ORIGINAL ARTICLE

Relationship between Insomnia and Blood Oxygen Levels in COVID-19 Patients Admitted to the Intensive Care Unit

Khadijeh Alizadeh Feremi[1], Nouraddin Mousavinasab[2], Zahra Gholipour[3]

Received on: 07 September 2022; *Accepted on:* 11 October 2022; *Published on:* 19 October 2022

Abstract

Introduction: It seems that inadequate sleep affects the oxygen levels in patients infected with coronavirus disease-2019 (COVID-19). However, few studies have worked on the effect of insomnia on the blood oxygen level. Therefore, this study aimed to determine the effect of insomnia on the blood oxygen level in patients admitted to the intensive care unit (ICU) due to infection with COVID-19.

Materials and methods: This study was performed on 100 patients with COVID-19 referred to Imam Khomeini Hospital, affiliated with Mazandaran University of Medical Sciences, Sari, Iran. The insomnia severity index (ISI) was used to assess the severity of insomnia in the patients. They were then divided into four groups of patients with no insomnia, subthreshold, moderate, and severe insomnia. The patient's oxygen saturation was measured repeatedly at different times of day after hospitalization.

Results: The findings demonstrated no significant differences between the four study groups regarding gender, marital status, education level, and occupational status (p >0.05). Moreover, no significant difference was observed between the four groups concerning lung involvement (F = 0.64; p = 0.58) and hospital stay (F = 1.23; p = 0.29). The mean of oxygen saturation in patients without insomnia was higher than in those who had insomnia before the study and on days 1–5 after hospitalization (F = 30.97; p <0.001).

Conclusion: The results confirm the association between oxygen saturation and sleep disorder. The oxygen saturation level decreases in patients with different levels of insomnia (i.e., severe, moderate, and threshold insomnia) and patients affected by COVID-19 with acute pulmonary involvement. These patients are more susceptible to being hospitalized in specialized departments and mortality.

Keywords: COVID-19, Insomnia, Intensive care unit, Oximetry.

Indian Journal of Sleep Medicine (2022): 10.5005/jp-journals-10069-0103

Introduction

The outbreak of COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), occurred as an epidemic in 2019 in Wuhan, China.[1] Coronavirus has led to social dysfunction, mass hysteria, and constant anxiety due to the high infection and mortality rates.[2]

Progressive pneumonia, acute lung injury, and acute respiratory distress syndrome (ARDS) are the main complications of the disease.[3,4] Furthermore, studies have reported moderate-to-severe depression, anxiety, and insomnia in patients suffering from COVID-19.[5,6] Stress, anxiety, and depression due to COVID-19 reduce serotonin levels, leading to sleep disorders. Sleep disorder lowers energy and results in shortness of breath and a decline in blood oxygen level. Abrupt disruption in regular sleep patterns (circadian rhythms) has been reported in the general population during the COVID-19 pandemic.[7] In addition, sleep disorders are among health problems that can aggravate systemic and pulmonary inflammation during viral infections.[8,9]

There is a dearth of evidence on sleep-related disorders caused by COVID-19, and insomnia is one of the most critical complications in these patients. Some studies have focused on the prevalence of insomnia among hospital care staff, nurses, and physicians, while they have paid less attention to insomnia risk factors.[10,11]

Based on the evidence, lack of energy caused by insomnia decreases the patients' ability to breathe. Moreover, the reduced COVID-19 patient's ability to breathe due to pulmonary involvement can decline blood oxygen level and result in a respiratory crisis.[12] Based on the evidence, more than 75% of patients with COVID-19 hospitalized in the ICU need supplemental oxygen, and about 17–35% of them require high-pressure oxygen.[13]

Regarding the effect of adequate sleep on the immune system and energy supply, the amount of sleep can also affect the person's oxygen level. However, based on the literature review, no study has yet investigated the effect of insomnia on blood oxygen levels.

[1,3]School of Nursing and Midwifery, Mazandaran University of Medical Sciences, Sari, Iran

[2]Department of Biostatistics, School of Health Sciences, Mazandaran University of Medical Sciences, Sari, Iran

Corresponding Author: Khadijeh Alizadeh Feremi, School of Nursing and Midwifery, Mazandaran University of Medical Sciences, Sari, Iran, Phone: +98 9113141948, e-mail: rahaalizade18@outlook.com

How to cite this article: Feremi KA, Mousavinasab N, Gholipour Z. Relationship between Insomnia and Blood Oxygen Levels in COVID-19 Patients Admitted to the Intensive Care Unit. Indian J Sleep Med 2022; 17(3):72–76.

