



DOI: <https://doi.org/10.56936/18290825-2.v19.2025-61>

## THE EFFECT OF COVID-19 OUTBREAK AND VACCINATION ON SLEEP QUALITY, SLEEP CHRONOTYPE (MORNINGNESS-EVENINGNESS), DEPRESSION, ANXIETY AND STRESS; A CROSS-SECTIONAL STUDY AMONG ISFAHANI RESIDENTS

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Received 12.07.2024; Accepted for printing 28.03.2025

### ABSTRACT

**Background.** Have been reports suggesting physical or psychological complications associated with for anti-COVID-19 vaccination. We aimed to investigate the effect of COVID-19 infection and vaccination on sleep quality, chronotype, depression, anxiety, and stress among Isfahani population.

**Materials and methods.** 2000 adult residents (aged  $\geq 18$  years) were enrolled between January 10 to September 10, 2022. The participants completed three questionnaires: the Pittsburgh Sleep Quality Index Questionnaire, the Reduced Morningness-Eveningness Questionnaire, and the Depression, Anxiety and Stress Scale – 21 items, in addition to demographics (age and gender), history of COVID-19 (severity and management), and vaccination. The questionnaire scores were calculated and compared between the groups with and without COVID-19 infection, based on vaccination status and disease severity using IBM SPSS Statistics (version 25).

**Results.** The mean age of participants was  $33.04 \pm 10.52$  years; and most were female (61.65%). A history of COVID-19 was positive in 926 individuals (186 with inpatient and 740 with outpatient management), and negative in the remaining participants ( $N=1074$ ). Patients with COVID-19 had a greater Pittsburgh Sleep Quality Index score ( $P=0.024$ ) with significant difference based on the severity of COVID-19 ( $P<0.001$ ). Anxiety severity was different between patients with and without COVID-19 ( $P=0.001$ ). Among all participants, 144 were unvaccinated for COVID-19, 191 had received one dose, and 1665 had completed immunization (two doses). Those who received two doses had a lower mean score on the Reduced Morningness-Eveningness Questionnaire, compared to unvaccinated and one-dose participants, and lower mean depression and anxiety scores, compared to the one-dose group ( $P<0.05$ ). Chronotype and severity of depression and anxiety differed significantly by vaccination status ( $P<0.001$ ).

**Conclusion.** COVID-19 infection and vaccination may affect sleep quality and anxiety levels. Therefore, strategies for managing sleep hygiene and improving sleep quality during COVID-19 rehabilitation are recommended, along with raising physicians' awareness for the proper diagnosis and treatment of these complications.

**KEYWORDS:** COVID-19, COVID-19 Vaccines, Sleep Quality, Chronotype, Depression, Anxiety, Stress

### CITE THIS ARTICLE AS:

Amra B., Soltaninejad F., Ghaderi F., Masnavi E., Robillard R., Hassanzadeh S. (2025). The Effect of COVID-19 Outbreak and Vaccination on Sleep Quality, Sleep Chronotype (Morningness-Eveningness), Depression, Anxiety and Stress; A Cross-sectional Study Among Isfahani Residents; The New Armenian Medical Journal, vol.19 (2), 61-70; <https://doi.org/10.56936/18290825-2.v19.2025-61>

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## INTRODUCTION

The novel deadly disease, Coronavirus disease 2019 (COVID-19), which emerged since December 2019 and became a pandemic a few months later, affected millions of people around the world and resulted in extensive global mortality (approximately 7 million deaths as of June 2023) [Li H, Burm SW et al., 2019]. The early versions of the virus (Alpha and Beta) turned the lungs into a virus-producing factories and spread extensively through the body, eventually involving multiple organs and triggering a cytokine storm, which can lead to acute respiratory distress syndrome, multi-organ failure, and death [Ragab D et al., 2020]. With the introduction of the vaccines and implementation of specific personal and social measures, such as lockdown, hand-washing, social distancing, and wearing masks, the spread of the virus gradually decreased [Brüssow H et al., 2022]. However, due to the lockdowns, many lost their jobs and faced economic problems that added to the hardship caused by the pandemic. Although the next generations of the virus (such as Omicron) the long-term effects of this disease remain present in the society [Ameratunga R et al., 2022].

