Original Article

Mental Health Outcomes and Sleep Status among Patients with Coronavirus Disease 2019

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Abstract

Objective: The immediate impacts of coronavirus disease 2019 (COVID-19) on mental health of affected patients and psychiatric morbidities of these patients has been neglected by researchers. We assessed mental health outcomes and sleep status among inpatients and outpatients with COVID-19 who were initially referred to our COVID-19 clinic in Mashhad, Iran during April-October 2020.

Method: In this ethically approved cross-sectional study, 130 patients with confirmed COVID-19 who were referred to outpatient clinics and wards of a referral hospital in Mashhad, Iran were surveyed during April-October 2020. Demographic data were collected after obtaining informed written consent. Validated Persian versions of insomnia severity index (ISI), 9-item patient health questionnaire (PHQ-9), and 7-item generalized anxiety disorder (GAD-7) and revised impact of event scale (IES-R) were used as main outcome measures (i.e. status of anxiety, depression, insomnia, and event-related distress). Analysis was performed with SPSS using binary logistic regression. P-values < 0.05 were considered significant.

Results: Overall, 65 inpatients and 65 outpatients were surveyed. The two groups did not significantly defer in terms of insomnia and depression severity, but the outpatients showed higher levels of anxiety (52.3% vs. 24.6%, P = 0.005) and distress compared to inpatients (80.0% vs. 64.6%, P < 0.001). Male sex (OR = 0.017, 95%CI = 0.000-0.708, P = 0.032) exhibited independent and inverse association with depression in COVID-19 patients. Being married (OR = 0.102, 95% CI = 0.018-0.567, P = 0.009) was independently and inversely associated with anxiety. Insomnia was independently associated with event-related distress (OR = 7.286, 95%CI = 2.017-26.321, P = 0.002). Only depression was independently associated with insomnia (OR = 49.655, 95%CI = 2.870-859.127, P = 0.007).

Conclusion: We found symptoms of psychological distress and anxiety to be more prevalent among outpatients with COVD-19 than inpatients. Insomnia can be a potential risk factor for adverse mental health outcomes in these patients.

Key words: *Anxiety; COVID-19; Depression; Insomnia; Mental Health*

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With over 280 million reported cases and 5 million deaths by end of December 2021, coronavirus disease 2019 (COVID-19) continues to affect global health in an unprecedented manner (1). Despite vast efforts to control the pandemic by rapid vaccination against COVID-19 (more than 8.5 billion doses until early 2022) or applying preventive measures such as lockdowns, social distancing, or using face-masks (1, 2), new mutations of the virus, namely Delta and recently Omicron variants (3), still invade human societies (4).

It was expected that the COVID-19 pandemic could affect psychological well-being of many people around the globe (5). Long-term quarantine and lockdown orders, diminished interpersonal connections, facing fear of death or contagion, or losing jobs and subsequent economic consequences could all be considered as leading factors of perceived psychological distress in the general population (6, 7). Therefore, as soon as the COVID-19 pandemic was documented in early 2020, many researchers have focused on the impacts of the pandemic on mental health across the world (8, 9). Infected patients are one of the target populations in these studies.

Studies on previous epidemics of the coronavirus, namely severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), report psychiatric manifestations and long-term cognitive complications in infected patients (10, 11). Therefore, some researchers have focused on psychological presentations associated with COVID-19 in infected patients (6, 12). Reports have indicated high prevalence of depression, anxiety, post-traumatic distress, panic disorder, obsessive-compulsive disorder, psychological distress, sleep disturbance, new-onset psychosis, and neurocognitive impairments among COVID-19 patients (6, 10-12).

The broad spectrum of mental illnesses associated with COVID-19 may be better explained if they were categorized based on time of presentation, as this infection may have immediate or long-term consequences on mental health of patients (13). They may immediately be affected by isolation from society, losing emotional support of family members and friends, experiencing threat of death, feeling stigmatized, and even experience direct invasion of the virus into the central nervous system (5, 6, 14). Hospitalized patients may also experience uncertainty about duration of hospitalization and treatment procedures, possible neuropsychiatric side effects of medications such as antiviral agents or glucocorticoids, and different levels of hypoxia which could affect their mental function (7, 14, 15).

