

# ความชุกและปัจจัยที่เกี่ยวข้องกับอาการนอนไม่หลับในผู้หญิงวัย หมดประจำเดือนที่คลินิกวัยทอง โรงพยาบาลจุฬาลงกรณ์

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\*\*\*ศูนย์ความเป็นเลิศทางการแพทย์ด้านการดูแลผู้สูงอายุและภาควิชาสูติศาสตร์-นรีเวชวิทยา คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย

## บทคัดย่อ

**วัตถุประสงค์** เพื่อศึกษาความชุกและปัจจัยที่เกี่ยวข้องกับอาการนอนไม่หลับในผู้หญิงวัยหมดประจำเดือนที่คลินิกวัยทอง โรงพยาบาลจุฬาลงกรณ์

**วิธีการศึกษา** การศึกษาเชิงพรรณนา ณ จุดเวลาใดเวลาหนึ่งในผู้หญิงวัยหมดประจำเดือนที่คลินิกวัยทอง โรงพยาบาลจุฬาลงกรณ์ จำนวน 102 คน โดยการตอบแบบสอบถามข้อมูลส่วนตัว แบบประเมินอาการนอนไม่หลับ (insomnia severity index; ISI) และแบบสอบถามอาการวิตกกังวลและอาการซึมเศร้า ฉบับภาษาไทย (Thai Hospital Anxiety and Depression Scale scores) สถิติวิเคราะห์ใช้สถิติเชิงพรรณนาและการวิเคราะห์ถดถอยโลจิสติก

**ผลการศึกษา** พบความชุกของอาการนอนไม่หลับ ร้อยละ 52 (ISI  $\geq$  8) พบว่าอาการวิตกกังวลสัมพันธ์กับอาการนอนไม่หลับอย่างมีนัยสำคัญทางสถิติ (OR 12.57, 95% CI 1.56 - 101.5, p-value = 0.018) จากการวิเคราะห์ถดถอยโลจิสติกพบว่า ประวัติการใช้ฮอร์โมนทดแทนในปัจจุบันมีความสัมพันธ์กับอาการนอนไม่หลับ (aOR 0.36, 95% CI 0.13 - 0.97, p-value = 0.044)

**สรุป** จากการศึกษพบว่าความชุกของอาการนอนไม่หลับในผู้หญิงวัยหมดประจำเดือนค่อนข้างสูง โดยสัมพันธ์กับอาการวิตกกังวล ในขณะที่ประวัติการใช้ฮอร์โมนทดแทนเป็นปัจจัยป้องกันอาการนอนไม่หลับได้ การประเมินผู้หญิงวัยหมดประจำเดือนจึงควรประเมินอาการนอนไม่หลับ ภาวะวิตกกังวล และอาการอื่นๆ ทางจิตเวช เพื่อกำหนดแนวทางการรักษาที่มีประสิทธิภาพ และพัฒนาคุณภาพชีวิตของผู้ป่วยได้อย่างเหมาะสม

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# The Prevalence and Associated Factors of Sleep Disturbance in Menopause at Menopause Clinic, King Chulalongkorn Memorial Hospital

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## ABSTRACT

**Objective:** This study aimed to evaluate the prevalence of insomnia at a Menopause clinic in a tertiary hospital and to identify the associated factors of insomnia.

**Methods:** A survey of 102 female patients aged 45 - 60 at a Menopause Clinic collected demographic data, Insomnia Severity Index (ISI) scores, and Thai Hospital Anxiety and Depression Scale scores. Descriptive statistics, univariate, and multivariate logistic regression analyses were used to identify associations.

**Results:** The prevalence of insomnia was 52% (ISI  $\geq$  8). Anxiety symptoms were significantly associated with insomnia (OR 12.57, 95% CI 1.56 - 101.50, p-value = 0.018). Multivariate logistic regression analyses revealed significant associations between insomnia and currently using hormone replacement therapy (aOR 0.36, 95% CI 0.13 - 0.97, p-value = 0.044).

