JoCASS
Çukurova Anestezi ve Cerrahi Bilimler Dergisi
2018 Adana

SLEEP DISORDERS IN THE FOLLOW-UP OF COVID-19 INFECTION: A SINGLE CENTER EXPERIENCE

Selahattin Ayas[1], Anıl Uçan [2]

1 *Eskişehir City Hospital, Department of Neurology, Eskişehir, Türkiye*
2 *Eskişehir City Hospital, Department of Internal Medicine, Eskişehir, Türkiye*

Abstract

Aim: This study aims to investigate sleep-related disorders and their possible causes after COVID-19 infection.

Methods: The data of patients over the age of 18 with a history of COVID-19 infection who applied to our Sleep Disorders Unit in the last 3 months were obtained retrospectively from anamnesis, laboratory, imaging, and polysomnography examinations. The data of Pittsburgh sleep quality index (PSQI), Epworth sleepiness scale and Beck anxiety inventory (BAI) tests of patients were included in the study.

Results: After COVID-19 infection, in all patients, reason for admitting to our Sleep Disorders Unit was complaints of insomnia. Another sleep-related disorder was determined in 64% of the patients (Obstructive Sleep Apnea Syndrome (OSAS) is the most common with 52%). The history of the chronic cardiorespiratory, cerebral, endocrine-metabolic disease was significantly higher in patients having complaints of insomnia and another accompanying sleep-related disorders (68% vs 0%, p=0.001). Also, the history of hospitalization in these patients was higher, although not statistically significant (50% vs 11%, p=0.088). For all patients, the median BAI value and the mean PSQI value were high (13 and 11.6, respectively), but no correlation was found between them (p=0.336).

Conclusions: The most common reason for sleep-related admission after COVID-19 infection is complaints of insomnia and if there is a history of chronic cardiorespiratory, cerebral, endocrine-metabolic disease and/or hospitalization because of COVID-19 infection, another accompanying sleep-related disorders, especially OSAS, should investigate. Also, the severity of anxiety disorder as a cause of insomnia complaints is not correlated with the deterioration in sleep quality.

Keywords: *Insomnia, COVID-19, comorbidity, polysomnography.*

Corresponding Author: Selahattin Ayas, e-mail: ayastr@hotmail.com

Received: 15.08.2022, Accepted: 08.10.2022, Available Online Date: 31.12.2022

Cite this article as: Ayas S, Uçan A. Sleep disorders in the follow-up of COVID-19 infection: A Single Center Experience. J Cukurova Anesth Surg. 2022;5(3):325-33.

doi: 10.36516/jocass.1162315

Introduction

Coronavirus disease (COVID-19) was accepted as a pandemic by the World Health Organization on March 11, 2020. Severe psychiatric and neuropsychiatric diseases in patients with history of COVID-19 infection have been reported between 14% to 61% during infection and between 14.8% and 76.9% after infection similar to other coronavirus pandemics, such as Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) [1]. Primary mental health disorders in affected individuals include depression, anxiety disorder, post-traumatic stress disorder (PTSD), insomnia, and sleep disorders.

The prevalence of insomnia varies between 3.9% and 22% worldwide [2]. The community-based studies have shown the prevalence of insomnia during the COVID-19 pandemic is close to or higher than the upper limit of the worldwide prevalence of insomnia, varying between 19.1% and 37% [3–5].

Anxiety and depression stand out as the primary cause of insomnia during the COVID-19 pandemic [6]. In both cases, increased cognitive arousals and changing cerebral monoamine concentrations, as well as an increase in proinflammatory cytokines caused by psychological stressors such as C-reactive protein (CRP), Tumor-necrosis factor (TNF) and interleukin-6 (IL-6), neuroinflammation, irregularity of the hypothalamic-pituitary-adrenal axis, genetic factors and circadian rhythm irregularity may play a role in the pathophysiology of insomnia [7–9]. However, it is known that sleep-related disorders, which can cause poor sleep quality such as insomnia, lead to increased susceptibility to depression and infectious processes by increasing these proinflammatory cytokines and causing changes in T lymphocyte expression and proliferation [10,11]. For this reason, early diagnosis and treatment of sleep-related disorders, especially insomnia that may occur during and after COVID-19 infection, is essential in terms of neurological, immunological and psychological processes.

