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**Analysis of Sleep Quality in Patients with Hereditary Angioedema**

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## ABSTRACT

**Introduction:** Sleep plays a crucial role in human health, both physiologically and mentally, responsible for body repair and regeneration. This may be affected by patients with Hereditary Angioedema (HAE), a rare and serious genetic disease of the immune system. **Objective:** To analyze sleep quality in patients with HAE. **Methods:** A cross-sectional study involving 31 patients, with a mean ( $\pm$  standard deviation,  $\pm$ SD) age of 43 ( $\pm$ 18.49) years, comprising 25 women and 6 men. Sleep analysis was conducted using the Pittsburgh Sleep Quality Index (PSQI) and the Epworth Sleepiness Scale (ESS). Statistical analysis was performed using SPSS software. Data were expressed as means  $\pm$  SD, medians, and interquartile ranges ([IQR]), or absolute and relative frequencies. Associations between variables were assessed using Chi-square, independent samples t-, or Mann-Whitney tests, with a significance level set at 5%. **Results:** PSQI analyses showed that approximately 80% of patients had poor or very poor sleep quality, characterized by various sleep disturbances such as inadequate sleep, impaired sleep frequency, and efficiency. Main reported sleep difficulties included waking up in the middle of the night, getting up to use the bathroom, coughing, loud snoring, and feeling hot. ESS analyses indicated that about 77% of patients experienced average or abnormal daytime sleepiness. **Conclusion:** This is the first Brazilian study to characterize sleep in patients with HAE. In the sample, there was an association with sleep disorders, likely because of HAE.

**Keywords:** Angioedemas, hereditary; Complement C1 Inhibitor Protein; Sleep Quality; Sleep Wake Disorders; disorders of excessive somnolence.

## INTRODUCTION

Sleep plays a pivotal role in human health, both physiologically and mentally, facilitating repair and regeneration within the body, while also regulating the hormone cortisol, which keeps us alert during the day and plays a crucial role in immune system regulation. The immune system, particularly the Complement System, is closely linked to the pathogenesis of Hereditary Angioedema (HAE). Therefore, for HAE patients, adequate sleep is imperative<sup>1-3</sup>.

Cortisol, a hormone produced by the adrenal glands, is vital in the body's immune and inflammatory response. In patients with HAE, cortisol levels may be affected by physical and emotional stress caused by the disease's recurrent symptoms and attacks<sup>4,5</sup>.

HAE is a rare, serious, and potentially life-threatening genetic disorder characterized by frequent episodes of edema resulting from a deficiency or dysfunction of C1 esterase inhibitor (C1-INH). Although C1-INH inhibits the activation of the complement system pathways, the primary mechanism involved in HAE is the dysregulation of the kallikrein-kinin system, leading to excessive release of bradykinin (BK), which is the main mediator of edema episodes. These often-unpredictable symptoms cause anxiety and negatively impact sleep quality, resulting in difficulties falling asleep, nighttime awakenings, and excessive daytime sleepiness<sup>6-8</sup>. Inadequate sleep can trigger comorbidities such as cardiovascular diseases, metabolic disorders, obesity, diabetes, and memory consolidation problems<sup>9-11</sup>.

Studies on sleep quality in HAE patients are crucial not only for a better understanding of their quality of life but also for identifying and developing effective clinical approaches and actions<sup>6,12,13</sup>.

Buysse et al.<sup>14</sup> developed a tool to assess sleep quality called the Pittsburgh Sleep Quality Index (PSQI). This tool was validated for Brazilian Portuguese by Bertolazi et al.<sup>15</sup>. In 1991, Johns<sup>16</sup> developed a questionnaire, the Epworth Sleepiness Scale (ESS), which evaluates

eight possibilities of dozing off. This instrument was validated for Brazil in 2009 by Bertolazi et al.<sup>17</sup>.

There are no similar studies in the literature evaluating this outcome in HAE patients using both instruments. The study's objective was to analyze sleep quality in adults with HAE, expanding knowledge and understanding of the challenges patients face regarding sleep, thereby providing healthcare professionals with a basis for developing new interventions aimed at improving the quality of life of HAE patients.

## **METHODS**

### **Study Design and Ethical Considerations**

A cross-sectional design was utilized in this study to analyze sleep quality and daytime sleepiness in patients with HAE residing in the state of Paraná in southern Brazil. The study was approved by the Research Ethics Committee of the Federal University of Paraná [CAAE: 83071518.7.1001.0096]. Patients provided signed informed consent agreeing to participate in the study, and the confidentiality of their data was strictly maintained throughout the research process. The study was conducted by the principles outlined in the Declaration of Helsinki and relevant national regulations regarding research involving human subjects.

### **Participants**

The study involved 31 patients (25 women and 6 men) during outpatient consultations. Patients were invited to complete a questionnaire assessing sleep quality and daytime sleepiness in February 2024. The average time for questionnaire completion was 10 minutes.

Eligibility criteria included: inclusion criteria: a) clinical medical diagnosis of HAE; b) patients who completed the questionnaire responses; c) patients who signed the informed consent form. Exclusion criteria included patients who did not meet the inclusion criteria.

After admission, patients were invited to participate in the study, briefed on the procedures, and then signed the informed consent form to begin completing the Pittsburgh Sleep Quality Index (PSQI) and Epworth Sleepiness Scale (ESS) questionnaires.

