Menopausal symptoms appear before the menopause and persist 5 years beyond: a detailed analysis of a multinational study

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ABSTRACT

Objective   Few Latin American studies have described menopausal symptoms in detail by means of a standardized assessment tool. The objective of this study was to assess the prevalence and severity of menopausal symptoms and their impact over quality of life among mid-aged Latin American women.

Method   In this cross-sectional study, 8373 otherwise healthy women aged 40–59 years from 12 Latin American countries were asked to fill out the Menopause Rating Scale (MRS) and a questionnaire containing personal sociodemographic data. Menopause status (pre-, peri- and postmenopausal) was defined according to the criteria of the Stages of Reproductive Aging Workshop.

Results   Of all the studied women, 90.9% had at least one menopausal symptom (complaint) that they rated. Muscle and joint discomfort, physical and mental exhaustion and depressive mood were highly prevalent and rated as severe–very severe (scores of 3 and 4), at a higher rate than vasomotor symptoms (15.6%, 13.8% and 13.7% vs. 9.6%, respectively). Of premenopausal women (40–44 years), 77.0% reported at least one rated complaint, with 12.9% displaying MRS scores defined as severe (>16). The latter rate increased to 26.4% in perimenopausal, 31.6% in early postmenopausal and 29.9% among late postmenopausal women. As measured with the MRS, the presence of hot flushes increased the risk of impairment of overall quality of life in both premenopausal (odds ratio 12.67; 95% confidence interval 9.53–16.83) and peri/postmenopausal women (odds ratio 9.37; 95% confidence interval 7.85–11.19).

Conclusion   In this large, mid-aged, female Latin American series, muscle/joint discomfort and psychological symptoms were the most prevalent and severely rated menopausal symptoms. The symptoms appear early in the premenopause, significantly impair quality of life and persist 5 years beyond the menopause.

INTRODUCTION

The existence *per se* of a climacteric syndrome and its composite symptoms is still controversial. Although many have claimed a causal relation between the cessation of menses and symptom appearance in order to consider the syndrome a valid entity[1], this link is in fact unclear and may cloud the understanding of the syndrome. For instance, although hot flushes and sweats, also known as vasomotor symptoms, are more prevalent in the postmenopause, other symptoms such as psychological ones may already appear during the menopausal transition and may not increase after the menopause[2–5]. Although vasomotor symptoms are, for both women and physicians, the most identifiable non-menstrual indicators of the menopausal transition[6,7], recent studies have determined the contrary. Indeed, the US multi-ethnic SWAN study found muscle and joint stiffness (54.3%) and being tense (51.9%) as the two most prevalent complaints among women aged 40–55 years. Surprisingly, vasomotor symptoms affected only 27.5% of studied women[1]. Similarly,

using a validated instrument, a study from India found fatigue and joint pains to be more prevalent than vasomotor symptoms among postmenopausal women[8]. Stiff shoulders (75.4%) and fatigue (64.7%) were more frequent among Japanese women in their fifties as compared to vasomotor symptoms, which were present in only 36.9%[9]. Although these studies show that vasomotor symptoms may not have been the most severe or prevalent complaint, they still may be considered a relevant signal, correlating with other complaints such as psychological ones, in the pre- and postmenopausal phases. Women with vasomotor symptoms present more psychological symptoms than those without vasomotor symptoms, and vasomotor symptoms may, in fact, increase the risk for depression, stress, sexual dysfunction and anxiety[10]. In premenopausal women, vasomotor symptoms act as a red flag linking psychological symptoms to decline of ovarian function in a similar way as amenorrhea does in postmenopausal women.

Menopausal symptoms are highly prevalent among mid-aged women world-wide and have been related to impaired quality of life. In a previous multicenter study, our research group – known as the Collaborative Group for Research of the Climacteric in Latin America (REDLINC) – found that 24.9% of Latin American women aged 40–59 years had severe impairment of quality of life in relation to menopausal symptoms[11]. In recent years, the Menopause Rating Scale (MRS) has allowed many researchers world-wide (including REDLINC) to assess in detail the clinical manifestations of the menopause and adequately compare results between populations[12,13]. Bearing this in mind, we decided to explore more profoundly both the prevalence and severity of menopausal symptoms and their impact over quality of life among mid-aged women (pre-, peri- and postmenopausal).

METHOD

Study design and participants

This was a cross-sectional study (the REDLINC IV[11]) designed to assess menopausal symptoms and related risk factors in mid-aged women in 22 health centers located in 18 Latin American cities with populations of more than 500 000 inhabitants in 12 different countries. Involved researchers, cities, clinical centers, number of women studied per center and more details of the methodology used have recently been published elsewhere[11,14]. This study included Hispanic-Mestizo women aged 40–59 years who accompanied patients attending consultations at participating health centers. Participants had normal health, as defined by the National Center for Health Statistics as that compatible with the performance of daily routines[15]. Women of other ethnic groups, with mental or physical handicaps impairing the capacity of understanding and/or providing answers during the interview, and those unwilling to give written consent for participation were excluded.

