuberculosis (yes/no). Collected gynecologic and obstetric history factors included menarche, menopause onset age, years after menopause, number of natural childbirths, parity (0 or >1), abortions (yes/no), contraceptive method (ever used, currently used, never used), sexual activity (yes/no), bladder surgery (yes/no), breast surgery (yes/no), other gynecological surgeries (yes/no), urinary incontinence (yes/no), vaginal dryness (yes/no), vaginal itching (yes/no), and dyspareunia (yes/no).

The questionnaire used to collect the data was structured in eight sections: sociodemographic evaluation, general health aspects, gynecological and reproductive aspects, menopause symptoms, knowledge about menopause, search and completion of menopause treatments, aspects of sexuality, and classification of socioeconomic strata. The socioeconomic

level classification was made in two ways: using median household income reported (R\$2,500) and the Brazilian Economic Classification Criterion (A/B, C, and D).²³ The instrument was previously tested with volunteer participants from the Menopause Outpatient Clinic of the University of Campinas Women's Hospital. Any issues that generated uncertainties were adapted once again and tested until the participants reported no more doubts about or difficulties answering the questions. A final version of the instrument was obtained through this evaluative feedback process. The interviews lasted 30 to 40 minutes.

Quality control

The quality control of the interviews was due to the reinterview of part of the sample, by regular analysis during the research of the frequency of the investigated variables and by the consistency analysis of the database. Reinterviews were made through telephone calls, and a standardized questionnaire was applied to those randomly selected. The values obtained were compared routinely with the latest research findings.

Statistical analyses

The analyses were performed using the statistical program "Statistical Analysis System for Windows version 9.2" (SAS Institute Inc., Cary, NC), using the command set appropriate for the analysis of complex samples and guaranteeing the necessary weighting, considering the sample design. An exploratory descriptive analysis of all the variables involved in the study was performed, through summary measures (mean, standard deviation, minimum, median, maximum). The variables were compared using Fisher's exact test, the χ^2 test, the Mann-Whitney test, or the Kruskal-Wallis test. Univariate analysis was made using the χ^2 test, to compare the categorical variables among the four groups, followed by Bonferroni correction (multiple comparison method). The level of statistical significance was set at 5%. The polytomous logistic multivariate regression analysis was also made, with *P* values adjusted for age. Poisson regression analysis, simple and multiple, was used to study the factors associated with medication use (prevalence ratio estimation), with forward stepwise variable selection criteria (95% CI).

RESULTS

A total of 749 women (mean age, 52.5 ± 4.4 y; mean age at menopause, 46.5 ± 5.8 y) were included in the present study. By menopause stage, 16% were premenopausal and 84% were peri- or postmenopausal. The overall prevalence of medication use was 68.8%; of these patients, 9.8% were using exclusive medication for the climacteric symptoms, 41.2% were using nonexclusive medication for the climacteric symptoms, and 17.8% were using both (exclusive and nonexclusive medications for climacteric symptoms). Only 20.8% of the participants reported previous or current use of systemic and/or vaginal hormone therapy. The overall frequency of polypharmacy was 24.6%. The most commonly prescribed

medications were those for treatment of cardiovascular diseases (34.6%), antidepressants (14.7%), oral lipid-lowering agents (13%), anxiolytics (12%), treatment of osteoarticular diseases (12%), and treatment of diabetes (9.6%). Polypharmacy was more frequent in women aged 55 to 60 years ($P<0.001$), with menopause onset after 40 years of age ($P<0.001$), with peri- or postmenopausal status ($P<0.001$), or with multimorbidity ($P<0.001$) (data not shown).

Table 1 shows the results of the association between medication use and sociodemographic and clinical variables in the bivariate analysis, followed by the Bonferroni correction (multiple comparison method). As age is a very strong a priori confounding factor, the polytomous logistic multivariate regression analysis was also performed, with values adjusted for age, as a continuous variable. The use of exclusive medication for climacteric symptoms was higher in women with menopause onset over 45 years ($P<0.001$), those in menopause for less than 10 years ($P<0.001$), those with peri- or postmenopausal status ($P<0.001$), those with BMI <25 ($P=0.003$), and those without chronic diseases ($P<0.001$). Longer time since menopause ($P<0.001$), peri- or postmenopausal status ($P<0.001$), overweight or obese status ($P=0.003$), and the presence of chronic diseases or multimorbidity ($P<0.001$) were

associated with the use of nonexclusive medications. The use of any medication (concomitant exclusive and nonexclusive medication for climacteric symptoms) was associated with more than 5 years since menopause ($P<0.001$), postmenopausal status ($P<0.001$), overweight/obesity status ($P<0.001$), and multimorbidity ($P<0.001$). The other sociodemographic variables were not associated with medication use.