## **Research Instrument**

The PSQI questionnaire consists of 19 questions with 7 components, with scores ranging from zero (no difficulty) to three (severe difficulty). The components of the PSQI are: C1 subjective sleep quality, C2 sleep latency, C3 sleep duration, C4 habitual sleep efficiency, C5 sleep disturbances, C6 use of sleep medications, and C7 daytime dysfunction due to sleepiness. The sum of the values assigned to the seven components ranges from zero to twenty-one in the total questionnaire score, with higher scores indicating poorer sleep quality<sup>14,15</sup>.

The ESS questionnaire consists of 8 questions about the likelihood of dozing off in everyday situations, using a scale from 0 (no chance) to 3 (high chance). Scores of 1 to 6 points determine a normal sleepiness scale, 7 to 8 points indicate moderate sleepiness, while scores of 9 to 24 are considered abnormal sleepiness, potentially pathological<sup>16,17</sup>.

Questionnaire scores are obtained using a Likert scale, where each scale is assigned a numerical value from 0-3.

To interpret the scores of the seven PSQI components, the total sum of the questionnaire is calculated, ranging from 0 to 21, where scores of 0-4 are considered good sleep quality, 5-10 indicate poor sleep, and above 10 indicates the presence of sleep disorders<sup>14,15</sup>.

For interpretation of the ESS questionnaire, the sum of the 8 possibilities of dozing off during the day is calculated and assigned a value from 0 to 24 points, where scores of 0-6 are considered normal, 7-8 indicate moderate sleepiness, and 9-24 indicate abnormal sleepiness, potentially pathological<sup>16,17</sup>.

## Statistics

Data processing, double data entry into the database, review, and analysis were performed using SPSS software, version 29.0 [SPSS Inc. Released 2022. PASW Statistics for Windows, Version 29.0. Chicago: SPSS Inc.

Descriptive analyses were conducted, with quantitative data expressed as mean  $\pm$  standard deviation ( $\pm$ SD) or median and interquartile range ([IQR], percentiles 25th-75th), depending on the Shapiro-Wilk distribution test. Qualitative variables were described in terms of absolute frequencies (n) and relative frequencies (%).

Possible associations between qualitative variables were analyzed using the Chi-square test with adjusted residual analysis ( $\chi^2$ ). Comparisons between means ( $\pm$ SD) were conducted using Student's t-test for independent samples (t), and between medians [IQR] using the Mann-Whitney test. For all analyses, the significance level was set at 5%.

## RESULTS

The participant selection flowchart is presented in Figure 1 of the supplementary material. Among the 69 patients subjected to eligibility analysis, 38 were excluded (9 for non-response to the instruments, 25 due to loss of contact/follow-up, and 4 for refusal to participate in the research). Thus, the definitive sample comprised 31 participants, of whom 25 were female and 6 were male.

Sociodemographic and clinical characterization is described in Table 1. In summary, the mean ( $\pm$ SD) age was 43 ( $\pm$ 18.49) years, ranging from 18 to 83, with a predominance of adults aged 30 or older (71.0%). The mean ( $\pm$ SD) age at symptom onset was 14.77 ( $\pm$ 8.52) years, ranging from 3 to 36 years. Regarding HAE, a significant proportion of women were associated with the normal C1-INH subtype (56.0%), with most participants reporting having experienced severe (87.1%) or moderate (71.0%) episodes. At the time of the research instrument

administration, all patients reported that their episodes were well-controlled. A high frequency of facial (87.1%), abdominal (83.9%), and upper limb (81.1%) edema was observed, with vomiting (38.7%) and diarrhea (35.5%) emerging as commonly reported symptoms. Concerning medications, Danazol (54.8%) and Firazyr (40,8%) were the most reported, with four participants (12.9%) not using any pharmacotherapy.

Data from the Pittsburgh Sleep Quality Index is presented in Table 2. Approximately half (54.8%) of the participants reported taking less than 15 minutes to fall asleep, with many (51.6%) indicating a sleep duration of 6 to 7 hours per night over the past month, with sleep efficiency exceeding 85% in 21 (67.7%) participants. The main reported difficulties in sleeping were waking up in the middle of the night or early in the morning (25.8%), coughing or snoring heavily (16.1%), and getting up to use the bathroom (16.1%). A considerable proportion of men (50.0%) reported difficulty due to feeling hot, and marginal significance was observed for men (33.3%) also having trouble sleeping due to feeling cold.

The medians [IQR] of each component of the Pittsburgh Sleep Quality Index are described in Table 3. The total score of this index ranged from 3 to 17 points, with a median [IQR] of 6 [5-9] points. No significant differences were identified between any of the analyzed components.

Data regarding the Epworth Sleepiness Scale are detailed in Table 4. The most frequently associated situations with sleepiness were "sitting quietly after lunch" (35.5%) and "lying down in the afternoon to rest" (32.3%). The mean ( $\pm$ SD) total score was 8.831 ( $\pm$ 4.86) points, ranging from 1 to 19. Categorizing sleep based on this instrument, it was found that seven (23.3%) participants exhibited an adequate sleep profile, eleven (36.7%) had inadequate sleep, and twelve (40.0%) showed some indication of sleep disturbance.

## DISCUSSION

This is the first study characterizing the sleep profile of patients with HAE in Brazil. In this study, sleep quality in patients with HAE followed at a reference center in the state of Paraná was evaluated.

The sample comprised 31 patients with a mean age of 43 years, including 25 females and 6 males. Most of the women presented with HAE with normal C1-INH, a phenotype more commonly observed in women, which is consistent with reports in the literature<sup>18-20</sup>. Among the patients analyzed, 48% C1-INH deficiency, 6% C1-INH dysfunction, and 46% normal C1-INH, with 87% experiencing severe attacks, primarily affecting the face, glottis, upper and lower limbs, and abdomen. Most patients reported symptom onset between the ages of 10 to 17.