Source of support: Nil

Conflict of interest: None

Ethical approval: This study was approved by the Ethics Committee of Mazandaran University of Medical Sciences under the code of IR.MAZUMS.REC.1400.9124. All the procedures performed in the study were in accordance with the ethical standards of the Ethics Committee of Mazandaran University of Medical Sciences.

Informed consent: Informed consent was obtained from all the participants included in the study

Therefore, the present study aimed to determine the effect of insomnia on the blood oxygen level in patients hospitalized in the ICU due to COVID-19 infection.

Materials and Methods

The present study was performed on 100 patients with insomnia infected with COVID-19. They were admitted to the ICU of Imam Khomeini Teaching Hospital, affiliated with Mazandaran University of Medical Sciences, Sari, Iran.

Inclusion and Exclusion Criteria

The inclusion criteria included the age range of 18–70 years, positive polymerase chain reaction (PCR) for COVID-19, oxygen saturation level ≤92%, pulmonary involvement less than 50%, and a minimum hospital stay of 5 days. However, the patients with mental disorders, ventilator-dependent patients, obese and pregnant subjects, and those using other medications were excluded from the study.

Study Design

The sample size for this study was calculated to be 25 patients in each group, considering the power of 80%, $\alpha = 0.5$, $r = 0.2$, and the effect size of 0.5. The sample size was measured based on a comparison of means. Therefore, the sample size of each study group was increased to 27 cases, considering the attrition rate.

Data Collection

The data collected from patient's medical records were recorded in a sociodemographic form. The samples were selected from the patients with insomnia who were admitted to the ICU due to COVID-19 infection.

Instruments

At the admission of patients in the ICU, their insomnia severity was assessed using the ISI. The collected questionnaires were then scored on a 5-point Likert scale, with higher scores representing more severe sleep problems (0 = no sleep problem, 4 = very severe sleep problem). The total scores of the questionnaires range from 0 to 28. The scores between 0 and 7, 8 and 14, 15 and 21, and 22 and 28 are regarded as no clinically significant insomnia, subthreshold insomnia, clinical insomnia (moderate severity), and clinical insomnia (severe), respectively. A previous study has confirmed the reliability and validity of the scale.[14] The severity of patients' insomnia was calculated after completing questionnaires, and they were divided into four groups (27 in each) of no insomnia, subthreshold, moderate, and severe insomnia.

The oximetry technique was used to assess the oxygen saturation of ICU admitted COVID-19 patients. It is a technique for continuous evaluation of oxygen saturation that measures light transmission through the blood based on different absorption spectra of oxygenated or deoxygenated hemoglobin.[15] A 95% or more saturation rate is normal, and a 92% or less indicates low oxygen levels.[16] The oxygen saturation of patients admitted to ICU was repeatedly measured over 5 days of hospitalization. The data collected from the four study groups were compared afterward.

Statistical Analysis

This study presented quantitative data with the means and standard deviation (SD), and categorical data were presented with frequencies and percentages. In addition, the analysis of variance (ANOVA) was employed to compare the mean blood oxygen levels, the patients' insomnia, and oxygen levels over 5 days of hospitalization in the four study groups. In all measurements, a *p*-value <0.05 was considered statistically significant.

Ethical Considerations

The Research Ethics Committee of Mazandaran University of Medical Sciences approved the study protocol (Code: IR.MAZUMS.REC.1400.9124). The study objectives were explained to the patients, and they were ensured about the confidentiality of their personal information. Before the study, informed written consent was obtained from patients and their families.