Several patients were and still are being admitted to the intensive care units and require mechanical ventilation, which results in dependency on intensive care unit and increases the risk of mortality [Ohbe H et al., 2023]. The experience of the intensive care unit and mechanical ventilation is distressing in itself, as many patients report sleep and psychological disorders after discharge [Guck AJ et al., 2021]. Survivors may experience several problems (such as fatigue and dyspnea) after the acute phase, known as long COVID or post-acute sequelae of COVID-19 [Chen C et al., 2021]. The problems patients face during the acute and post-acute phases can induce a great psychosocial burden and result in depression, anxiety, and stress within communities, especially the elderly and female population [Megatsari H et al., 2020]. Not only patients but also the family members are influenced by the negative effect of COVID-19 on mental health, considering the fear of death and the economic burden of the treatment [Salameh P et al., 2020]. These problems have resulted in increased rates of panic, anxiety, obsessive behavior, depression, paranoia, and post-traumatic stress disorder in the society [Dubey S et al., 2020].

Sleep is one of the determinants of an individual's mental health and has several features, including sleep quality and circadian clock (chronotype); both have been reported to be altered by COVID-19 [Herz RS et al., 2021].

The negative impact of COVID-19 on mental health (including depression, anxiety, and stress) is suggested as a major etiology of sleep disorders, known as the "coronasomnia" phenomenon, manifested by insufficient sleep, poor sleep quality, insomnia, sleep apnea, and disturbances of sleep-wake schedules [Casagrande M et al., 2020; Sher L et al., 2020]. A review of studies indicated sleep problems in 35.7% of the general population and 74.8% of patients with COVID-19 (54,231 participants from 13 countries) [Jahrami H et al., 2021].

A nationwide study in Iran also revealed poor sleep quality in 73.5% and depressive symptoms in 41.4% of the population (3,446 participants) [Torkian S et al., 2021]. Another study in Mazandaran Province (1075 respondents) revealed that 22.5%, 38.5%, and 47.2% of the population had moderate-to-severe depression, anxiety, and stress, respectively [Reskati MH et al., 2020]. Poor sleep quality has also been documented in Iranian adolescents during COVID-19 pandemic [Chehri A et al., 2023].

The anxiety and sleep disorders caused by COVID-19 pandemic may be alleviated by vaccination, as it can reduce individual's fear of contracting the disease in the individuals; although there is limited literature available on this topic [Al-Amer R et al., 2022]. Therefore, in this study, we investigated the effect of COVID-19 infection and vaccination on sleep quality, depression, anxiety, and stress in a sample of Isfahani population. To ensure greater accuracy in the research, we also examined participant's sleep chronotype in the post-COVID era and its association with COVID-19 infection and vaccination.

## MATERIALS AND METHODS

**Study design and participants:** This cross-sectional analytic survey included 2000 adult residents (aged 18 years and older) of Isfahan, Iran, after the COVID-19 pandemic, from January 10 to September 10, 2022.

**Ethical Considerations:** This study was carried out in accordance with the latest version of the Declaration of Helsinki on human studies and

Institutional Research Ethics guidelines; anonymity and confidentiality were addressed. The study's protocol was approved by the Local Ethics Committee of Isfahan University of Medical Sciences (Approval ID: IR.ARI.MUI.REC.1401.034). Before enrollment, the study's objectives were explained to the participants and they were asked to read and sign the written informed consent form.

**Instruments and data gathering:** Three questionnaires were used in this study, including the Pittsburgh Sleep Quality Index (PSQI), the Reduced Morningness–Eveningness Questionnaire (rMEQ), and the Depression, Anxiety and Stress Scale–21 Items (DASS-21). The questionnaires were distributed via several routes, including college, social media, and organizations. Before completing the questionnaires, the researcher explained the purpose of the questionnaire and how they should be completed to the participants. The participants were asked to complete the questionnaire in a quiet environment and in a relaxed condition, paying full attention to the questions.