This study aimed to evaluate possible sleep-related disorders retrospectively in our patients who were followed up in the Sleep Disorders Unit of our hospital in the last three months and who had a history of COVID-19 infection.

Materials and Methods

After the approval of Eskişehir Osmangazi University, Faculty of Medicine, Clinical Research Ethics Committee (Date: 26.10.2021, No: 05), the study was organized according to the Principles of the Declaration of Helsinki. All patients over 18 who applied to Eskişehir City Hospital Sleep Disorders Unit between 15.01.2021 and 15.04.2021 and had a history of COVID-19 Polymerase Chain Reaction (PCR) test positivity were retrospectively screened and included in the study. The exclusion criteria were being younger than 18 years of age, being pregnant, using medication that may cause sleep disturbance, not having a sleep disorder complaint, not having a history of COVID-19 infection and insufficient data.

In all patients fulfilling including criteria in the study, the reason for admitting to our Sleep Disorders Unit was complaints of insomnia. In addition, age, gender, characteristics and duration of sleep disturbance complaints, body mass indices, history of hospitalization or intensive care unit admission due to COVID-19 infection, presence of an additional sleep-related disease, chronic cardiac, respiratory, cerebral, endocrine-metabolic disease and psychiatric disorders were recorded. Data for this study were collected using the hospital information management system in detail from patient's history, anamnesis, laboratory, imaging and polysomnography (PSG) examinations. All medications used by the patients were noted. The data obtained from the Pittsburgh sleep quality index test (PSQI), Epworth sleepiness scale (ESS) and Beck anxiety inventory (BAI)

tests were included in the study. A clinical neurophysiology specialist applied these tests to all patients who applied with complaints of insomnia.

The PSQI test, developed by Buysse et al. [12], is a scale consisting of 24 questions evaluating sleep quality and disturbance in the past month. Nineteen questions are self-report questions, and five questions are answered by spouse or roommates of the patient. Questions answered by the spouse or roommates are not included in the scoring. PSQI includes seven components: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleeping pills, and daytime dysfunction. The score obtained from these components varies between 0-21. A total score above 5 indicates "poor sleep quality".

ESS, developed by Johns et al. [13], is a scale consisting of 8 questions and indicates daytime sleepiness. In each question, the scoring method is the same. The probability of falling asleep is calculated with scale. On an ordinary day when the patient is not excessively tired is given 0 points if there is no probability of falling asleep, 1 point if it is a low probability, 2 points if it is a medium probability, and 3 points if it is a high probability. A total score of 10 and above indicates the presence of excessive daytime sleepiness.

BAI, developed by Beck et al. [14], is a scale consisting of 21 questions in total and in which each question scoring between 0-3 is used to measure the anxiety of the individual. A total score of 8-15 indicates a mild level of anxiety, between 16-25 indicates moderate anxiety, and between 26-63 indicates a high level of anxiety.

The data of type 1 PSG performed during all night in laboratory conditions as well as scored and reported according to the guideline organized by American Academy of Sleep Medicine (AASM) in 2020 [15] were included in the study in the patients applying with complaints of insomnia accompanied by symptoms including snoring, witnessed apnea, waking from sleep with shortness of breath, night sweats, nocturia, restless sleep, and fatigue.

Statistical evaluation was analyzed using the SPSS-24 (Statistical Package for the Social Sciences) program. Categorical data were compared using Fisher's exact test. Non-parametric data were evaluated with the Mann-Whitney U test, and parametric data were evaluated with the Student-t and One-way ANOVA test. Pearson correlation analysis was used in the correlation analysis of parametric data. According to the analysis results, the p-value of 0.05 and below was accepted as statistically significant.

Results

A total of 25 patients who applied with the complaints of insomnia after COVID-19 infection between 15.01.2021 and 15.04.2021 were included in the study.

In the study, the first set of questions aimed to evaluate the baseline characteristics of the patients. As shown in Table 1, 16 (64%) of the patients were female, and 9 were male. Their mean age was 48±14 years, and the median duration of insomnia complaints was two months (Interquartile Range [IQR]: 1.5-3 months). The mean body mass index was 27±5.7 kg/m^2.

A total of 9 patients (36%) had a history of hospitalization due to COVID-19 infection, and 2 (0.5%) patients needed treatment in the intensive care unit (Table 1).

