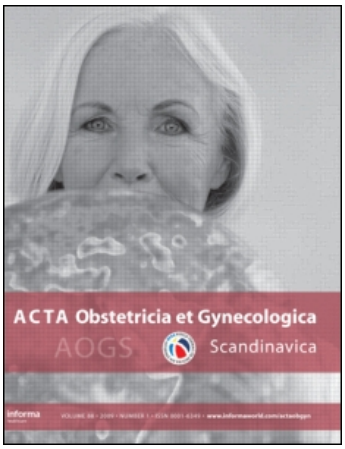


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**ORIGINAL ARTICLE**

# Clinical profile of menopausal insomniac women referred to sleep laboratory

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**Abstract**

*Objective.* The primary purpose of this study was to assess the overall clinical profile of menopausal women complaining of insomnia who were referred to a sleep laboratory. *Methods.* A total of 206 menopausal women who had complaints related to insomnia were interviewed. Each participant completed a questionnaire in order to obtain data on general health, menopausal status, medications, and sleep patterns. *Results.* The mean age of the participants was 55.9 years. Clinical profiles revealed that the most prevalent health problems were systemic arterial hypertension (33.9%) and osteoporosis (19%), though there was no association between insomnia and incidence of chronic disease. Our data demonstrate an overall prevalence of insomnia of 4–5 times a week in 62% of the women, with 68.9% complaining of hot flashes. However, there was no association between hot flashes and frequency of insomnia across the menopausal transition period. Only 7% of women had already undergone polysomnography. Less than 5% of the participants were undergoing treatment for menopause, while 8% were taking benzodiazepines for sleep problems. *Conclusions.* This study provides evidence that insomnia in postmenopausal women was not associated with incidence of chronic disease. In addition, the majority of the participants were not undergoing treatment for menopause or for sleep disturbance.

**Key words:** *Menopause, sleep, insomnia, sleep disorders, hypertension, hot flashes, hormonal therapy, benzodiazepines, hormones*

## Introduction

Questionnaire-based studies reveal that menopausal women frequently complain of problems with their sleep (1,2). Indeed, menopausal women frequently report hot flashes and night sweats, where these are both associated with insomnia (3). Ohayon et al. (4) stated that severe hot flashes are strongly associated with chronic insomnia in midlife women and suggested that hot flashes should be systematically investigated in women with insomnia. However, there is evidence that hot flashes may not be a cause of sleep disturbances (5), which suggests that complaints of insomnia by postmenopausal women may co-exist with other causes of sleep disturbance such as apnea or periodic leg movements (PLM) (6–8).

It is well documented that menopause is a critical period in the lives of women that leads to several noticeable symptoms. Women commonly attribute these symptoms to their disrupted or non-refreshing sleep (9). For instance, a high incidence of insomnia in postmenopausal women has been reported, with estimates ranging from 28 to 63% (10,11). A previous study from our lab indicated that insomnia was reported by 63% of postmenopausal women, with 83% of such cases being confirmed by polysomnography (PSG) (2). It is notable that subjects with

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chronic insomnia reported higher incidences of heart disease, high blood pressure, neurologic disease, breathing problems, urinary problems, chronic pain, and gastrointestinal problems compared to those without insomnia (11). Given this correlation, Lai et al. (12) suggest that insomnia and emotional disturbances should be taken into consideration in the management of climacteric women who seek medical advice.

The lack of studies describing the sleep complaints reported during menopause combined with the paucity of studies investigating the association between insomnia and chronic diseases led us to evaluate the overall clinical profile of a large sample of women in postmenopause who had been referred to a Brazilian sleep laboratory. The symptoms chosen for investigation were those that had been observed to increase in prevalence during the menopausal transition and, therefore, that had been hypothesized to be related to changes in sleep quality. As a secondary aim, we also examined the characteristics of those seeking medical assistance and determined the prevalence of women who were currently taking medication for these symptoms.



## Material and methods

The study protocol and consent forms were approved by the Ethical Committee of UNIFESP (# 564/02). The methods of this study have been described in detail elsewhere, as have the results pertaining specifically to hot flashes (9). Briefly, women aged 50–66 years complaining of insomnia were recruited from the general population by advertisements in newspapers and on the radio. Women who were interested in participating were screened by telephone and an appointment was scheduled for a clinical visit if they were eligible. A total of 228 women participated in the investigation. Seven of these women were excluded because they did not report amenorrhea and another 12 were excluded due to lack of complaints of insomnia at the time of the study. Three women were excluded because they had undergone hysterectomy and/or oophorectomy.