**Demographic data** were gathered by adding this information at the top of one of the forms; age, gender, history of COVID–19 infection, anti–COVID vaccination status. For participants who had been infected with COVID–19, additional information regarding disease severity, management approach, and the number of infections was also recorded (table 1).

**Pittsburgh Sleep Quality Index (PSQI):** The Pittsburgh Sleep Quality Index (PSQI) is a widely used instrument for assessing self-reported (subjective) sleep quality to discriminate between good and poor sleepers [Buysse DJ *et al.*, 1989]. This questionnaire consists of 19 items that evaluate sleep behavior profiles (bedtime, wake-up time, and time spent in bed), sleep-onset latency (minutes), total sleep time (hours), sleep efficiency (percentage) and global subjective sleep quality. Each domain is scored from 0 to 3, where 3 indicates greatest dysfunction. Sum of these scores results in a total score of 0 to 21. A total PSQI score of greater than 5 indicates poor sleep quality. A study by Chehri and colleagues validated the Persian version of the PSQI (used in the present study); reliability was confirmed by Cronbach's alpha of 0.81, and goodness of fit of the structural equation model was confirmed using confirmatory

TABLE 1.

Characteristics of the study population at the time of survey completion in Post Covid–19

| General demographics and Categories | With CO-VID-19 (N= 926) | Without COVID-19 (N=1074) | P-value* |
|-------------------------------------|-------------------------|---------------------------|----------|
| Age (years) n(%)                    |                         |                           |          |
| 10–20                               | 72(7.8%)                | 143(13.3%)                | <0.001   |
| 21–40                               | 634(65.5%)              | 732(68.2%)                |          |
| 41–60                               | 205(22.1%)              | 186(17.3%)                |          |
| 61–80                               | 15(1.6%)                | 13(1.2%)                  |          |
| Sex n(%)                            |                         |                           |          |
| Male                                | 403(43.5%)              | 384(25.8%)                | <0.001   |
| Female                              | 523(56.5%)              | 690(64.2%)                |          |
| Marital status n(%)                 |                         |                           |          |
| Single                              | 313(33.8%)              | 431(40.1%)                | 0.001    |
| Married                             | 556(60%)                | 586(54.6%)                |          |
| Widow                               | 22(2.4%)                | 12(1.1%)                  |          |
| Divorced                            | 27(2.9%)                | 23(2.1%)                  |          |
| Cohabiting                          | 8(.09%)                 | 22(2%)                    |          |
| Education n(%)                      |                         |                           |          |
| No college degree                   | 286(30.9%)              | 433(40.3%)                | <0.001   |
| Attending college                   | 482(52.1%)              | 494(46%)                  |          |
| Academic degree                     | 158(17.1%)              | 147(13.7%)                |          |
| Employment status n(%)              |                         |                           |          |
| Employee                            | 437(47.3%)              | 368(34.3%)                | <0.001   |
| Retired                             | 15(1.6%)                | 22(2%)                    |          |
| Housewife                           | 158(17.1%)              | 271(25.2%)                |          |
| Business                            | 277(29.9%)              | 368(34.3%)                |          |
| Laborer                             | 39(4.2%)                | 38(3.5%)                  |          |
| Medical conditions n(%)             |                         |                           |          |
| Healthy                             | 782(84.4%)              | 958(89.2%)                | 0.001    |
| Diabetic mellitus                   | 53(5.7%)                | 47(4.4%)                  |          |
| Cardiovascular disease              | 70(7.6%)                | 39(3.6%)                  |          |
| Malignancy                          | 4(0.4%)                 | 4(0.4%)                   |          |
| Lung disease                        | 6(0.6%)                 | 15(1.4%)                  |          |
| Arthritis                           | 11(1.2%)                | 11(1%)                    |          |
| Medication use n(%)                 |                         |                           |          |
| Sleeping aids                       | 74(8%)                  | 36(3.4%)                  | <0.001   |
| Antidepressant                      | 37(4%)                  | 17(1.6%)                  |          |
| Anxiolytics and/or benzodiazepines  | 44(4.8%)                | 19(1.8%)                  |          |
| None                                | 771(83.3%)              | 102(93.3%)                |          |
| COVID-19 vaccination n(%)           |                         |                           |          |
| Fully (2 doses)                     | 770(83.2%)              | 895(83.3%)                | 0.001    |
| Partially (1 dose)                  | 107(11.6%)              | 84(7.8%)                  |          |
| None                                | 49(5.3%)                | 95(8.8%)                  |          |