PSG examination was performed all night in laboratory conditions in 16 patients (64%) who had insomnia complaints accompanied by symptoms such as snoring, witnessed apnea, awakening from sleep with shortness of breath, night sweats, nocturia, restless sleep, and fatigue during the day. According to the result of PSG and clinical evaluation, at least one other sleep-related disease accompanying insomnia complaints was observed in 16 (64%) patients. Further analysis showed the presence of obstructive sleep apnea syndrome (OSAS) in 13 patients (52%),

Table 1. Demographic characteristics of all patients presenting with complaints of insomnia

Demographic characteristics (n=25)	
Gender, female/male, n (%)	16/9 (64/36)
Age, years, mean (SD)	48 (14)
Insomnia duration, months, median (IQR)	2 (1.5-3)
Body mass index, kg/m2, mean (SD)	27 (5.7)
Number of patients with a history of hospitalization, n (%)	9 (36)
Number of patients treated in the Intensive Care Unit, n (%)	2 (8)
Duration of hospitalization, days, mean (SD)	17.1 (13.7)

SD, Standard deviation; IQR, interquartile range
Mean values (SD) were used for parametric (normally distributed) data, and median values (IQR) for non-parametric (non-normally distributed) data.

restless legs syndrome / Willis-Ekbom disease (RLS/WED) in 3 patients (12%), periodic limb movement disease (PLMD) in 2 patients (8%), and central sleep apnea syndrome associated with Cheyne-Stokes respiration in 1 patient (4%). According to clinical and PSG data, while 10 patients (40%) had a history of cardiorespiratory and/or endocrine-metabolic diseases, 2 patients (8%) had a generalized anxiety disorder, and 1 patient (4%) had epilepsy (Table 2).

Patients who applied with the complaint of insomnia after COVID-19 infection were divided into those with and without accompanying sleep-related disorders. Demographic and clinical data of these two groups were compared. Further statistical tests revealed that chronic cardiorespiratory/endocrine-metabolic/cerebral disease history was significantly higher in the group with a history of the concomitant sleep-related disease (p=0.001). The history of hospitalization was also higher in this group, although not statistically significant (p=0.088). Two patients with a history of hospitalization in the intensive care unit were also in this group. Other demographic and clinical data between the two groups were similar and detailed in Table 3.

When sleep-related data were evaluated, it was noted that the median value of subjective sleep latency (sSL) was 60 minutes and increased, while the mean value of subjective total sleep time (sTST) was 312 minutes and decreased. The mean PSQI value was found to be high with 11.6±3.2 and indicated poor sleep quality and also, the median value of the BAI score was high with 13 (IQR:6-26.5). The mean ESS score was 4.6±3.7 and was low, indicating decreased daytime sleepiness, consistent with insomnia complaints (Table 4).

According to BAI scores, 5 patients had mild anxiety, 5 patients had moderate anxiety, and 6 patients had high anxiety (10.8±3.1, 19.8±2.7, and 35.8±3.7, respectively). The mean PSQI score of each group was found to be high (11±2.5, 11.4±5.1 and 12.5±5.6, respectively), but no significant difference was found between the groups in terms of PSQI score (p=0.803). Similarly, no correlation was found between BAI and PSQI scores in all patients with insomnia and with or without anxiety (p=0.336).

Patients with insomnia complaints were divided into two groups: those with a history of hospitalization (n: 9, 36%) and those without (n: 16, 64%). Both groups had a high BAI score (18.2±12.2 and 9 [IQR:5.2-27.7], respectively, p=0.452) and PSQI score (12 [IQR:9.5-16] and 11.1±2.9, respectively, p=0.357).

However, no statistically significant difference was found between the two groups.

Patients with insomnia were also divided into two groups: those with comorbid sleep-related respiratory disorders (n:14, 56%) and those without (n:11, 44%). When all sleep-related data were compared, it was observed that both groups had low sTST,

Table 2. Distribution of comorbidities in patients presenting with complaints of insomnia

All patients diagnosed with insomnia (n:25)	
Presence of sleep-related illness, n (%)*	16 (64)
Mild OSAS (AHI:5-14), n (%)	1 (4)
Moderate-severe OSAS (AHI≥15), n (%)	12 (48)
CSAS associated with Cheyne-Stokes respiration, n (%)	1 (4)
RLS/WED, n (%)	3 (12)
PLMD, n (%)	2 (8)
Presence of chronic cardiorespiratory/endocrine disease, n (%)	10 (40)
Presence of chronic cerebral disease, n(%)	1 (4)
Presence of psychiatric disorder, n (%)	2 (8)

