Depression, Anxiety, and Stress 1 **Among Patients with COVID-19:** 2 **A Cross-Sectional Study** 3 Malihe Sadat Moayed, Amir Vahedian-Azimi, 4 Golshan Mirmomeni, Farshid Rahimi-Bashar, 5 Keivan Goharimoghadam, 6 Mohamad Amin Pourhoseingholi, 7 Mohsen Abbasi-Farajzadeh, Mostafa Hekmat, 8 Thozhukat Sathyapalan, Paul C. Guest, and Amirhossein Sahebkar 10 Abstract Material and Methods 11 21 This cross-sectional survey was conducted in 22 Aim 2020. All confirmed patients with COVID-19 12 Patients with confirmed COVID-19 infection were included in the study by census sam-13 24 can develop several psychological consepling. Assessment of depression, stress, and 14 25 quences. Epidemiological data on mental anxiety was performed using the DASS-21 15 26 health and psychological disorder inpatients questionnaire. All statistical analyses were 27 16 infected with COVID-19 pneumonia are not performed using R version 3.5.1. 17 28 available in Iranian patients. The purpose of 18 this study was to evaluate the anxiety, stress, Results 29 19 and depression of patients with COVID-19. The questionnaires were completed by 221 20 30 patients with COVID-19 infection (204 males,

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17 females). The mean age was 45.90 ± 7.73 years. Our results indicated that the mean scores of depression and anxiety were at "extremely severe" levels, while stress levels were "severe." The prevalence of "extremely severe" symptoms of depression and anxiety was 54.29% and 97.29%, respectively. The prevalence of severe stress was 46.61%.

Keywords Corona irus 2019, COVID-19, patient, depression, anxiety, stress

Conclusion

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In this study, patients infected with COVID-19 reported severe and extremely severe experience psychological distress. Further studies should focus on the combined use of psychological and molecular biomarker testing to increase accuracy. Overall, the findings demonstrate the necessity of special intervention programs for the confirmed patients with emerging infectious disease COVID-19 to promote mental health needs.

Keywords

COVID-19 · Coronavirus · Patient · Depression · Anxiety · Stress · Iran

19.1 Introduction

Coronavirus disease 2019 (COVID-19) is mainly a respiratory system infection with a newly diagnosed coronavirus thought to have originated as a

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Laboratory of Neuroproteomics, Department of Biochemistry and Tissue Biology, Institute of Biology, University of Campinas (UNICAMP), Campinas, Brazil zoonotic virus which has human pathogenicity [1]. The virus transmits from person to person through close contact or airborne probably as respiratory droplets [2]. At the time of writing (April 28, 2020), there have been approximately three million cases worldwide, with approximately 923,000 having recovered and 211,000 having died [3].

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Therefore, virtually all patients with confirmed or suspected COVID-19 experience fear due to complications of the disease relating to the severe disability and potential death, in the absence of any definitive treatment or vaccine. In addition, symptoms such as fever, hypoxia, and cough, as well as adverse effects of treatment, could lead to worsening of anxiety and mental distress [4, 5]. In the early phases of the severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) outbreaks, a range of psychiatric morbidities, including persistent depression, anxiety, panic attack, psychomotor excitement, psychotic symptoms, delirium, and even suicidality, were reported [6, 7]. The persistence of depression in MERS survivors leads to prolonged chronic post-traumatic stress symptoms even 18 months after the infection [8]. A 14-day quarantine period and restrictions on social contact, which form part of the public health responses to the COVID-19 pandemic, could cause individuals to experience signs such as boredom, a higher level of depression, loneliness, and anger. It also could increase patients' guilt and anxiety about the effects of pathogenesis, quarantine, and stigma on their families and friends [4, 9]. Among the survivors of the SARS outbreak, stress levels were persistently elevated

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1 year later, compared to people who were not infected with SARS. SARS survivors had high levels of psychological distress even 1 year after the outbreak. This evidence suggests that the long-term psychological implications of infectious diseases should not be ignored and mental health services could play an important role in the rehabilitation of patients [6].

To date, epidemiological data on the mental health of patients with COVID-19 in Iran has not been established. The main purpose of this study was to measure the prevalence and severity of this psychological distress and gauge the current mental health burden on patients with a diagnosis of COVID-19 infection.