Procedure

Women fulfilling the inclusion criteria were requested to fill out the MRS and a general data questionnaire after being informed about the research, its purpose, the MRS and its content. Written consent was obtained from all participants prior to any interview according to the Helsinki Declaration[16]. The research protocol of this study was reviewed and approved by the Bioethics Committee of the PROSAM Foundation, Santiago de Chile, Chile. Using statistical software (EPI-INFO 6.04, 2001, Centers for Disease Control and Prevention, Atlanta, GA, USA), a minimal sample size of 380 participants per center was calculated, considering that each center covered an estimated population of 50 000 women[17] and assuming that 50% of the surveyed population would present vasomotor symptoms[18] with a 5% desired precision and a 95% confidence interval.

Instruments and variables

General data questionnaire

In order to record all data, an itemized questionnaire was constructed and validated among 50 women before being implemented at Latin American centers affiliated to REDLINC participating in this study.

Study variables and definitions

Studied variables included: age (years), educational level (years), parity, menopausal status, years since menopause onset, surgical menopause (yes/no), marital status, sexual status in last 4 weeks (active or inactive), accessed health-care system (free-minimal cost or paid). Lifestyle and other personal factors included in this section were: smoking habit, church attendance, history of sexual abuse (rape) and if currently having a partner. Current medical care and drug use (during the last 4 weeks) were also assessed and included: psychiatric attention (%) and the use of psychotropic drugs (%), menopausal hormone therapy (HT) (%), alternative therapies for the menopause (%) or oral contraceptive pill use (%). Each REDLINC group was assigned a center number (city and country), and maximum average daily temperature and sea level altitude were also registered for each one. As previously reported, insufficient educational level was defined as 12 years or less of study[19]. Menopausal status was defined according to the criteria of the Stages of Reproductive Aging Workshop as premenopausal (women having regular menses); perimenopausal (irregularities >7 days from their normal cycle); and postmenopausal (no more menses), which was further divided as early postmenopausal (1–4 years) and late postmenopausal (≥5 years)[20].

The Menopause Rating Scale

The present research used the MRS[21], which is a validated questionnaire that assesses both the presence and severity of 11 menopausal symptoms grouped in three subscales:

(1) *Somatic*: hot flushes, sweating (vasomotor symptoms), heart discomfort, sleep problems, muscle and joint discomfort (items 1–3 and 11, respectively); (2) *Psychological*: depressive mood, irritability, anxiety and physical and mental exhaustion (items 4–7, respectively); and (3) *Urogenital*: sexual problems, bladder problems and vaginal dryness (items 8–10, respectively). Each item can be rated as: 0 (absent), 1 (mild), 2 (moderate), 3 (severe) and 4 (very severe) and displayed as mean and standard deviations. For a particular individual, scores obtained for each item contained in a given subscale are summed to provide a total subscale score. The sum of the subscales scores provides the total MRS score. Higher scores are indicative of worse impairment of quality of life. Indeed, values above 8 (somatic), 6 (psychological), 3 (urogenital) and 16 (total MRS) were defined as severe (impaired quality of life)[22]. This instrument has been translated into 27 languages[23] and validated in Spanish[24,25].

Statistical analysis

Data analysis was performed using the EPI-INFO statistical program (Version 3.5.1, 2008, Centers for Disease Control and Prevention, Atlanta, GA, USA; WHO, Basel, Switzerland). Results are presented as mean ± standard deviations and percentages (95% confidence intervals, CI). The Kolmogorov–Smirnov test was used to assess the normality of data distribution, and the Bartlett test was used to evaluate the homogeneity of the measured variance. According to this, group comparisons were performed with ANOVA (various independent samples, parametric) or the Kruskal–Wallis test (various independent samples, non-parametric). Percentages between groups were evaluated with the χ^2 test.

Logistic regression analysis was performed for the simultaneous assessment of several variables influencing quality of life in pre- as well as peri/postmenopausal women. For this, the total MRS score (dependent variable) was transformed into a categorical one, and cases (quality of life impairment) were considered who exhibited scores above 16 (severe MRS scoring). Independent variables to be entered in the regression model were: older age (yes, ≥50 years, median), hot flushes (yes/no), peri/postmenopausal status (yes/no), premature menopause (<40 years), surgical menopause (yes/no), nulliparity (yes/no), having a partner (yes/no), sexually active (yes/no), medication use (contraceptives, HT/alternatives for the menopause, psychiatric drugs), psychiatric consulting (yes/no), history of rape (yes/no), high-altitude residency (yes, city location >2500 m), hot-climate city (yes, average maximum temperature >30°C), access to free health care (yes/no), low schooling (<12 years), current smoking (yes/no), church attendance (yes/no) and self-perceived healthiness (yes/no). Entry of variables into the regression model was considered with a 20% significance level and the stepwise procedure performed. Interactions between significant variables found during regression model construction were also considered for the final model. Adequacy of the regression model was demonstrated with the Hosmer–Lemeshow goodness-of-fit test. For all calculations, a *p* value of < 0.05 was considered as statistically significant.

RESULTS

A total of 8394 women fulfilled inclusion criteria and were surveyed in the 22 participating health centers in 12 Latin American countries. The refusal rate for study participation was 6.5%; the data of 21 subjects were incomplete and excluded, leaving 8373 surveys for analysis. The general characteristics of all studied women, and in accordance with their menopausal stage, are depicted in Table 1.