Approximately 80% of the sample was identified with some sleep disorder. The most frequent disturbances were in the sleep disorder and daytime dysfunction components, with 76.7% of the sample reporting excessive daytime sleepiness. The most prevalent issues were sitting quietly after lunch and lying down in the afternoon to rest.

In the characterization of the Pittsburgh Sleep Quality Index, 80.7% of patients exhibited sleep disturbances, with 58.1% reporting poor sleep and 22.6% reporting very poor sleep. Components 5 (sleep disturbances) and 7 (daytime dysfunction) received the lowest ratings, although alterations were observed in all components. Patients also reported delays in falling asleep (45%), a few hours of sleep (71%), and reduced sleep efficiency (32%).

Ozer et al.<sup>21</sup>, Matsumoto et al.<sup>22</sup> and Sharman<sup>23</sup>, evaluating patients with Systemic Lupus Erythematosus, Hypothyroidism, and Multiple Sclerosis, respectively, reported sleep disturbances such as sleep latency, sleep efficiency, and difficulties in maintaining sleep, similar to the findings in this study. This supports the hypothesis that chronic patients have

more sleep dysfunctions, and the psychosocial and depressive symptoms of patients can negatively influence sleep quality.

In the Epworth Sleepiness Scale questionnaire, high rates of patients experiencing mild (23%), moderate (37%), or severe (40%) daytime sleepiness were observed across the eight questions presented. For example: sitting and reading (81%), watching TV (87%), sitting in a public place (45%), sitting as a passenger in a car (58%), lying down in the afternoon to rest (87%), sitting to talk with another person (29%), sitting quietly after lunch (84%), and 26% reported daytime sleepiness while sitting in a stopped car in traffic. These alarming situations raise constant concerns about the physical, social, mental, emotional, and occupational well-being of these patients, as daytime sleepiness negatively impacts their daily lives.

Ates et al.<sup>24</sup> investigated the Epworth Sleepiness Scale index in patients with Chronic Idiopathic Urticaria and reported that half of their sample had excessive daytime sleepiness, while Shakoei et al.<sup>25</sup> reported that 11.4% of their patients with Alopecia Areata suffered from severe sleepiness. Bellofatto et al.<sup>26</sup> described in their study with Charcot-Marie-Tooth patients that these patients had severe daytime sleepiness, and these results were related to pain and sensory abnormalities. Although HAE is not associated with immune dysfunction or autoimmune diseases, it is relevant to consider the association between excessive daytime sleepiness and other chronic genetic conditions, highlighting the negative impact that unpredictable and debilitating symptoms can have on sleep quality, as observed in HAE<sup>26,27</sup>.

Sleep disorders in chronic patients have been associated with anxiety, depression, social stigmatization, pain, discomfort, unpredictability of attacks, fatigue, and tiredness, corroborating the findings of this research<sup>28-32</sup>.

A study conducted by our research group analyzed the quality of life of this same group of patients, and important findings highlighted a loss of quality of life in these patients, with sleep being one of the impacting factors.

The literature suggests psychoeducation strategies and behavioral psychotherapies for good sleep hygiene, strategies that can be adopted in the therapeutic management of these patients as a means of relief for coping with HAE attacks.

Despite the significant findings characterizing the sleep profile in this study, which are unprecedented in Brazil and corroborate the literature on the subject, it is important to highlight the limitations identified in the study, with the main one being the sample size, a common limitation in articles on rare genetic diseases. Another limitation was the absence of articles using these instruments in HAE patients. Despite these limitations, we were able to characterize the sleep profile and demonstrate the discrepancies on the topic in patients with HAE.

This study was conducted using a questionnaire applied exclusively to patients with HAE, without the inclusion of a control group, which limits direct comparisons between individuals with the disease and healthy subjects. Future studies are suggested to include patient samples compared to healthy controls to provide additional data on the assessment of sleep quality in HAE patients. These observations emphasize the need for further studies on HAE, investigating sleep, an important component in the quality of life of patients<sup>24-27</sup>.

## **Conclusion**

Quality of life is multidimensional, with sleep being one of its important components. Based on the sample and the instruments used, it is concluded that individuals with HAE experience sleep disturbances. This study provides important evidence regarding the clinical issue and the proposed objectives and suggests relevant issues to be discussed by the medical community for the therapeutic management of these patients.

Future research should consider longitudinal studies with larger samples and gold standard assessment tools, such as polysomnography and actigraphy, to enable physiological analyses of the outcome and further explore these sleep dysfunctions in patients with HAE.

