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ORIGINAL ARTICLE

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Sleep disorders and menopausal symptoms: a Latin American perspective on postmenopausal health

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ABSTRACT

Objective: This cross-sectional, observational study, conducted in nine Latin American countries, aimed to examine the association between hot flashes and insomnia, and whether the severity of vasomotor symptoms (VMS) correlates with sleep disturbances.

Method: The study collected sociodemographic and clinical data, and evaluated the presence of sleep disorders using Jenkin's Sleep Scale (JSS-4) and menopausal symptoms using the Menopause Rating Scale (MRS) questionnaire.

Results: The study included 1185 postmenopausal women with average age 56.9 ± 5.7 years, body mass index (BMI) of 26.5 ± 5.2 kg/m^2 and 8.6 ± 6.4 years since menopause. Overall, 20.6% reported sleep disturbances. Compared to those without sleep problems, affected women had longer postmenopausal duration (12 ± 9.0 vs. 10.8 ± 7.8, $p < 0.03$), had higher BMI (27.9 ± 5.6 vs. 26.1 ± 5.0, $p < 0.001$), were more often smokers and homemakers, and had more comorbidities. They were also less likely to have a partner or have used menopausal hormone therapy. Sleep disturbances increased proportionally with VMS severity ($p < 0.01$). In multivariate analysis, sleep disorders were associated with VMS (odds ratio [OR] 4.47), psychotropic use (OR 1.84), obesity (OR 1.45) and comorbidities (OR 1.45).

Conclusion: Women with VMS were more likely to experience sleep disorders and this effect was proportional to the magnitude of the hot flashes. The study also presents several factors associated with sleep disorders in postmenopausal women that should be considered to help prevent these disturbances.

PLAIN LANGUAGE SUMMARY

This study examined the impact of hot flushes on sleep disorders in 1185 postmenopausal women, averaging 56.9 ± 5.7 years of age.

Of the total, 244 had sleep disturbances and had significantly more postmenopausal years, higher body mass index, were more frequently housewives, smoked more, used more psychotropic drugs and had more comorbidities. Conversely, they were less likely to have a partner, had fewer partners, used less MHT, and had lower sexual activity and physical activity. There were no differences in age, age at menopause, years of education, parity, sexual activity and physical activity.

A significant association was found between the severity of hot flashes and the extent of sleep disruptions.

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Insomnia; sleep disorders; menopause; vasomotor symptoms

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Introduction

During the menopausal transition and postmenopausal period, many women experience hot flashes and insomnia, which can significantly impact their quality of life [1,2]. Hot flashes, characterized by sudden episodes of heat, flushing and sweating, are reported by up to 75% of menopausal women [3,4]. These symptoms are attributed to fluctuations and eventual decline in estrogenic levels, which disrupt the hypothalamic thermostat, triggering a vasodilation response [5].

Insomnia, defined as difficulty in initiating or maintaining sleep, is a prevalent symptom that affects up to 60% of women during menopause [6]. It not only worsens fatigue and irritability but is also linked to an increased risk of mood disorders such as depression and anxiety [7]. The domino hypothesis suggests that hot flashes disturb sleep, thereby causing insomnia, which in turn increases vulnerability to depression [8,9].

In addition to declining estrogen, stress, anxiety, depression and race may also influence sleep [10–12]. The variability in symptom presentation and the influence of cultural factors add another layer of complexity to understanding this phenomenon [13].

Epidemiological studies have found that insomnia was associated with an increased risk of obesity, hypertension, diabetes, coronary heart disease and other cardiovascular diseases [14–16]. Therefore, sleep problems among perimenopausal and postmenopausal women should be paid more attention. Moreover, there is evidence that sleep disorders have shown a steady increase in prevalence over the last few years [17].

This study aims to examine the connection between hot flashes and insomnia in a large cross-sectional survey of Latin American women. Additionally, the study seeks to determine whether there is a relationship between the severity of vasomotor symptoms (VMS) and the extent of sleep disorders.