OSAS, obstructive sleep apnea syndrome; AHI, apnea hypopnea index; CSAS, central sleep apnea syndrome; RLS/WED, Restless legs syndrome / Willis-Ekbom disease; PLMD, periodic limb movement disorder
**Subgroup analysis indicates the presence of more than one accompanying sleep-related disease in a patient.*

Table 3. Comparison of demographic characteristics of all patients with and without accompanying sleep disorder diagnosed with insomnia

Groups, n (%)	Patients without concomitant sleep disorder 9 (36)	Patients with concomitant sleep disorders 16 (64)	p
Demographic characteristics			
Gender, female/male, n (%)*	5/4 (55/45)	11/5 (68/32)	0.671
Age, years, mean (SD)**	43 (11.9)	50.8 (14.6)	0.187
Insomnia duration, months, mean (SD)**	2 (0.9)	2.4 (1.4)	0.513
Body mass index, kg/m2, mean (SD)**	25.9 (3.9)	28.5 (6.4)	0.290
Presence of chronic cerebral/endocrine/cardiorespiratory disease, n (%)*	0 (0)	11 (68)	0.001
Presence of psychiatric disorder, n (%)*	0 (0)	2 (12.5)	0.520
Number of patients with a history of hospitalization, n (%)*	1 (11)	8 (50)	0.088
Number of patients treated in the Intensive Care Unit, n (%)*	0 (0)	2 (12.5)	0.520

SD, Standard deviation; *Fisher's Exact test was used.**Student T test was used. Mean values (SD) were used for parametric (normally distributed) data.

Table 4. Analysis of sleep-related data of all patients presenting with complaints of insomnia

Sleep-related data	
sSL, minutes, median (IQR)	60 (60-165)
sTST, minutes, mean (SD)	312 (109.2)
Pittsburgh sleep quality index score, mean (SD)	11.6 (3.2)
Epworth sleepiness scale score, mean (SD)	4.6 (3.7)
Beck anxiety inventory score, median (IQR)	13 (6-26.5)

SD, Standard deviation; IQR, interquartile range; sSL, subjective sleep latency; sTST, subjective total sleep time, Mean values (SD) were used for parametric (normally distributed) data, and median values (IQR) for non-parametric (non-normally distributed) data.

Table 5. Comparison of sleep-related data in patients with and without sleep-related respiratory disorder who presented with complaints of insomnia

	Patients without sleep-related breathing disorders (n=11)	Patients with sleep-related breathing disorders (n=14)	p
sSL, minutes, median (IQR)*	60 (60-180)	75 (60-157.5)	0.851
sTST, minutes, mean (SD)**	316.3 (146.5)	308.5 (73.8)	0.874
Pittsburgh sleep quality index score, mean (SD)**	11.1 (3.6)	12 (2.9)	0.540
Epworth sleepiness scale score, mean (SD)**	4.4 (3.2)	4.7 (4.1)	0.831
Beck anxiety inventory score, median (IQR)/mean (SD)*	8 (6-36)	15.2 (11.5)	0.687

SD, Standard deviation; IQR, interquartile range; sSL, subjective sleep latency; sTST, subjective total sleep time;
** Mann-Whitney U test was used. **T-test was used. Mean values (SD) were used for parametric (normally distributed) data, and median values (IQR) for non-parametric (non-normally distributed) data.*

high sSL, PSQI and BAI scores, but no statistically significant difference was found between the two groups (Table 5).

