RESEARCH ARTICLE

Assessment of sleep quality in severe COVID-19 hospitalised patients

Nida Zeb Abbasi[1], Kainaat Baig[2], Muhammad Hassan[3], Fibhaa Syed[4], Muhammad Anas Waheed Jami[5], Muhammad Usman[6]

Abstract

Objective: To evaluate the quality of sleep in patients hospitalised with coronavirus disease-2019, and its impact on hospitalisation duration, need for intensive care unit admission and mortality.

Methods: The cross-sectional study was conducted at the Pakistan Institute of Medical Sciences, Islamabad, Pakistan, from May 2, 2021 to April 30, 2022, and comprised hospitalised coronavirus disease-2019 patients. Data was gathered using the Pittsburgh Sleep Quality Index questionnaire, including demographics, comorbidities, length of hospital stay, need for intensive care unit admission, C-reactive protein and D-dimer values at admission, and the outcome. The patients were divided into group A having good sleep quality score >5 and group B having poor sleep quality score <5. Data was analysed using SPSS 25.

Results: Of the 1,250 patients, 559(44.7%) were males and 691(55.3%) were females. There were 560(44.8%) patients in group A with mean age 53.80±14.85 years, and 690(55.2%) patients in group B with mean age 53.71±14.32 years. There were no significant intergroup differences in terms of age and high-resolution computed tomography scan ($p>0.05$). The difference was significant with respect to gender, comorbid conditions, education status as well C-reactive protein and D-dimer levels ($p<0.001$). Group B patients had a longer duration of hospitalisation ($p<0.001$) and a higher need for intensive care unit admission ($p<0.001$) compared to group A. The outcome was death in 166(13.28%) patients in group B compared to 40(3.2%) in group A ($p<0.001$).

Conclusion: Poor sleep quality was found to be associated with longer hospital stay, increased need for mechanical ventilation, and higher mortality rate in coronavirus disease-2019 patients.

Keywords: Sleep condition, COVID-19, PSQI. (JPMA 74: 445; 2024) **DOI: https://doi.org/10.47391/JPMA.7704**

Introduction

Coronavirus disease-2019 (COVID-19) was declared a pandemic by the World Health Organization (WHO) on March 11, 2020. It was declared a health emergency all over the world, including Pakistan. In Pakistan from January 3, 2020, to June 7, 2022, there were 1,530,564 confirmed cases and 30,379 deaths that were reported to the WHO. As the number of COVID-19 cases increased dramatically, the healthcare system of Pakistan faced lots of challenges due to lack of medical facilities and awareness among population. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) severely affected health, ranging from asymptomatic infections to fatal respiratory distress. In addition to physical effects, SARS-COV-2 also has psychological effects. Previous studies showed the negative impact on mental health and sleep duration due to disturbance in their daily lifestyle routines and isolation from their family members.[1] The body's immune system is also affected by mental health and sleep status, as good mental health and sleep protect against viral infections.[2] The cells of the immune system and the neurons in the central nervous system (CNS) communicate in a two-way manner. The immune system can be of innate or adaptive type, both of which use cytokines as their way of communication for intercellular and intracellular responses. Interleukin-6 (IL-6) and tumour necrosis factor-alpha (TNF-α) are involved in sleep and innate immunity. IL-6 as a proinflammatory cytokine increases energy expenditure by increasing catabolic state, and TNF-α is involved in lipolysis, immunomodulation, apoptosis and pathological responses. The hormones, neurotransmitters, cytokines and chemokines between the nervous and immune systems are the same and can cross the blood-brain barrier in two directions. The cells of the immune system travel to the whole body and come in close contact with the nerve endings and brain.[3] As a result of infection or inflammatory diseases, cytokine levels are altered, activating the peripheral immune system and causing sleep disturbance with suppression of both rapid eye movement (REM) and NREM sleep.

The immune system and health are harmed by prolonged sleep loss. Studies showed rise in inflammatory markers

[1,2,5,6]Department of Internal Medicine, Pakistan Institute of Medical Sciences, Shaheed Zulfiqar Ali Bhutto Medical University, Islamabad, Pakistan; [3]Department of Neurology, Pakistan Institute of Medical Sciences, Shaheed Zulfiqar Ali Bhutto Medical University, Islamabad, Pakistan; [4]Department of General Medicine, Pakistan Institute of Medical Sciences, Shaheed Zulfiqar Ali Bhutto Medical University, Islamabad, Pakistan.

Correspondence: Nida Zeb Abbasi. e-mail: nidaabbasi02@hotmail.com
ORCID ID. 0000-0001-8265-5075

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secondary to prolonged sleep deprivation. Sleep loss for eight hours or limited sleep to 4 hours per night for 10 days raises the levels of inflammatory biomarkers, including C-reactive protein (CRP).[4] It has been shown that even mild restriction of sleep can increase levels of pro-inflammatory cytokines.