General data

Sociodemographic characteristics

The mean age of the women was 49.1 ± 5.7 years; 31.7% (*n* = 2655) of the women were premenopausal, 19.7% (*n* = 1648) perimenopausal and 48.6% (*n* = 4070) postmenopausal. In the postmenopausal group, 26.9% (*n* = 2249) had been postmenopausal for 5 or more years. Younger premenopausal women had significantly more years of schooling than older postmenopausal ones (12.2 ± 4.4 vs. 10.9 ± 4.6 years, *p* < 0.0001). Overall, 56.2% of the women had access to free health care. The rate of women in a stable couple relationship significantly decreased in relation to age and the menopausal stage. Indeed, while 60.7% of younger premenopausal women were part of a stable couple, less than 50% were in a stable relationship after the menopause (*p* < 0.0001). The decrease in the rate of women being in a stable relationship correlated with a decrement in sexual activity (premenopausal, 62.1% vs. late postmenopausal, 41.9%, *p* < 0.0001).

Geographical characteristics

A total of 31.9% of the studied women lived in cities located at more than 2500 m above sea level and 45.4% lived in places with an average daily temperature higher than 30°C.

Gynecological and obstetric characteristics

It was interesting to observe a meaningful decrease in parity within the 20-year sample range. Women who were 5 or more years postmenopausal (mean age 54.8 ± 3.9 years) reported on average 3.0 ± 1.9 births, while premenopausal women <45 years only reported 2.2 ± 1.3 births (*p* < 0.0001). Overall, the surgical menopause rate was 14.1%, which was significantly higher among late postmenopausal women (34.1%). Overall, the use of HT and contraceptives was 14.7% and 6.0%, respectively. As would be expected, HT use increased from 3.0% in the younger premenopausal women to 23.6% in early postmenopausal women. Of all surveyed women, 6.7% elected alternative therapies to treat their menopausal symptoms. This rate was lower than the 14.7% of women who elected HT.

Table 1 Characteristics of the studied mid-aged Latin American women, according to their menopausal status. Data are presented as mean ± standard deviations or percentages

| | All (n = 8373) | Premenopause (age) | | Perimenopause (n = 1648) | Postmenopause | | p Value* |
		40–44 years (n = 1523)	≥45 years (n = 1132)		Early (n = 1821)	Late (n = 2249)	
Age (years)	49.1 ± 5.7	41.8 ± 1.4	47.9 ± 3.0	47.2 ± 4.1	50.8 ± 4.4	54.8 ± 3.9	0.0001[1]
Educational level (years)	11.6 ± 4.4	12.2 ± 4.4	11.6 ± 4.7	11.7 ± 4.6	11.3 ± 4.7	10.9 ± 4.6	0.0001[1]
Access to free health care	56.2	61.4	58.6	56.1	52.4	54.4	0.0001[2]
Part of a stable couple	51.3	60.7	49.3	55.7	48.6	46.6	0.0001[2]
Has sexual activity	47.3	62.1	44.7	53.4	40.7	41.9	0.0001[2]
Living at high altitude	31.9	36.3	35.2	36.8	25.7	28.8	0.0001[2]
Living in hot climate (>30°C)	45.4	50.4	46.3	44.2	42.8	44.7	0.0001[2]
Parity (number of children)	2.6 ± 1.6	2.2 ± 1.3	2.4 ± 1.5	2.4 ± 1.5	2.6 ± 1.6	3.0 ± 1.9	0.0001[3]
Surgical menopause	14.1	0	0	0	22.5	34.1	0.0001[2]
Use of hormone therapy	14.7	3.0	4.9	10.4	23.6	23.4	0.0001[2]
Use of contraceptives	6.0	17.8	10.1	5.6	1.0	0.4	0.0001[2]
Use of alternative therapy	7.6	2.5	6.1	6.9	9.5	10.9	0.0001[2]
Current smoker	17.4	19.8	17.9	18.1	17.3	15.1	0.003[2]
History of psychiatric consulting	11.6	8.7	10.3	12.0	12.0	13.4	0.0008[2]
Use of psychotropic drugs	8.0	5.4	6.6	6.9	9.3	10.3	0.0001[2]
History of rape	4.4	4.4	3.8	5.0	4.2	4.3	NS
Good health (self-perception)	90.5	93.3	91.1	89.9	89.6	89.5	0.0002[2]

*, p values as determined by the Kruskal–Wallis test[1], the χ² test[2] or ANOVA[3] ; NS, non-significant

Other characteristics

Current smoking significantly declined in relation to the menopausal stage, from 19.8% in younger premenopausal women to 15.1% in late postmenopausal ones ($p < 0.003$). Of all studied women, 11.6% reported psychiatric consultation at some point in their lives, 8% had a history of psychotropic drug use and 4.4% a history of rape; 90.5% reported themselves as healthy. However, this rate displayed a significant decrease in relation to the reproductive stage ($p < 0.0002$).