Despite the broad spectrum of psychological consequences of COVID-19 among patients, many studies have focused on the general population or healthcare workers (16), and there exists a lack of studies on psychiatric morbidities in patients infected with this virus. Moreover, limited data reflected on psychological outcomes of COVID-19 in the Iranian population. To address these concerns, we aimed to assess the immediate mental health outcomes of COVID-19 infection in a group of Iranian patients and to compare them between inpatient and outpatient groups. We hypothesized that patients may experience a high prevalence of psychological symptoms immediately after they're diagnosed with COVID-19, which could be even higher among hospitalized patients.

Materials and Methods

Ethics Approval
This study followed the ethical guidelines of the Declaration of Helsinki. This study has been approved by the Ethics Committee of Mashhad University of Medical Sciences (approval number IR.MUMS.REC.1399.062). All participants gave informed consent before enrollment. Data was collected anonymously and the confidentiality of information was assured. Patients were permitted to leave the study if they desired at any time.

Participants
Based on the reported 30% prevalence of depression among hospitalized patients with COVID-19 (17), keeping an alpha error of 0.05, a d = 0.078, and a p = 0.3, the target sample size was calculated to be 130 patients, including 65 inpatients and 65 outpatients. Recruitment of patients was continued until we received 65 questionnaire responses in each group.

Inclusion criteria were literacy and education level of at least middle school, confirmed diagnosis of COVID-19 based on clinical presentations and RT-PCR, age of 20-75 years, and giving written informed consent to participate in the study. Patients with severely deteriorated general condition who could not respond to the questionnaires were excluded from the study.

Study Design and Settings
This cross-sectional study was conducted on confirmed cases of COVID-19 who were referred to COVID-19 center of Imam Reza Hospital, Mashhad, Iran from April 10, 2020 to October 10, 2020. Imam Reza Hospital serves as the main center for referral of patients diagnosed with COVID-19 in Mashhad, Iran. Patients highly suspected to have COVID-19 are referred to the outpatient COVID-19 clinic of Imam Reza Hospital, where they are visited and assessed thoroughly to work out the definitive COVID-19 diagnosis based on the clinical presentations and real-time polymerase chain reaction (RT-PCR). Patients positive for COVID-19 are then managed in the clinic and sent home or admitted to the COVID-19 inpatient wards of the hospital if they have the indications for hospitalization based on the National COVID-19 Guideline (18).

We used the contact information of outpatients who were confirmed to have COVID-19 and reached them through phone calls on the 7th day after their first visit at

the clinic. After obtaining informed consent, we sent them a link to an online platform containing our study checklist and questionnaires and they were requested to respond within three days (7th-10th days after their first visit). For the hospitalized patients, the process was done in-person, by a researcher going to their room at the inpatient ward on the 7th day, obtaining informed consent and providing the questionnaires. The researcher then returned for collecting the response within the next three days.

Data were collected from the patients 7-10 days after their first visit at the COVID-19 clinic, through online checklist and questionnaires. Demographic data were gathered in self-reported checklists including age, sex, height, weight, marital status, education, occupation status, income level, history of psychiatric visit, history of psychiatric drug use, history of medical comorbidities, history of close contact with COVID-19 patients, and loss of loved ones due to COVID-19. Duration of hospital stay in hospitalized patients was recorded as well. Body mass index (BMI) was calculated based on reported height and weight. Participants were also asked to complete four questionnaires to assess their psychiatric symptoms (i.e., main outcomes of the study). We tried to select patients using rigorous criteria (all patients originating from the same general population, included in a prospective design) in an attempt to prevent selection bias. We also used objective sources to collect data whenever possible to prevent recall bias.

Tools
Using the validated Persian versions of the following measurement tools, we assessed symptoms of depression, anxiety, insomnia, and distress in all enrolled patients.

• The 7-item Insomnia Severity Index (ISI)
The ISI is a measurement tool designed to assess perception of respondents in regards to their insomnia and sleep problems. It evaluates problems in sleep initiation and continuation, satisfaction with sleep pattern, interference with daily function, significance of sleep-related difficulties, and the distress caused by sleep disturbance. Items are scored on a 5-point Likert scale between 0 (never) and 4 (very much). Scores for all item are added to give a final score between 0 and 28, with larger values indicating a higher perception of sleeplessness. Severity of insomnia is stratified into none (0-7), subthreshold (8-14), moderate (15-21), and severe (22-28) based on the total score (19).