**NOTES** \*-The results of Chi square test; N(%) - Total number(%) of patients. n(%) - number (percent) of patients in a subgroup.



factor analysis; the internal consistency of PSQI was 0.81 and correlation scores ranged from 0.48–0.71 [Chehri A et al., 2020].

Reduced Morningness–Eveningness Questionnaire (rMEQ): The reduced Morningness–Eveningness Questionnaire (rMEQ) evaluates sleep chronotype through five items; it has been derived from the original MEQ (the gold standard tool for evaluating chronotype, containing 19 items. Due to the length of MEQ, rMEQ was designed by Adan and Almirall (1991) with 5 items (items 1, 7, 10, 18, and 19 of the original MEQ), appropriate for screening larger populations and much easier to complete [Adan A et al., 1991]. Global scores range from 4 to 26; higher scores indicates morningness chronotype; specifically scores of greater than 17 indicate morning type, less than 12 indicate evening type, and 12–17 represent neither type. The validity of this questionnaire has been approved in different populations [Danielsson K et al., 2019]. The Persian version of this questionnaire, used in the present study, was validated by Rahafar and colleagues, with Cronbach's alpha of 0.71 (confirmed by factor analysis) [Rahafar A et al., 2015].

The Depression, Anxiety and Stress Scale – 21 Items (DASS–21): The Depression, Anxiety and Stress Scale–21 Items is a self-report scale, designed to measure the severity of depression, anxiety and stress symptoms. This version is a shortened version of the original DASS (42 items). The three scales of the DASS have been shown to have high internal consistency, labeled collectively as “general affective distress”. Each of the three scales contain 7 items, each rated on a 4-point scale. It evaluates the participants' distress during the past week. It has been validated among different populations [Sarıçam H, 2018; Oei TP et al., 2013]. The Persian version of this questionnaire, used in the present study, was validated by Kakeman and colleagues by acceptable Cronbach's alpha coefficient for depression (0.93), anxiety (0.79), and stress (0.91), as well as acceptable test–retest reliability (0.74–0.88) [Kakemam E et al., 2022].

Statistical Analysis: Statistical analyses were performed using the IBM SPSS Statistics (version 25). Mean and standard deviation (SD) were calculated for continuous variables; comparisons between groups were made using the independent samples t-test. Frequencies and percentages were

calculated for categorical variables; comparisons were made using the Chi-square test. A P-value of <0.05 was considered statistically significant.

## RESULTS

A total of 2,000 participants completed the study. The mean age of participants was  $33.04 \pm 10.52$  years; and the majority (68.3%) were between 21 and 40 years old. Most participants were female (61.65%). Among all participants, 926 had a history of COVID–19 infection, while 1,074 did not. Regarding disease severity, 186 participants were hospitalized, and 740 received outpatient management.

The mean rMEQ score was  $13.88 \pm 3.01$ , and the mean PSQI score was  $9.38 \pm 2.93$ . Patients with or without COVID–19 did not differ in terms of mean rMEQ score or chronotype ( $P=0.117$ ), but those with COVID–19 had a significantly higher PSQI score ( $P=0.024$ ; Table 2). Approximately half of patients without COVID–19 had poor PSQI ( $P=0.011$ ; Table 2). There was a significant difference in PSQI classes based on the severity of COVID–19 ( $P<0.001$ ). The proportion of participants with good PSQI scores was 7.8% among those without COVID-19, 0% among hospitalized patients, and 6.5% among outpatients. In contrast, poor PSQI scores were observed in 92.2% of participants without COVID-19, 100% of hospitalized patients, and 93.5% of outpatients.