Menopausal symptoms

Overall, 24.9% of women presented at least one menopausal symptom scored as severe–very severe (scores of 3 and 4) (Table 2). The mean total MRS score for the whole sample was 11.27 ± 8.54. Psychological symptoms (four items) contributed with an average 4.60 points (40.8% of the total MRS score); the four somatic symptoms contributed 4.12 points and the three urogenital symptoms, 2.54 points. The most severely rated specific symptoms were: muscle and joint discomfort (1.25 ± 1.23 points), followed by physical and mental exhaustion (1.24 ± 1.18 points) and irritability (1.20 ± 1.13 points). Overall, 90.9% of all studied women experienced at least one symptom rated at any degree. Muscle and joint discomfort, physical and mental exhaustion and depressive mood were rated as severe–very severe (scores of 3 and 4) at a higher rate compared to vasomotor symptoms (15.6%, 13.8% and

13.7% vs. 9.6%, respectively). It is important to mention that 77.0% of premenopausal women aged 40–44 years presented at least one symptom rated at any degree.

MRS scores and symptom prevalence

In order to obtain a clearer profiling of symptoms in this mid-aged sample, MRS scores and symptoms were analyzed in detail for each menopausal stage (Table 3).

Somatic symptoms

Vasomotor symptoms of any degree were present in 29.7% of premenopausal women aged 40–44 years, a rate that increased to 68.5% in early postmenopausal women (12.3% were rated as severe–very severe). As one can observe, vasomotor symptoms were still present in 60.6% of women even after 5 or more years since menopause onset, with an 11.5% still rating them as severe–very severe (includes scores of 3 and 4). In general, the prevalence of heart discomfort was lower than that of vasomotor symptoms but this also increased throughout the menopausal stages, reaching its highest frequency and severity among late postmenopausal women (any degree, 50.6% and severe–very severe, 6.2%). Sleeping problems affected almost 50% of premenopausal women aged 40–44 years, with a significant increase observed in the late postmenopausal phase (any degree, 75.8% and severe–very severe, 16.2%). Although for all studied women

Table 2 Menopause Rating Scale (MRS) scores and prevalence of menopausal symptoms in the studied women ($n = 3373$). Data are presented as mean $\pm$ standard deviations or percentages

Symptoms	MRS score	Symptom prevalence (95% confidence interval)*	
		Any degree	Severe–very severe
Somatic			
1. Hot flushes, sweating	1.02 ± 1.14	54.5 (53.5–55.6)	9.6 (9.0–10.3)
2. Heart discomfort	0.73 ± 0.97	43.8 (42.8–44.9)	5.0 (4.6–5.5)
3. Sleep problems	1.13 ± 1.18	59.0 (57.9–60.1)	13.2 (12.5–14.0)
11. Muscle and joint discomfort	1.25 ± 1.23	63.0 (61.9–64.0)	15.6 (14.8–16.4)
Total subscale	4.12 ± 3.36	84.2 (83.4–84.9)[†]	10.8 (10.1–11.4)**
Psychological			
4. Depressive mood	1.17 ± 1.19	60.5 (59.4–61.5)	13.7 (13.0–14.4)
5. Irritability	1.20 ± 1.13	64.6 (63.6–65.6)	12.3 (11.7–13.1)
6. Anxiety	0.99 ± 1.13	53.9 (52.8–55.0)	10.7 (10.1–11.4)
7. Physical mental exhaustion	1.24 ± 1.18	64.8 (63.7–65.8)	13.8 (13.0–14.5)
Total subscale	4.60 ± 3.83	84.4 (83.6–85.2)[†]	28.7 (27.7–29.7)**
Urogenital			
8. Sexual problems	0.90 ± 1.16	46.6 (45.6–47.7)	10.8 (10.2–11.5)
9. Bladder problems	0.76 ± 1.07	42.1 (41.0–43.1)	8.2 (7.6–8.8)
10. Vaginal dryness	0.89 ± 1.15	45.9 (44.9–47.0)	11.2 (10.5–11.9)
Total subscale	2.54 ± 2.72	66.4 (65.4–67.4)	31.3 (30.3–32.3)
Total	11.27 ± 8.54	90.9 (90.2–91.5)[†]	24.9 (24.0–25.8)**

*, Symptom prevalence rated as any degree (1–4) or severe–very severe (3 and 4); at least one item is present and rated as any degree[†] or severe–very severe**

muscle and joint discomfort was the most severely rated complaint (Table 2), this trend was not found when women were stratified according to their menopausal stage. In this case, sleep problem was the most prevalent symptom rated as any degree and as severe–very severe within each menopausal stage.

Psychological symptoms

For all studied women, MRS psychological subscale scores were found to be higher compared to those obtained for the somatic and urogenital subscales. As with somatic symptoms and except for certain items, in general the psychological symptom prevalence (any degree and severe–very severe) also displayed an overall increasing trend from one menopausal stage to the next. As observed for all studied women, irritability and physical and mental exhaustion were also the most prevalent and severely rated symptoms in each menopausal stage.

Urogenital symptoms

Sexual problems are multifactorial but have been included in the MRS as related to urogenital health. A clear increase in both severity and prevalence of urogenital problems was observed throughout the menopausal stages. Indeed, sexual problems increased from 31.3% (any degree) among premenopausal women (40–44 years) to 55.3% in early postmenopausal women. The prevalence of vaginal dryness (any

degree and severe–very severe) displayed a significant rise from one menopausal stage to the next. Contrary to this, the prevalence of bladder problems (any degree and severe–very severe) displayed a peak among perimenopausal women (any, 46.0% and severe–very severe, 11.1%). It is worth mentioning that, contrary to what might be expected, there was no dramatic increase in both symptoms after the menopause.