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**Table 1:** Sociodemographic and clinical Characterization of participants:

| Variable                   | Female (n = 25) | Male (n = 6) | Total (N = 31) |
|----------------------------|-----------------|--------------|----------------|
| Age                        |                 |              |                |
| 18 – 21 years              | 3 (12,0)        | 0 (0,0)      | 3 (9,7)        |
| 22 – 24 years              | 0 (0,0)         | 1 (16,7)     | 1 (3,2)        |
| 25 – 29 years              | 4 (16,0)        | 1 (16,7)     | 5 (16,1)       |
| ≥ 30 years                 | 18 (72,0)       | 4 (66,7)     | 22 (71,0)      |
| Age of onset of symptoms   |                 |              |                |
| < 10 years                 | 8 (32,0)        | 1 (16,7)     | 9 (29,0)       |
| 10 – 17 years              | 6 (24,0)        | 4 (66,7)     | 10 (32,3)      |
| ≥ 18 years                 | 11 (44,0)       | 1 (16,7)     | 12 (38,7)      |
| HAE                        |                 |              |                |
| C1-INH Deficiency          | 10 (40,0)       | 5 (83,3)     | 15 (48,5)      |
| C1-INH Dysfunction         | 1 (4,0)         | 1 (16,7)     | 2 (6,5)        |
| Normal C1-INH              | 14 (56,0)       | 0 (0,0)      | 14 (45,2)      |
| Severity of attacks        |                 |              |                |
| Mild attacks               | 11 (44,0)       | 2 (33,3)     | 13 (41,9)      |
| Moderate attacks           | 18 (72,0)       | 4 (66,7)     | 22 (71,0)      |
| Severe attacks             | 23 (92,0)       | 4 (66,7)     | 27 (87,1)      |
| Signs and symptoms (edema) |                 |              |                |
| Glottis                    | 15 (60,0)       | 5 (83,3)     | 20 (64,5)      |
| Face                       | 22 (88,0)       | 5 (83,3)     | 27 (87,1)      |
| Genitals                   | 10 (40,0)       | 5 (83,3)     | 15 (48,4)      |
| Upper limbs                | 21 (84,0)       | 6 (100,0)    | 27 (81,1)      |
| Lower limbs                | 20 (80,0)       | 4 (66,7)     | 24 (77,4)      |
| Abdominal distension       | 22 (88,0)       | 4 (66,7)     | 27 (83,9)      |
| Diarrhea                   | 9 (36,0)        | 2 (33,3)     | 11 (35,5)      |
| Vomiting                   | 9 (36,0)        | 3 (50,0)     | 12 (38,7)      |
| Dyspnea                    | 8 (32,0)        | 2 (33,3)     | 10 (32,3)      |
| Pharmacotherapy in use     |                 |              |                |
| Danazol/Ladogal            | 13 (52,0)       | 4 (66,7)     | 17 (54,8)      |
| Stanozolol                 | 0 (0,0)         | 1 (16,7)     | 1 (3,2)        |
| Oxandrolone                | 1 (4,0)         | 0 (0,0)      | 1 (3,2)        |
| Icatibant/ Firazyr         | 11 (50,0)       | 2 (28,6)     | 13 (40,8)      |
| Berinert                   | 1 (4,0)         | 1 (16,7)     | 2 (6,5)        |
| Tranexamic acid/ Transamin | 5 (22,7)        | 0 (0,0)      | 5 (17,2)       |
| Promethazine               | 1 (4,0)         | 0 (0,0)      | 1 (3,2)        |
| Adrenaline                 | 2 (8,0)         | 0 (0,0)      | 2 (6,5)        |
| Corticosteroids            | 1 (4,0)         | 0 (0,0)      | 1 (3,2)        |
| No medication              | 4 (16,0)        | 0 (0,0)      | 4 (12,9)       |

Data expressed as absolute frequencies (n) and relative frequencies (%), means  $\pm$  standard deviations of the means ( $\pm$ SD), or medians and interquartile ranges ([IQR], 25th and 75th percentiles). Legend: HAE – estrogen-dependent hereditary angioedema. C1-INH – C1-esterase inhibitor. Chi-Square test with adjusted residual analyses, Student's t-test for independent samples, or Mann-Whitney test, where applicable. Significance set at 5% for all analyses.