The mean anxiety score was  $4.86 \pm 4.40$ , the mean depression score was  $5.95 \pm 4.85$ , and the mean score of stress was  $7.37 \pm 4.93$ . Participants with or without COVID–19 did not differ in terms of mean depression score or its categories, mean stress score or its categories, and mean anxiety scores ( $P>0.05$ ; Table 2). However, the distribution of anxiety severity levels were significantly different between patients with and without COVID–19 ( $P=0.001$ ; Table 2).

Of all patients, 144 were unvaccinated, 191 had received one dose, and 1665 had completed their immunization (two doses). There was a significant difference in mean rMEQ, depression, and anxiety scores of patients based on their vaccination status. Participants who received two doses had a lower mean rMEQ score, compared to the unvaccinated and one-dose groups, and lower mean depression and anxiety scores, compared to the one-dose

group ( $P < 0.05$ ; Table 3). In addition, the chronotype and the severity of depression and anxiety differed significantly based on patients' COVID-19 vaccination status ( $P < 0.001$ ; Table 3). However, there was no significant difference in PSQI categories, stress categories, or their mean scores based on their vaccination status ( $P > 0.05$ ; Table 3).

### DISCUSSION

The present study showed that most participants (93.4%) had poor sleep quality during post-COVID era and this effect was even larger in patients who were infected with COVID-19. The issue of sleep disorders in the era of COVID-19 pandemic has been the focus of attention, since sleep is not just for relaxing, but has several important roles in the body; including maintaining homeostasis and regulating the immunity [Ono BHVS et al., 2020].

Correspondingly, sleep disorders can result in neuroinflammation and changes in blood-brain barrier [Semyachkina-Glushkovskaya O et al., 2021]. Evidently, the experience of COVID-19 infection causes great stress and anxiety for the patients, the fear of dying, the pain and respiratory distress, post-viral fatigue, the horrible experiences of intensive care unit admission and mechanical ventilation (including intensive care unit delirium) are the major causes of sleep disorders in the post-acute phase [Voulgaris A et al., 2020].

Respiratory distress may also result in sleep-disordered breathing, such as sleep apnea, leading the patients to require positive airway pressure devices or sleep medicine for sleep. During the pandemic, one individual were infected with the disease several times, and many are affected by long-COVID complications [Raveendran A et al., 2020]. This explains sleep disorders have

been so prevalent during the COVID-19 pandemic and during lockdown periods [Pinto J et al., 2020]. However, our study investigated sleep quality of population in 2021, more than three years after the outbreak, at the time when the World Health Organization had already declared an end to the global emergency status for COVID-19 and expressed hope for the conclusion of the pandemic in near future. Yet, the results of our study showed that poor sleep quality in the majority of participant during this period. Notably, even vaccination could not change the pattern of poor sleep quality among the studied population.

One hypothesis is that the disturbed sleep, present in the acute and post-acute phase, is maintained in the chronic phase. A review of studies indicates significant poor sleep quality in the first year

Comparing sleep quality, chronotype, depression, anxiety, and stress between participants with or without COVID-19 infection