**Conclusion:** Insomnia is highly prevalent among menopausal women, especially those with anxiety, while usage of hormone replacement therapy has been shown to alleviate symptoms. Clinicians should emphasize the assessment of anxiety and insomnia in menopausal women to provide appropriate care. A comprehensive evaluation of other mental health conditions, vasomotor symptoms, and history of hormonal therapy is crucial for determining the most effective treatment approach.

**Keywords:** insomnia, menopause, anxiety

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## INTRODUCTION

The American Insomnia Survey, conducted in 2008 - 2009 among more than 10,000 people, found that over half experienced sleep disturbances, and 22.1% met the criteria for insomnia according to the Diagnostic and Statistical Manual of Mental Disorders, 4<sup>th</sup> edition (DSM-IV). The issue was statistically significantly more common in females than in males (27.1%, 19.7%;  $P = 0.001$ ), with a higher prevalence observed among those in menopause.<sup>1-3</sup> Insomnia can associate to various diseases, including diabetes (hazard ratio [HR], 1.28; 95% CI, 1.24 - 1.33), dementia (relative risk, 1.53; 95% CI, 1.07 - 2.18), stroke (HR, 1.54; 95% CI, 1.38 - 1.72), and chronic kidney disease (HR, 1.39; 95% CI, 1.34 - 1.44).<sup>4-7</sup>

A study conducted by the Thai Department of Mental Health in 2020 found that 19 million Thai people experience sleep disturbances, affecting individuals across all age groups. While most people experience symptoms for just one or two nights, some suffer from these disturbances for weeks, months, or even years. Women and the elderly are particularly affected.<sup>8</sup>

The hormonal changes associated with menopause can impact physical, emotional, mental, and social well-being. The symptoms experienced during and after the menopausal transition vary greatly from person to person. Some individuals experience few, if any, symptoms, while others may have severe symptoms that affect daily activities and quality of life.<sup>9</sup>

A cross-sectional study found that chronic insomnia during menopause is related to vasomotor symptoms, with a higher prevalence of insomnia in those experiencing more severe vasomotor symptoms. Among individuals with severe vasomotor symptoms, 80% experienced insomnia. Furthermore, insomnia was found to be bidirectionally associated with depression.<sup>10,11</sup> Insomnia was also bidirectionally associated with menopausal symptoms, as sleep disturbances can result from hormonal fluctuations, vasomotor instability, and mood disturbances, while poor sleep quality can worsen these symptoms, creating a cycle of mutual reinforcement. This complex interplay highlights the need for targeted

interventions addressing both sleep quality and menopausal symptoms to improve health outcomes in menopausal individuals.

A literature review reveals that many studies have explored insomnia during menopause. Although research has been conducted in both Western and Asian populations, there remains a limited focus on menopausal insomnia in Thailand. While studies in Thailand have examined menopause and its effects, specific investigations into the prevalence and contributing factors of insomnia are scarce. This gap in knowledge highlights the need for a focused study to better understand the extent of the problem and its potential risk factors in a Thai population. Therefore, the objectives of this research are to evaluate the prevalence of insomnia in a menopause clinic at King Chulalongkorn Memorial Hospital and to identify the factors associated with insomnia.

## METHODS

### Study designs and study population

We conducted a cross-sectional descriptive study on female patients in a menopause clinic at a tertiary hospital, Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University. The sample size was calculated using Cochran's formula, determining a minimum of 102 participants. We included female patients aged 45 - 60 years attending the menopause clinic through convenience sampling. We excluded patients who declined to participate and those who worked night shifts for more than half of the previous month. Our study received approval from the Institutional Review Board of the Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand (COE No. 382/66).