**Table 2:** Characterization of the Pittsburgh Sleep Quality Index (PSQI-BR)

| Variable                                           | Female (n=25)                            | Male (n=6)                               | Total (n=31)                             |
|----------------------------------------------------|------------------------------------------|------------------------------------------|------------------------------------------|
| During the last month                              |                                          |                                          |                                          |
| Usual bedtime<br>(minimum–maximum)                 | 22:30 [22:00 – 23:00]<br>(21:00 – 00:00) | 23:30 [23:00 – 00:00]<br>(22:00 – 01:00) | 22:30 [22:00 – 23:00]<br>(21:00 – 01:00) |
| Minutes to fall asleep                             |                                          |                                          |                                          |
| ≤15 minutes                                        | 13 (52,0)                                | 4 (66,7)                                 | 17 (54,8)                                |
| 16 – 30 minutes                                    | 6 (24,0)                                 | 2 (33,3)                                 | 8 (25,8)                                 |
| 31 – 60 minutes                                    | 2 (8,0)                                  | 0 (0,0)                                  | 2 (6,5)                                  |
| >60 minutes                                        | 4 (16,0)                                 | 0 (0,0)                                  | 4 (12,9)                                 |
| Usual wake-up time<br>(minimum–maximum)            | 06:50 [06:00 – 8:00]<br>(03:15 – 09:15)  | 06:30 [05:50 – 07:00]<br>(05:30 – 10:00) | 06:50 [05:55 – 08:00]<br>(03:15 – 10:00) |
| Hours of sleep per night                           |                                          |                                          |                                          |
| 7 hours                                            | 7 (28,0)                                 | 2 (33,3)                                 | 9 (29,0)                                 |
| 6 – 7 hours                                        | 14 (56,0)                                | 2 (33,3)                                 | 16 (51,6)                                |
| 5 – 6 hours                                        | 3 (12,0)                                 | 1 (16,7)                                 | 4 (12,9)                                 |
| <5 hours                                           | 1 (4,0)                                  | 0 (0,0)                                  | 2 (6,5)                                  |
| Hours in bed per night<br>(minimum–maximum)        | 8 [7 – 9]<br>(4 – 10)                    | 7 [6 – 8]<br>(6 – 9)                     | 8 [7 – 9]<br>(4 – 10)                    |
| Sleep efficiency                                   |                                          |                                          |                                          |
| >85%                                               | 17 (68,0)                                | 4 (66,7)                                 | 21 (67,7)                                |
| 75% - 84%                                          | 1 (4,0)                                  | 1 (16,7)                                 | 2 (6,5)                                  |
| 65% - 74%                                          | 5 (20,0)                                 | 0 (0,0)                                  | 5 (16,1)                                 |
| <65%                                               | 2 (8,0)                                  | 1 (16,7)                                 | 3 (9,7)                                  |
| Difficulty falling asleep for                      |                                          |                                          |                                          |
| Not falling asleep within 30 minutes.              |                                          |                                          |                                          |
| None in the last month                             | 10 (40,0)                                | 3 (50,0)                                 | 13 (41,9)                                |
| Less than once a week                              | 4 (16,0)                                 | 2 (33,3)                                 | 6 (19,4)                                 |
| Once or twice a week                               | 8 (32,0)                                 | 0 (0,0)                                  | 8 (25,8)                                 |
| Three or more times a week                         | 3 (12,0)                                 | 1 (16,7)                                 | 4 (12,9)                                 |
| Waking up in the middle of the night/early morning |                                          |                                          |                                          |
| None in the last month                             | 3 (12,0)                                 | 0 (0,0)                                  | 3 (9,7)                                  |
| Less than once a week                              | 4 (16,0)                                 | 0 (0,0)                                  | 4 (12,9)                                 |
| Once or twice a week                               | 13 (52,0)                                | 3 (50,0)                                 | 16 (51,6)                                |
| Three or more times a week                         | 5 (20,0)                                 | 3 (50,0)                                 | 8 (25,8)                                 |
| Getting up to use the bathroom                     |                                          |                                          |                                          |
| None in the last month                             | 6 (24,0)                                 | 0 (0,0)                                  | 6 (19,4)                                 |
| Less than once a week                              | 6 (24,0)                                 | 2 (33,3)                                 | 8 (25,8)                                 |
| Once or twice a week                               | 9 (36,0)                                 | 3 (50,0)                                 | 12 (38,7)                                |
| Three or more times a week                         | 4 (16,0)                                 | 1 (16,7)                                 | 5 (16,1)                                 |
| Not being able to breathe.                         |                                          |                                          |                                          |
| None in the last month                             | 14 (56,0)                                | 5 (83,3)                                 | 19 (61,3)                                |
| Less than once a week                              | 7 (28,0)                                 | 0 (0,0)                                  | 7 (22,6)                                 |
| Once or twice a week                               | 3 (12,0)                                 | 1 (16,7)                                 | 4 (12,9)                                 |
| Three or more times a week                         | 1 (4,0)                                  | 0 (0,0)                                  | 1 (3,2)                                  |
| Coughing or snoring loudly                         |                                          |                                          |                                          |
| None in the last month                             | 10 (40,0)                                | 2 (33,3)                                 | 12 (38,7)                                |
| Less than once a week                              | 5 (20,0)                                 | 0 (0,0)                                  | 5 (16,1)                                 |
| Once or twice a week                               | 6 (24,0)                                 | 3 (50,0)                                 | 9 (29,0)                                 |
| Three or more times a week                         | 4 (16,0)                                 | 1 (16,7)                                 | 5 (16,1)                                 |
| Feeling very cold                                  |                                          |                                          |                                          |
| None in the last month                             | 19 (76,0)                                | 4 (66,7)                                 | 23 (74,2)                                |
| Less than once a week                              | 1 (4,0)                                  | 2 (33,3)                                 | 3 (9,7)                                  |
| Once or twice a week                               | 5 (20,0)                                 | 0 (0,0)                                  | 5 (16,1)                                 |
| Three or more times a week                         | 0 (0,0)                                  | 0 (0,0)                                  | 0 (0,0)                                  |
| Feeling very hot                                   |                                          |                                          |                                          |
| None in the last month                             | 6 (24,0)                                 | 3 (50,0)                                 | 9 (29,0)                                 |
| Less than once a week                              | 9 (36,0)                                 | 0 (0,0)                                  | 9 (29,0)                                 |
| Once or twice a week                               | 7 (28,0)                                 | 0 (0,0)                                  | 7 (22,6)                                 |
| Three or more times a week                         | 3 (12,0)                                 | 3 (50,0)                                 | 6 (19,4)                                 |
| Having nightmares/bad dreams                       |                                          |                                          |                                          |
| None in the last month                             | 9 (36,0)                                 | 1 (16,7)                                 | 10 (32,3)                                |
| Less than once a week                              | 9 (36,0)                                 | 4 (66,7)                                 | 13 (41,9)                                |
| Once or twice a week                               | 4 (16,0)                                 | 0 (0,0)                                  | 4 (12,9)                                 |
| Three or more times a week                         | 3 (12,0)                                 | 1 (16,7)                                 | 4 (12,9)                                 |
| Feeling pain                                       |                                          |                                          |                                          |
| None in the last month                             | 10 (40,0)                                | 3 (50,0)                                 | 13 (41,9)                                |
| Less than once a week                              | 6 (24,0)                                 | 2 (33,3)                                 | 8 (25,8)                                 |
| Once or twice a week                               | 7 (28,0)                                 | 0 (0,0)                                  | 7 (22,6)                                 |