Results

The participants in the study included 108 patients with insomnia admitted to ICU due to COVID-19 infection. The mean age of participants was 53.73 ± 1131 ranging from 26 to 70. Moreover, the mean age of patients with no insomnia, subthreshold, moderate, and severe insomnia were 45.15 ± 11.69, 55.67 ± 9.81, 54.15 ± 11.64, and 55.96 ± 11.29 years, respectively. There were no significant differences among the four study groups regarding the mean age

Table 1: Comparison of demographic characteristics among four study groups

	No insomnia		*Subthreshold insomnia*		*Moderate insomnia*		*Severe insomnia*		*Total*			
Variable	*No*	*%*	*No*	*%*	*No*	*%*	*No*	*%*	*No*	*%*	χ^2	*p-value*
Gender												
Male	9	33.3	12	44.4	13	48.1	9	33.3	43	39.8	1.97	0.57
Female	18	66.7	15	55.6	14	51.9	18	66.7	65	60.2		
Marriage status												
Single	2	7.4	0	0	2	7.4	0	0	4	3.7	4.15	0.24
Married	25	92.6	27	100	25	92.6	27	100	104	96.3		
Education level												
Under diploma	16	59.3	19	70.4	21	77.8	23	85.2	79	73.1	5.04	0.16
Diploma and higher	11	40.7	8	29.6	6	22.2	4	14.8	29	26.9		
Occupational status												
Self-employed	9	33.3	8	29.6	10	37	4	14.8	31	28.7	4.8	0.56
Housewife	14	51.9	12	44.4	12	44.4	17	63	55	50.9		
Worker and employee	4	14.8	7	25.9	5	18.5	6	22.2	22	20.4		

Table 2: Comparison of percentage of lung involvement and mean of hospital stay among four study groups

	No insomnia		*Subthreshold insomnia*		*Moderate insomnia*		*Severe insomnia*		*Total*			
Variable	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*F*	*p-value*
Lung involvement	46.48	6.76	46.85	6.95	47.96	6.83	48.70	5.81	47.5	6.57	0.64	0.58
Length of hospital stay	8.52	2.59	10.04	8.32	9.52	2.39	10.96	3.006	9.76	4.77	1.23	0.29

Table 3: Mean of oxygen saturation among four groups at various times

	No insomnia		*Subthreshold insomnia*		*Moderate insomnia*		*Severe insomnia*		*Total*			
Time	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*F*	*p-value*
Day 0	90.37	1.52	89.56	2.66	88.41	3.15	86	3.32	88.58	3.18	12.82	<0.001
Day 1	91.48	1.77	91	2.66	90.308	3.02	87.13	2.61	89.98	3.04	15.74	<0.001
Day 2	93.08	1.93	91.85	2.09	89.93	3.7	87.82	3.309	90.67	3.45	17.405	<0.001
Day 3	93.32	1.95	91.407	3.04	89.69	3.94	87.81	3.03	87.81	3.03	15.82	<0.001
Day 4	93.33	2.43	91.33	2.97	89.96	3.14	87.93	3.29	90.64	3.54	15.7	<0.001
Day 5	93.28	3.03	91.71	2.88	90.12	2.37	87.76	2.77	90.72	3.42	19.42	<0.001

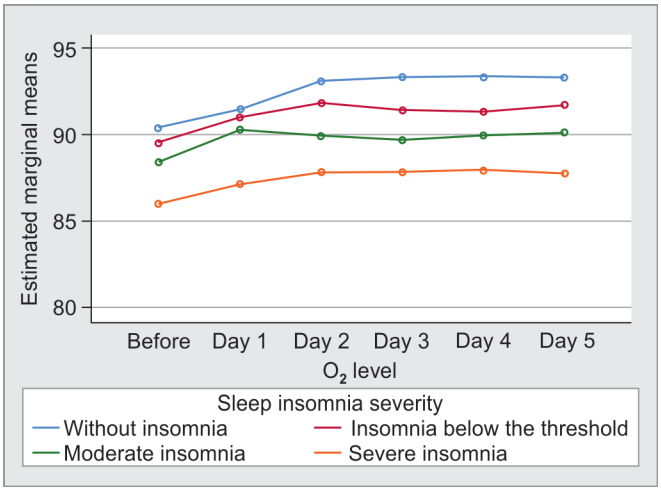

Fig. 1: Oxygen saturation change among the four groups before hospitalization and on days 1–5 after hospitalization

($Z = 2.17, p = 0.09$). Table 1 presents the demographic characteristics of each group. The results demonstrated no significant differences among the four study groups concerning gender, marital status, education level, and occupational status ($p > 0.05$).

On the other hand, Table 2 compares four study groups regarding lung involvement percentage and hospital stay. The results indicate no significant differences among the four study groups concerning the lung involvement mean ($Z = 0.64, p = 0.58$) and the length of hospital stay ($Z = 1.23, p = 0.29$). Moreover, none of the patients presents obesity, drug abuse, and mental disorder.