Participants answered a sleep survey designed to quantify subjective sleep quality. The sleep questionnaire consisted of an instrument developed by the team at the Sleep Institute/AFIP. The frequency, type of insomnia (initial, middle, final insomnia), subjective latency to sleep, and duration of sleep were probed by the questionnaire. In order to evaluate the presence of sleep disorders, women were also asked whether they had undergone PSG and whether they were taking medication to induce and/or maintain sleep.

The definition of menopausal status was from the consensus statement on a staging system for the reproductive aging of women, standardized in the Climacteric Section of University Medical Center (that is, menopause is defined as 12 months of amenorrhea). Participants underwent a complete screening interview that included questions about hot flashes, whether they had any other diseases, and whether they were undergoing hormone replacement therapy (HT) or taking isoflavone compounds.

### *Statistical analysis*

Data from the questionnaire and interview were quantified as variables indicating the prevalence of insomnia and other clinical conditions. Results are expressed as mean $\pm$ SD or as a percentage of subjects. In order to evaluate any possible association between variables, the Chi-Square Test was performed. The level of significance adopted was $p<0.05$.

## Results

The clinical characteristics of the population are given in Table I. In our sample of postmenopausal women, the mean age was 55.9 (50–66) years and the most prevalent health problems were systemic arterial hypertension and osteoporosis.

An assessment of insomnia revealed that the proportion of women who complained of insomnia 3–4 times/week was higher than the participants reporting insomnia five or more times/week ($p<0.01$) or 1–2 times/week ($p<0.01$), as depicted in Figure 1A. Nevertheless, there was no association between the frequency of insomnia and the presence of chronic disease (df = 2; $p = 0.46$). As illustrated in Figure 1B,

Table I. Clinical profile of menopausal women complaining of insomnia ($n = 206$).

| Characteristics | Profile |
|---|---|
| Mean age | 55.9 years (4.9) |
| Years of postmenopause | 9.1 years (6.2) |
| Systemic diseases | |
| Hypertension | 33.9% |
| Osteoporosis | 19% |
| Thyroid dysfunction | 7.2% |
| Type 2 Diabetes | 5.8% |
| Depression | 1.4% |

Data expressed in percentage.
For mean age and years of menopause, standard deviations are given in the parenthesis.

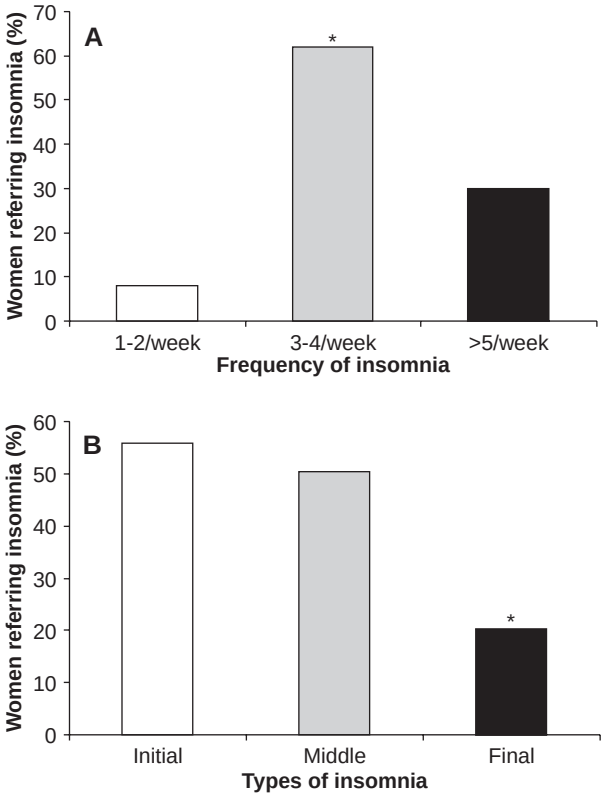


Figure 1. Frequency (panel A) and types of insomnia (panel B) reported by postmenopausal women. *Different from the other groups.

insomnia was reported to occur most commonly at the beginning and middle of the night than at the end ($p<0.01$). Indeed, only 20.4% of the women reported difficulties in maintaining sleep at the end of the night, as compared to 55.8% who indicated problems falling asleep.