|                                        |           |          |           |
|----------------------------------------|-----------|----------|-----------|
| Three or more times a week             | 2 (8,0)   | 1 (16,7) | 3 (9,7)   |
| Other reasons                          |           |          |           |
| None in the last month                 | 20 (80,0) | 4 (66,7) | 24 (77,4) |
| Less than once a week                  | 1 (4,0)   | 0 (0,0)  | 1 (3,2)   |
| Once or twice a week                   | 3 (12,0)  | 1 (16,7) | 4 (12,9)  |
| Three or more times a week             | 1 (4,0)   | 1 (16,7) | 2 (6,5)   |
| During the last month                  |           |          |           |
| Overall sleep rating                   |           |          |           |
| Very good                              | 1 (4,0)   | 0 (0,0)  | 1 (3,2)   |
| Good                                   | 17 (68,0) | 3 (50,0) | 20 (64,5) |
| Poor                                   | 5 (20,0)  | 3 (50,0) | 8 (25,8)  |
| Very poor                              | 2 (8,0)   | 0 (0,0)  | 2 (6,5)   |
| Taking sleep medication                |           |          |           |
| None in the last month                 | 19 (76,0) | 3 (50,0) | 22 (71,0) |
| Less than once a week                  | 1 (4,0)   | 1 (16,7) | 2 (6,5)   |
| Once or twice a week                   | 1 (4,0)   | 0 (0,0)  | 1 (3,2)   |
| Three or more times a week             | 4 (16,0)  | 2 (33,3) | 6 (19,4)  |
| Difficulty staying awake               |           |          |           |
| None in the last month                 | 16 (64,0) | 3 (50,0) | 19 (61,3) |
| Less than once a week                  | 3 (12,0)  | 1 (16,7) | 4 (12,9)  |
| Once or twice a week                   | 3 (12,0)  | 2 (33,3) | 5 (16,1)  |
| Three or more times a week             | 3 (12,0)  | 0 (0,0)  | 3 (9,7)   |
| Feeling a lack of enthusiasm/energy    |           |          |           |
| No difficulty                          | 2 (8,0)   | 2 (33,3) | 4 (12,9)  |
| A slight problem                       | 6 (24,0)  | 2 (33,3) | 8 (25,8)  |
| A reasonable problem                   | 13 (52,0) | 1 (16,7) | 14 (45,2) |
| A major problem                        | 4 (16,0)  | 1 (16,7) | 5 (16,1)  |
| Partner, spouse, or roommate           |           |          |           |
| Partner/roommate                       |           |          |           |
| No                                     | 8 (32,0)  | 1 (16,7) | 9 (29,0)  |
| In another room                        | 2 (8,0)   | 0 (0,0)  | 2 (6,5)   |
| Same room, different bed               | 0 (0,0)   | 0 (0,0)  | 0 (0,0)   |
| Same room, same bed                    | 15 (60,0) | 5 (83,3) | 20 (64,5) |
| He/She snores loudly <sup>§</sup>      |           |          |           |
| None in the last month                 | 5 (33,3)  | 2 (40,0) | 7 (35,0)  |
| Less than once a week                  | 3 (20,0)  | 1 (20,0) | 4 (20,0)  |
| Once or twice a week                   | 3 (20,0)  | 0 (0,0)  | 3 (15,0)  |
| Three or more times a week             | 4 (26,7)  | 2 (40,0) | 6 (30,0)  |
| He/She has sleep apnea <sup>§</sup>    |           |          |           |
| None in the last month                 | 11 (73,3) | 4 (80,0) | 15 (75,0) |
| Less than once a week                  | 1 (6,7)   | 0 (0,0)  | 1 (5,0)   |
| Once or twice a week                   | 1 (6,7)   | 1 (20,0) | 2 (10,0)  |
| Three or more times a week             | 2 (13,3)  | 0 (0,0)  | 2 (10,0)  |
| He/She moves a lot <sup>§</sup>        |           |          |           |
| None in the last month                 | 7 (46,7)  | 2 (40,0) | 9 (45,0)  |
| Less than once a week                  | 3 (20,0)  | 1 (20,0) | 4 (20,0)  |
| Once or twice a week                   | 4 (26,7)  | 1 (20,0) | 5 (25,0)  |
| Three or more times a week             | 1 (6,7)   | 1 (20,0) | 2 (10,0)  |
| He/She becomes confused <sup>§</sup>   |           |          |           |
| None in the last month                 | 8 (53,3)  | 4 (80,0) | 12 (60,0) |
| Less than once a week                  | 5 (33,3)  | 0 (0,0)  | 5 (25,0)  |
| Once or twice a week                   | 2 (13,3)  | 1 (20,0) | 3 (15,0)  |
| Three or more times a week             | 0 (0,0)   | 0 (0,0)  | 0 (0,0)   |
| He/She has other symptoms <sup>§</sup> |           |          |           |
| None in the last month                 | 8 (61,5)  | 1 (25,0) | 9 (52,9)  |
| Less than once a week                  | 3 (23,1)  | 1 (25,0) | 4 (23,5)  |
| Once or twice a week                   | 1 (7,7)   | 1 (25,0) | 2 (11,8)  |
| Three or more times a week             | 1 (7,7)   | 1 (25,0) | 2 (11,8)  |
| Pittsburgh classification              |           |          |           |
| Overall sleep quality                  |           |          |           |
| Good sleep quality                     | 6 (20,0)  | 1 (16,7) | 6 (19,4)  |
| Poor sleep quality                     | 14 (56,0) | 4 (66,7) | 18 (58,1) |
| Very poor sleep quality                | 6 (24,0)  | 1 (16,7) | 7 (22,6)  |

Data expressed as absolute frequencies (n) and relative frequencies (%) or medians and interquartile ranges ([IQR], 25th and 75th percentiles). Legend: §N=17 – 20. \*Chi-square test with adjusted residual analyses or Mann-Whitney test, when applicable. Significance set at 5% for all analyses.