Table 3 compares the four study groups' mean oxygen saturation on various occasions. Based on the obtained results, the mean oxygen saturation is significantly different among the four study groups ($p < 0.005$). Mauchly's test validated the ANOVA assumptions ($p < 0.005$). Figure 1 presents the oxygen saturation changes in the four study groups over 5 days of hospitalization. Repeated measure ANOVA demonstrates statistically significant differences in the oxygen levels of the patients on different days ($F = 15.73$; $p < 0.001$) and among the study groups ($F = 30.97$; $p < 0.001$).

Table 4 presents the mean oxygen saturation in the four groups before the intervention and on days 1–5 after hospitalization. Mauchly's test was used to validate a repeated-measures ANOVA ($p < 0.005$). Based on the obtained results, the mean oxygen saturation is higher in patients without insomnia than in those with insomnia during the morning, evening, and night of different days after hospitalization ($F = 28.04$; $p < 0.005$). Figure 1 presents changes in the patient's oxygen saturation in the four study groups over 5 days of hospitalization. Figure 2 illustrates the changes in patient's oxygen saturation in the four study groups that were measured during the morning, evening, and night before hospitalization and on 5 days of hospitalization. In addition, repeated measure ANOVA reveals a statistically significant difference in patients' insomnia on different days ($F = 8.33$; $p < 0.001$) and among the study groups ($F = 28.05$; $p < 0.001$).

Discussion

The COVID-19 pandemic is a severe life-threatening health problem. Moreover, mental health is a healthcare priority for these patients. Recently, the sleep condition of patients infected with COVID-19 seems to be a source of concern because COVID-19 infection is associated with difficulty in breathing and the development of pneumonia.[8,9]

The study results indicate that the mean oxygen saturation is higher in patients without insomnia on various days after hospitalization during the morning, evening, and night.

Sleep disorder has been a common problem during the COVID-19 pandemic. It may aggravate the systemic and lung inflammation by affecting some neurotransmitters, such as serotonin (the primary sleep regulator) that binds to GABA receptors and decreases in patients with insomnia.[17–19] It is believed that serotonin has immunomodulatory effects by activating central and peripheral mechanisms. It regulates sleep, body temperature, motor control, and systemic inflammation.[20] The immune cells are activated in patients infected with SARS-CoV-2; therefore, massive production and release of inflammatory mediators may disrupt the functioning of other organs, such as brain that controls serotonin release.[21]

Based on the evidence, the respiratory system and breathing pattern can directly affect insomnia. Pneumonia is one of the complications of insomnia that causes a decrease in blood oxygen level.[6] On the other hand, reducing blood oxygen levels in COVID-19

Table 4: Mean of oxygen saturation during various times on days 1–5 of hospitalization among four study groups

		No insomnia		*Subthreshold insomnia*		*Moderate insomnia*		*Severe insomnia*		*Total*	
Time	*Oxygen saturation*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*
Day 1	Morning	90.41	1.575	90.07	2.495	88.63	3.543	85.85	3.195	88.74	3.302
	Evening	91.96	1.931	91.15	2.811	91.07	3.999	87.89	3.446	90.52	3.471
	Night	92.07	2.881	91.78	3.693	91.22	3.262	87.67	4.048	90.69	3.881
Day 2	Morning	92.26	3.133	91.81	2.746	89.74	4.443	87.44	3.906	90.31	4.050
	Evening	93.30	2.127	91.96	2.157	90.67	3.627	88.44	3.446	91.09	3.397
	Night	93.70	2.035	91.78	2.501	89.41	4.956	87.59	4.002	90.62	4.220
Day 3	Morning	93.52	2.408	91.19	2.883	89.93	4.242	88.30	3.593	90.73	3.822
	Evening	92.93	2.218	91.89	3.166	89.52	4.552	87.44	4.060	90.44	4.152
	Night	93.52	2.225	91.15	3.850	89.63	4.226	87.70	3.429	90.50	4.071
Day 4	Morning	93.26	2.669	91.00	3.711	89.81	4.306	87.41	4.126	90.37	4.268
	Evening	93.33	2.646	91.44	3.262	90.22	3.490	87.89	3.651	90.72	3.798
	Night	93.41	2.678	91.56	3.297	89.85	2.713	88.52	3.435	90.83	3.527
Day 5	Morning	93.15	3.110	92.11	2.873	89.26	3.133	87.59	3.377	90.53	3.802
	Evening	93.33	3.113	91.59	3.092	90.30	2.367	88.00	3.162	90.81	3.506
	Night	93.37	3.586	91.44	3.401	90.81	2.450	87.70	2.743	90.83	3.662