This work offers additional context on the intricate connection between VMS and sleep disorders, both of which are highly prevalent during the postmenopausal period.

Subjects and methods

Study design and participants

The multinational and observational, Latin American, cross-sectional study (REDLINC XII) was conducted between January and October 2023 in general gynecology consultations across nine countries in Latin America: Argentina, Bolivia, Brazil, Colombia, Costa Rica, Ecuador, Mexico, Panama and Peru [18]. Participants were postmenopausal women aged under 70 years who attended a routine gynecological check-up (convenience sampling). Researchers at the participating centers were asked to complete 100 surveys. The study included postmenopausal women (1 year of amenorrhea) who were otherwise healthy. All participants were required to be able to read and write in their native language. Most women had middle-income levels and received medical care at either private or public clinical centers. We excluded women who had undergone chemotherapy or radiotherapy, those with hearing or vision impairments, or those with a diagnosis of dementia that would interfere with their understanding of the questionnaires.

This study is a sub-analysis of the REDLINC XII study, which aimed to investigate the impact of menopause type on cognitive function. The analysis utilized the original database to explore the connections between the frequency of VMS and the severity of sleep disorders.

The participants were 1185 postmenopausal women who met the requirements of the REDLINC XII study described earlier.

Studied variables

The following data were collected: age, years of schooling, body mass index (BMI), parity or number of children, current partner, sexual activity, homemaker status, smoker, age at menopause, hysterectomy, bilateral oophorectomy, current use of menopausal hormone therapy (MHT), prior use of MHT, current use of antidepressants, hypnotics or anxiolytics and comorbidities (treatment for hypertension, diabetes or dyslipidemia).

The Spanish-language validated versions of the Jenkins Sleep Scale (JSS-4) and the Menopause Rating Scale (MRS) were used, which have been previously applied in Latin American populations [19,20]. The JSS-4 is a four-item tool that evaluates the frequency and intensity of sleep problems over the past 4 weeks. Each item is assessed on a Likert scale with five response options: never (0 points), 1–3 days (1 point), 4–7 days (2 points), 8–14 days (3 points), 15–21 days (4 points) and 22–31 days (5 points). The JSS-4 is known for being a brief, user-friendly tool with strong psychometric properties [21]. A score of 12 points or more suggests the presence of a sleep disorder [22].

The MRS was used to characterize menopausal symptoms in the study. This is a standardized self-administered scale to assess symptoms/complaints of aging women under different conditions, to evaluate the severity of symptoms over time [23] and to measure changes in premenopause and postmenopause replacement therapy [24]. A score of 14 points or higher indicates the presence of menopause symptoms [23].

Statistical analysis

Statistical analysis was performed using SPSS software (version 21.0 for Windows; SPSS Inc., Chicago, IL, USA). Data are presented as the mean and standard deviation or frequency. Variance homogeneity was assessed using Levene's test ($p > 0.05$). The normality of data distribution was tested with the Kolmogorov–Smirnov test. Accordingly, differences between numerical variables were analyzed using the Mann–Whitney test (non-parametric data) or Student's *t*-test (parametric data). Comparison of categorical data was performed using the chi-square test. Categorical covariables were entered into the model as presented, while continuous covariables were categorized based on the median. Variables were included in the model using a stepwise procedure, considering a significance level of 10%. The variance inflation

factor was used to address multicollinearity in the regression analysis (variance inflation factor <10). Interactions between variables that were statistically significant in the bivariate analysis were also considered. The Omnibus test and the Hosmer–Lemeshow test were used to determine the adequacy of the regression model. For all calculations, $p < 0.05$ was considered statistically significant.

Studied variables

The following data were collected: age (years), age of menopause (years), years since menopause (years), BMI (weight [kg]/squared height [m]), years of education, homemaker defined as a woman who has primarily assumed that role throughout her life (yes/no), number of children, having a current partner (yes/no), sexual activity (at least one sexual intercourse in the last year, yes/no), physical activities (defined as performing >75 min/week of intense aerobic physical activities such as running, gym workouts, tennis, etc., or >150 min/week) or moderate aerobic physical activities (fast walking, cycling or dancing), ever smoker (%), ever MHT user (%), use of psychotropics drugs (anxiolytics, hypnotics or antidepressants) (yes/no) and comorbidities defined as being treated for dyslipidemia, diabetes mellitus or hypertension (yes/no).