**Table 3:** Characterization of the components of the Pittsburgh Sleep Quality Index (PSQI-BR).

| Variable                                                | Female (n=25)         | Male (n=6)              | Total (n=31)           |
|---------------------------------------------------------|-----------------------|-------------------------|------------------------|
| Subjective sleep quality<br>(minimum–maximum)           | 1 [1 – 2]<br>(0 – 3)  | 1,5 [1 – 2]<br>(1 – 2)  | 1 [1 – 2]<br>(0 – 3)   |
| Sleep latency<br>(minimum–maximum)                      | 1 [0 – 2]<br>(0 – 3)  | 0,5 [0 – 1]<br>(0 – 2)  | 1 [0 – 1]<br>(0 – 3)   |
| Sleep duration<br>(minimum–maximum)                     | 1 [0 – 1]<br>(0 – 3)  | 1 [0 – 2]<br>(0 – 3)    | 1 [0 – 1]<br>(0 – 3)   |
| Typical sleep efficiency<br>(minimum–maximum)           | 0 [0 – 2]<br>(0 – 3)  | 0 [0 – 1]<br>(0 – 3)    | 0 [0 – 1,5]<br>(0 – 3) |
| Sleep disturbances<br>(minimum–maximum)                 | 1 [1 – 2]<br>(0 – 3)  | 1,5 [1 – 2]<br>(1 – 2)  | 1 [1 – 2]<br>(0 – 3)   |
| Use of sleep medication<br>(minimum–maximum)            | 0 [0 – 0]<br>(0 – 3)  | 0,5 [0 – 3]<br>(0 – 3)  | 0 [0 – 1]<br>(0 – 3)   |
| Daytime sleepiness and dysfunction<br>(minimum–maximum) | 1 [1 – 2]<br>(0 – 3)  | 2 [0 – 2]<br>(0 – 2)    | 1 [1 – 2]<br>(0 – 3)   |
| Total score<br>(minimum–maximum)                        | 6 [5 – 9]<br>(3 – 17) | 8,5 [7 – 9]<br>(3 – 12) | 6 [5 – 9]<br>(3 – 17)  |

Data expressed as medians and interquartile ranges ([IQR], 25th and 75th percentiles). Legend: \*Mann-Whitney test. Significance set at 5% for all analyses.

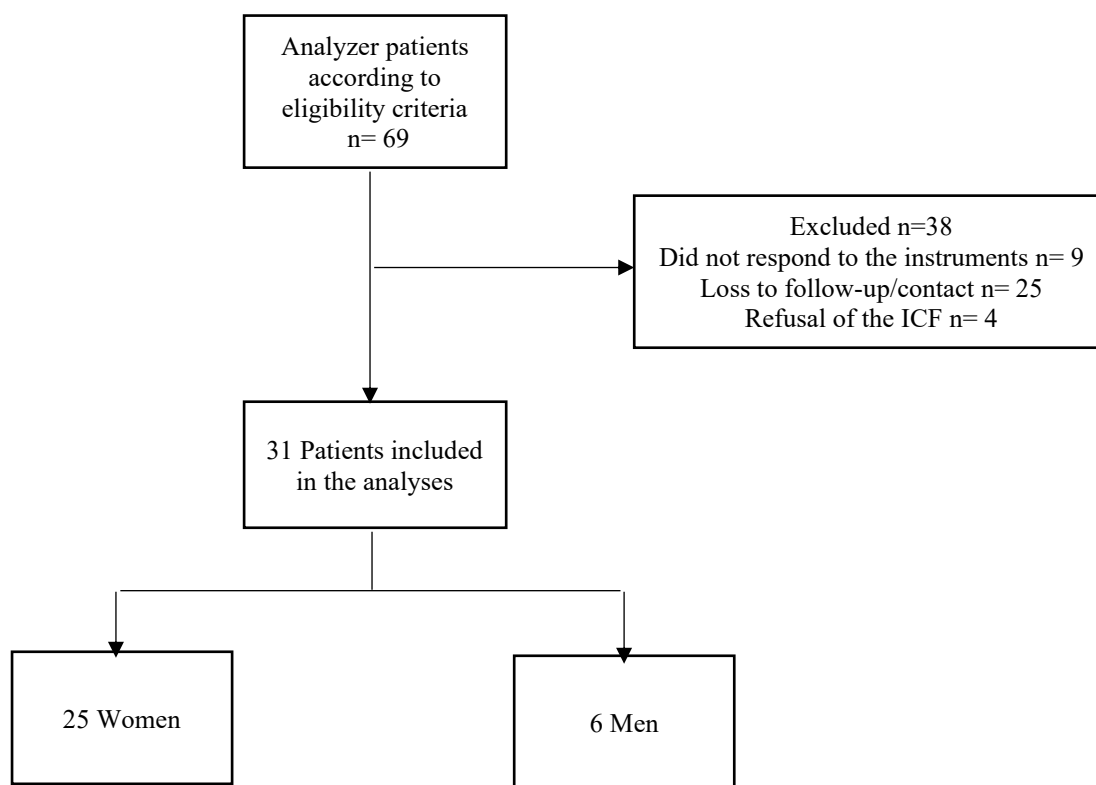
**Table 4:** Characterization of the Epworth Sleepiness Scale (ESS).