We collected demographic data, including age, weight, height, educational status, marital status, occupation, number of children, underlying diseases, psychiatric conditions, history of hormone replacement therapy, medication, menopausal status, and severity of vasomotor symptoms. Prolonged vasomotor symptoms can worsen insomnia, while chronic insomnia may exacerbate menopausal symptoms, highlighting their

bidirectional relationship. These variables were selected based on a literature review indicating their potential relationship with and influence on insomnia. Previous studies have suggested that demographic, medical, and hormonal factors may play a role in sleep disturbances during menopause, making it essential to include them in our analysis. Additionally, we assessed depression and anxiety in participants using the Thai Hospital Anxiety and Depression Scale (Thai HADS). The Thai HADS is a short self-assessment questionnaire validated in Thai, divided into two sections: depression and anxiety, each comprising seven items. The items are scored on a 4-point Likert scale ranging from 0 to 3. Participants were considered to be depressed or anxious if they scored 11 or higher.<sup>12</sup>

Assessment of insomnia was conducted using the Insomnia Severity Index (ISI) scale, which has been validated in Thai. The ISI scale includes seven items that evaluate the pattern, intensity, and impact of insomnia. The items assess the following dimensions: severity of sleep onset, sleep maintenance, early morning awakening issues, sleep dissatisfaction, interference of sleep difficulties with daytime functioning, noticeability of sleep issues by others, and distress caused by sleep issues. The items are scored on a 5-point Likert scale, ranging from 0 (not at all) to 4 (nearly every day). Total scores range from 0 to 28, with higher scores indicating more severe insomnia symptoms. The severity of symptoms is categorized as follows: 0 - 7 = no clinically significant insomnia, 8 - 14 = subthreshold insomnia, 15 - 21 = clinical insomnia (moderate severity), and 22 - 28 = clinical insomnia (severe).<sup>13,14</sup>

### Data analysis

Descriptive statistics were used to summarize the demographic data. Categorical variables were reported as counts and percentages, while continuous variables were reported as means with standard deviations. The association between factors and insomnia was assessed using univariate analyses with the chi-square test and Fisher's exact test. Candidate variables for multivariate logistic regression analysis were selected based on their

association with insomnia, as identified through a literature review and univariate analyses with a p-value of less than 0.1.<sup>15</sup> Additionally, clinically relevant variables known to influence insomnia, regardless of statistical significance, were included to account for potential confounding effects. We also assessed the associations between variables to identify potential confounders and understand their interactions. In the multivariate logistic regression analysis, potential confounders were controlled by adjusting for key demographic and clinical variables identified in previous studies and those showing significant associations in univariate analyses. Statistical analysis was performed using SPSS version 20.0, with a p-value of less than 0.05 considered statistically significant.

## RESULTS

The mean age of the participants was 52.97 years ( $\pm 3.79$ ), and 60.8% were married. Regarding educational and occupational status, 73.5% of the participants had attained a bachelor's degree or higher, and 62.7% were employed. Most participants had children (55.9%). Most participants were in postmenopausal period (90.2%), while the minorities were in perimenopause period (9.8%). The majority of participants experienced vasomotor symptoms (77.5%), categorized as mild (18.6%), moderate (54.9%), and severe (3.9%). Currently using hormone replacement therapy was reported by 30.4% of participants. Additionally, 63.7% had underlying medical conditions such as diabetes, hypertension, dyslipidemia, ovarian cancer, and thyroid disease. Furthermore, 17.6% of participants had underlying psychiatric conditions, including major depressive disorder, anxiety, and others. According to the Thai-HADS, 6.9% of participants were found to have depression, and 11.8% had anxiety. (Table 1)

The study found that the mean total score of the Insomnia Severity Index (ISI) was 8.28 (SD = 6.56), with the prevalence of insomnia being 52.0% (ISI  $\geq 8$ ). Among those with insomnia, 32.4% had mild insomnia, 16.7% had moderate insomnia, and 2.9% had severe insomnia. (Table 2) Univariate analysis revealed that anxiety was statistically significantly associated with insomnia