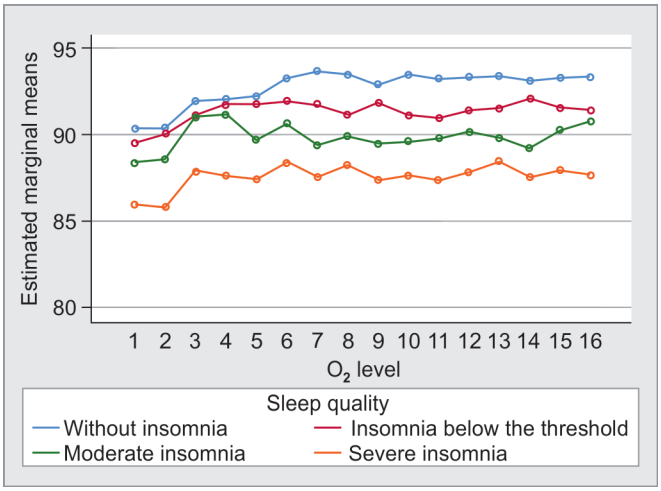

Fig. 2: Oxygen saturation change in the four groups during the morning, evening, and night on various days

patients with pulmonary involvement leads to a respiratory crisis.[22] Inadequate oxygen saturation can lead to a wide range of adverse conditions, such as chest pain, shortness of breath, increased heart rate, and the need to receive oxygen. Therefore, many hospitalized patients with COVID-19 need supplemental or high-flow oxygen.[23] The number of patients requiring hospitalization in the specialized wards of the hospital or ICU increases after such complications.[24] Insomnia results in high anxiety and stress levels, increases the heartbeat and breath rate, and surges the metabolism. All these complications decrease the oxygen level in patients with different levels of insomnia. Therefore, COVID and its effects on the lungs increase pulmonary problems.[25]

Although there is no similar study to assess the oxygen saturation in patients with a sleep disorder, some studies have assessed sleep dysfunction in patients infected with COVID-19. For example, Thorpy et al. have considered sleep dysfunction (e.g., sleep apnea) in patients infected with COVID-19. The results indicate that obstructive sleep apnea is a significant risk factor for hospitalization in the ICU, cardiovascular complications (e.g., ischemia and cardiac arrhythmia), and pulmonary complications such as pneumonia.[12] Correspondingly, Salles et al. has confirmed the role of sleep deprivation on the severity of the pulmonary inflammatory process in COVID-19 patients.[26] Moreover, a study has shown that sleep deprivation leads to inflammatory cytokines, such as interleukin 6 and 17.[27]

Based on findings, positive airway pressure therapy can be helpful in patients in the early stages of COVID-19 before hospitalization. Moreover, the application of positive end-expiratory pressure can help hospitalized COVID-19 patients breathe easier during sleep.[12]

Some sleep evaluation activities were ceased during the COVID-19 outbreak leading to complications in managing patients with sleep disorders, such as obstructive sleep apnea. In some cases, the symptoms of obstructive sleep apnea (e.g., snoring) may recur due to failure to apply positive airway pressure at home.[28] However, positive airway pressure devices are still used in patients with COVID-19 without a standard ventilator to prevent the patient's condition from getting worse.[29,30]

Based on a study conducted by Yun Xia et al., the COVID-19 pandemic has caused fear, anxiety, depression, and insomnia in Parkinson's patients infected with COVID-19. Insomnia and sleep disorders lead to Parkinson's disease and aggravation of symptoms, such as tremors, muscular stiffness, bradykinesia, and pain which are essential in increasing the need for oxygen. Therefore, the severity of pain following insomnia can be a factor in the reduced level of oxygen blood in COVID-19 patients.[31]

In general, this study's results shed light on the impact of sleep disorders on the blood oxygen levels of patients with COVID-19 and indicate the necessity of further studies. Furthermore, future studies can answer some critical questions, such as this one: "Is the severity of insomnia an aggravating factor for reducing blood oxygen levels in COVID-19 patients?"