| Variable                                            | Female<br>(n=25) | Male<br>(n=6) | Total<br>(n=31) |
|-----------------------------------------------------|------------------|---------------|-----------------|
| Classify the situations associated with sleepiness. |                  |               |                 |
| Sitting and reading                                 |                  |               |                 |
| No chance of dozing                                 | 4 (16,0)         | 2 (33,3)      | 6 (19,4)        |
| Slight chance of dozing                             | 12 (48,0)        | 3 (50,0)      | 15 (48,4)       |
| Moderate chance of dozing                           | 5 (20,0)         | 0 (0,0)       | 5 (16,1)        |
| High chance of dozing                               | 4 (16,0)         | 1 (16,7)      | 5 (16,1)        |
| Watching TV                                         |                  |               |                 |
| No chance of dozing                                 | 3 (12,0)         | 1 (16,7)      | 4 (12,9)        |
| Slight chance of dozing                             | 8 (32,0)         | 3 (50,0)      | 11 (35,5)       |
| Moderate chance of dozing                           | 9 (36,0)         | 1 (16,7)      | 10 (32,3)       |
| High chance of dozing                               | 5 (20,0)         | 1 (16,7)      | 6 (19,4)        |
| Sitting quietly in a public place §                 |                  |               |                 |
| No chance of dozing                                 | 12 (50,0)        | 4 (66,7)      | 16 (53,3)       |
| Slight chance of dozing                             | 5 (20,8)         | 1 (16,7)      | 6 (20,0)        |
| Moderate chance of dozing                           | 5 (20,8)         | 1 (16,7)      | 6 (20,0)        |
| High chance of dozing                               | 2 (8,3)          | 0 (0,0)       | 2 (6,7)         |
| Sitting as a passenger in a car                     |                  |               |                 |
| No chance of dozing                                 | 9 (36,0)         | 4 (66,7)      | 13 (41,9)       |
| Slight chance of dozing                             | 7 (28,0)         | 0 (0,0)       | 7 (22,6)        |
| Moderate chance of dozing                           | 5 (20,0)         | 1 (16,7)      | 6 (19,4)        |
| High chance of dozing                               | 4 (16,0)         | 1 (16,7)      | 5 (16,1)        |
| Lying down in the afternoon to rest                 |                  |               |                 |
| No chance of dozing                                 | 3 (12,0)         | 1 (16,7)      | 4 (12,9)        |
| Slight chance of dozing                             | 7 (28,0)         | 1 (16,7)      | 8 (25,8)        |
| Moderate chance of dozing                           | 9 (36,0)         | 0 (0,0)       | 9 (29,0)        |
| High chance of dozing                               | 6 (24,0)         | 4 (66,7)      | 10 (32,3)       |
| Sitting and talking with another person             |                  |               |                 |
| No chance of dozing                                 | 18 (72,0)        | 4 (66,7)      | 22 (71,0)       |
| Slight chance of dozing                             | 6 (24,0)         | 2 (33,3)      | 8 (25,8)        |
| Moderate chance of dozing                           | 1 (4,0)          | 0 (0,0)       | 1 (3,2)         |
| High chance of dozing                               | 0 (0,0)          | 0 (0,0)       | 0 (0,0)         |
| Sitting quietly after lunch                         |                  |               |                 |
| No chance of dozing                                 | 5 (20,0)         | 0 (0,0)       | 5 (16,1)        |
| Slight chance of dozing                             | 7 (28,0)         | 2 (33,3)      | 9 (29,0)        |
| Moderate chance of dozing                           | 6 (24,0)         | 0 (0,0)       | 6 (19,4)        |
| High chance of dozing                               | 7 (28,0)         | 4 (66,7)      | 11 (35,5)       |
| Sitting in a stopped car due to traffic             |                  |               |                 |
| No chance of dozing                                 | 18 (72,0)        | 5 (83,3)      | 23 (74,2)       |
| Slight chance of dozing                             | 4 (16,0)         | 1 (16,7)      | 5 (16,1)        |
| Moderate chance of dozing                           | 3 (12,0)         | 0 (0,0)       | 3 (9,7)         |
| High chance of dozing                               | 0 (0,0)          | 0 (0,0)       | 0 (0,0)         |
| Total score §                                       | 8,88±5,11        | 8,67±4,13     | 8,83±4,86       |
| (minimum–maximum)                                   | (1 – 19)         | (4 – 14)      | (1 – 19)        |
| Sleepiness classification §                         |                  |               |                 |
| Adequate sleep (0-4 points)                         | 5 (20,8)         | 2 (33,3)      | 7 (23,3)        |
| Inadequate sleep (5-10 points)                      | 9 (37,5)         | 2 (33,3)      | 11 (36,7)       |
| Sleep disorder (≥11 points)                         | 10 (41,7)        | 2 (33,3)      | 12 (40,0)       |

Data expressed as absolute frequencies (n) and relative frequencies (%), means and standard deviations of the means (±SD), or medians and interquartile ranges ([IQR], 25th and 75th percentiles). Legend: §n=30.

\*Chi-square test with adjusted residual analyses, Student's t-test for independent samples, or Mann-Whitney test, when applicable. Significance set at 5% for all analyses.

**Figure 1:** Participant Selection Flowchart.



Legend: n – absolute frequency.