

**Factors related to insomnia symptoms among people living with HIV***Fatores relacionados aos sintomas de insônia entre pessoas vivendo com HIV**Factores relacionados con los síntomas de insomnio entre personas que viven con el VIH*Luciana Fidalgo Ramos Nogueira<sup>1</sup>, Pollyanna Pellegrino<sup>1</sup>, Thais Carvalho da Fonseca<sup>2</sup>, Patrick Herman Paterlini<sup>2</sup>, Adriana de Sousa Duarte<sup>3</sup>, Elaine Cristina Marqueze<sup>1</sup>

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**ABSTRACT**

**Objective:** To evaluate the prevalence of insomnia symptoms and its relationship with nutritional aspects, gastrointestinal symptoms and chronic diseases among people living with HIV. **Methods:** a cross-sectional study of 307 people living with HIV in antiretroviral therapy attended by the Specialized AIDS Service of the municipality of Santos (SP), Brazil. The variables evaluated were insomnia symptoms, gastrointestinal symptoms and chronic noncommunicable diseases. **Results:** the prevalence of insomnia symptoms was 79.2%. There was a greater proportion of people living with HIV with insomnia symptoms who had weight changes after HIV diagnosis, unpleasant stomach sensations, poor digestion, poor appetite, respiratory and skin diseases. **Conclusion:** the high prevalence of insomnia symptoms was related to the presence of gastrointestinal symptoms, as well as respiratory and dermatological diseases.

**Keywords:** HIV; Sleep Initiation and Maintenance Disorders; Chronic disease; Nutrition in Public Health.

**RESUMO**

**Objetivo:** avaliar a prevalência dos sintomas de insônia e sua relação com os aspectos nutricionais, sintomas gastrointestinais e doenças crônicas entre pessoas vivendo com HIV. **Métodos:** estudo transversal com 307 pessoas vivendo com HIV em terapia antirretroviral atendidas pelo Serviço de Assistência Especializada em AIDS do município de Santos (SP), Brasil. As variáveis avaliadas foram sintomas de insônia, sintomas gastrointestinais e doenças crônicas não transmissíveis. **Resultados:** a prevalência de sintomas de insônia foi de 79,2%. Verificou-se uma maior proporção de pessoas vivendo com HIV com sintomas de insônia que tiveram mudança de peso após o diagnóstico do HIV, sensações desagradáveis no estômago, má digestão, falta de apetite, doenças respiratórias e de pele. **Conclusão:** a elevada prevalência de sintomas de insônia foi relacionada à presença de sintomas gastrointestinais, bem como de doenças respiratórias e dermatológicas.

**Descritores:** HIV; Distúrbios do Início e da Manutenção do Sono; Doença crônica; Nutrição em Saúde Pública.

**RESUMÉN**

**Objetivo:** evaluar la prevalencia de los síntomas de insomnio y su relación con los aspectos nutricionales, los síntomas gastrointestinales y las enfermedades crónicas entre las personas que viven con el VIH. **Métodos:** estudio transversal con 307 personas viviendo con VIH en terapia antirretroviral atendidas por el Servicio de Asistencia Especializada en SIDA del municipio de Santos (SP), Brasil. Las variables evaluadas fueron síntomas de insomnio, síntomas gastrointestinales y enfermedades crónicas no transmisibles. **Resultados:** la prevalencia de síntomas de insomnio fue del 79,2%. Hubo una mayor proporción de personas que viven con el VIH con síntomas de insomnio que tuvieron cambios de peso después del diagnóstico de VIH, sensaciones estomacales desagradables, mala digestión, falta de apetito, enfermedades respiratorias y de la piel. **Conclusión:** la alta prevalencia de síntomas de insomnio se relacionó con la presencia de síntomas gastrointestinales, así como con enfermedades respiratorias y dermatológicas.

**Descriptores:** VIH; Trastornos del inicio y del mantenimiento del sueño; Enfermedad crónica; Nutrición en Salud Pública.