About 79% of women reported having some type of chronic disease. The most prevalent morbidities were hypertension (36%), depression (34%), anxiety (27%), osteoarticular diseases (27%), dyslipidemia (22%), asthma (10.5%), diabetes mellitus (10.4%), and osteoporosis (7.3%). Only 21.2% denied having morbidities; however, approximately half of the population studied (47.3%) reported 1 or 2 comorbidities and 31.5% had multimorbidity. About 15% of the women with chronic diseases did not use any type of medication (data not shown on table).

Table 2 shows the results of the association between medication types and climacteric symptoms, in the bivariate analysis, followed by the Bonferroni correction (multiple comparison method). Values were adjusted for age using the polytomous logistic multivariate regression analysis. Women, who had the most severe climacteric symptoms

TABLE 1. Association between medication types and sociodemographic factors ($n=749$)—not adjusted^a and adjusted^b for age

Characteristic	Without medication		Exclusive medication		Nonexclusive medication		Both		Total	P^a	P^b
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%			
Age, y										<0.001	—
45-49	110	47.0^c	19	26.0	78	25.0	21	16.0	228		
50-54	76	32.5	23	31.5	102	32.8	41	31.3	242		
55-60	48	20.5	31	42.5^d	131	42.1^d	69	52.7^d	279		
Age at menopause, y										<0.001	<0.001
Without menopause	113	48.3^c	9	12.3	78	25.0^c	9	6.87	209		
<40	13	5.56	5	6.85	22	7.07	14	10.7	54		
40-44	21	8.97	13	17.8	37	11.9	24	18.3	95		
≥45	87	37.2	46	63.0^d	174	55.9^d	84	64.1^d	391		
Time since menopause (y)										<0.001	<0.001
Without menopause	113	48.3^c	9	12.3	78	25.0^c	9	6.87	209		
<5	57	24.4	27	36.9^d	86	27.7	34	25.9	204		
5-9	31	13.3	20	27.4^e	71	22.8	42	32.0^e	164		
≥10	33	14.1	17	23.3	76	24.4	46	35.1^f	172		
Menopause status										<0.001	<0.001
Pre	72	30.7^c	5	6.85	39	12.5	4	3.05	120		
Peri/Pos	162	69.2	68	93.1^d	272	87.5^d	127	96.9^d	629		
BMI										<0.001	0.003
<25	88	41.9^c	34	50.0^c	71	24.4	42	33.0	235		
≥25	122	58.1	34	50.0	220	75.6^d	85	66.9^d	461		
Diseases										<0.001	<0.001
0	125	53.4^c	34	46.6^c	0	0.00	0	0.00	159		
1-2	95	40.6	32	43.8	169	54.3^d	58	44.3	354		
≥3	14	5.98	7	9.59	142	45.7^e	73	55.7^e	236		
Socioeconomic level										0.003	0.309
A/B	116	50.0	52	71.2^c	148	47.7	80	61.1^c	396		
C	104	44.8^d	18	24.7	143	46.1^d	41	31.3	306		
D	12	5.17	3	4.11	19	6.13	10	7.63	44		
Family income (median)										0.021	0.961
<R\$2,500.00	95	46.1	21	32.3	139	53.0^c	49	44.9	304		
≥R\$2,500.00	111	53.8	44	67.7^d	123	46.9	60	55.0	338		

Bold values indicate statistical significance.

BMI, body mass index.

^a χ^2 test—bivariate analysis.

^b Polytomous Logistic Regression Analysis, adjusted for age (in years), as a continuous variable.

^{c,d,e,f} Groups with different letters are significantly different.