**Table 1** Demographic data (n = 102)

Variable	N (%) or mean ± SD
Age (years)	52.97 ± 3.79
Educational level	
Bachelor's degree or higher	75 (73.5%)
Lower than bachelor's degree	27 (26.5%)
Marital Status	
Married	62 (60.8%)
Single	29 (28.4%)
Divorced	7 (6.9%)
Widow	4 (3.9%)
Employment Status	
Employed	64 (62.7%)
Not employed	38 (37.3%)
Having Children	
Yes (1 - 4 children)	57 (55.9%)
No	45 (44.1%)
Menopausal Status	
Perimenopausal	10 (9.8%)
Postmenopausal	92 (90.2%)
Vasomotor Symptoms	
Present	79 (77.5%)
Mild	19 (18.6%)
Moderate	56 (54.9%)
Severe	4 (3.9%)
Not present	23 (22.5%)
Currently Using Hormone Replacement Therapy	
Yes	31 (30.4%)
No	71 (69.6%)
Underlying Medical Conditions	
Present	65 (63.7%)
Not present	37 (36.3%)
Underlying Psychiatric Condition	
Present	18 (17.6%)
Not present	84 (82.4%)
Having Depression (Thai-HADS depression ≥ 11)	7 (6.9%)
Having Anxiety (Thai-HADS anxiety ≥ 11)	12 (11.8%)

Note: Thai-HADS = Thai Hospital Anxiety and Depression Scale

(OR 12.57, 95% CI 1.56 - 101.50, p-value = 0.018). (Table 3) Additionally, vasomotor symptoms (OR 2.48, 95% CI 0.94 - 6.53, p = 0.065) and currently using of hormone replacement therapy (OR 0.462, 95% CI 0.195 - 1.095, p = 0.079), depression (OR 6.13, 95% CI 0.71 - 52.86, p = 0.099), and underlying psychiatric conditions (OR 2.86, 95% CI 0.94 - 8.74, p = 0.065) showed a trend toward statistical significance. However, these associations did not reach conventional significance, potentially due to the limited sample size, which may have reduced statistical power. Moreover, the sample size was calculated primarily to address the research question regarding the prevalence of insomnia, and therefore may not be sufficient to reliably detect associations between insomnia and its potential correlates.

Multivariate logistic regression, with factors selected for adjustment based on their association with insomnia and univariate analysis findings with a p-value of less than 0.1, showed that currently using hormonal therapy was a protective factor against insomnia, reducing the likelihood by 0.36 times compared to those not currently using (adjusted OR 0.36, 95% CI 0.13 - 0.97, p = 0.044). (Table 4) Variables included in the model were those that demonstrated a trend toward statistical significance in univariate analysis, as they may still have a meaningful association with insomnia despite not reaching conventional significance. This approach helps account for potential confounding factors and ensures that important contributors to insomnia are not overlooked due to sample size limitations or statistical power constraints.

**Table 2** Prevalence of insomnia

Clinical insomnia	Criteria	Prevalence (%)
Insomnia	ISI ≥ 8	52.0
Subthreshold insomnia	ISI 8 – 14	32.4
Moderate insomnia	ISI 15 – 21	16.7
Severe insomnia	ISI 21 – 28	2.9
No insomnia	ISI 0 – 7	48.0

Note: ISI = Insomnia Severity Index

**Table 3** Factors associated with insomnia by univariate analysis

Variable	No insomnia n (%)	Insomnia n (%)	Crude OR	95% CI of OR Lower	95% CI of OR Upper	p-value
<b>Marital Status</b>						
Others	21 (42.9%)	19 (35.8%)	1			
Married	28 (57.1%)	34 (64.2%)	1.34	0.61	2.98	0.47
<b>Educational level</b>						
Lower than bachelor's degree	13 (26.5%)	14 (26.4%)	1			
Bachelor's degree or higher	36 (73.5%)	39 (73.6%)	1.006	0.42	2.43	0.99
<b>Employment Status</b>						
Not employed	22 (44.9%)	16 (30.2%)	1			
Employed	27 (55.1%)	37 (69.8%)	1.88	0.84	4.24	0.13
<b>Having Children</b>						
No	23 (46.9%)	22 (41.5%)	1			
Yes	26 (53.1%)	31 (58.5%)	1.24	0.57	2.73	0.58
<b>Menopausal Status</b>						
Perimenopausal	6 (12.2%)	4 (7.5%)	1			
Postmenopausal	43 (87.8%)	49 (92.5%)	1.71	0.45	6.46	0.43
<b>Vasomotor Symptoms</b>						
Not present	15 (30.6%)	8 (15.1%)	1			
Present	34 (69.4%)	45 (84.9%)	2.48	0.94	6.53	0.065
<b>Currently Using Hormone Replacement Therapy</b>						
No	30 (61.2%)	41 (77.4%)	1			
Yes	19 (38.8%)	12 (22.6%)	0.46	0.14	1.0	0.079
<b>Having Depression</b>						
Not present	48 (98%)	47 (88.7%)	1			
Present	1 (2%)	6 (11.3%)	6.13	0.71	52.86	0.099
<b>Having Anxiety</b>						
Not present	48 (98%)	42 (79.2%)	1			
Present	1 (2%)	11 (20.8%)	12.57	1.5	101.50	0.018
<b>Underlying Medical Conditions</b>						
Not present	16 (32.7%)	21 (39.6%)	1			
present	33 (67.3%)	32 (60.4%)	0.739	0.328	1.66	0.465
<b>Underlying Psychiatric Conditions</b>						
Not present	44 (89.8%)	40 (75.5%)	1			
Present	5 (10.2%)	13 (24.5%)	2.860	0.93	8.74	0.065