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## INTRODUCTION

People living with HIV (PLWH) have a high prevalence of sleep disorders, which are associated with poorer functioning of the immune system.<sup>1</sup> According to a study conducted to characterize the sleep quality of this population, the lower the lymphocyte count TCD4, the greater the prevalence of problems related to sleep.<sup>2</sup>

Significant changes in sleep patterns may occur soon after infection, but they also appear to be associated with long periods of exposure to antiretroviral therapy (ART). In a study of adults living with HIV who started ART early, it was found that difficulty sleeping, total sleep time reduction and daytime sleepiness were the main reported complaints.<sup>3</sup> In a systematic review of the implications pathophysiology of insomnia in PLWH, it was pointed out that the prevalence of sleep disorders varies from 29 to 97%, and this wide variability is justified by the absence of a gold standard for the evaluation of these disorders, from subjective questionnaires to clinical evaluations.<sup>4</sup>

The occurrence of sleep disorders, may be related to the onset or aggravation of chronic diseases. Unlike the era prior to high-potency antiretroviral treatment, when opportunistic infections were the main cause of death of PLWH, this population currently has a high prevalence of chronic diseases. As regards cardiovascular diseases, dyslipidemias, diabetes and non-AIDS cancers, PLWH present higher prevalences when compared to the general adult population.<sup>5</sup> It is worth mentioning that the presence of sleep disorders is associated not only with the chronic diseases themselves, but also to

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risk factors for its development, such as smoking, alcoholism and poor dietary habits.<sup>6</sup> In addition, it is a bidirectional relationship, since chronic diseases can promote changes in the sleep-wake cycle, with consequent damages on physical and mental recovery.<sup>6</sup> Thus, the presence of gastrointestinal symptoms and nutritional aspects, such as body mass and changes in body weight, are also strongly associated with poor sleep quality.<sup>7</sup>

It is not possible to understand the sleep problems and the factors related to their occurrence among PLWH, based on studies that have been carried out for more than 10 years, with different ART regimens. In addition, the difficulty of sleeping also results in low adherence to ART, which prevents the control of viral replication and leads to a worse prognosis of the clinical evolution of HIV.<sup>8</sup> Given the current HIV epidemic situation, this problem deserves attention, since sleep disorders can significantly influence the integrity of the immune system and the quality of life.<sup>9</sup>

In this context, the objective of the present study was to evaluate the prevalence of insomnia symptoms and its relationship with nutritional aspects, gastrointestinal symptoms and chronic diseases among people living with HIV (PLWH) in antiretroviral therapy.

## METHODS

This is a cross-sectional epidemiological study carried out with 307 PLWH in ART (sample power = 80%, G \* Power 3.1.4), aged 18 years or older, attended by the Specialized Assistance Service (SAS) in AIDS of the municipality of Santos, São Paulo Brazil.

Data collection was performed at the SAS, from February to June 2016, on alternating days and times (Monday to Friday, from 08:00 to 18:00, according to office hours). The instrument of data collection consisted of a structured questionnaire that was applied by undergraduate students. In a pilot study, it was verified that the majority of the participants had difficulty reading the questionnaire. Therefore, it was decided to standardize its application through interviews, in which the students performed the individual reading of each question and recorded the answers of the participants. The interviews lasted an average of 45 minutes and the undergraduates were properly trained to guide the participants without interfering with their responses.

The study-dependent variable was the symptoms of insomnia, assessed using the Karolinska Sleep Questionnaire (KSQ). Participants who reported having at least one of the seven symptoms investigated, with a minimum frequency of three times a week, were classified as positive for insomnia symptoms in the six months prior to the study.<sup>10</sup>

The independent variables of the study were:

1) Nutritional aspects: Body mass index (BMI) was used as an indicator of nutritional status, and its score was classified as low weight (<18.5 kg/m<sup>2</sup>), eutrophy (18.5-24.9 kg/m<sup>2</sup>), overweight (25.0-29.9 kg/m<sup>2</sup>) and obesity (≥30.0 kg/m<sup>2</sup>).<sup>11</sup> Participants also answered two questions about body weight changes, one after HIV infection and another last 12 months. Both admitted three response options: "Not changed", "Decreased \_\_\_ kg" or "Increased \_\_\_ kg";