Quality of life throughout the stages of the menopause

Mean total MRS scores significantly increased from one menopausal stage to the next (Table 4). The prevalence of women displaying total MRS scores defined as severe (above 16), and hence impaired quality of life, increased significantly throughout the menopausal stages. Compared to younger premenopausal women, the risk of impaired quality of life increased 1.5-fold in older premenopausal women and nearly three-fold among postmenopausal women (early and late).

Sociodemographic and other female factors related to impaired quality of life

Sociodemographic and other female factors that may influence quality of life during mid-life are included in Table 5. The studied women were divided in premenopausal and peri/postmenopausal women in order to assess possible hormone-related

Table 3 Menopause Rating Scale (MRS) scores and menopausal symptom prevalence according to menopausal stages in the studied women. The scores are given as mean ± standard deviation; prevalences are given as percentage (95% confidence interval)

Symptoms	Premenopause (40–44 years)	Premenopause (≥ 45 years)	Perimenopause	Early postmenopause	Late postmenopause	p Value**
Somatic						
Hot flushes, sweating						
mean score	0.54 ± 0.96	0.85 ± 1.07	1.07 ± 1.14	1.31 ± 1.16	1.15 ± 1.15	0.0001[1]
prevalence*: any degree	29.7 (27.4–32.1)	47.1 (44.1–50.0)	58.9 (56.5–61.3)	68.5 (66.3–70.7)	60.6 (58.5–62.6)	0.0001[2]
prevalence: severe–very severe	4.7 (3.7–5.9)	6.6 (5.3–8.3)	10.8 (9.4–12.4)	12.3 (10.8–13.9)	11.5 (10.2–12.9)	0.0001[2]
Heart discomfort						
mean score	0.41 ± 0.80	0.62 ± 0.93	0.78 ± 0.98	0.85 ± 0.98	0.87 ± 1.02	0.0001[1]
prevalence: any degree	26.1 (23.9–28.4)	38.3 (35.4–41.2)	47.8 (45.3–50.2)	50.2 (47.9–52.6)	50.6 (48.5–52.6)	0.0001[2]
prevalence: severe–very severe	3.3 (2.5–4.4)	4.7 (3.6–6.1)	5.5 (4.5–6.8)	4.7 (3.8–5.8)	6.2 (5.2–7.3)	0.0002[2]
Sleep problems						
mean score	0.78 ± 1.10	0.96 ± 1.16	1.17 ± 1.16	1.23 ± 1.19	1.34 ± 1.20	0.0001[1]
prevalence: any degree	49.6 (47.8–52.9)	61.6 (58.7–64.4)	74.3 (72.1–76.4)	76.8 (74.7–78.7)	75.8 (74.0–77.6)	0.0001[2]
prevalence: severe–very severe	9.5 (81–11.1)	10.5 (8.8–12.5)	13.6 (12.1–15.4)	14.0 (12.5–15.7)	16.2 (14.7–17.8)	0.0001[2]
Muscle and joint discomfort						
mean score	0.81 ± 1.08	1.11 ± 1.22	1.17 ± 1.20	1.37 ± 1.25	1.57 ± 1.23	0.0001[1]
prevalence: any degree	45.9 (43.4–48.4)	56.3 (53.3–59.2)	62.1 (59.7–64.5)	66.9 (64.7–69.0)	75.4 (73.5–77.1)	0.0001[2]
prevalence: severe–very severe	7.9 (6.6–9.4)	13.2 (11.3–15.3)	13.5 (11.9–15.2)	18.3 (16.6–20.2)	21.4 (19.8–23.2)	0.0001[2]
Psychological						
Depressive mood						
mean score	0.80 ± 1.10	1.06 ± 1.18	1.26 ± 1.19	1.32 ± 1.20	1.28 ± 1.19	0.0001[1]
prevalence: any degree	44.3 (41.7–46.8)	56.1 (53.1–59.0)	65.4 (63.1–67.7)	66.2 (63.9–68.3)	65.4 (63.4–67.4)	0.0001[2]
prevalence: severe–very severe	8.9 (7.5–10.4)	12.8 (10.9–14.9)	14.9 (13.3–16.8)	15.3 (13.7–17.1)	15.2 (13.7–16.7)	0.0001[2]
Irritability						
mean score	0.83 ± 1.04	1.11 ± 1.15	1.35 ± 1.14	1.34 ± 1.12	1.26 ± 1.14	0.0001[1]
prevalence: any degree	48.5 (46.0–51.1)	58.9 (56.0–61.8)	71.0 (68.7–73.2)	72.0 (69.9–74.0)	67.6 (65.6–69.6)	0.0001[2]
prevalence: severe–very severe	7.3 (6.1–8.7)	11.5 (9.7–13.5)	14.7 (13.0–16.5)	13.8 (12.3–15.5)	13.3 (12.0–14.8)	0.0001[2]
Anxiety						
mean score	0.69 ± 1.02	0.92 ± 1.12	1.06 ± 1.13	1.11 ± 1.17	1.08 ± 1.14	0.0001[1]
prevalence: any degree	39.7 (37.2–42.2)	50.4 (47.4–53.3)	58.9 (56.4–61.2)	57.9 (55.6–60.2)	58.5 (56.4–60.5)	0.0001[2]
prevalence: severe–very severe	6.8 (5.6–8.2)	11.0 (9.3–13.0)	11.2 (9.8–12.9)	12.5 (11.0–14.1)	11.5 (10.2–13.0)	0.0001[2]
Physical mental exhaustion						
mean score	0.87 ± 1.13	1.15 ± 1.18	1.26 ± 1.15	1.47 ± 1.14	1.35 ± 1.19	0.0001[1]
prevalence: any degree	48.1 (49.3–54.4)	59.9 (57.0–62.8)	68.1 (65.8–70.3)	74.3 (72.2–76.3)	68.3 (66.4–70.3)	0.0001[2]
prevalence: severe–very severe	9.7 (8.3–11.3)	13.2 (11.3–15.3)	13.2 (11.6–15.0)	15.2 (13.6–16.9)	16.1 (14.6–17.7)	0.0001[2]
Urogenital						
Sexual problems						
mean score	0.59 ± 1.02	0.71 ± 1.06	0.92 ± 1.12	1.09 ± 1.19	1.05 ± 1.25	0.0001[1]
prevalence: any degree	31.3 (28.9–33.7)	38.0 (35.2–40.9)	51.0 (48.5–53.4)	55.3 (53.0–57.6)	51.2 (49.1–53.3)	0.0001[2]
prevalence: severe–very severe	7.0 (5.8–8.5)	7.2 (5.8–8.9)	10.0 (8.6–11.5)	12.9 (11.4–14.5)	14.3 (12.9–15.8)	0.0001[2]
Bladder problems						
mean score	0.47 ± 0.92	0.64 ± 1.04	0.85 ± 1.13	0.80 ± 1.09	0.89 ± 1.00	0.0001[1]
prevalence: any degree	26.5 (24.3–28.8)	35.2 (32.5–38.1)	46.0 (43.6–48.4)	43.7 (41.4–46.0)	41.8 (39.7–43.9)	0.0001[2]
prevalence: severe–very severe	5.1 (4.0–6.3)	7.2 (5.8–9.0)	11.1 (9.6–12.7)	9.4 (8.1–10.8)	7.6 (6.6–8.8)	0.0001[2]
Vaginal dryness						
mean score	0.53 ± 0.99	0.66 ± 1.02	0.93 ± 1.16	1.03 ± 1.18	1.09 ± 1.22	0.0001[1]
prevalence: any degree	28.7 (26.4–31.1)	37.5 (34.6–40.4)	49.8 (47.4–52.3)	52.5 (50.2–54.8)	53.7 (51.6–55.8)	0.0001[2]
prevalence: severe–very severe	6.8 (5.6–8.2)	6.8 (5.4–8.5)	11.7 (10.2–13.3)	13.3 (11.8–15.0)	14.2 (12.8–15.8)	0.0001[2]