Note: Thai-HADS = Thai Hospital Anxiety and Depression Scale, CI = confidence interval, OR = odds ratio

**Table 4** Factors associated with insomnia by multivariate logistic regression

Variable	Adjusted OR	95% CI of Adjusted OR Lower	95% CI of Adjusted OR Upper	p-value
Vasomotor symptoms	1.89	0.68	5.29	0.224
Currently using hormone replacement therapy	0.36	0.13	0.97	0.044
Having anxiety	6.69	0.68	66.15	0.104
Having depression	1.50	0.12	17.81	0.747
Underlying psychiatric condition	2.76	0.72	10.57	0.138

Note: CI = confidence interval, OR = odds ratio

## DISCUSSION

Our study was among the first to assess the prevalence and associated factors of insomnia among women in the Menopause Clinic at King Chulalongkorn Hospital. We found that 52% of women experienced some level of insomnia, including 2.9% who reported severe insomnia. This finding was quite similar to a study conducted in Japan, where approximately 51% of peri- and postmenopausal women in a menopause clinic sample suffered from sleep disturbances.<sup>16</sup>

In 2014, the research conducted by D. Sun et al., found that 33.2% of middle-aged Chinese women in a community-based sample experienced sleep disturbances, as measured by a PSQI global score of  $\geq 8$ .<sup>17</sup> Similarly, the study conducted by Chung and Tang in 2020, reported that 26% of women aged 45 - 55 years in a community-based sample in Hong Kong were poor sleepers.<sup>18</sup>

The higher prevalence of sleep disturbance in this study, compared to community-based samples, may be due to selection bias from the hospital-based sample. Women seeking medical care are more likely to have severe symptoms, potentially overestimating the true prevalence of insomnia. Additionally, hospital patients may be more aware of menopausal symptoms, leading to higher self-reporting. While this highlights the clinical burden of insomnia, future population-based studies are needed for more generalizable estimates.

The 2005 State-of-the-Science Conference Statement from the National Institutes of Health identified sleep disturbances as a key symptom of menopause.<sup>19</sup>

Recent research consistently showed that subjective sleep quality gradually declined during the perimenopausal phase. The common sleep complaints included disrupted sleep, frequent awakenings, and generally poor sleep quality. Several factors may contribute to the decrease in sleep quality, including vasomotor symptoms, hormonal fluctuations, age-related changes, and an increase in conditions like mental health problems (i.e., depression and anxiety) and sleep-disordered breathing.<sup>20</sup>

The findings in this research indicated that women with anxiety had a higher likelihood of experiencing insomnia, while using hormone replacement therapy was significantly associated with a reduced risk of insomnia. Although previous studies suggested that poor sleep was linked to higher levels of both anxiety and depression<sup>21</sup>, our study did not find a significant association between depression and sleep disturbance. Instead, anxiety was found to have a more detrimental influence on sleep problems. The lack of a significant association between depression and insomnia in our study differs from previous research, which may be due to the study's sample size and design. Since the sample size was primarily calculated to estimate the prevalence of insomnia rather than to examine associations, it may not have been optimal for detecting certain relationships between variables. While a trend toward an association with depression was observed, further studies with larger sample sizes specifically designed for assessing these associations are needed to confirm this relationship.