Discussion

Insomnia is a condition characterized by complaints about sleep, which can occur alone or as a result of many diseases such as anxiety, depression, chronic pain, and sleep apnea [16]. Insomnia is diagnosed by the presence of symptoms associated with sleep causing deterioration in at least one of the patient's cognitive, mental, behavioral, social, occupational, and familial functions such as difficulty initiating sleep, inability to continue sleep, waking up early in the morning, resistance to going to bed at the appropriate sleep time [17]. For the diagnosis of acute insomnia, these sleep-related complaints that occur at least 3 times a week should continue less than 3 months, and for the diagnosis of chronic insomnia, these complaints should continue longer than 3 months. The prevalence of insomnia varies between 3.9% and 22% worldwide [2].
It has been shown in studies that mental disorders and sleep-related disorders, especially insomnia, occur during and after COVID-19 infection in people who are infected with COVID-19. In these studies, it has been reported that the prevalence of depression is three times higher (15.97% vs 4.4%), anxiety disorder is four times higher (3.6% vs 15.15%), and PTSD is five times higher (21.94% vs 4%) in people infected with COVID-19 compared to the general population [18–20]. Community-based studies have shown that the prevalence of insomnia during the COVID-19 pandemic is close to or higher than the upper limit of the worldwide prevalence of insomnia. It varied between 19.1% and 37% [3–5]. In our study, the reason for admission in all patients who applied to our Sleep Disorders Unit after COVID-19 infection in the last 3 months was complaints of insomnia and these results were consistent with the literature. In our study, the mean duration of insomnia complaints was determined as 2 months. Consistent with general population, in this study it was observed that the patients who applied with insomnia complaints were predominantly female and were in the middle-advanced age group [21]. After detailed questioning of these patients who applied with insomnia complaints, PSG examination was performed on 16 patients. According to clinical, PSG and laboratory data, two-thirds (64%) of the patients had another sleep-related disorder accompanying the complaints of insomnia, and the most common sleep-related disorder was found to be obstructive sleep apnea syndrome (OSAS)

with 52%. The prevalence of OSAS is around 10-15% in the general population in this age group, and complaints of insomnia in OSAS cases can reach up to 50% [22,23]. According to our results, it was seen that the frequency of OSAS in the COVID-19 population is higher than the prevalence of OSAS in the general population, and one of the most important symptoms in these patients may be insomnia rather than daytime sleepiness. In our study, the patients were divided into two groups as those with or without a concomitant sleep-related disorder; it was observed that the rate of chronic cardiorespiratory, cerebral and endocrine-metabolic diseases was significantly higher in the group with a concomitant sleep-related disorder. Also, it was observed that the history of hospitalization was higher in this group, although not statistically significant. This has demonstrated that the patients applying with complaints of insomnia after COVID-19 infection should be evaluated in detail in terms of other underlying sleep-related disorders, especially OSAS, if they have a history of chronic cardiorespiratory, cerebral, endocrine-metabolic disease and/or hospitalization. In this group, effective treatment of comorbid sleep-related respiratory disorders suggested that it could both improve insomnia complaints and reduce the number and duration of hospitalizations during COVID-19 infection by controlling the systemic effects of other comorbid chronic diseases.

Objective sleep tests such as polysomnography and actigraphy in diagnosing insomnia have less sensitivity and specificity than the self-reports used to define insomnia [24]. Based on the self-reports of the person, the diagnosis of insomnia can be mentioned if the sleep latency and duration of wakefulness after sleep onset are over 30 minutes [25]. However, the PSQI is a test used effectively to evaluate sleep quality and complaints of insomnia. Consistent with the literature, in our study, the median value of sSL is high and 60 minutes and also the mean sTST has reduced and is 312 minutes in patients who applied insomnia complaints after COVID-19 infection. In this study, the mean PSQI test score has been determined as 11.6 in these patients, indicating poor sleep quality. In previous study have reported that 40% of insomnia patients fulfill the criteria of any psychiatric disorders; this rate is 23% for major depression and 24% for anxiety disorders [26]. And also insomnia has determined in 90% of the patients with major depression [27]. Studies have shown that the prevalence of anxiety disorder in people with COVID-19 infection is four times higher than the general population (3.6% vs 15.15%) [18]. Consistent with this, in our study, the median value of the BAI score used in evaluating anxiety disorder as a cause of insomnia was found to be 13 and increased. However, no correlation was found between the severity of anxiety disorder and sleep quality. In addition, in our study, although high anxiety levels and poor sleep quality were detected in those with a history of hospitalization as a cause of anxiety and those with respiratory disorder associated with sleep, no significant difference was found compared to those who did not. In a study, PSQI scores of healthcare workers employed in COVID-19 services show correlation with BAI scores positively [28]. In contrast, according to our results, the association between PSQI and BAI scores suggests that the effect of level of anxiety disorders on deterioration of sleep quality is subjective and this suggests that treating mild anxiety disorder after COVID-19 infection could effectively ameliorate severe insomnia complaints.