*, Symptom prevalence rated as any degree (1–4) or severe–very severe (3 and 4); **, p value as determined with the Kruskal–Wallis test[1] or the χ^2 test[2]

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Table 4 Mean total Menopause Rating Scale (MRS) scores, frequency of severe MRS scores (impaired quality of life) and risk of impaired quality of life throughout the menopausal stages

Reproductive stage	Total MRS score (mean ± standard deviation)	Impaired quality of life[†] (95% confidence interval)	Impaired quality of life[‡] (95% confidence interval)
All women	11.27 ± 8.54	23.0 (21.7–24.4)	–
Premenopause (40–44 years)	7.32 ± 7.80	12.9 (11.2–14.7)	1.00
Premenopause (≥ 45 years)	9.78 ± 8.11	18.1 (15.9–20.5)	1.50 (1.20–1.82)
Perimenopause	11.82 ± 8.41	26.4 (24.3–28.6)	2.43 (2.00–2.94)
Early postmenopause	12.91 ± 8.46	31.6 (29.5–33.8)	3.12 (2.60–3.76)
Late postmenopause	12.94 ± 8.40	29.9 (28.0–31.8)	2.89 (2.41–3.46)
p Value*	0.0001[1]	0.0001[2]	0.0001[2,3]

[†], Prevalence of women displaying total MRS scores above 16; [‡], non-adjusted odds ratios; *, *p* value as determined with the Kruskal–Wallis test[1] or the χ^2 test[2]; odds ratio 2.34 (95% confidence interval 2.07–2.65)[3]

differences. The presence of hot flushes was the most important factor related to impaired quality of life (total MRS scores >16) in all, pre- and peri/postmenopausal women. Only hot flushes were considered in this analysis as they are the most common and well-known symptom related to the menopause. Psychotropic drug use and psychiatric consulting were the next two most important factors related to impaired quality of life. Church attendance, HT and contraceptive use, and self-perceived health status were factors related to lower risk.

DISCUSSION

In general, menopausal symptoms are the consequence of the decline in ovarian function. Nevertheless, their presence and severity may not only depend on hormonal status but on socio-cultural, ethnic and geographical aspects as well (i.e. city temperature or altitude)[11]. Upon analyzing the characteristics of

our studied population, it may be immediately highlighted that some factors influencing the prevalence and severity of menopausal symptoms may change as women age and progress through the menopausal transition. Compared to younger premenopausal women (40–44 years), those with 5 or more years since menopause onset display a range of features that have been associated with a higher risk of presenting menopausal symptoms[26–30]. Indeed, not only were they older (13 years average) yet also less educated, less sexually active, used HT less often and reported a higher rate of psychiatric consultation and psychotropic drug use, not to mention the fact that they reported a worst self-perception of health. Hence, menopausal symptom prevalence may be reported as higher in older women due to the presence of these factors.