• The 22-item Impact of Event Scale–Revised (IES-R)
The IES-R includes 22 items and has been designed to evaluate the subjective response to a specific traumatic event and related distress. IES-R contains three subscales (intrusion, avoidance, and hyperarousal), besides a total subjective stress score, together measuring the mental disability of respondents in facing specific traumatic events. Each item is scored on a 5-point scale from 0 (no symptom) to 4 (an extremely high level of symptoms) according to the severity of

symptoms in the past seven days. The total score falls in the 0-88 range, where scores 0-23 mean no distress, 24-32 mean partial distress, 33-38 indicate definitive distress, and ≥ 39 indicate severe distress (20).

• The 9-item Patient Health Questionnaire (PHQ-9)
The PHQ-9 comprises nine items, each of which can be scored based on a Likert 4-point scale from 0 (not at all) to 3 (nearly every day). The total score for this questionnaire ranges between 0 and 27, with larger values indicating higher severity of depression in the respondent. Based on the PHQ-9 scores, the severity of depression can be classified into none (≤ 4), mild (5-9), moderate (10-14), moderately severe (15-19), and severe (≥ 20) (21).

• The 7-item Generalized Anxiety Disorder (GAD-7)
The GAD-7 is a 7-item tool that quantifies the extent of generalized anxiety and its impact on function of the respondent. Each item in GAD-7 can be scored 0 (not at all), 1 (several days), 2 (more than half the days), and 3 (almost every day). The total score varies between 0 and 21, larger total scores indicating greater impairment. Intensity of anxiety in this scale is stratified as none to mild (0-9), moderate (10-14), and severe (15-21) (22).

Statistical Analysis
Data was analyzed by SPSS 24 (IBM Statistics, Chicago, IL). Kolmogorov-Smirnov test was used to test the normality of the data. Data conforming to a normal distribution were reported in mean ± standard deviation (SD), while non-normal data were reported using median and interquartile range (IQR). Independent sample t-test, Mann-Whitney U test, and Chi-square test were used to perform inter-group comparison for variables.

We performed multivariate binary logistic regression models to evaluate the potential associated factors with symptoms of anxiety, depression, insomnia, and event-related distress in COVID-19 patients, by removing the effects of potential confounding factors. Outcomes of the regression analyses are reported as odds ratio (OR) and 95% confidence interval (95%CI). $P < 0.05$ was considered statistically significant in all analyses.

Results
Overall, 130 patients with COVID-19, including 65 inpatients (50.0%) and 65 outpatients (50.0%), were surveyed in this study. Of the 130 patients, 60 (46.1%) were female and the remaining 70 (53.9%) were male. The mean age of the patients was 43.90 ± 11.84 years (45.96 ± 11.99 years in the inpatients and 41.81 ± 11.41 years in the outpatients). Among the inpatient group, the mean hospitalization time (at the time of responding to the questionnaires) was 9.30 ± 6.58 days.

Personal and demographic variables for the outpatients and inpatients were compared in Table 1. As seen in the table, females composed 53.8% of the outpatients and 38.5% of the inpatients (35 vs. 25, P = 0.079). The median (IQR) age of the outpatients was 40.0 (32.5-48.0), while it was 45.0 (37.5-52.5) in the inpatient group (P = 0.019). Inpatients had a significantly higher

BMI compared with the outpatients (27.72 ± 6.24 vs. 25.74 ± 2.83, P = 0.038). The frequency of higher education levels and contact with COVID-19 patients were significantly higher among the outpatients (76.9% vs. 46.2%, P < 0.001 and 38.5% vs. 15.4%, P = 0.003, respectively), while medical comorbidities were significantly more prevalent among inpatients (53.8% vs. 30.8%, P = 0.008). However, the two groups did not have any significant difference regarding occupation, income, psychiatric history, and loss of loved ones due to COVID-19 (Table 1).

Primary study outcomes are shown and compared between the inpatient and outpatient participants in Table 2. Among all participants, 72 (55.4%) had experienced moderate to severe depression, 50 (38.5%) had reported moderate to severe anxiety, 69 (53.1%) had reported definitive to severe levels of event-related distress, and 51 (39.2%) had experienced moderate to severe insomnia. As shown in Table 2, although the two groups did not significantly differ in terms of insomnia

and depression severity, the outpatient group showed significantly higher levels of anxiety (52.3% vs. 24.6%, P = 0.005) and event-related distress compared to the inpatients (80.0% vs. 64.6%, P < 0.001).