Various diseases, like type 2 diabetes mellitus (T2DM), cardiovascular disease (CVD), and obesity, are also linked with sleep deprivation, which is associated with systemic inflammation. Immunodeficiency also occurs in response to prolonged sleep loss. Research showed that immune response to influenza vaccination reduced following a sleep loss for six days.[5] Moreover, chronic sleep loss leads to increase susceptibility to common cold infections.

The current study was planned to assess the association of COVID-19 pneumonia on sleep quality in terms of duration of hospital stay, intensive care unit (ICU) admission and mortality.

Patients and Methods

The cross-sectional study was conducted at the Pakistan Institute of Medical Sciences (PIMS), Islamabad, Pakistan, from May 2, 2021 to April 30, 2022. After approval from the ethics review board of Shaheed Zulfiqar Ali Bhutto Medical University, Islamabad, the sample size was calculated using the WHO calculator[6] with confidence level 95%, absolute precision 2.56%, and 69.2% anticipated population proportion rate of sleep disturbance. The sample was raised using non-probability consecutive sampling technique from among patients admitted with severe COVID-19 pneumonia, as per the WHO classification.[7] Those included were patients regardless of age and gender who were well-oriented, capable of understanding the study questionnaire, and accessible during the study period. Those diagnosed with any psychiatric illness, patients who were previously on medication for sleep issues, and patients who were unwilling to participate in the study were excluded.

After taking informed consent from all the subjects, basic demographic information, including age, gender and education level, was collected, as well as other parameters, such as comorbid conditions, duration of hospital stay, high-resolution computed tomography (HRCT) findings, need for ICU admission, and outcome. During hospital admission, CRP and D-dimer levels were also recorded.

Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI) questionnaire,[8] consisting of 19 questions; 4 open-ended questions and 15 that were rated 0-3. The items were then further grouped into 7 components specifying sleep quality, latency, duration, habitual sleep efficiency, disturbance of sleep, use of sleep medication, and dysfunction during daytime. The total PSQI score was the sum of the 7 components, with score up to 5 indicating good quality of sleep and >5 or more indicating poor quality of sleep. All patients responded to the questionnaire before the final outcome. The patients were divided into group A having good sleep quality score >5 and group B having poor sleep quality score <5.

Data was analysed using SPSS 25. Continuous variables were expressed as mean±standard deviation, and categorical variables as frequencies and percentages. The association of sleep quality in patients with moderate to severe COVID-19 pneumonia with the duration of hospital stay, requirement of oxygen, need for ICU admission, and outcome was checked using chi-square test. Association of PSQI with continuous variables was calculated using independent t-test. Data normality was checked for quantitative variable before the application of *t*-test.

Multivariate analysis was performed to assess the confounding factors associated with the outcome of the patients. P<0.05 indicated statistical significance.

Results

Of the 1,250 patients, 559(44.7%) were males and 691(55.3%) were females. There were 1210(97%) patients with typical HRCT findings, while 40(3%) had atypical findings. In addition, 894(71.5%) participants tested positive for COVID-19 PCR, and 356(28.5%) had negative COVID-19 PCR. The COVID-19 antigen was positive for 580(46.4%) participants, and negative for 670(53.6%) (Figure). There were 560(44.8%) patients in group A with mean age 53.80±14.85 years, and 690(55.2%) patients in group B with mean age 53.71±14.32 years. Of the total, 29.5% were university graduates and 22.3% were illiterate. In terms of chronic illness, 38.2% participants had no chronic illness, 25.6% had multiple comorbidities, and 36.1% had a single chronic disease. There were no

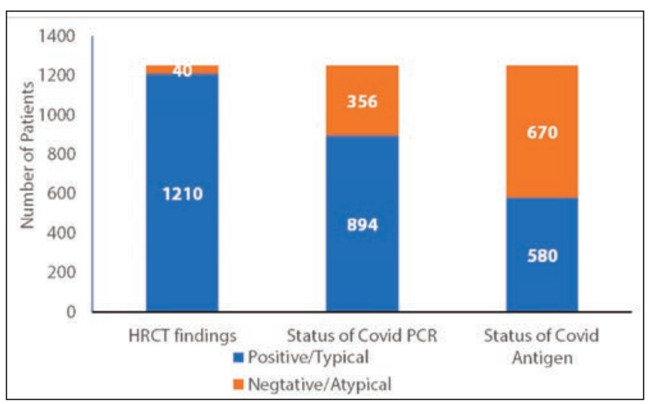

Figure: High-resolution computed tomography (HRCT) and coronavirus disease-2019 (COVID-19) polymerase chain reaction (PCR)/antigen in the study cohort.