In a similar study conducted in Taiwan by Cheng et al., 46% of middle-aged women reported

dissatisfaction with their sleep.<sup>22</sup> The study found that anxiety, as measured by the Hospital Anxiety and Depression Scale (HADS), was strongly associated with insomnia symptoms, including difficulty initiating sleep (OR = 2.35, 95% CI = 1.28 - 4.29, p-value = 0.006), sleep fragmentation (OR = 2.48, 95% CI = 1.36 - 4.50, p-value = 0.003), and early morning awakenings (OR = 4.16, 95% CI = 1.85 - 9.37, p-value = 0.001). Further research is needed to determine causality-whether anxiety worsens sleep quality or whether insomnia induces an anxious mood.

Our finding that using hormone replacement therapy was significantly associated with a reduced risk of insomnia aligned with the established role of menopausal hormonal therapy (MHT) as an effective treatment for sleep disturbances in menopausal women (adjusted OR 0.356, 95% CI 0.136 - 0.97, p = 0.044). However, the wide confidence interval observed in our study suggests some uncertainty around the exact magnitude of the effect. This may be due to the limited sample size, which could reduce the precision of the estimate, as well as variations in the duration of hormone therapy use among participants. The duration of hormonal therapy may play a critical role in the effectiveness of treatment, and further studies should explore how varying durations of use affect the risk of insomnia.

The relationship between insomnia, anxiety, and hormonal changes is complex and likely involves a bidirectional interaction. Hormonal fluctuations during menopause, particularly the decline in estrogen and progesterone, have been shown to disrupt sleep patterns and contribute to sleep disturbances such as insomnia. These hormonal changes can also increase the likelihood of experiencing anxiety, which in turn may exacerbate sleep problems. Anxiety, characterized by heightened stress and worry, may intensify the physiological responses to hormonal changes, such as increased heart rate, muscle tension, and disrupted autonomic regulation, all of which can impair sleep quality. Conversely, persistent insomnia can exacerbate anxiety by impacting mood regulation, cognitive function, and overall well-being, creating a

vicious cycle. This interaction between anxiety and hormonal changes may explain why individuals with high anxiety are more prone to sleep disturbances during menopause.

A recent meta-analysis reported an improvement in quality of life with MHT only in patients with vasomotor symptoms. MHT may improve sleep by alleviating other symptoms that disrupt sleep during menopause, especially vasomotor symptoms. However, our study did not find statistically significant association between hormonal therapy and vasomotor symptom. In terms of MHT, estrogens may exert an antidepressant effect through the norepinephrine and histamine pathways, along with direct action on sleep and body thermoregulation. Progesterone, on the other hand, has a direct sedative function by stimulating benzodiazepine receptors, leading to increased production of GABA receptors during non-rapid eye movement sleep.<sup>23</sup> Additionally, it may have an anxiolytic effect as a GABA agonist, though the exact mechanism remains unclear.

#### Limitation

This study's findings reflect a higher prevalence of insomnia, likely due to the hospital-based sample, which may not represent the general population. Additionally, as a cross-sectional study, it cannot establish causality between the associated factors and insomnia. Future longitudinal research is recommended to differentiate the effects of aging from other contributing factors.

#### CONCLUSION

Insomnia is highly prevalent among menopausal women, especially those with anxiety, while usage of hormone replacement therapy has been shown to alleviate symptoms. Clinicians should emphasize the assessment of anxiety and insomnia in menopausal women to provide appropriate care. A comprehensive evaluation of other mental health conditions, vasomotor symptoms, and history of hormonal therapy is crucial for determining the most effective treatment approach.

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## Conflict of Interest

The authors declare that they have no competing interests.

## Authors' Contributions

Nichakorn Sirisivanart: study design, ethical approval process, data collection, data analysis, and manuscript writing; Naphat Sirinimnuakul: review and revision of the study design, data analysis, and manuscript editing; Nalina Orprayoon: review and revision of the study design, and manuscript editing.

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