For statistical analyses, women were divided into two groups according to the presence or absence of sleep disturbances.

Table 1. Clinical characteristics of studied women according to the presence of sleep disorders.

Parameter	*Sleep disturbances* (n = *244*)	*Non-sleep disturbances* (n = *941*)	p-*Value*
Age (years)	55.5 ± 7.8	55.3 ± 6.6	ns
Age at menopause (years)	43.5 ± 7,4	44.5 ± 7.0	ns
Years since menopause	12.0 ± 9.0	10.8 ± 7.8	0.03[a]
Body mass index (kg/m^2)	27.9 ± 5.6	26.1 ± 5.0	0.001[a]
Years of education	12.8 ± 5.46	13.4 ± 5.0	ns
Homemakers (%)	43.0 (36.8–49.3)	35.4 (32.3–38.5)	0.027[b]
Number of children	2.4 ± 1.8	2.5 ± 1.7	ns
With a partner (%)	66,4 (60.4–72.4)	74,1 (71.3–76.9)	0.017[b]
With sexual activity (%)	68.1 (65.1–71.1)	62.7 (56.6–68.8)	ns
Physical activities	46.3 (40.0–52.6)	49.2 (46.0–52.4)	ns
Ever smoker (%)	32.8 (26.9–38.7)	25.4 (22.6–28.2)	0.020[b]
Ever MHT users (%)	28.7 (23.0–34.4)	37.7 (34.6–40.8)	0.009[b]
Use of psychotropic drugs (%)	45.5 (39.2–51.8)	30.2 (27.2–33.1)	0.001[b]
Comorbidities (%)	57.4 (51.1–63.6)	41.7 (38.5–44.8)	0.001[b]

[a]Determined with the Mann–Whitney *U*-test.
[b]Determined with the chi-square test.
Data presented as mean ± standard deviation or percentage (95% confidence interval). MHT, menopausal hormone therapy; ns, not significant.

Results

Out of the total of 1185 women studied, 244 (20.6%) reported experiencing sleep disturbances. Table 1 presents a comparison of the characteristics of women with and without sleep disorders. The study revealed that women with sleep disorders had been postmenopausal for a longer duration, had higher BMI, were more frequently homemakers, smoked more, used more psychotropic drugs and had more comorbidities. Additionally, they were less likely to have a partner or use MHT. There were no significant differences between the two groups in terms of age, age at menopause, years of education, number of children or level of physical activity (Table 1).

Figure 1 depicts the relationship between the percentage of sleep disturbances, as assessed by the JSS-4, and the intensity level of hot flushes measured using the MRS questionnaire. The data indicate a gradual increase in sleep disturbance scores as the severity of symptoms rises, starting at 6.4% in women without hot flushes (MRS 0) and increasing to 13.9% in women with very severe hot flushes (MRS 4).

Table 2 presents the average score for each type of sleep disorder as assessed by the JSS-4 score, based on the presence or absence of VMS. The results indicate that patients experiencing VMS encounter greater difficulty in staying asleep, waking up multiple times during the night, an inability to fall back asleep and experiencing non-restorative sleep.