Table-1: Demographics and clinical parameters.

Demographics & Clinical Parameters	PSQI SCORE >5	PSQI SCORE <5	*p*-value
Age (years)	53.80±14.85	53.71±14.32	0.33
Gender			
Male	213 (17.04%)	346 (27.68%)	<0.001
Female	347 (27.76%)	344 (27.52%)	
Education			
Illiterate	150 (12%)	129 (10.32%)	
Primary	128 (10.24%)	245 (19.6%)	
Intermediate	109 (8.72%)	120 (9.6%)	<0.001
Bachelor	95 (7.6%)	116 (9.28%)	
Higher	78 (6.24%)	80 (6.4%)	
Comorbids			
Single (DM, HTN, IHD, Respiratory Illness)	156 (12.48%)	246 (19.68%)	
Multiple	180 (14.4%)	140 (11.2%)	<0.001
Others	20 (1.6%)	30 (2.4%)	
Nil	204 (16.32%)	274 (21.92%)	
Hospitalisation Period	8.29±6.0	14.16±8.6	<0.001
HRCT			
Typical	540 (43.2%)	670 (53.6%)	0.50
Atypical	20 (1.6%)	20 (1.6%)	
Outcome			
Discharge	520 (41.6%)	524 (41.92%)	<0.001
Death	40 (3.2%)	166 (13.28%)	
ICU Admission			
Yes	0 (0%)	196 (15.68%)	<0.001
No	560 (44.8%)	494 (39.52%)	
CRP			
At Admission	60.41±48.09	101.30±70.42	<0.001
Before Outcome	19.40±28.09	30.14±39.58	
D-Dimers			
At Admission	707.51±927.09	1580.79±2040.10	<0.001
Before Outcome	377.59±397.80	1197.36±1810.30	

PQSI: Pittsburgh sleep quality index, HTN: Hypertension, DM: Diabetes mellitus, IHD: Ischaemic heart disease, HRCT: High-resolution computed tomography, ICU: Intensive care unit, CRP: C-reactive protein.

significant intergroup differences in terms of age and HRCT scan ($p>0.05$). The difference was significant with respect to gender, comorbid conditions, education status as well CRP and D-dimer levels ($p<0.001$). Group B patients had a longer duration of hospitalisation ($p<0.001$) and a higher need for ICU admission ($p<0.001$) compared to group A. The outcome was death in 166(13.28%) patients in group B compared to 40(3.2%) in group A ($p<0.001$) (Table 1).

Multivariate analysis revealed that participants with a higher oxygen requirement at admission, positive COVID-19 antigen and increased levels of CRP and D-dimer had poor outcomes and poor sleep quality ($p<0.05$). A significant association of PSQI score was observed with gender, COVID-19 PCR, duration of hospital stay, oxygen requirement at admission and outcome, CRP levels at admission, and D-dimer levels at admission and outcome ($p<0.05$). There was also a significant association involving ICU admission and age, gender, comorbidities, COVID-19 PCR, COVID-19 antigen, oxygen requirement at admission as well CRP and D-dimer levels at admission and outcome ($p<0.001$) (Table 2).

Table-2: Multivariate analysis of outcome and confounding factors.

Variable	Independent Variable	Correlation coefficient (F)	*p*-value
PSQI			
	Gender	3.994	0.046
	COVID-19 PCR	7.151	0.008
	Duration hospital	133.956	<0.001
	Oxygen requirement at admission	92.790	<0.001
	Oxygen requirement at outcome	92.093	<0.001
	CRP levels at admission	69.666	<0.001
	D-Dimers levels at admission	43.916	<0.001
	D-Dimers levels at outcome	22.875	<0.001
ICU			
	Age (years)	11.891	0.001
	Gender	19.115	<0.001
	Co-morbids	17.568	<0.001
	COVID-19 PCR	24.383	<0.001
	COVID-19 antigen	31.932	<0.001
	Oxygen requirement at admission	126.991	<0.001
	CRP levels at admission	79.264	<0.001
	CRP levels at outcome	150.420	<0.001
	D-Dimers levels at admission	17.713	<0.001
	D-Dimers levels at outcome	143.312	<0.001
OUTCOME			
	COVID-19 antigen	22.264	<0.001
	Oxygen requirement at admission	7.970	0.005
	CRP levels at admission	16.857	<0.001
	D-Dimers levels at outcome	8.966	0.003
	ICU admission	223.354	<0.001
	PSQI score	67.632	<0.001

PQSI: Pittsburgh sleep quality index, ICU: Intensive care unit, PCR: Polymerase chain reaction, CRP: C-reactive protein.