The limited number of patients and the fact that PSG was not performed on all patients can be counted among the limitations of the study. Our study is single-center, and we consider that it would be beneficial to expand our study with a multicenter study, including more patients. In addition, PSG was not routinely applied to patients with only insomnia complaints, except for the patients in whom considered a diagnosis of paradoxical insomnia as well as the patients with symptoms accompanying insomnia complaints and suggesting the presence of an-

other sleep-related disease. Therefore, we consider that a prospective study in which PSG will be performed as a routine will provide more objective data about complaints associated with sleep of the patients. Thus, we believe that a multicenter and prospective study will support our study. In this study, the demographic and clinical characteristics of all patients with complaints of insomnia were compared to the literature. And also, patients with complaints of insomnia and concomitant sleep-related disorders generated the control group of study and, therefore, in the second stage of the study, the demographic and clinical characteristics of all patients with insomnia complaints were evaluated according to the presence of accompanying sleep-related disorders.

Conclusion

In summary, the study showed that the most common sleep-related symptom after COVID-19 infection was insomnia. If these patients presenting with complaints of insomnia have a history of chronic cardiorespiratory, cerebral, endocrine-metabolic disease and/or hospitalization, should investigate in terms of another sleep-related disease, especially OSAS. The effective treatment of these comorbid sleep-related diseases provides improving complaints of insomnia and also can play an effective role in reducing the number and duration of hospitalizations due to COVID-19 infection via controlling the systemic effects of other chronic diseases. In addition, it has been shown that anxiety disorder occurring after COVID-19 infection causes different levels of insomnia and thus poor sleep quality in patients. Therefore, we also suggest that treating mild anxiety disorder after COVID-19 infection may effectively cure severe insomnia complaints.

Author contributions
Concepts: 1,2
Design:1,2
Literature search:1
Clinical studies:1
Data acquisition:1,2
Data analysis:1
Statistical analysis:1
Manuscript preparation:1
Manuscript editing:1
Manuscript review:1,2

Conflict of interest
The authors declare that they have no conflict of interest.

Funding
This research did not receive any funding from the public, commercial, or not-for-profit agencies.

Ethical approval
Eskişehir Osmangazi University, Faculty of Medicine, Clinical Research Ethics Committee (Date: 26.10.2021, No: 05), the study was organized according to the Principles of the Declaration of Helsinki.

References

1. Rogers JP, Chesney E, Oliver D, et al. Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: a systematic review and meta-analysis with comparison to the COVID-19 pandemic. The lancet Psychiatry. 2020;7(7):611-27. https://doi.org/10.1016/S2215-0366(20)30203-0
2. Kay-Stacey M, Attarian H. Advances in the management of chronic insomnia. BMJ. 2016;354. https://doi.org/10.1136/bmj.i2123
3. Kokou-Kpolou CK, Megalakaki O, Laimou D, et al. Insomnia during COVID-19 pandemic and lockdown: Prevalence, severity, and associated risk factors in French population. Psychiatry Res. 2020;290. https://doi.org/10.1016/j.psychres.2020.113128
4. Morin CM, Carrier J. The acute effects of the COVID-19 pandemic on insomnia and psychological symptoms. Sleep Med. 2021;77:346-7. https://doi.org/10.1016/j.sleep.2020.06.005
5. Voitsidis P, Gliatas I, Bairachtari V, et al. Insomnia during the COVID-19 pandemic in a Greek population. Psychiatry Res. 2020;289:113076. https://doi.org/10.1016/j.psychres.2020.113076
6. Cukrowicz K, Otamendi A, Pinto J, et al. The impact of insomnia and sleep disturbances on depression and suicidality. Dreaming. 2006; 16(1):1. https://doi.org/10.1037/1053-0797.16.1.1
7. Mazza MG, De Lorenzo R, Conte C, et al. Anxiety and depression in COVID-19 survivors: Role of inflammatory and clinical predictors. Brain Behav Immun. 2020;89:594-600. https://doi.org/10.1016/j.bbi.2020.07.037