Table 3 elaborates significant associations between psychiatric symptoms and different studied variables. Multivariate logistic regression showed that male sex (OR = 0.017, 95%CI = 0.000-0.708, P = 0.032) and insomnia (OR = 175.935, 95%CI = 6.173-5014.155, P = 0.002) were the only independent factors associated with depression in COVID-19 patients. Being married (OR = 0.102, 95%CI = 0.018-0.567, P = 0.009) and insomnia (OR = 10.679, 95%CI = 1.445-78.901, P = 0.020) were independently associated with anxiety. However, only insomnia was found to be independently associated with event-related distress (OR = 7.286, 95%CI = 2.017-26.321, P = 0.002). In a binary logistic regression model, only depression was independently associated with insomnia (OR = 49.655, 95%CI = 2.870-859.127, P = 0.007).

Table 1. Personal and Demographic Characteristics of Patients with COVID-19

Variable	Outpatients (N = 65)	Inpatients (N = 65)	P
Age (years)	40.00 (32.50 - 48.00)	45.00 (37.50-52.50)	0.019*
BMI (kg/m²)	25.74 ± 2.83	27.72 ± 6.24	0.038**
Sex (female)	35 (53.8%)	25 (38.5%)	0.079***
Marital status (single)	11 (16.9%)	11 (16.9%)	
Education (primary)	15 (23.1%)	35 (53.8%)	< 0.001***
Occupation (unemployed)	19 (29.2%)	25 (38.5%)	0.266***
Income (low)	14 (21.5%)	19 (29.2%)	0.083***
History of psychiatric visits	8 (12.3%)	13 (20.0%)	0.233***
Psychiatric drug use	3 (4.6%)	8 (12.3%)	0.115***
Medical comorbidity	20 (30.8%)	35 (53.8%)	0.008***
Contact with COVID-19 patients	25 (38.5%)	10 (15.4%)	0.003***
Loss due to COVID-19	3 (4.6%)	4 (6.2%)	> 0.99***

BMI: body mass index; COVID-19: coronavirus disease 2019
*Mann-Whitney test
**Independent samples t-test
***Chi-square test

Table 2. Mental Health and Sleep Status in Patients with COVID-19

Variable	Outpatients (N = 65)	Inpatients (N = 65)	P
Depression			
None	8 (12.3%)	10 (15.4%)	
Mild	16 (24.6%)	24 (36.9%)	
Moderate	18 (27.7%)	16 (24.6%)	0.219
Moderately severe	13 (20.0%)	12 (18.5%)	
Severe	10 (15.4%)	3 (4.6%)	
Anxiety			
None to mild	31 (47.7%)	49 (75.4%)	
Moderate	12 (18.5%)	6 (9.2%)	0.005
Severe	22 (33.8%)	10 (15.4%)	
Distress			
None	13 (20.0%)	23 (35.4%)	< 0.001
Partial	5 (7.7%)	20 (30.8%)	

Definitive	7 (10.8%)	4 (6.2%)	
Severe	40 (61.5%)	18 (27.7%)	
Insomnia			
None	19 (29.2%)	23 (35.4%)	
Subthreshold	20 (30.8%)	17 (26.2%)	0.486
Moderate	21 (32.3%)	16 (24.6%)	
Severe	5 (7.7%)	9 (13.8%)	

Chi-square test

Table 3. Regression Analysis Summary for Factors Affecting Psychiatric Symptoms in Patients with COVID-19

Symptom Covariate	Odds Ratio	95%CI		P
		Lower bound	Upper bound	
Depression				
Male sex	0.017	0.000	0.708	0.032
Insomnia	175.935	6.173	5014.155	0.002
Anxiety				
Married	0.102	0.018	0.567	0.009
Insomnia	10.679	1.445	78.901	0.020
Distress				
Insomnia	7.286	2.017	26.321	0.002
Insomnia				
Depression	49.655	2.870	859.127	0.007

Discussion

In this survey, we assessed immediate mental health outcomes in 130 patients infected with COVID-19. Half of the participants were inpatients and half were outpatients with confirmed COVID-19 infection. We found moderate to severe levels of depression, anxiety, event-related distress, and insomnia among 55.4%, 38.5%, 53.1%, and 39.2% of the participants, respectively. Although the two groups did not significantly differ in terms of insomnia and depression severity, the outpatients showed higher levels of anxiety and event-related distress compared to the inpatients.