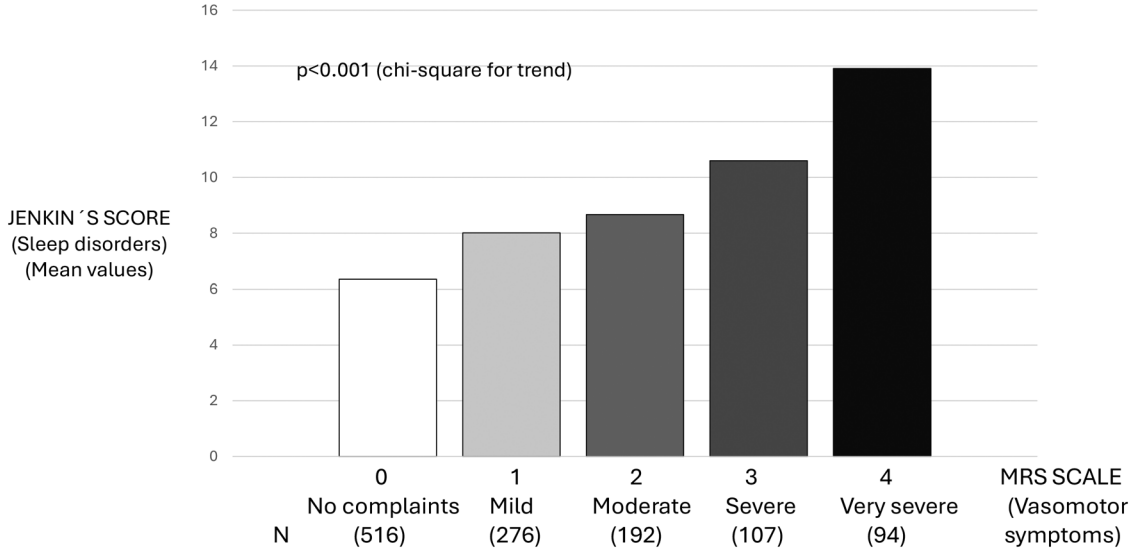


Figure 1. Average sleep disturbance assessed using the Jenkins Sleep Scale (JSS-4), according to the intensity level of hot flashes, as measured by the Menopause Rating Scale (MRS) questionnaire.

Table 2. Impact of hot flashes on the different domains of sleep quality according to the Jenkins Sleep Scale (JSS-4).

Vasomotor symptoms	*Difficulty staying asleep*	*Waking up multiple times during the night*	*Having trouble falling back asleep*	*Non-restorative sleep*	*Total score*
No	1.50 ± 1.14	1.77 ± 1.4	1.49 ± 1.18	1.58±1.13	6.35±4.07
Yes	2.22 ± 1.65	2.59 ± 1.81	2.20 ± 1.63	2.43±1.71	9.45±5.71
p-Value[a]	0.0001	0.0001	0.0001	0.0001	0.0001

[a]Determined with the Mann–Whitney *U*-test.
Data presented as mean ± standard deviation.

This is further supported by a significant increase in the total JSS-4 score, which rose from 6.35 to 9.45 ($p < 0.0001$).

Table 3 presents the results of a multivariate study that examined the factors related to sleep disturbances. The study found that VMS were strongly associated with sleep disorders, with an odds ratio of 4.46 and a 95% confidence interval of 3.12–6.40. Other significant factors associated with sleep disturbances were the use of psychotropic drugs, obesity and the presence of comorbidities. An association was observed between being in a relationship and lower levels of sleep disturbances. There was no collinearity between the variables, as all variance inflation factor values ranged from 1.046 to 1.258.

Discussion

Our research has shown that VMS are an important factor associated with sleep disturbances. Sleep scores deteriorate as the severity of flashes increases.

Hot flashes occur when estrogen levels decrease. The mechanism behind them is quite complex and involves central noradrenergic activity [25] as well as the activity of hypothalamic kisspeptin, neurokinin B and dynorphin (KNDy) neurons [26]. KNDy neurons project to structures that are important for regulating body temperature, and their effects on temperature regulation are influenced by estrogen.

Self-reported VMS are consistently associated with poorer self-reported sleep quality and chronic insomnia [27]. Longitudinal Study of Women's Health Across the Nation (SWAN) data show that women with moderate to severe hot flashes are almost three times more likely to report sleep disturbances [28].

Nocturnal hot flashes therefore have a significant impact on sleep disturbance, although there is considerable individual variability [29]. Some women going through menopause-related sleep problems do not have hot flashes, and not all hot flashes result in waking up. It is important to consider other factors that can affect sleep, such as the direct impact of changes in reproductive hormones.