The present study found that many of the studied women (90.9%) presented at least one menopausal symptom rated at any degree. This percentage is slightly lower than the 96.4% reported in Brazil by Pedro and colleagues[31], probably because

Table 5 Sociodemographic and female factors associated with impaired quality of life (total score on Menopause Rating Scale >16) according to menopausal status: logistic regression analysis. Data are presented as odds ratio (95% confidence intervals)

Factors	Premenopausal (n = 2655)	Peri/postmenopausal (n = 5718)	All (n = 8373)
Hot flush presence	12.67 (9.53–16.83)	9.37 (7.85–11.19)	10.28 (8.84–11.95)
Use of psychotropic drugs	1.98 (1.24–3.17)	2.01 (1.59–2.53)	2.00 (1.63–2.46)
Premature menopause	–	–	1.80 (1.23–2.64)
History of psychiatric consulting	1.37 (0.94–2.00)	1.86 (1.52–2.26)	1.76 (1.48–2.10)
History of rape	1.23 (0.71–2.13)	1.92 (1.43–2.58)	1.70 (1.31–2.20)
Peri/postmenopausal	–	–	1.45 (1.26–1.67)
Living at high altitude (2500 m)	1.46 (1.14–1.88)	1.36 (1.18–1.56)	1.39 (1.23–1.57)
Current smoking habit	1.76 (1.30–2.37)	1.17 (0.99–1.39)	1.28 (1.10–1.48)
Use of alternative therapy	1.04 (0.61–1.78)	1.29 (1.05–1.59)	1.26 (1.04–1.52)
Church attendance	0.89 (0.70–1.14)	0.82 (0.72–0.93)	0.83 (0.74–0.93)
Sexually active	1.11 (0.80–1.56)	0.70 (0.61–0.81)	0.75 (0.66–0.85)
Use of hormone therapy	0.89 (0.50–1.57)	0.72 (0.61–0.85)	0.74 (0.63–0.87)
Use of contraceptives	0.62 (0.42–0.91)	0.72 (0.44–2.00)	0.70 (0.52–0.94)
Good health (self-perception)	0.53 (0.36–0.77)	0.60 (0.49–0.73)	0.58 (0.49–0.70)

the authors did not include, as we did, younger women (40–44 years), an age group usually presenting a lower symptom prevalence when compared to older ones. Although menopausal symptoms affected almost all of our studied women, only 24.9% presented at least one symptom rated as severe–very severe and overall 23.0% presented total MRS scores defined as severe (>16). The latter rate was higher than that reported by the authors of a study using the MRS in Asian women (9.5%) yet similar to those found in European (24.3%), North American (22.5%) and Latin American (22.7%) women[22].

Muscle and joint discomfort was the most frequently reported menopausal symptom (63.0%) rated at any degree among all our studied women; 15.6% rated this complaint as severe–very severe. As already mentioned, this complaint has also been reported in the SWAN as the most prevalent, affecting 54.3% of women aged 40–55 years[1]. A similar trend has been observed in Thailand, where 56.4% of postmenopausal women were affected within the first year of amenorrhea[32]. Another prevalent symptom in our series was physical and mental exhaustion; nevertheless, the percentage of women rating this symptom as severe–very severe was slightly lower when compared to muscle and joint discomfort (13.8% vs. 15.6%). Interestingly, other complaints assessed with the MRS psychological subscale, such as irritability, depressive mood and anxiety, although being less prevalent, were more severely rated and contributed to 40.8% of the total MRS score. Vasomotor symptoms, very commonly reported menopausal symptoms, were ranked ninth in the present series. Contrarily, vasomotor symptoms were the most frequently reported complaints among postmenopausal European women (up to 74%)[33]. Finally, although the prevalence of any degree-rated urogenital symptoms in our women was lower than for somatic and psychological complaints, a higher number of women rated these symptoms as severe–very severe (31.3% vs. 10.8% and 28.7% respectively). Using the MRS, Chuni and Sreemareddy[34] have reported severe vaginal dryness among 23.6% of women aged 40–65 years in Nepal.

It was found in the present study that menopausal symptoms appear early in the premenopausal stage even before menstrual irregularities begin; thus, for example, 29.7% of premenopausal women under 45 years of age have vasomotor symptoms, 26.1% heart discomfort, 49.6% sleeping problems and 45.9% muscle and joint discomfort, with 70.0% experiencing at least one complaint rated at any degree. The latter is consistent with a Finnish study that found 64% of women aged 42–46 years present menopausal symptoms[35]. It is important to mention that 3.3–9.7% of our studied younger premenopausal women present symptoms rated as severe–very severe. The majority of these symptoms became more prevalent in postmenopausal women and continued to be present 5 or more years after menopause onset. Vasomotor symptoms are amongst the few symptoms that tend to decline in late postmenopausal women. In our study, a similar trend was also observed for symptoms composing the psychological and urogenital

subscales of the MRS, which were present in younger premenopausal women and increased throughout the menopausal stages, with a slight decrease observed in late postmenopausal women. It should be highlighted that, in the present study, general menopausal symptoms were found in young premenopausal women, who still exhibited regular menstrual cycles, with a prevalence that increased with age and the menopausal phase. These symptoms may last for years, as was found in the present study in which late postmenopausal women, 5 or more years since menopause onset, continue to present symptoms with a similar frequency and intensity as peri- and early postmenopausal women at the time when menopausal symptoms classically appear[1,36]. In agreement with our results, an Australian study found that the prevalence of menopausal symptoms was still high 7 years after menopause[37].