2) Gastrointestinal symptoms: evaluated from three drawn questions of validated version and translated into Portuguese Self-Reporting Questionnaire.<sup>12</sup> The questions were: "Do you have unpleasant sensations in the stomach?" "You have no appetite?" and "You have poor digestion?", having as answer options "Yes" or "No";

3) Chronic diseases: obtained from a list of 51 lesions and diseases included in the validated version and translated into Portuguese of the Workability Index<sup>13</sup>, which was used as an important tool for rapid completion and simple and can be used both individually and collectively, subsidizing information for directing preventive measures.<sup>14</sup> The diseases with medical diagnosis referred to are grouped into 11 categories: genitourinary, neurological, dermatological, endocrine or metabolic, musculoskeletal, digestive, emotional, cardiovascular, hematological, respiratory and tumors. This variable was evaluated only among the 122 of the 307 PLHIV who worked for remunerated activity and who responded to the Work Ability Index (WAI).

The treatment of the data included the description of the sample studied through absolute and relative frequencies of the qualitative variables. To test the normality of the quantitative variables, the Shapiro-Wilk test was used. Parametric variables were described by mean and standard deviation (SD), while nonparametric variables were described by median and Interquartile Interval (IQI = P25-P75).

For the comparison of the study variables, Pearson's chi-square or Fisher exact

test were performed. The internal consistency and reliability of the insomnia symptom questionnaire were assessed by Cronbach's Alpha test ( $\alpha=0.76$ ). A significance level of 5% was used for all tests. The analyzes were performed in software Stata 12.0 and STATISTICA 7.

The present study was authorized by the Municipal Health Department of Santos and approved by the Research Ethics Committee (n° 1,237,142), respecting the ethical aspects of research with human beings in accordance with resolution 466/2012.

## RESULTS

The mean age of participants was 48 years (SD 12.1 years). The majority were female (52.4%), and identified themselves as women (54.9%), had a high school education (83.4%) and had financial difficulties at the end of the month (53.9%). 49.5% were single, 39.7% reported having formal employment and about 1/3 had children up to 14 years old at home (29.6%),

The majority (96.4%) stated that they were not an alcoholic, and 24.4% declared that they were smokers. Regarding the use of illicit drugs, 21.2% had used them in the last six months and 10.1% still used them. Among the illicit drugs, the most mentioned were marijuana (19.5%), cocaine (17.9%) and crack (9.8%).

The mean time to diagnosis of HIV was 12.9 years (SD 8.1 years), with little more than half reporting that the current drug regimen was neither the first nor the only one used (51.9%). The median time of use of the current drug regimen was 9.4 years (SD 7.6 years), with the

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most used drugs being lamivudine (51.8%), tenofovir (51.5%) and efavirenz (44.2 %).

In the year prior to the survey, 47.1% reported changes in body weight, 30.3% with a median loss of 6.0 kg (Interquartile Interval - IQI 3.0-12.0 kg) and 16.8% with a median gain of 6.0 kg (IQI 3.0-10.0 kg). After the discovery of HIV, 20.7% presented a change in weight, 14.5% with a median loss of 12.5 kg (IQI 8.5 - 20.0 kg) and 5.6% with a median gain of 11 kg (IQI 5.0 - 19.0 kg). Approximately half of the participants were overweight (44.9%), being 30.6% overweight and 14.3% obese. Regarding gastrointestinal symptoms, 23.4% reported having poor digestion, 30.6% had a lack of appetite and 32.8% had unpleasant sensations in the stomach.

The symptoms of insomnia were verified in 79.2% of the evaluated ones, being the early awakening (43,8%) and the difficulty of falling asleep (38,0%) the most prevalent symptoms.

Among those who reported having other diagnosed diseases, the most prevalent were respiratory (23.3%), cardiovascular (20.8%), emotional (15.6%) and digestive (15.4%), followed by musculoskeletal diseases, 83%), endocrine (11.7%), skin (10.5%), neurological (8.4%), genitourinary (5.9%), hematologic (2.6%) and tumors (0.7 %).

Although most participants reported no maldigestion, unpleasant sensations in the stomach and lack of appetite, these gastrointestinal symptoms were found to be more frequent among the PLWH who had symptoms of insomnia (Table 1).

**Table 01** - Proportion test of nutritional aspects and gastrointestinal symptoms as a function of insomnia symptoms among people living with HIV.