8. Griffin SC, Williams AB, Mladen SN, et al. Reciprocal Effects Between Loneliness and Sleep Disturbance in Older Americans. J Aging Health. 2020;32(9):1156-64. https://doi.org/10.1177/0898264319894486
9. Fang H, Tu S, Sheng J, et al. Depression in sleep disturbance: A review on a bidirectional relationship, mechanisms and treatment. J Cell Mol Med. 2019;23(4):2324-32. https://doi.org/10.1177/0898264319894486
10. Ibarra-Coronado EG, Pantaleón-Martínez AM, Velazquéz-Moctezuma J, et al. The Bidirectional Relationship between Sleep and Immunity against Infections. J Immunol Res. 2015;2015. https://doi.org/10.1155/2015/678164
11. Irwin MR, Opp MR. Sleep Health: Reciprocal Regulation of Sleep and Innate Immunity. Neuropsychopharmacology. 2017;42(1):129-55. https://doi.org/10.1038/npp.2016.148
12. Buysse DJ, Reynolds CF, Monk TH, et al. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res. 1989;28(2):193-213. https://doi.org/10.1016/0165-1781(89)90047-4
13. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep. 1991;14(6):540-5. https://doi.org/10.1093/sleep/14.6.540
14. Beck AT, Epstein N, Brown G, et al. An inventory for measuring clinical anxiety: psychometric properties. J Consult Clin Psychol. 1988;56(6):893-7. https://doi.org/10.1037//0022-006X.56.6.893
15. Academy of Sleep Medicine A. The AASM Manual for the Scoring of Sleep and Associated Events Summary of Updates in Version 2.6. Published online 2020.
16. Perez MN, Salas RME. Insomnia. Continuum (Minneap Minn). 2020;26(4):1003-15. https://doi.org/10.1212/CON.0000000000000879
17. Sateia MJ. International classification of sleep disorders-third edition: highlights and modifications. Chest. 2014;146(5):1387-94. https://doi.org/10.1378/chest.14-0970
18. Kessler RC, Aguilar-Gaxiola S, Alonso J, et al. Trauma and PTSD in the WHO World Mental Health Surveys. Eur J Psychotraumatol. 2017;8(5). https://doi.org/10.1080/20008198.2017.1353383
19. Liu H, Petukhova M V., Sampson NA, et al. Association of DSM-IV Posttraumatic Stress Disorder with Traumatic Experience Type and History in the World Health Organization World Mental Health Surveys. JAMA psychiatry. 2017;74(3):270-81. https://doi.org/10.1001/jamapsychiatry.2016.3783
20. Organization WH. Depression and other common mental disorders: global health estimates. Published online 2017. Accessed December 13, 2021. https://apps.who.int/iris/bitstream/handle/10665/254610/W?sequence=1
21. Ohayon MM, Sagales T. Prevalence of insomnia and sleep characteristics in the general population of Spain. Sleep Med. 2010;11(10):1010-18. https://doi.org/10.1016/j.sleep.2010.02.018
22. Punjabi NM. The epidemiology of adult obstructive sleep apnea. Proc Am Thorac Soc. 2008;5(2):136-43. https://doi.org/10.1513/pats.200709-155MG
23. Buysse DJ. Insomnia. JAMA. 2013;309(7):706-16. https://doi.org/10.1001/jama.2013.193
24. Rosa RR, Bonnet MH. Reported chronic insomnia is independent of poor sleep as measured by electroencephalography. Psychosom Med. 2000;62(4):474-82. https://doi.org/10.1097/00006842-200007000-00004
25. Lichstein KL, Durrence HH, Taylor DJ, et al. Quantitative criteria for insomnia. Behav Res Ther. 2003;41(4):427-45. https://doi.org/10.1016/S0005-7967(02)00023-2
26. Ford DE, Kamerow DB. Epidemiologic study of sleep disturbances and psychiatric disorders. An opportunity for prevention? JAMA. 1989;262(11):1479-84. https://doi.org/10.1001/jama.262.11.1479
27. Seow LSE, Subramaniam M, Abdin E, et al. Sleep disturbance among people with major depressive disorders (MDD) in Singapore. J Ment Health. 2016;25(6):492-9. https://doi.org/10.3109/09638237.2015.1124390
28. Korkmaz S, Kazgan A, Çekiç S, et al. The anxiety levels, quality of sleep and life and problem-solving skills in healthcare workers employed in COVID-19 services. J Clin Neurosci. 2020;80:131-6. https://doi.org/10.1016/j.jocn.2020.07.073