Certainly, our observations cannot be extrapolated to other populations. Various studies performed in a given country show differences in symptom prevalence in relation to various ethnic groups. In the US, Im and colleagues[38] have reported that feeling hot or cold was the most frequently experienced menopausal symptom among Caucasian, Hispanics and African Americans, whereas decreased sexual interest was more frequently seen among Asians. These ethnic differences have also been found in the SWAN. After controlling for age, education, health, and economic status, Caucasian women reported significantly more psychosomatic symptoms than other ethnic groups and African-American women reported more vasomotor symptoms[1]. In Colombia, Monterrosa and colleagues[28] have determined that menopausal symptom severity (total MRS score) is significantly higher in Afro-Colombian women as compared to non-Afro-Colombians and is related to higher somatic and psychological subscale scores. Ojeda and colleagues[39] have also determined with the MRS that indigenous women display a high prevalence of menopausal symptoms, hypothesizing that ethnic blending (mestizo) may be a critical factor explaining the severity of menopausal symptoms found among climacteric Latin American women. As mestizo ethnicity is predominant in Latin America, studies involving pure Caucasian women are lacking. In light of these data, the results of the present study can only be applicable to mestizo Latin American women aged 40–59 years.

The high prevalence and severity of menopausal symptoms found in the women of our study throughout the different stages of the menopause correlate with a high rate of women displaying severely compromised quality of life. Indeed, as assessed with the MRS, 12.9% of our younger premenopausal women displayed severely compromised quality of life. This percentage rises steadily, with a peak observed 4 years after the menopause of 31.6% and then slightly declining in the late postmenopause. In accordance with our results, a Chilean study, assessing quality of life with the Menopause Specific Quality of Life Questionnaire, found that women 40–59 years displayed a gradual impairment in quality of life after the premenopausal stage and then reached a further deterioration 5 or more years after menopause onset[40].

The fact that vasomotor symptoms are the most common menopausal symptoms led us to analyze their possible role as a marker of impaired quality of life. Logistic regression analysis found that their presence implied a ten-fold risk of presenting impaired quality of life (MRS total scores >16), even among premenopausal women. This observation is consistent with other studies that have suggested that vasomotor symptoms increase the risk of impaired quality of life[41]. Reports also indicate that, independent of the vital events, premenopausal women with family dysfunction or poor social support and experiencing vasomotor symptoms have more stress and psychological and somatic symptoms[10]. The fact that our regression model found that HT and contraceptive use decreased the risk for impaired quality of life leads us to encourage HT use in premenopausal women, especially in those with hot flushes who display the greatest symptomatology. Our study showed that premenopausal women have impaired quality of life due to menopausal symptoms and that these complaints may persist several years after menopause onset. HT use significantly decreased the risk of impaired quality of life. Despite this, no scientific society has stated guidelines for the treatment of premenopausal women with impaired quality of life due to severe menopausal symptoms. Most clinicians expect menses to cease in order to indicate therapy. The present study found that 5.5% of younger and 11.0% of older premenopausal women use HT or alternatives to treat their symptoms. Our results point to the need to regulate premenopausal HT use. The prevalence of HT use found in our study among early postmenopausal women (23%) does not differ to that currently found in Western countries in the post-WHI era[42,43]. In addition, measures that improve lifestyles and thus reduce menopausal symptoms and the risk of chronic diseases in young women should be encouraged. Physical activity is associated with less intense menopausal symptoms[44] and may decrease obesity, a condition also associated with more severe symptoms[45].

Finally, the limitations of the present study include its cross-sectional design and the fact that the sample is not representative of the Latin American population, but only of women who accompanied their relatives to the participating Latin American health-care centers. Defining the menopause only by the presence of amenorrhea can also be seen as a drawback. As a strength of our study, one can highlight the large number of surveyed women and the multiplicity of participating cities. Including vasomotor symptoms in the logistic regression model instead of the other more prevalent non-classical menopausal symptoms found in the study may also be considered a potential weakness. However, vasomotor symptoms were chosen as a marker of impaired quality of life in view of the fact that they are the most commonly known symptom world-wide and their presence has also been included in the definition of severely compromised quality of life.

CONCLUSION

In this large, mid-aged, Latin American female series, muscle and joint discomfort and psychological symptoms were the most prevalent and severely rated menopausal symptoms. They occur early in the premenopause, increase with age and with each menopausal phase and significantly impair quality of life, with an impact lasting 5 years beyond the menopause. This is in contrast to vasomotor symptoms which have classically been reported in the literature as the most common menopausal complaint, ranked ninth in the present series. In light of our findings, guidelines for the treatment of symptomatic premenopausal women are strongly recommended.

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Appendix: Participating countries, investigators and cities

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