TABLE 2. Association between medication types and severity of climacteric symptoms—not adjusted^a and adjusted^b for age

Variables	Without medication (n = 234)		Exclusive medication (n = 73)		Nonexclusive medication (n = 309)		Both (n = 130)		Total n	P ^a	P ^b
	n	%	n	%	n	%	n	%			
Total MRS (median)										0.001	0.001
<8	150	64.1^c	41	56.2^c	139	44.9	42	32.2	372		
≥8	84	35.9	32	43.8	170	55.1^d	88	67.7^d	374		
Somatic MRS (median)										0.001	0.001
≤3	151	64.5^c	39	53.4^c	144	46.3	44	33.6	378		
>3	83	35.5	34	46.6	167	53.7^d	87	66.4^d	371		
Psychological MRS (median)										0.001	0.001
≤2	156	66.7^c	40	54.8^c	148	47.7	54	41.2	398		
>2	78	33.3	33	45.2	162	52.3^d	77	58.8^d	350		
Urogenital MRS (median)										0.001	0.001
≤1	156	66.7^c	38	52.0	159	51.3	59	45.4	412		
>1	78	33.3	35	48.0^d	151	48.7^d	71	54.6^d	335		

Bold values indicate statistical significance.

MRS, Menopause Rating Scale.

^aχ² test—bivariate analysis.

^bPolytomic Logistic Regression Analysis, adjusted for age (in years), as a continuous variable.

^{c,d}Groups with different letters are significantly different.

(MRS >8), were more likely to use nonexclusive medication for climacteric symptoms or both (exclusive and nonexclusive medication for climacteric symptoms) (*P*<0.001). Women who had the most severe somatic and psychological symptoms related to menopause were more likely to use nonexclusive medication for climacteric symptoms or both (exclusive and nonexclusive medication for climacteric symptoms) (*P*<0.001). Women who had the most severe urogenital symptoms were using both medications (exclusive, nonexclusive, and both) (*P*<0.001). A higher intensity of climacteric symptoms was also observed in those women who reported polypharmacy (70% of women) (data not shown on table).

Table 3 shows the main factors associated with medication use according to the Poisson multiple regression analysis, adjusted for age (in years) as a continuous variable. Women with a higher prevalence of using exclusive medication for climacteric symptoms were those without diseases (PR = 8.2; 95% CI = 3.5-18.9; *P*<0.001) and with a menopause onset between 40 and 44 years (PR = 4.9; 95% CI = 2.0-11.9; *P*<0.001). Women who were using nonexclusive medication for climacteric symptoms were those with at least 1 chronic disease (1 or 2 diseases: PR = 30.7; 95% CI = 7.7-122.4; *P*<0.001; ≥3 diseases: PR = 37.8; 95% CI = 9.4-150.8; *P*<0.001) and those with overweight/obesity status (PR = 1.3; 95% CI = 1.03-1.7; *P* = 0.031). Women with a higher prevalence of concomitant use of exclusive and nonexclusive medication for climacteric symptoms (both) were those with at least 1 chronic disease (1 or 2 diseases: PR = 3.8; 95% CI = 1.3-11.3; *P*<0.001; ≥3 diseases: PR = 6.7; 95% CI, 2.5-17.9; *P*<0.001) and those with menopause onset between 40 and 44 years (PR = 3.7; 95% CI = 1.6-8.7; *P* = 0.002). Women with a higher prevalence of polypharmacy were those with multimorbidity (PR = 10.6; 95% CI = 4.6-24.2; *P*<0.001) and with somatic MRS score >3 (PR = 1.4; 95% CI = 1.01-1.9; *P* = 0.044).

DISCUSSION

The aim of this study was to evaluate the prevalence of medication use by middle-aged women and its association with sociodemographic factors, morbidities, and climacteric symptoms.

According to IBGE, the Brazilian age structure of the last decade shows the same tendency to the marked aging of the population registered in the other Latin American countries: there is an increase in the segment of 45 years of age or more, as well as the female population. The percentage of middle-aged women (45-60 y) corresponds to 9% of the total Brazilian population (18,861,113 women).⁷ Thus, there is an expectation of a progressive increase in the demand for health services and medication use by women with climacteric symptoms. To the best of our knowledge, no other Brazilian study has specifically assessed data about medication use and polypharmacy in this large and specific group of women. The data from the present study showed a high prevalence of medication use, mainly associated with age of menopause onset, overweight and obesity, the presence of morbidities, and intensity of menopause somatic symptoms.