Variables	Insomnia		p-value
	No symptoms n (%)	With symptoms n (%)	
<b>Nutritional aspects</b>			
<i>BMI</i>			
Eutrophic	32 (50.8)	110 (46.8)	0.66*
Low weight	3 (4.8)	19 (8.1)	
Overweight	17 (27.0)	74 (31.5)	
Obesity	11 (17.5)	32 (13.6)	
<i>Weight change in last year</i>			
None	34 (54.0)	127 (53.4)	0.51
Decreased	16 (25.4)	74 (31.1)	
Increased	13 (20.6)	37 (15.5)	
<i>Weight change after HIV</i>			
None	46 (73.0)	195 (81.9)	0.12
Decreased	10 (15.9)	35 (14.7)	
Increased	7 (11.1)	8 (3.4)	
<b>Gastrointestinal symptoms</b>			
<i>Unpleasant sensations in the stomach</i>			
No	50 (79.4)	154 (64.2)	0.02
Yes	13 (20.6)	86 (35.8)	
<i>Indigestion</i>			
No	54 (85.7)	178 (74.5)	0.06
Yes	9 (14.3)	61 (25.5)	
<i>Lack of appetite</i>			
No	55 (87.3)	155 (64.8)	<0.01
Yes	8 (12.7)	84 (35.2)	

In addition, although the majority of the participants did not mention the diagnosis of respiratory and dermatological diseases, it was

verified that both were more frequent among the PLWH who had symptoms of insomnia (Table 2).

**Table 02** - Proportion of chronic diseases as a function of insomnia symptoms among people living with HIV.

Independent variables	Insomnia		p-value
	No symptoms n (%)	With symptoms n (%)	

**Chronic diseases**

## Musculoskeletal

Not	54 (85.7)	207 (87.3)	0.73
Yes	9 (14.3)	30 (12.7)	

## Cardiovascular

Not	51 (82.3)	185 (78.1)	0.47
Yes	11 (17.7)	52 (21.9)	

## Respiratory

Not	54 (87.1)	172 (73.5)	0.03
Yes	8 (12.9)	62 (26.5)	

## Emotional

Not	56 (88.9)	199 (82.9)	0.24
Yes	7 (11.1)	41 (17.1)	

## Neurological

Not	58 (93.5)	212 (91.0)	0.36*
Yes	4 (6.5)	21 (9.0)	

## Digestive

Not	55 (88.7)	199 (83.3)	0.29
Yes	7 (11.3)	40 (16.7)	

## Genitourinary

Not	59 (93.6)	225 (94.1)	0.54*
Yes	4 (6.3)	14 (5.9)	

## Dermatological

Not	60 (95.2)	209 (87.8)	0.06*
Yes	3 (4.8)	29 (12.2)	

## Endocrine and Metabolic

Not	54 (85.7)	213 (88.7)	0.50
Yes	9 (14.3)	27 (11.3)	

**DISCUSSION**

The high prevalence of insomnia symptoms was related to the presence of gastrointestinal symptoms, respiratory and skin diseases. This result is corroborated by the study findings that found a high prevalence of poor sleep quality and insomnia symptoms, as well as a greater predisposition for the development of gastrointestinal problems and skin diseases among PLWH.<sup>15</sup> In studies on gastrointestinal

problems previously performed with the adult population in general, a strong association with sleep disorders was also found, which is related to higher levels of proinflammatory cytokines.<sup>16-17</sup> It is important to emphasize that there is evidence indicating that problems in the gastrointestinal tract may affect sleep physiology, just as sleep disturbances may

influence the functioning of the gastrointestinal tract, making this two-way problem.<sup>18</sup>

In a study carried out in Switzerland with 268 PLWH, the perception of several health symptoms was analyzed, and insomnia was one of the ten most prevalent (42%) in relation to severity, frequency, discomfort and being uncontrollable, indicating their relevance in this population.<sup>19</sup> In addition to insomnia, the authors also highlighted the high prevalence of dry skin (52.2%), diarrhea (47%) and gas (45%) among PLHIV. Among the most severe, lack of appetite and constipation have also been reported, as well as vomiting among the most troublesome and nausea among the least controllable. Another study, using data from a Canadian cohort, found that the most prevalent gastrointestinal symptoms among PLHIV consisted of swelling and abdominal pain (41%), diarrhea (40%), lack of appetite 25%, nausea and vomiting (21%).<sup>20</sup>