As is evident in Figure 2, there is no association between the presence of hot flashes and the frequency of insomnia across the menopausal transition (Chi-square: 0.83; df = 2; $p = 0.66$). During the first years of menopause, the frequency of insomnia ranged from 4.3 to 3.5 times/week. After being in menopause for 20 years, the complaint of insomnia reached five times/week, and all women in the study reported the occurrence of hot flashes. There was no association between the number of years postmenopause and the type of insomnia ($p = 0.17$), hot flashes or type of insomnia ($p = 0.65$), or between hot flashes and frequency of insomnia ($p = 0.66$). Only 7% of the women had already undergone PSG.

The use of medication to alleviate climacteric symptoms was indicated by only 4.8% of the women interviewed. Hormonal and isoflavones were the most common therapies (in both cases, five women out of 206: 2.4%). Eight percentage of the participants used drugs in order to mitigate their sleep disturbances. Among those drugs, benzodiazepines were the most commonly used, where their use was observed mainly in women reporting less than six hours sleep per night. The other medications reported were: antihypertensive (26.2%), antidepressants (8.2%), thyroid medications (2.4%), anti-inflammatories (2.4%), osteoporosis medications (1.9%), hypoglycemia medications (1.4%), and corticoids and gastric pills (0.9%; data not shown).

## Discussion

The current study revealed that postmenopausal women suffering from insomnia did not generally present with other comorbid conditions and that only a minority of subjects had previously been under treatment for menopause or sleep disorders. Moreover, there was no association between the presence of hot flashes and the frequency of insomnia.

In light of the large number of women suffering from climacteric syndrome, there is a surprising lack of research investigating the sleep difficulties experienced by postmenopausal women. Indeed, sleep disturbance is a common complaint in these women, who report difficulty falling asleep as well as frequent awakenings with difficulty falling back to sleep, as we have previously observed (9). The association between hot flashes and insomnia has been raised in several studies, because women usually attribute poor sleep quality to nocturnal sweats (13,14). However, Freedman et al. (5) showed a lack of association between hot flashes and insomnia. Nevertheless, the complaint of hot flashes was more frequent in young women than in old ones (47.9 vs. 57.5 years old; data not shown). Most menopausal women suffered from the climacteric syndrome in the first years following the cessation of menses (15). In the current study, the frequency of hot flashes ranged from 66.7 to 94.4% of the women in the youngest group (those with less than five years of menopause). Similar incidences of hot flashes were also reported by postmenopausal women in Europe and North America (70–80%, respectively) (16). In contrast, Ohayon (4) showed that severe hot flashes were strongly associated with chronic insomnia in midlife women. Some studies using PSG have reported that women who exhibit hot flashes also experience more waking episodes, alterations in sleep stages, and less sleep efficiency (17).

Although bouts of insomnia occurring in the middle of the night have been attributed to nocturia, hot flashes or depression, our data, compiled from a considerable sample ($n = 206$), suggest that other reasons might be involved, given that we do not find a relationship between insomnia and hot flashes (Figure 2). This association is not unequivocally

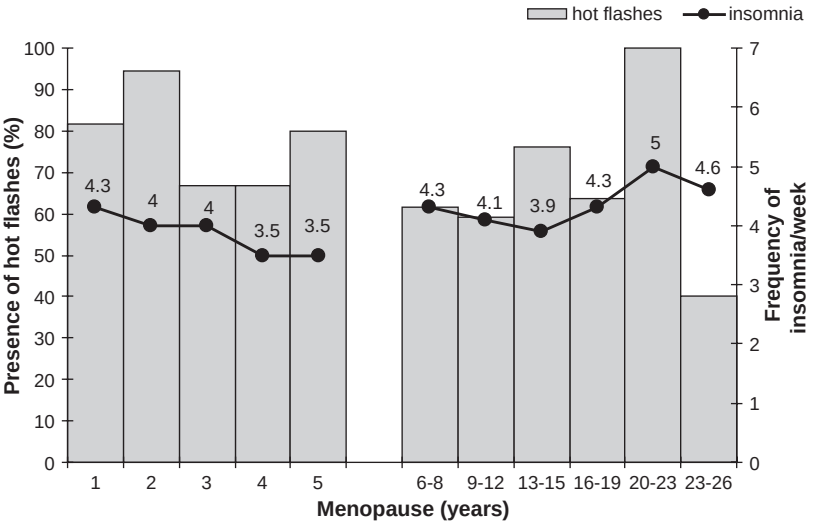


Figure 2. Fluctuations in the frequency of insomnia in relation to the percentage of women reporting hot flashes across menopause transition period.