The overall prevalence of medication use was 68.8%. Age is a predictor of medication use, and its effect occurs even before 60 years, as medication use increases starting in the fourth decade of life.²⁴ The vast majority of women (about 80%) experience vasomotor symptoms during the menopausal transition.^{18,25} Those symptoms typically last from 5 to 7.4 years (median total duration), but, for many women, its duration could be much longer.²⁶ Consequently, it is expected that the pharmacologic therapy for menopausal symptoms is higher in this group. Bertoldi et al performed a population-based study of 41,433 individuals that recorded a prevalence of medication use of 36% to 61%, accounting for women in the age group of 40 to 60 years with a trend toward greater use with aging.⁶ Our results confirm such evidence with an even higher prevalence of medication use (68.8%) among middle-

TABLE 3. Factors associated with medication use, adjusted for age (y) as a continuous variable—Poisson multiple regression analysis (n = 689)

Factors associated with the use of exclusive medication for the climacteric symptoms (n = 68 with exclusive medication for the climacteric symptoms and n = 621 others)				
Variables ^a	Categories	PR	95% CI PR	P
Age	Continuous variable (y)	0.975	0.916-1.038	0.423
Number of diseases	≥3 (ref.)	1.00	—	—
	1-2	3.39	1.49-7.72	0.004
	0	8.20	3.54-18.97	<0.001
Age at menopause	Premenopause (ref.)	1.00	—	—
	<40 y	3.82	1.25-11.65	0.019
	40-44 y	4.91	2.02-11.93	<0.001
	≥45 y	3.89	1.73-8.74	0.001
Factors associated with the use of nonexclusive medication for the climacteric symptoms (n = 288 with nonexclusive medication for the climacteric symptoms and n = 401 others)				
Variables ^a	Categories	PR	95% CI PR	P
Age	Continuous variable (y)	0.995	0.969-1.022	0.735
Number of diseases	0 (ref.)	1.00	—	—
	1-2	30.76	7.73-122.46	<0.001
	≥3	37.82	9.48-150.86	<0.001
BMI (kg/m ²)	<25 (ref.)	1.00	—	—
	≥25	1.35	1.03-1.77	0.031
Factors associated with the use of both medications (exclusive and nonexclusive) (n = 126 with both medications and n = 563 others)				
Variables ^a	Categories	PR	95% CI PR	P
Age	Continuous variable (y)	1.062	1.012-1.114	0.015
Number of diseases	0 (ref.)	1.00	—	—
	1-2	3.86	1.32-11.31	<0.001
	≥3	6.73	2.53-17.93	<0.001
Age at menopause	Premenopause (ref.)	1.00	—	—
	<40 y	2.93	1.15-7.43	0.024
	40-44 y	3.78	1.64-8.70	0.002
	≥45 y	2.89	1.31-6.32	0.008
Factors associated with polypharmacy (n = 175 with polypharmacy and n = 514 without polypharmacy)				
Variables ^a	Categories	PR	95% CI PR	P
Age	Continuous variable (y)	1.066	1.028-1.105	<0.001
Number of diseases	0 (ref.)	1.00	—	—
	1-2	2.65	1.12-6.24	0.026
	≥3	10.60	4.64-24.20	<0.001
Somatic MRS	≤3 (ref.)	1.00	—	—
	>3	1.41	1.01-1.96	0.044

95% CI PR, confidence interval for the prevalence ratio; PR, prevalence ratio; Ref. reference level.

^aVariables considered: age at menopause, time since menopause, menopause status, marital status, schooling, physical activity, smoking, alcoholism, BMI (body mass index), social stratum, family income, number of diseases, total MRS (Menopause Rating Scale), somatic MRS, psychological MRS and urogenital MRS.

aged women. Besides the high prevalence of medication use observed, it is necessary to point out that 7 of 10 women were using some type of medicine.

After the regression analysis adjusted for age as a continuous variable, the main factors associated with the use of exclusive medication for climacteric symptoms were the absence of diseases and menopause onset between 40 to 44 years. These findings can be justified by the higher prevalence of symptoms in the menopausal transition. Hormone therapy represents a safe and effective option for the treatment of menopause symptoms for postmenopausal women aged younger than 60 years or within 10 years of menopause onset (treatment window).²⁵ Furthermore, the absence of diseases possibly influenced the higher number of prescriptions of hormone therapy for younger women who were in the treatment window without contraindication for its use.