| Variable                                                         | Categories  | Total<br>(N = 2000) | With<br>COVID-19<br>(N= 926) | Without<br>COVID-19<br>(N=1074) | P-<br>value |
|------------------------------------------------------------------|-------------|---------------------|------------------------------|---------------------------------|-------------|
| rMEQ score, (mean±SD)                                            |             | 13.88±3.01          | 13.92±3.07                   | 13.85±2.94                      | 0.117*      |
| rMEQ categories,<br>N(%)                                         | Eveningness | 458(22.9)           | 222(11.1)                    | 236(11.8)                       | 0.372†      |
|                                                                  | Morningness | 259(13)             | 125(6.3)                     | 134(6.7)                        |             |
|                                                                  | Neither     | 1283(64.2)          | 579(29)                      | 704(35.2)                       |             |
| PSQI score, (mean±SD)                                            |             | 9.38±2.93           | 9.52±2.81                    | 9.26±3.02                       | 0.024*      |
| PSQI category,<br>N(%)                                           | Good        | 132(6.6)            | 48(2.4)                      | 84(4.2)                         | 0.011†      |
|                                                                  | Poor        | 1868(93.4)          | 878(43.9)                    | 990(49.5)                       |             |
| Depression, Anxiety and Stress Scale ( DASS)-21 score, (mean±SD) |             |                     |                              |                                 |             |
| Depression score                                                 |             | 5.95±4.85           | 6.21±4.85                    | 5.73±4.84                       | 0.333*      |
| Depression severity,<br>N(%)                                     | None        | 894(44.7)           | 396(19.8)                    | 498(24.9)                       | 0.473†      |
|                                                                  | Mild        | 343(17.2)           | 158(7.9)                     | 185(9.3)                        |             |
|                                                                  | Moderate    | 446(22.3)           | 217(10.9)                    | 229(11.5)                       |             |
|                                                                  | Severe      | 145(7.3)            | 73(3.7)                      | 72(3.6)                         |             |
|                                                                  | Very severe | 172(8.6)            | 82(4.1)                      | 90(4.5)                         |             |
| Anxiety score, mean±SD                                           |             | 4.86±4.40           | 5.25±4.48                    | 4.49±4.29                       | 0.956*      |
| Anxiety severity,<br>N(%)                                        | None        | 911(45.6)           | 379(19)                      | 532(26.6)                       | 0.001†      |
|                                                                  | Mild        | 372(18.6)           | 172(8.6)                     | 200(10)                         |             |
|                                                                  | Moderate    | 252(12.6)           | 128(6.4)                     | 124(6.2)                        |             |
|                                                                  | Severe      | 190(9.5)            | 103(5.2)                     | 87(4.4)                         |             |
|                                                                  | Very severe | 275(13.8)           | 144(7.2)                     | 131(6.6)                        |             |
| Stress score, mean±SD                                            |             | 7.37±4.93           | 7.56±4.88                    | 7.20±4.97                       | 0.113*      |
| Stress severity,<br>N(%)                                         | None        | 1069(53.5)          | 492(24.6)                    | 577(28.9)                       | 0.859†      |
|                                                                  | Mild        | 290(14.5)           | 139(7)                       | 151(7.6)                        |             |
|                                                                  | Moderate    | 359(18)             | 164(8.2)                     | 195(9.8)                        |             |
|                                                                  | Severe      | 172(8.6)            | 76(3.8)                      | 96(4.8)                         |             |
|                                                                  | Very severe | 110(5.5)            | 55(2.8)                      | 55(2.8)                         |             |

NOTES \* Results of Mann-Whitney U test, †Result of Chi square test

after COVID-19 infection that requires telehealth and strategies for treatment. The lack of appropriate treatment of this disorder can result in the persistence of sleep problem [Becker PM et al., 2022]. Another mechanism, suggested for the persistence of sleep disorder, induced by COVID-19 infection, is the disruption of circadian rhythms of the individuals during the pandemic. The results of the present study showed that the majority of the participants had neither morningness, nor eveningness, and the chronotype patterns were not influenced by COVID-19 infection; but were influenced by vaccination status. Other studies have also referred to the altered chronotype of the population after COVID-19 outbreak, including increased sleep duration and delayed sleep timing, documented by comparing the sleep timing between 2019 and 2020 across 20 countries [Yuan RK et al., 2022].

One of the factors identified was the widespread shift to working from home that contributed to disturbed sleep time, with tendency towards eveningness, and daytime napping [Rome O et al., 2021], later bedtime and wake-ups [Bhat S et al., 2022]. As suggested, the positive correlation between sleep duration and morningness observed before the pandemic shifted to a negative correlation after the outbreak. Additionally, both wake time and bedtime were found to influence morningness-eveningness pattern [Staller N et al., 2021]. Most of these disorders have been studied during the lockdown period and compared with the before outbreak phase [Leone MJ et al., 2020], which may be the factor for the differences in chronotype findings compared to the present study. The disorder in sleep-wake cycle and

chronotype have been suggested to be related to the depression and anxiety in affected individual [Ono BHVS et al., 2020].