19.2 Material and Methods

19.2.1 Study Design

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This cross-sectional survey was conducted in February and March, 2020.

19.2.2 Settings and Participants

Bagiyatallah Hospital is one of the main referral centers for the specialized diagnosis and treatment of patients with COVID-19 in Tehran, Iran. Participants were recruited mainly as patients referred to this hospital and patients from other centers who gave consent to participate in the study. Other centers also participated in this study, but since the number of participants from other centers was not high enough to obtain a separate ethics code, the Dean of each center approved data collection for their respective institutions. All patients over 18 years of age who were interested in participating in this study, who could read and write, with no preexisting physical disabilities or mental disorders, were included. All participants were confirmed COVID-19 positive. Census sampling was used.

19.2.3 Sample Size

Cochran's sample size estimation formula in the epidemiologic study was used [10]. The first and second type errors were considered five-hundredth and two-tenths, respectively. A 50% satisfaction probability was assumed to estimate the maximum sample size. The sample size was calculated at 87 patients. According to the nature of the study and the probability of sample size drop, a 20% dropout was considered and the final sample size was therefore calculated to be 110.

19.2.4 Research Tools

Demographic characteristics were self-reported by participants. These included sex, age, job, marital status, educational qualification, and history of chronic disease. The Depression Anxiety Stress Scale (DASS) was used to collect data. This questionnaire was designed and validated by Lovibond in 1995 [11] to measure psychological distress among the community with 21 items. This questionnaire included three subscales and each subscale had seven questions. In the translated version, the choices were never, little, moderate, and many for each question. The lowest score for each question was 0 and the highest score was 3. Validity and reliability of this questionnaire were previously established in Iran. According to the original questionnaire, the three subscales had high internal consistency with Cronbach's alpha values of 0.77, 0.79, and 0.78 for depression, anxiety, and stress, respectively [12]. Another study reported Cronbach's alpha values greater than 0.80 for all scales in an analysis of the effect of the 2008 Sichuan earthquake in China [13].

The questions 3, 5, 10, 13, 16, 17, and 21 were related to depression. Questions 1, 6, 8, 11, 12, 14, and 18 assessed stress. Q questions 2, 4, 7, 9, 15, 19, and 20 were related to anxiety. The cutoff points of the subscales were as follows:

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176 19.2.5 Depression Scores

- 0-4 = normal
- 178 5-6 = mild
- 7-10 = average
- 11-13 = severe
- > 14 = very severe

19.2.6 Stress Scores

- 0-7 = normal
- 8-9 = mild
- 10-12 = average
- 13-16 = severe
- >17 = very severe

188 19.2.7 Anxiety Scores

- 0-3 = normal
- 4-5 = mild
- 6-7 = average
- 8-9 = severe

>10 = very severe

194 19.2.8 Ethical Consideration

The study was approved by the Ethics Committee of Baqiyatallah University of Medical Sciences with code IR.BMSU.REC.1398.438. The objectives of the study were explained to all patients, and informed consent was obtained from the patients to participate in the study. They were also assured of confidentiality.

19.2.9 Statistical Analysis

All analyses were performed using R statistical software (version 3.5.1). The variables included gender (male, female), age (>30, 41–50, <40 years), marital status (married, unmarried), job (governmental, nongovernmental, unemployed, student, and housewife), background disease (yes, no), and qualification (diploma or lower, associate, bachelor's degree, master's

degree, or higher). The values for each variable were presented as the mean and standard deviation. Independent samples *t*-test was applied as a parametric test to compare psychological symptom (stress, depression, and anxiety) scores by gender and marital status. One-way analysis of variance (ANOVA) test was applied to compare the mean differences in psychological factors in terms of age group, job, and educational qualification. A *p*-value of <0.05 was considered significant.

19.3 Results

The DASS-21 questionnaires were completed by 221 patients with COVID-19 (204 males, 17 females). The demographic characteristics are summarized in Table 19.1. The mean age was 45.9 ± 7.73 years. A high proportion of patients reported a nongovernmental (37.1%) job. Most of the participants were unmarried (55.21%). In addition, 31.22% and 29.41% of the patients had "Bachelor" or "Associate" education level, respectively (Table 19.1).

The study results demonstrated that the comparison of mean scores for stress, depression, and anxiety subscales was not statistically significant in terms of "age," "gender," "job," "marital status," "background disease," and "qualification" variables (Table 19.1).