Conclusion

The present study confirms the association between oxygen saturation and sleep disorder in COVID-19 patients. In addition,

the mean oxygen saturation is higher in patients without insomnia than in those with insomnia.

Authors' Contributions

The idea for the article was raised by KAF. The scales and statistical analysis were completed by NM. Subjects' samples were collected and processed by ZG. The data were collected by KAF. The draft of the manuscript was written by KAF, revised the manuscript, and supervised the work.

Acknowledgment

The authors would like to express our gratitude to officials of Imam hospital in Amol, Mazandaran.

Orcid

Khadijeh Alizadeh Feremi https://orcid.org/0000-0002-5793-5750
Nouraddin Mousavinasab https://orcid.org/0000-0002-0631-4233
Zahra Gholipour https://orcid.org/0000-0003-0583-5974

References

1. Gozalbo-Rovira R, Gimenez E, Latorre V, et al. SARS-CoV-2 antibodies, serum inflammatory biomarkers and clinical severity of hospitalized COVID-19 patients. J Clin Virol 2020;131:104611. DOI: 10.1016/j.jcv.2020.104611.
2. Jain A, Singariya G, Kamal M, et al. COVID-19 pandemic: Psychological impact on anaesthesiologists. Indian J Anaesth 2020;64(9):774–783. DOI: 10.4103/ija.IJA_697_20.
3. George PM, Wells AU, Jenkins RG. Pulmonary fibrosis and COVID-19: The potential role for antifibrotic therapy. Lancet Respir Med 2020; 8(8):807–815. DOI: 10.1016/S2213-2600(20)30225-3.
4. Franceschini C, Musetti A, Zenesini C, et al. Poor sleep quality and its consequences on mental health during the COVID-19 lockdown in Italy. Front Psychol 2020;11:574475. DOI: 10.3389/fpsyg.2020.574475.
5. Zhuo K, Gao C, Wang X, et al. Stress and sleep: A survey based on wearable sleep trackers among medical and nursing staff in Wuhan during the COVID-19 pandemic. Gen Psychiatr 2020;33(3):e100260. DOI: 10.1136/gpsych-2020-100260.
6. De Mello MT, Silva A, Guerreiro R de C, et al. Sleep and COVID-19: Considerations about immunity, pathophysiology, and treatment. Sleep Sci 2020;13(3):199–209. DOI: 10.5935/1984-0063.20200062.
7. Brooks SK, Webster RK, Smith LE, et al. The psychological impact of quarantine and how to reduce it: Rapid review of the evidence. The Lancet 2020;395(10227):912–920. DOI: 10.1016/S0140-6736(20) 30460-8.
8. Sattar N, McInnes IB, McMurray JJ. Obesity is a risk factor for severe COVID-19 infection: multiple potential mechanisms. Circulation 2020;142(1):4–6. DOI: 10.1161/CIRCULATIONAHA.120.047659.
9. Lighter J, Phillips M, Hochman S. Obesity in patients younger than 60 years is a risk factor for Covid-19 hospital admission. Clin Infect Dis 2020;71(15):896–897. DOI:10.1093/cid/ciaa415.
10. Zhan Y, Liu Y, Liu H, et al. Factors associated with insomnia among Chinese front-line nurses fighting against COVID-19 in Wuhan: A cross-sectional survey. J Nurs Manag 2020;28(7):1525–1535. DOI: 10.1111/jonm.13094.
11. Vitale E, Mea R, Dio FD, et al. Anxiety, insomnia and body mass index scores in Italian nurses engaged in the care of COVID-19 patients. Endocr Metab Immune Disord Drug Targets 2020;21(9):1604–1612. DOI: 10.2174/1871530320666201016150033.
12. Thorpy M, Figuera-Losada M, Ahmed I, et al. Management of sleep apnea in New York City during the COVID-19 pandemic. Sleep Med 2020;74:86–90. DOI: 10.1016/j.sleep.2020.07.013.
13. Daher A, Balfanz P, Aetou M, et al. Clinical course of COVID-19 patients needing supplemental oxygen outside the intensive care unit. Sci Rep 2021;11(1):2256. DOI: 10.1038/s41598-021-81444-9.
