Original Article

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TANAFFOS

Pulmonary Function, Anxiety, Depression, and Sleep Quality after Recovery from COVID-19

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Background: The COVID-19 pandemic has affected human beings worldwide. After recovery from the disease, the pulmonary function and physiological characteristics of COVID-19 patients are not well documented. The current study aims to assess post-COVID-19 lung function, anxiety, depression, and sleep quality within three months after recovery from the disease.

Materials and Methods: Ninety-seven patients (21 outpatients and 76 inpatients) with COVID-19 were followed three months after recovery. They were divided into two groups according to the severity of the disease. The spirometric parameters included FEV1, FVC, and FEV1/ FVC. A 6-minute walk test (6-MWT) was recorded. Besides, sleep quality using Pittsburgh Sleep Quality Index (PSQI) and mood status in two dimensions of anxiety and depression using the Hospital Anxiety and Depression Scale (HADS) were compared between the groups.

Results: More than 70% of the studied population presented at least one of the COVID-19 infection-related symptoms within three months after recovery. spirometric measurements revealed non-significant differences between the patients with severe versus non-severe COVID-19 in terms of FVC (P=0.805), FEV1 (P=0.948), FEV1/FVC (P=0.616), and 6MWT (P=0.409). Based on PSQI, sleep quality was significantly associated with the severity of disease (P=0.031), but HADS assessments were not significant (P>0.05).

Conclusion: This study demonstrated that a significant proportion of COVID-19 patients have corona symptoms and abnormal pulmonary function tests three months after recovery. Besides, sleep quality was considerably affected by the severity of the disease and was directly associated with the post-COVID-19 mood of the patients. It seems necessary to consider and control the long-term consequences of this infection regardless of the disease severity.

Keywords: Pulmonary Function; Anxiety; Depression; Sleep Quality; COVID-19

INTRODUCTION

In December 2019, a novel coronavirus emerged in Wuhan, China, and became a serious threat to human health (1). WHO introduced the coronavirus disease 2019 (COVID-19) as a world pandemic in March 2020 (2). By 15 October 2021, the disease infected more than 239 million people worldwide.

COVID is a complex disease; the infection can present as a mild disease with spontaneous recovery, but some patients show multi-organ failure (3). Lung distress and damage, liver injury, anosmia, encephalitis, myocardial infarction, and acute kidney injury have been reported in COVID-19 patients (4).

The lung is the main site of COVID-19 infection (5, 6). In a meta-analysis study on 46,959 patients in China, acute respiratory distress syndrome (ARDS), bilateral and unilateral pneumonia, irregular lesions, thickening of the bronchovascular bundles, grid form shadow, and hydrothorax were found in COVID patients (7). However, as more patients are recovered from illness, the aftereffects of the disease may threaten their health (4, 6, 8). Outcomes of COVID-19 are still unknown, but there are documents presenting pulmonary fibrosis and lung lesions in patients with SASR-CoV1 and MERS after recovery (9, 10). A patient's health conditions and age are important factors in recovery time (4).

COVID-19 is also a significant stressor for many people. Some documents show that COVID-19 is associated with altered sleep quality, anxiety, and stress. All of these factors have an essential effect on health (11).

Usually, stress symptoms are observed in the COVID-19 recovered patients. The signs disappear after several weeks, but patients may experience psychophysical symptoms such as depression and anxiety for a longer time. The hospital environment, lingering effects of the virus, quarantine, avoiding some rehabilitation services from improved patient admissions, and social distancing might increase the risks of psychological symptoms (4).

If, after some time, the diseases were observed in COVID-19-recovered patients, healthcare workers will face a big challenge. Hence, monitoring infected people can have many benefits. Also, until an effective drug and vaccine are discovered, it is necessary to know intermediate and long-term outcomes to support patients.

In this study, we followed up COVID-19 patients to identify problems with pulmonary function, anxiety, depression, and sleep quality.

MATERIALS AND METHODS

Patient population

Ninety-seven patients (21 outpatients and 76 inpatients) with COVID-19 from different hospitals in Isfahan city were included in this study from 9 July to 10 December 2020. Infection with SARS-CoV-2 in patients had been confirmed by real-time PCR and clinical symptoms. Patients were invited to refer to our clinic in the third month after recovery from the disease. Patients with a previous history of Chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF), ischemic heart disease (IHD), age <18 years, and people with movement disorders who were unable to do exercise tests such as six-minute walk test (6MWD), were excluded from the study. The incomplete records were not analyzed. According to the severity of COVID-19 disease, patients were categorized into two groups: group 1: The patients who required intensive care unit (ICU) admission, non-invasive ventilation (NIV), intubation, or had O_2 saturation of less than 90% were categorized as severe COVID-19 (13); otherwise, as non-severe.