The main factors associated with the use of nonexclusive medication for climacteric symptoms were having at least one chronic disease and overweight/obesity status. Menopause transition has been linked to increased propensity for weight gain. Prospective studies have shown a greater increase of abdominal fat after menopause, leading to a shift from a gynoid to an android pattern of fat distribution, due to estrogen deficiency.^{26,27} The excess of central fat is associated with insulin resistance and high prevalence of metabolic syndrome, which are risk factors for cardiovascular disease.²⁸ Thus, the nonuse of exclusive medication for climacteric symptoms could lead to overweight and obesity status, predisposing to the appearance of chronic diseases in middle-aged women, which, in turn, increases the medication intake. These findings are aligned with a recent prospective study, the OsteoLau Cohort, which demonstrated that active hormone

therapy use is associated with significantly lower levels of visceral adipose tissue.²⁹ In our population sample, 61% of the women had BMI above 25. Overweight and obesity were also associated with earlier menopause onset in European women.³⁰ With increasing obesity in America, the age of natural menopause may be trending downward in regions with the greatest obesity, as we have observed in our population studied.

The main factors associated with the concomitant use of exclusive and nonexclusive medication for climacteric symptoms were having at least one chronic disease and menopause onset between 40 and 44 years. Being in the peri- or postmenopausal period was associated with a higher frequency of the use of all medication categories, probably because of a higher number of medical consultations due to climacteric symptom complaints and by the eventual opportunity to diagnose chronic diseases during the menopausal transition.

The main factors associated with polypharmacy were multimorbidity and intensity of somatic menopause symptoms. The hypotheses for this scenario are justified by the demographic transition of the last decades and the feminization of aging. Women, who have a longer life expectancy and live longer with chronic degenerative processes, are more affected by nonfatal health problems and more aware of their health. In addition, they usually express more signs and symptoms to healthcare professionals, resulting in a higher number of prescriptions. Costa et al studied the prevalence of medication use by the adult population in the city of Campinas, São Paulo, and the determinants of this use according to demographic, socioeconomic, health-related, and morbidity factors. The prevalence was higher among women and in age groups over 40 years, highlighting the prevalence of 88.4% in the age group of 70 years or more.³¹ Regarding the relationship between polypharmacy and age, it may be associated with the increase or worsening of diseases in older women as well as the higher use of health services by this age group. A previous study showed that this group of middle-aged women had a high demand for medical services to treat climacteric symptoms (80%).³² Therefore, the greater the contact with health services, the greater the possibility of the diagnosis of diseases that begin during this phase of life, which could justify the high prevalence of medicalization. In Brazil, some population-based studies have described a 25% to 35% prevalence of polypharmacy in the older population with positive associations with female sex, older age (75 y of age or older), low educational level, and living with a partner.³³⁻³⁵ No previous study evaluated the prevalence of polypharmacy for the specific group of middle-aged women (45-59 y) in Brazil. The overall frequency of polypharmacy in our group of women was 24.6%, very similar to that of the older population.

Chronic diseases and their treatments may worsen and/or simulate somatic menopause symptoms.³⁶⁻⁴¹ The appearance of chronic diseases is inherent to the aging process, justifying the greater medicalization and polypharmacy, found in patients with multimorbidity. The overlapping of the somatic

menopause symptomatology with the existence of any chronic diseases may lead to a higher occurrence of polypharmacy, characterized by the simultaneous use of multiple medications. Our findings reinforce the need to address women earlier, preferably in the period before the menopausal transition, to promote health through lifestyle modifications, thus preventing the onset of chronic degenerative diseases at earlier ages.

The limitations of the present study include the difficulty of establishing a cause-effect relationship with the cross-sectional study design and self-reported measures. Another limitation is that self-reported information may be more subject to recall bias. The strengths of this research include its sample size, the fact that it was population-based, and the rigorous data collection. To minimize possible memory bias, interviewers used standardized procedures by the interviewers during data collection, such as prescription request, packaging, or package insert. The information collected regarding the use of medication was comprehensive and complete.

CONCLUSIONS

The prevalence of medication use among middle-aged women was high and was associated with the age of menopause onset, chronic diseases, and obesity/overweight status. The main factors associated with polypharmacy were multimorbidity and intensity of somatic menopause symptoms. Understanding and controlling these factors can help reduce symptoms, rationalize drug prescriptions, prevent chronic diseases, and improve overall care during the climacteric period and aging process.

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