The decline of estrogen contributes to sleep disturbances. An 8-week study using daily sleep diaries showed that low estrogen levels and elevated follicle stimulating hormone (FSH), typical of perimenopause, are independent risk factors for insomnia, irrespective of hot flashes [10]. While night-time VMS remained the leading cause of disturbed sleep continuity in this population, the data also suggest that fluctuating hormone levels play a role in sleep difficulties for perimenopausal women without night-time VMS.

Table 3. Factors associated with sleep disturbances: logistic regression model.

Condition	*OR*	*95% CI for OR*	p-*Value*
Presence of vasomotor symptoms	4.47	3.12–6.40	0.0001
Use of psychotropic drugs	1.84	1.35–2.52	0.0001
Obesity	1.45	1.06–1.97	0.019
Comorbidities	1.45	1.06–1.98	0.019
Having a partner	0.70	0.51–0.96	0.028

CI, confidence interval; OR, odds ratio.

Estrogen signaling is most impactful on sleep regulation. Estrogen receptors are found in various neural centers regulating sleep in rats, including in the basal forebrain, hypothalamus, dorsal raphe nucleus and locus coeruleus [30] and in the sleep-active ventrolateral preoptic area [31].

Another possible explanation for sleep disturbances could be related to changes in the hypothalamic neuropeptide orexin-A levels, which promote wakefulness, and how these levels change during menopause. Estradiol affects the expression of orexin receptor 1 in the hypothalamus and anterior pituitary [32]. Plasma orexin levels are three times higher in postmenopausal than premenopausal women, whereas postmenopausal women taking estrogen therapy have levels like premenopausal women [33]. These findings suggest that estradiol may impact sleep during the perimenopausal transition through various pathways.

In our study, women who experience sleep disturbances had more postmenopausal years. This can be understood as a period during which there is a gradual decrease in ovarian steroids, particularly testosterone, androstenedione and estrone. Estrone is the predominant estrogen in postmenopausal women and is derived from its peripheral conversion from androstenedione. This decrease in ovarian steroids can be associated with experiencing more hot flashes [34,35].

In addition, the group with sleep disorders had higher BMI. The relationship between sleep disturbances and obesity seems to be bidirectional. Obesity can disrupt sleep due to the high prevalence of obstructive sleep apnea [36]. Moreover, all definitions of short sleep duration (<7 h, <6 h, <5 h or <4 h per night) were linked to a higher risk of obesity in adults. Importantly, the duration of sleep appeared to have a more significant effect on body fat in females [37]. The latter might be attributed to different hormonal profiles and socioeconomic status [38]. In addition, a reduction in body weight could lead to changes in sleep duration. Significant weight loss was associated with decreased sleepiness during the day and time to fall asleep, and increased sleep duration in people with short sleep duration (≤7 h) [39]. Furthermore, people with short sleep duration or poor sleep quality lost less fat mass, while having a 600 kcal restricted diet during a longitudinal study over 24 weeks [40], another argument in favor of bi-directionality that was mentioned earlier. Fat loss, in this study, increased by 0.72 kg for each additional hour of sleep.

From the pathophysiological point of view, reduced sleep is associated with low levels of leptin and glucagon-like peptide-1 (GLP1) and elevated levels of ghrelin, free fatty acids, catecholamines, interleukin-6 and tumor necrosis factor-α (TNFα) (representing inflammation), sympathetic activity and brain activation in response to food cues. Most

of these changes can lead to insulin resistance/reduced β-cell activity and changes in energy balance which can eventually be associated with obesity/type 2 diabetes mellitus [41].

The study found that homeowners are at a higher risk of experiencing sleep problems. This was identified as a risk factor for more sleep problems in our study and is usually associated with a lower socioeconomic situation, as they are responsible for taking care of children and doing household chores. In addition, they tend to have lower cultural levels [42]. There is also a relationship between low income/education and obesity [43], and through this mechanism could be more prone to sleep disorders, as recently analyzed.