The inpatient participants were significantly older, with higher BMI levels, and more medical comorbidities compared to the outpatients. Many other studies reported old age, obesity, and underlying medical conditions to be associated with longer hospitalization (23, 24). On the other hand, education level and history of close contact with COVID-19 patients were significantly higher among the outpatients. The association between higher educational attainment and lower severity of COVID-19 is shown in other populations (25). However, we did not find any reported association between positive history of close contact with COVID-19 and severity or prognosis of COVID-19 in the infected patients. We hypothesized that as our study took place in the early months of the pandemic in Iran, the positive history of close contact could serve as a screening tool that makes people more aware of the threat of this infection. So, they may seek medical services sooner and in less severe stages of disease (26).

Mental health issues are very common in patients suffering from COVID-19. Studies report depression in almost 31-45% of patients (27-29), anxiety in 31-47%

(27-29), event-related distress (post-traumatic stress symptoms) in 28-96% (28, 30), and sleep problems in 34-43% (29, 31). These findings are partly in line with high rates of depression, anxiety, distress, and sleep problems we found in our patients. The observed discrepancies in the reported rates could be explained by the differences in the study population (inpatients/outpatients/both), measurement tools, and the intervals between COVID-19 diagnosis and time of the study which correlated with the disease phase (27).

Comparing the rate and severity of mental health outcomes between inpatients and outpatients, our hypothesis regarding higher prevalence of psychological side-effects among the inpatient population was not supported by the findings in this study. None of the mental health outcomes were more prevalent or more severe in the hospitalized patients. In this study, similar to the findings of Mazza *et al.*, patients who were managed at home experienced significantly higher rates of anxiety (28). Our outpatient participants reported significantly higher rates of event-related distress. Patients managed at home may fear transmitting the disease to their family members, worry about the nature of their symptoms, or be concerned about disruption of medical care if they need intensive medical services (32, 33). While patients with severely deteriorated medical conditions were excluded from this study due to their inability to respond to the questionnaires, other hospitalized patients with less severe symptoms and better course of infection had the chance to share their concerns with the hospital staff and not be worried about availability of medical care. This may in turn lead to reduced levels of anxiety among them.

Considering the results of multivariate regression analysis, all mental health outcomes had direct or indirect (via insomnia or depression) correlation with each other. This finding is in line with many other reports as there is great overlap between dimensions of negative affect, symptoms, and treatment of these conditions (34). In general, people with depression, anxiety, or distress usually experience sleep problems, vice versa and sleep problems on the other hand can lead to these psychiatric disorders (35, 36). We also found inverse associations between male gender and experiencing depression, and between being married and experiencing anxiety. These findings are frequently reported in several previous studies. Studies have indicated that men are generally less likely to develop symptoms of depression compared to women (37, 38). In addition, being single can be a risk factor for anxiety disorders, which is often attributed to the ability of married people to share concerns and relieve the anxiety (39).

Findings from this study particularly showed that mental health issues in COVID-19 patients initiated early in the acute phase of the infection and infection and during the first two weeks of the disease course. Therefore, an immediate psychological assessment could properly address the possible psychological problems of the patients, even in the first few weeks after the diagnosis. Applying internet-based psychological interventions, such as tele-psychiatry, when patients are in isolation can improve mental health of COVID-19 patients (40).

Limitation

One of the limitations of this study was that since this was a real-world study, we could not match the demographic characteristics of the inpatient and outpatient groups. Another limitation was that we did not follow-up these patients and their long-term prognosis needs to be assessed in future studies. Moreover, we measured the outcomes using quick assessment tools that are appropriate for the pandemic conditions; prevalence of definitive psychiatric diagnoses in COVID-19 patients warrants further studies. Finally, while the prevalence and severity of psychological disorders might be higher in this population, we did not include critically ill patients if they could not fill the questionnaires due to their adverse general condition. This can affect our results by underreporting the prevalence and severity of mental health outcomes in COVID-19 patients. All of the above-mentioned issues could have limited the generalizability of our results and thus further large-scale studies are needed to tackle these issues.

Conclusion

In summary, we found the symptoms of psychological event-related distress and anxiety to be more prevalent among outpatients with COVD-19 than the inpatients.

Insomnia can be a potential risk factor for adverse mental health outcomes in these patients.

Acknowledgment

Conflict of Interest

None.

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