The respiratory problems in PLWH, evaluated in the present study, were also related to insomnia symptoms. According to a review study on lung infections in PLWH, respiratory problems remain associated with a high risk of mortality in this population even after the introduction of HAART.<sup>21</sup> Among patients with respiratory problems, reports of excessive drowsiness and fatigue are common; this implies directly in the quality of life and in the functional state of the same. In a study of 58 PLWH using ART, a greater risk of drowsiness was found among those with disordered breathing during sleep.<sup>22</sup> In addition, the authors also found an association between sleep and

respiratory problems, corroborating the findings of the present study.

Skin problems were also associated with insomnia symptoms in the present study. In a study conducted over a decade ago, skin problems were identified as one of the most prevalent manifestations of HIV, with a prevalence of 75% among PLWH in outpatient care.<sup>23</sup> There were no more recent studies on the prevalence of skin diseases in people living with HIV in clinical follow-up, however, in a study of population-based cohort recently conducted, it was observed that the risk of skin diseases was higher in patients with sleep disorders.<sup>24</sup> The authors emphasize that a bidirectional relationship should be considered, since the adverse effects of psychological stress and sleep disturbance itself may further aggravate the acne in question by interrupting the circadian rhythm of cortisol secretion.

It is noteworthy that all participants in the present study were on antiretroviral therapy. Among the most common adverse effects of these medications are insomnia, nightmares, nausea, lack of appetite, abdominal pain, diarrhea, constipation and heartburn, poor sleep quality, poor digestion and unpleasant sensations in the stomach. These problems, in fact, represent the most frequently reported by PLWH.<sup>25</sup>

This study has some limitations. The first refers to the list of injuries and diseases used to obtain chronic diseases. Because it integrates the Work Ability Index, which consists of an instrument used for self-rated assessment of the physical and mental health conditions of workers, it was answered only by the PLWH who

were engaged in paid activity. Because it is a cross-sectional study, it is not possible to infer about the temporal cause and effect relationship of the studied variables, however, according to the aforementioned studies, it is verified that such relationships exist among PLWH, corroborating the results of the present study. In some situations these relationships are bidirectional, so that the evaluated outcomes may not represent the essential cause of the symptoms of insomnia in the sample studied. Nevertheless, the need for preventive measures for both sleep problems, chronic diseases and gastrointestinal problems.

## CONCLUSION

It is concluded that the prevalence of insomnia symptoms was high among PLWH, being more frequent among those that presented gastrointestinal symptoms, as well as respiratory and skin diseases.

As discussed above, PLW Hoften suffer from the consequences of chronic sleep deprivation due to pathophysiological mechanisms of the infection itself and chronic diseases, but also due to the adverse effects of ART. Given the accumulation of determinants for the occurrence of changes in the sleep-wake cycle and its possible interference with the development of comorbidities, a strong point of this study is the description of a significant sample of IVHIV in a clinical follow-up in relation to the sociodemographic aspects of sleep and health.

Considering the lack of knowledge regarding the aspects related to sleep disorders

in PLWH, the presented results certainly can contribute with the discussions of public health policies for this population.

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**COLLABORATIONS**

LFRN: substantial contributions in the design or design of the work; in the collection, analysis and interpretation of data; in the writing of the article or in its critical revision; in the final version to be published. PP: contributions in the writing of the article or in its critical revision; in the final version to be published. TCF and PHP: contributions in data collection, analysis and interpretation; in the writing of the article or in its critical revision; in the final version to be published. ASD: writing or article contributions or in the critical review of the article or in its critical review, in the final version to be published. ECM: contributions in the design or design of the work; in the collection, analysis and interpretation of data; in the writing of the article or in its critical revision; in the final version to be published.

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**CONFLICTS OF INTEREST**

The authors declare that no have conflicts of interest.

**AVAILABILITY OF DATA**

Available upon request to the authors.

**FUDING SOURCE**

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