Our results showed that different grades of depression, anxiety, and stress were present in the studied population and patients with COVID-19 had a higher severity of anxiety symptoms. These results are in line with the previous research, which indicates an increased rate of depression, anxiety, and stress, caused by COVID-19 in different parts of the world [Othman N, 2010; Shah SMA et al., 2021]. These three components of mental health are also associated with individual personal characteristics, such as marital status, employment and life circumstances [Shah SMA et al., 2021]. Furthermore, the deadly pandemic caused a great distress in so-

TABLE 3.

Comparison of sleep quality, chronotype, depression, anxiety, and stress between patients based on COVID-19 vaccination status

| Variable                    | Categories  | None<br>(N=144) | One-dose<br>(N=191) | Two-doses<br>(N=1665) | P-value              |
|-----------------------------|-------------|-----------------|---------------------|-----------------------|----------------------|
| rMEQ, (mean±SD)             |             | 14.53±3.06      | 14.72±2.98          | 13.73±2.98            | <0.001 <sup>*†</sup> |
| rMEQ categories, N(%)       | Eveningness | 20(1)           | 30(1.5)             | 408(20.4)             | <0.001 <sup>†</sup>  |
|                             | Morningness | 28(1.4)         | 38(1.9)             | 193(9.7)              |                      |
|                             | Neither     | 96(4.8)         | 123(6.2)            | 1064(53.2)            |                      |
| PSQI, (mean±SD)             |             | 9.09±2.71       | 9.41±2.95           | 9.40±2.95             | 0.476 <sup>*</sup>   |
| PSQI class, N(%)            | Good        | 13(0.7)         | 13(0.7)             | 106(5.3)              | 0.464 <sup>†</sup>   |
|                             | Poor        | 131(6.6)        | 178(8.9)            | 1559(78)              |                      |
| DASS-21 score               |             |                 |                     |                       |                      |
| Depression score, (mean±SD) |             | 6.0±4.89        | 6.93±5.34           | 5.83±4.77             | 0.012 <sup>*§</sup>  |
| Depression severity, N(%)   | None        | 65(3.3)         | 75(3.8)             | 754(37.7)             | <0.001 <sup>†</sup>  |
|                             | Mild        | 32(1.6)         | 26(1.3)             | 285(14.3)             |                      |
|                             | Moderate    | 16(0.8)         | 48(2.4)             | 382(19.1)             |                      |
|                             | Severe      | 21(1.1)         | 16(0.8)             | 108(5.4)              |                      |
|                             | Very severe | 10(0.5)         | 26(1.3)             | 136(6.8)              |                      |
| Anxiety score, (mean±SD)    |             | 4.86±4.40       | 5.77±4.81           | 4.73±4.33             | 0.005 <sup>*  </sup> |
| Anxiety severity, N(%)      | None        | 62(3.1)         | 66(3.3)             | 783(39.2)             | 0.004 <sup>†</sup>   |
|                             | Mild        | 18(0.9)         | 44(2.2)             | 208(10.4)             |                      |
|                             | Moderate    | 22(1.1)         | 22(1.1)             | 208(10.4)             |                      |
|                             | Severe      | 16(0.8)         | 20(1)               | 154(7.7)              |                      |
|                             | Very severe | 26(1.3)         | 39(2)               | 210(10.5)             |                      |
| Stress score, (mean±SD)     |             | 7.03±4.99       | 7.85±5.18           | 7.35±4.90             | 0.277 <sup>*</sup>   |
| Stress severity, N(%)       | None        | 81(4.1)         | 97(4.9)             | 891(44.6)             | 0.094 <sup>†</sup>   |
|                             | Mild        | 23(1.2)         | 27(1.4)             | 240(12)               |                      |
|                             | Moderate    | 21(1.1)         | 38(1.9)             | 300(15)               |                      |
|                             | Severe      | 10(0.5)         | 10(0.5)             | 152(7.6)              |                      |
|                             | Very severe | 9(0.5)          | 19(1)               | 82(4.1)               |                      |