The habit of smoking, which is more frequent in our studied women with sleep disorders, is a common factor in environmental exposure and has become a serious public health problem [44]. Nicotine, the main active substance in tobacco, can influence the release of neurotransmitters such as dopamine and thus affect sleep [45]. In addition, nicotine can stimulate cholinergic neurons in the basal forebrain and cause physiological arousal [46]. A meta-analysis demonstrated that second-hand smoke exposure is also associated with short duration and poor-quality sleep [45]. Another study using polysomnography also showed that smokers had several insomnia-like sleep impairments compared to non-smokers [47]. In addition, tobacco is associated with greater estrogen metabolization in the thalamic area [48], which can be associated with greater VMS and greater sleep disorders.

In our study, we found that women with sleep disturbances used more psychotropic drugs such as anxiolytics, hypnotics and antidepressants. This is highly understandable as these drugs are used to control sleep disorders and alleviate the depressive and anxious symptoms they experience. Depression in the older population may present differently to that in the younger population, and older patients with depression may be more likely to report sleep disturbances [49,50]. A bi-directional relationship likely exists between sleep disturbance and depression, with sleep disturbance representing both a risk for and a symptom of depression [51].

The insomniac patients in the study had more comorbidities – defined as the presence of dyslipidemia, diabetes and/or hypertension – than those who were normal sleepers. This fact is well established in the literature and refers to a more extensive list of comorbidities than those described in this study [52]. Given that sleep impairment is associated with increased risks of mortality, cardiovascular disease, impaired quality of life and falls, it should be a target of holistic patient management, and not considered a normal phenomenon of aging [53,54].

The current study has also several limitations. First, its cross-sectional design prevents us from making conclusions about causality. Second, the study did not investigate the causes of insomnia, which could introduce biases. The study also did not assess objective measures of sleep quality, so our findings are based solely on subjective evaluations. While the study measured the frequency of sleep problems, this does not necessarily indicate the clinical presence of sleep disorders [55]. Additionally, the reported experiences of hot flashes may not always align with objective measurements of this discomfort [56]. Finally, the study lacked specificity regarding the type of MHT used, including whether it involved estrogens or progestogens, the method of administration and the duration of therapy. Furthermore, the low rate of MHT use observed among symptomatic women in our study aligns with previously reported trends in Latin America. Regional data indicate that MHT utilization remains limited, with estimates ranging from 1.7% to 32.9%, and an average of just 12–15% among women experiencing VMS. These low rates are thought to reflect not only restricted access to therapy but also under-prescription by healthcare providers and prevailing cultural perceptions regarding hormone use [57].

The strength of our data lies in the high number of participants, the robustness of the applied tests and the fact that, to our knowledge, it is the first study on sleep disorders in postmenopausal Latin American women. Additionally, the study identifies several factors associated with sleep disturbances that could be helpful for clinically managing these patients.

As a corollary, our study shows that hot flashes are closely linked to sleep disorders. This effect is proportional to the magnitude and intensity of the VMS.

In conclusion, healthcare professionals must prioritize addressing sleep problems in postmenopausal women, as these disturbances can significantly contribute to various physical and mental health issues. By paying closer attention to sleep-related concerns, practitioners could potentially intervene earlier in addressing ailments stemming from poor sleep quality, leading to better overall health outcomes and enhancing the quality of life for postmenopausal women.

Ethics statement

The current study received approval from the ethics committee of the Southern Metropolitan Health Service in Santiago de Chile, Chile (Memorandum 15/2022; 22 June 2022) and adheres to the principles of the Declaration of Helsinki. All participants were fully informed about the study, its objectives and the tools used. Subsequently, they provided written consent to participate.

Disclosure statement

The authors report no conflicts of interest and are alone responsible for the writing and content of this document.

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Data availability statement

There are no linked research data sets for this article. The data from this study are not publicly available but can be requested for research collaboration projects in compliance with ethical, privacy and legislation requirements.

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