Table 19.2 shows the prevalence and score severity ratings of psychological symptoms among patients with COVID-19 infection. Our results indicated that the mean scores of symptoms of depression and anxiety were "extremely severe," while stress was at "severe" levels. The prevalence of "extremely severe" symptoms of depression and anxiety was 54.29% and 97.29%, respectively. The prevalence of "severe" symptom of stress was 46.61%.

19.4 Discussion

The purpose of this study was to evaluate the anxiety, stress, and depression in hospitalized Iranian patients with confirmed COVID-19 infec-

Table 19.1 The mean (±SD) scores for psychological symptoms in terms of age group, gender, marital status, job, education level, and history of background disease (n = 221)

Variable		Frequency (%)	Anxiety score	Stress score	Depression score
Age	<40 years	70 (31.67)	27.83 ± 4.82	28.97 ± 5.21	27.86 ± 4.70
	41–50 years	103 (46.61)	27.51 ± 5.17	28.54 ± 5.34	28.25 ± 5.02
	>50 years	48 (21.72)	27.58 ± 5.55	28.17 ± 4.88	28.00 ± 5.75
<i>p</i> -value			0.923	0.705	0.876
Gender	Male	204 (92.31)	27.68 ± 5.07	28.47 ± 5.01	28.11 ± 4.84
	Female	17 (7.69)	27.06 ± 5.88	30.12 ± 6.98	27.65 ± 7.46
p-value			0.634	0.354	0.805
Marital status	Married	99 (44.79)	27.33 ± 5.05	28.42 ± 5.03	28.48 ± 5.47
	Unmarried	122 (55.21)	27.87 ± 5.19	28.74 ± 5.33	27.74 ± 4.71
<i>p</i> -value			0.441	0.656	0.277
Job	Governmental	34 (15.39)	28.00 ± 5.72	28.00 ± 4.90	27.59 ± 4.29
	Nongovernmental	82 (37.10)	27.73 ± 5.16	28.66 ± 5.38	28.44 ± 5.71
	Unemployed	54 (24.43)	27.07 ± 4.77	28.74 ± 5.43	28.67 ± 4.88
	Student	39 (17.65)	27.74 ± 5.30	28.31 ± 5.14	27.28 ± 4.91
	Housewife	12 (5.43)	28.00 ± 4.75	30.17 ± 3.95	26.83 ± 3.56
p-value			0.922	0.790	0.536
Qualification	Diploma or lower	30 (13.57)	26.73 ± 4.25	28.93 ± 4.63	28.27 ± 4.75
	Associate	65 (29.41)	28.21 ± 5.11	28.31 ± 5.79	27.97 ± 5.45
	Bachelor's degree	69 (31.22)	27.77 ± 5.29	28.14 ± 5.24	28.43 ± 4.63
	Master's degree or higher	57 (25.73)	27.26 ± 5.39	29.30 ± 4.70	27.65 ± 5.37
p-value			0.553	0.598	0.846
Background disease	None	144(65.16)	28.14 ± 5.08	28.81 ± 5.35	28.20 ± 5.13
	Cardiovascular	16 (7.24)	27.13 ± 6.41	29.13 ± 3.72	26.75 ± 5.05
	Diabetic	21(9.33)	26.95 ± 5.24	29.33 ± 5.03	28.00 ± 5.10
	Hypertension	16 (7.24)	25.88 ± 4.98	26.50 ± 4.10	27.75 ± 4.31
	Allergy	12 (5.44)	26.50 ± 4.10	25.17 ± 5.15	28.00 ± 5.66
	Chronic kidney	7 (3.33)	27.14 ± 5.27	31.14 ± 6.62	30.28 ± 5.71
	Chronic liver	5 (2.26)	26.40 ± 4.56	29.20 ± 2.28	26.80 ± 4.60

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Psychological variable		Frequency	%
Depression	Moderate	16	7.25
	Severe	85	38.46
	Extremely severe	120	54.29
	MEAN ± SD	28.07 ± 5.07	
Anxiety	Severe	6	2.71
	Extremely severe	215	97.29
	MEAN ± SD	27.62 ± 5.13	
Stress	Mild	1	0.45
	Moderate	94	42.53
	Severe	103	46.61
	Extremely severe	23	10.41

 28.59 ± 5.19

Table 19.2 Prevalence and score severity ratings of depression, anxiety, and stress among patients with coronavirus infection (n = 221)

tion. This can serve as important evidence to manage the promotion of mental health among patients with COVID-19. The results of the current study indicated that the patients with confirmed COVID-19 revealed a high prevalence of symptoms associated with mental disorders. All of the patients reported varying levels of depression, anxiety, and stress. Extreme anxiety was found in 97.27% of patients and severe depression signs were reported by 54.29% of patients.