accepted as the primary cause of sleep disturbance in menopause (5). Otherwise, the mood changes observed in postmenopause might result from sleep disorders attributed to the hot flashes that take place during sleep (13,18). In fact, it has been postulated that nocturnal urination, more than vasomotor symptoms, may cause sleep disorders in postmenopausal women (19). Thus, by treating atrophic genital alterations, we would expect a decrease in nocturia and thus be likely to minimize sleep fragmentation. The relationship between insomnia and chronic diseases has been previously proposed (20,21), as has the association between restless legs syndrome, depression, and heart disease (22). Our findings did not reveal an association between the presence of some diseases (e.g. osteoporosis, hypertension, diabetes) and insomnia. Thus, it can be assumed that the majority of postmenopausal women complaining of insomnia did not present systemic diseases as background.

The mechanisms that underlie insomnia in postmenopausal women are still obscure. It is unlikely that insomnia was related to either climacteric syndrome or other diseases. Despite the high prevalence of insomnia during postmenopause, most of the women reported that their sleep problems initiate during perimenopause. Young et al. (23) stated that, although women report sleep disturbance during both perimenopause and postmenopause, menopause itself was not a strong predictor of specific sleep-disorder symptoms. However, Shin et al. (24) found that insomnia was significantly associated with the menopausal period. According to these authors, the prevalence of insomnia increases significantly in the transition from pre-menopause to perimenopause, but not to postmenopause. Of note, among all climacteric symptoms, insomnia can, at least, be reversible, whereas the high prevalence of sleep disorders and PLM (9) require considerable treatment.

Overall clinical assessments such as Kupperman, Epworth, and other tools including sleep questions would provide a more integrated scenario regarding the diagnosis and could help guide specialists to the possible need for PSG to clarify whether complaints of insomnia are related to other sleep disorders such as PLM or sleep apnea. The presence of additional sleep disorders may be underestimated in insomnia cases, as our previous data demonstrated that nearly 50% of women complaining of insomnia present breathing disorders in sleep as well (8). Of note, 24.9% of the insomniac women also had PLM greater than five/hour, as previously reported (9).

Our results suggest that many cases of insomnia may be mishandled. At times, a given patient presents the symptoms of insomnia but does not meet the criteria for the diagnosis in the Diagnostic and Statistical Manual for Mental Disorders (DSM)-IV. A patient in postmenopause with symptoms of insomnia, even in the absence of DSM-IV determinants should (1) be treated for her hot flashes, nocturia, and other symptoms that are characteristic of the postmenopause syndrome. Often, once these symptoms are treated, the sleep complaints are resolved, and (2) address the diagnosis given to her sleep complaints, be they primary or secondary insomnia, apnea, or PLM. This will result in improvement of the symptoms associated with postmenopause.

As pointed out by Polo (25), insomnia is a particular symptom in the climacteric syndrome. In this study, we observed that the majority of the patients were not undergoing treatment for either climacteric syndrome or sleep problems. Proper assessment of symptomatology and adequate treatment could minimize symptoms such as hot flashes that inherently disrupt sleep. Under medical treatment, women would experience less depression and anxiety, as well as other situations that can lead to sleep disturbance. Foley et al. (26) reported that sleep complaints were associated with an increasing number of respiratory symptoms, physical disabilities, non-prescription medications, depressive symptoms, and poorer self-perceived health. Thus, sleep disturbances may be secondary to coexisting diseases. Nevertheless, the present findings fail to show this association. Additionally, the low concentrations of progesterone during the climacteric syndrome may contribute to apnea as progesterone is a respiratory stimulant (for a review, see Andersen et al. (27)).

Collectively, our data suggest that women underestimate their sleep quality. Although some had only occasional insomnia, they sought out sleep specialists to improve their sleep. Overall, a clinical assessment of women during menopause could lead to a better therapeutic approach to the symptoms, reducing not only insomnia but also undesired climacteric events. Insomnia in postmenopause is highly prevalent as a symptom. Gynecologists generally fail to prescribe adequate treatment, as they usually consider insomnia a postmenopausal symptom, and patients are misdiagnosed for PLM and apnea. Patients have responded overwhelmingly to calls for the treatment of insomnia at menopause, most likely because they feel that their condition has finally attracted the interest of specialists. According to the data collected in this investigation, insomnia in postmenopausal women was not associated with incidence of chronic disease, and the majority of participants were not undergoing any sort of treatment for menopause or for sleep disturbance.



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