14. Bastien CH, Vallières A, Morin CM. Validation of the Insomnia Severity Index as an outcome measure for insomnia research. Sleep Med 2001;2(4):297–307. DOI: 10.1016/s1389-9457(00)00065-4.
15. Nitzan M, Nitzan I, Arieli Y. The various oximetric techniques used for the evaluation of blood oxygenation. Sensors 2020;20(17):4844. DOI: 10.3390/s20174844
16. Andrés-Blanco AM, Álvarez D, Crespo A, et al. Assessment of automated analysis of portable oximetry as a screening test for moderate-to-severe sleep apnea in patients with chronic obstructive pulmonary disease. PLoS ONE 2017;12(11):e0188094. DOI: 10.1371/journal.pone.0188094.
17. Alizadeh K, Esmaeili R, Shorofi SS, et al. Effect of Urtica dioica (nettle) on quality of sleep in hemodialysis patients: A randomized clinical trial. J Herbal Med 2021;28:100356. DOI: 10.1016/j.hermed.2020.100356.
18. Bigalke JA, Greenlund IM, Carter JR. Sex differences in self-report anxiety and sleep quality during COVID-19 stay-at-home orders. Biol Sex Diff 2020;11(1):1–11.
19. Mello MTD, Silva A, Guerreiro RdeC, et al. Sleep and COVID-19: Considerations about immunity, pathophysiology, and treatment. Sleep Sci 2020;13(3):199–209. DOI: 10.5935/1984-0063.20200062.
20. Serrano MM, Pérez-Sánchez JR, Sánchez SP, et al. Serotonin syndrome in two COVID-19 patients treated with lopinavir/ritonavir. J Neurol Sci 2020;415:116944. DOI: 10.1016/j.jns.2020.116944.
21. Costa LHA, Santos BM, Branco LGS. Can selective serotonin reuptake inhibitors have a neuroprotective effect during COVID-19? Eur J Pharmacol 2020;889:173629. DOI: 10.1016/j.ejphar.2020.173629.
22. Marini JJ, Gattinoni L. Management of COVID-19 respiratory distress. JAMA 2020;323(22):2329–2330. DOI: 10.1001/jama.2020.6825.
23. Wang DH-M, Chen P-H, Yu TH-K, et al. The effects of corporate social responsibility on brand equity and firm performance. J Business Res 2015;68(11):2232–2236. DOI: 10.1016/j.jbusres.2015.06.003.
24. Iaccarino G, Grassi G, Borghi C, et al. Gender differences in predictors of intensive care units admission among COVID-19 patients: The results of the SARS-RAS study of the Italian Society of Hypertension. PLoS One 2020;15(10):e0237297. DOI: 10.1371/journal.pone.0237297.
25. Laharnar N, Grote L, Zou D, et al. Overnight pulse wave analysis to assess autonomic changes during sleep in insomnia patients and healthy sleepers. PLoS One 2020;15(5):e0232589. DOI: 10.1371/journal.pone.0232589.
26. Salles C, Barbosa HM. COVID-19 and obstructive sleep apnea. J Clin Sleep Med 2020;16(9):1647. DOI: 10.5664/jcsm.8606.
27. He S, Chen X-X, Ge W, et al. Are anti-inflammatory cytokines associated with cognitive impairment in patients with insomnia comorbid with depression? A pilot study. Nat Sci Sleep 2021;13:989–1000. DOI: 10.2147/NSS.S312272.
28. Dewan NA, Nieto FJ, Somers VK. Intermittent hypoxemia and OSA: Implications for comorbidities. Chest 2015;147(1):266–274. DOI: 10.1378/chest.14-0500.
29. Kryger M, Thomas R. Home PAP devices in patients infected with COVID-19. J Clin Sleep Med 2020;16(7):1217–1219. DOI: 10.5664/jcsm.8490.
30. Radovanovic D, Rizzi M, Pini S, et al. Helmet CPAP to treat acute hypoxemic respiratory failure in patients with COVID-19: A management strategy proposal. J Clin Med 2020;9(4):1191. DOI: 10.3390/jcm 9041191.
31. Xia Y, Kou L, Zhang G, et al. Investigation on sleep and mental health of patients with Parkinson's disease during the Coronavirus disease 2019 pandemic. Sleep Med 2020;75:428–433. DOI: 10.1016/j.sleep.2020.09.011.