Discussion

Sleep is indispensably essential for the wellbeing and sustenance of human life. Many physiological processes, systems and functions, such as homeostasis, energy metabolism, muscle restoration and the immune system, are largely dependent upon it.[9] Therefore, it is recommended that adults get 7-9 hours of sleep per night, yet today's population is typically short of 2-3 hours of sleep per night. The deprivation of sleep adversely affects human health, impacting mental alertness and well as cognitive and physical performance.[10]

Sleep plays an essential role in the proper functioning and sustenance of the immune system. It helps in forming and producing essential cells, such as macrophages, monocytes and dendritic cells, that are integral to the immune system. Hence, deprivation of sleep may weaken the immune system and increase the tendency for inflammatory infections.[11] Also, inflammatory mediators, like TNF-α, IL-1 beta and IL-6, rise in response to sleep deprivation, while anti-inflammatory cytokine receptors, like IL-10, tend to decrease following a lack of sleep. Raised pro-inflammatory gene expression may cause inflammatory diseases, and a reduction in antiviral gene expression leads to infectious sickness.[12] When sleep deprivation prevails for a long time, the function of antioxidant enzymes declines, eventually leading to oxidative stress.[13]

The current study found that poor sleep was associated with gender, education, comorbidities, period of hospitalisation, discharge, death, ICU admissions, CRP and D-dimer levels, both at the time of admission and before the outcome. The values have also been studied by Pingzheng Mo et al.[14] In terms of gender, differences have been reported in the context of COVID-19 by some countries, like China.[15] Of the countries that reported gender differences, Germany and Switzerland confirmed a higher incidence in males aged >60. The gender difference can be explained by differences in the lifestyles of both genders. For instance, females tend to wash their hands more frequently than men, making them less prone to infections, while men smoke more frequently than women, weakening the immune system and making them more prone to infections. In the current study, 27.7% of the males had poor sleep quality compared to 27.5% of females, thus proving gender difference compared to Catherine et al.[16] Gender is significant in the prevalence of sleep problems. Some studies reported that in COVID-19, females are more likely to be affected by sleep deprivation than males.[17] Although a longitudinal study illustrated that females who were quarantined for 4 weeks at home had poor sleep quality and more scores on PSQI and Insomnia Severity Index (ISI), their other psychological symptoms and insomnia improved. At the same time, the male gender during the lockdown period had higher PSQI and ISI scores, indicating a diminished gender gap in sleep quality.[18]

The current study found that patients with poor sleep quality had prolonged periods of hospitalisation compared to patients with good sleep quality. Similar findings were found by Jiancheng Zhang et al.[19]

Furthermore, the current study reported that 15.7% patients with higher PSQI score and poor sleep quality needed ICU care, while those patients with good sleep quality were not admitted to the ICU. These results were consistent with the 12% reported by Li Tan et al.[20] Nianqi Liu et al. reported bad sleep quality in 20.7% patients. The percentage of patients unable to sleep for more than half-an-hour for more than 2 times a week was 8.4%, and those who woke up more than 3 times a week was 13%.[21,22] These findings are consistent with studies reporting increased sleep deprivation with age.[23,24] Additionally, literature has noted that COVID-19 patients aged >30 years were more prone to sleep deprivation which was primarily attributed to two factors: social stress that patients experience during lockdown, and the effect of increasing age on circadian rhythm and sleep structure.[25]

A study, however, demonstrated that sleep deprivation was more common in young people aged 18-34 years than in older people. Along the same lines, three other cross-sectional studies showed a rise in sleep problems among college students who were home-quarantined during lockdowns.[26] This increase could be explained in terms of sleep being susceptible to the stress caused by dramatic changes in lifestyle, such as home confinement, decreased social gatherings, and all other outdoor activities during COVID-19 lockdowns. Therefore, it may not be possible to categorically comment on the effects of age on sleep during COVID-19. Sociopsychological factors could interfere with sleep and need further research.

The current study has limitations as it done at a single centre. Besides, it used only the PSQI score to assess sleep quality which means that some casual relationships might have been missed.

Conclusion

Poor sleep quality was associated with longer hospitalisation durations, higher rates of ICU admissions, and increased mortality. COVID-19 patients with multiple comorbidities, elevated CRP and D-dimer levels at the time of admission, and lower education levels were more likely to experience poor sleep quality. However, age and HRCT results did not significantly affect sleep quality.

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Author Contribution:

NZA: Study concept, design and literature search.
KB: Data collection, design and drafting.
MH: Drafting, review and literature search.
FS: Study concept, critical analysis and final review.
MAWJ: Data collection, analysis and writing.
MU: Literature search.