NOTE: <sup>\*</sup> - The results of One-way ANOVA test, <sup>†</sup> - The result of chi square test Pairwise comparison by post hoc test (Tukey HSD) revealed significant difference between one dose and two doses ( $P<0.001$ ) and none and two doses ( $P=0.006$ ) for rMEQ<sup>†</sup>, between one dose and two doses ( $P=0.008$ ) for depression<sup>§</sup>, and between one dose and two doses for anxiety ( $P=0.005$ )<sup>||</sup>



ciety and the problem was not only for the patients infected; but for the entire population, as many lost their family members and had to live with the fear of being infected every moment; many suffered from loneliness, caused by lockdowns and social distancing, and many lost their jobs [Wang S et al., 2022]. All types of distress increase the risk of daily life impairment and can have a negative impact on sleep quality. On the other hand, sleep disorders may also result in increased anxiety and stress [Stanton R et al., 2020]. If not treated, the vicious cycle would intensify both sleep disorders and depression, anxiety, and stress in the individuals, which is why it is important to pay greater attention to sleep disturbances and mental health in the general population during the post-COVID era.

A novel finding of the present study was the reduction of anxiety and depression symptoms in individuals who received two doses of anti-COVID vaccine. In another study on Jordanians, the researchers reported significant drop in the level of stress and anxiety after vaccination, compared to that before [Al-Amer R et al., 2022]. These findings are consistent with the results of the present study, although we did not assess anxiety or stress levels prior to vaccination.

Vaccination appears to ensure the individuals with lower vulnerability to the infection, thereby reducing their stress and anxiety. It has also been reported that individuals with high level of anxiety and fear of COVID-19 infection had a stronger intention to get vaccinated, while a higher rate of negative emotions are observed among those with anti-vaccination attitudes [Simione L, 2021; Bell S et al., 2021]. However, some others also receive the vaccine with the fear of post-vaccine complications that may temporarily intensify their stress and anxiety. This fear subsides after a few days, while the immunization effect of the vaccine makes the individual more assured about the effect of vaccine for reduced risk of infection [Garg RK et al., 2022]. Depression, on the other hand, seems to be a more internal component that may not be influenced by the vaccination. Interestingly, higher level of depression is associated negatively with antibody titers following vaccination [Kaneko H et al., 2023]. Therefore, it is important to diagnose

depressive symptoms in the general population in post-COVID era, in order to ensure appropriate treatment and prevent further complications. Depression, on the other hand, seems to be a more internalized psychological component that may not be directly influenced by vaccination. Interestingly, higher levels of depression have been reported to be negatively associated with antibody titers following vaccination [Kaneko H et al., 2023]. Therefore, it is important to diagnose depressive symptoms in the general population during the post-COVID era in order to ensure appropriate treatment and prevent further complications.

One of the limitations of the present study was its cross-sectional design, and we had no information about the individual's status before COVID-19 pandemic; therefore, we could not compare the results with pre-pandemic data. Another limitation was related to the subjective nature of the tools used, which made any potential bias in data recording immeasurable and unpredictable for the researchers.

### CONCLUSION

The newly-emerged pandemic, COVID-19, has resulted in significant stress and anxiety for the general population, with a greater effect on those infected with the disease. Complete vaccination appears to be an effective approach to reducing stress and anxiety in the population. Sleep quality is another factor influenced by the present pandemic, which can be the direct effect of the pandemic or the negative effect of impaired mental health on the sleep quality. The present study showed that although poor sleep quality was more prominent in those with history of COVID-19 infection, it is also observed in many individuals without a history of infection. This finding highlights poor sleep quality as a widespread issue in post-COVID era. Therefore, it is recommended to develop strategies for improving sleep hygiene and quality, as well as mental health of individuals (depression, anxiety, and stress), particularly in the rehabilitation of COVID-19 patients. Additionally, increasing physician awareness is essential for the early diagnosis and appropriate management of these complications.

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Copy editor: Kristina D Matevosyan

LLC Print in "Monoprint" LLC

Director: Armen Armentaakyan  
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