MEAN ± SD

All patients who participated in the study had signs of stress. The prevalence of severe symptoms of stress was 46.61%. Similar results were found in 90% of SARS-infected patients. There was an increased prevalence of general stress and negative psychological effects in patients infected with SARS [14]. Another study reported that patients with MERS infection had an increased incidence of clinically relevant depressive and post-traumatic stress disorder (PTSD) symptoms [8]. Mac et al. reported that 44% and 47.8% of survivors of SARS suffered from respective depressive symptoms and PTSD after infection [15].

None of the demographic variables appeared to contribute to the mean scores of depression, anxiety, and stress. We did not observe any effect of age in our sample of patients. However, Yang et al. reported that older adults in crisis conditions could experience significantly more distress. Therefore, the older population may need relative more mental health intervention [16].

Stress levels were not related to educational qualifications indicating that patients with all levels of educational qualifications who are positive for COVID-19 were adversely affected.

There is growing evidence that in confirmed or suspected COVID-19 infection, patients will need more advanced mental healthcare [17]. Despite the mental health problems reported among patients with COVID-19, few of the healthcare workers on the frontlines had received training in providing mental healthcare [8, 18, 19]. For individuals with suspected or confirmed COVID-19 infection who are under treatment (quarantine or at home), health service personnel should provide medical care and mental healthcare [20]. Special attention needs to be paid for the behavioral and mood changes of these patients. Insomnia, anxiety, anger, rumination, decreased concentration, low mood, and loss of energy are listed as warning symptoms that should be evaluated and managed by mental healthcare professionals [17]. In view of this, there is an urgent need to develop and recommend online and on-site mental health interventions such as psychotherapy [21]. This should involve multidisciplinary mental health teams with expertise in specialized psychiatric treatments to provide appropriate mental health services during and after this COVID-19 epidemic with specific treatment plans, progress reports, and health status updates. There is a need to services to provide psychological secure

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counseling in this group of patients. There should be more use of electronic devices and applications for affected patients as well as their families and members of the public. There is also a need to establish safe communication channels between patients and families. To date, mental health interventions are only provided for those presenting with more severe mental health problems [5]. Since personnel such as clinical psychiatrists, psychologists, and mental health social workers are unable to enter isolation wards for patients with COVID-19, frontline healthcare workers should be trained to provide psychological interventions for patients with COVID-19 in hospitals [20].

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One of the limitations of this study was the single-center cross-sectional survey design which limits the generalizability of the findings. In addition, this study was conducted at the onset of the COVID-19 outbreak, and, therefore, there might be further changes in the mental health status of these patients. Finally, we did not assess the risk factors that may have affected depression, anxiety, and stress in patients with COVID-19 infection, and the prior absence of mental disease in these patients was selfreported. Further studies should focus on the incorporation of molecular biomarkers into such tests to increase accuracy. Such biomarkers should be easily accessible for ease of sampling and to minimize patient discomfort. For example, this could include analysis of stress-related biomarkers such as cortisol and alpha-amylase A in saliva [22, 23] and proinflammatory cytokines such as tumor necrosis factor alpha and interleukin (IL)-1 and IL-6 in blood serum or plasma [24, 25].

19.5 Conclusions

In this study, patients infected with COVID-19 reported severe and extremely severe psychological distress. There is a need for introduction of the mental health interventions in this patient group. As the situation has now progressed to a pandemic, the effects on mental health could be even more profound. This is also complicated

by the risk of further outbreaks, the lack of treatments and a vaccine, as well as the effects on the economy at a global level. Given these challenges, it will be important to incorporate the use of molecular biomarkers to increase the accuracy of assessing the dynamic changes in mental health during the evolution of the pandemic.

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Conflict of Interest The author(s) declare no conflicts of interest with respect to the authorship and publication of this article

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