Assessment at follow-up

All discharged COVID-19 survivors were assessed for clinical symptoms including dyspnea at rest or on exertion and coughing. The patient's disease severity was determined according to the classification represented by the World Health Organization(12). They were categorized as severe versus non-severe COVID-19 infection. The spirometric variables, e.g., forced expiratory volume in the first second of exhalation (FEV1), forced vital capacity (FVC), FEV1/ FVC ratio, and 6-minute walk test in addition to parameters including oxygen saturation (O_2 sat), and heart rate were measured before and after exercise and distance walked according to the valid guidelines and references.

Demographic data, clinical symptoms, medical history, laboratory data, and drugs during hospitalization were extracted from the patient's medical record.

Two questionnaires, including the Pittsburg Sleep Quality Index (PSQI) for sleep quality and the Hospital Anxiety and Depression Scale (HADS) for mood disorders were filled out by the patients.

PSQI contains seven items and assesses the quality and quantity of sleep. Each item is scored between 0–3 and the total score ranges between 0 and 21(13). The higher score represents lower sleep quality (PSQI ≤ 5= good sleep, PSQI> 5= poor sleep).

HADS has 14 questions, seven for anxiety and seven for depressive symptoms(14). Each question is coded from 0 to 3, and the total scores can therefore vary from 0 to 21 (0 <HADS> 7=normal, 8<HADS> 10 = borderline, 11 <HADS> 21 = abnormal). Both questionnaires are valid and reliable.

Ethical issues

The study's goals were explained to the subjects while participation in the research was voluntary. Participants signed written informed consent. The study protocol was approved by the Ethics Committee of Isfahan University of Medical Sciences, Isfahan, Iran (approval number: IR.MUI.MEDREC.1399.065).

Statistical analysis

The analysis was conducted using SPSS software (version 21, 2007, SPSS Inc., Chicago, IL, USA). Continuous and categorical variables were reported using mean with standard deviation (SD) and percentage, respectively. Data were analyzed using the Chi-square test, Student's t-test, paired t-test, ANOVA, and Pearson's correlation coefficient. P-value <0.05 was considered significant.

RESULTS

Ninety-seven COVID-19 patients were referred to our clinic to assess their pulmonary, anxiety, depression, and sleep quality status within three months after recovery from the disease. Fifty-three patients met the criteria for severe disease and the others were categorized as non-severe group. Among all the included patients, seventy-six were hospitalized, among whom 25 were admitted to ICU, and 5 of the ICU-admitted patients were intubated.

The mean age of the studied patients was 52.48 ± 12.894 years (ranging from 19 -92), and the mean BMI was 28.63 ± 8.9 kg/m^2. Fifty-nine (60.82%) of the subjects had more than a high school education. At least one underlying disease was seen in 49 (50.51%) cases. Most common illnesses were hypertension, followed by diabetes. Six patients reported having a history of smoking.

Table 1 shows the demographic and chronic medical diseases among the studied population. Accordingly, the patients were similar in terms of age (P-value=0.121), gender distribution (P-value=0.140), BMI (P-value=0.455) and medical conditions including cardiovascular disease (P-value=0.201), hypertension (P-value=0.409), respiratory diseases (P-value=0.995), diabetes mellitus (P-value=0.178), kidney failure (P-value>0.99), and cancer (P-value=0624).

The chest pain complaint (P-value=0.001) and gastrointestinal symptoms (P-value=0.008) were significantly improved within three months after the hospitalization; however, the other symptoms revealed non-significant differences (P-value>0.05) (Table 2).

Spirometric parameters

54 (55.1%) and 40 (40.8%) of the subjects had FVC and FEV1 of less than 80 % of predicted, respectively; however, all participants had FEV1/FVC ratio above 0.7. The comparison of spirometric variables showed non-significant differences between the two assessed groups. Besides, other assessments, including 6MWD, heart rate before and after the test, and oxygen saturation after the test, did not reveal statistically significant differences comparing those with severe versus non-severe COVID-19 (P-value>0.05); however, oxygen saturation of the patients with a non-severe course of the disease was remarkably higher than the latter before the 6MWT.

Sleep quality, anxiety, and depression

Our study revealed that 19.8% of participants had suitable sleep quality. According to the HADS questionnaire, 50.5% and 22.6% of patients were within the

normal and borderline scores for anxiety and 48.4% and 37.6% for depression, respectively. The frequency of responses compatible with good sleep quality according to PSQI was remarkably higher among those with non-severe COVID-19 than those with a history of severe COVID-19 (P-value=0.031). HADS A (P-value=0.496) and HADS D (P-value=0.326) total scores did not differ between the groups. Gender (P-value=0.029) and anxiety (P-value=0.001) were risk factors for sleep quality. A statistically significant association was also observed between sleep quality and anxiety (P-value=0.006) (Table 4).

Table 5 represents the Spearman correlation test applied to assess the association of spirometric characteristics with various on-admission laboratory tests. Based on this table, none of the assessed variables were related to the spirometric measurements.

Table1. The baseline information and medical history in COVID patients

Variables		Total	Non-severe (n= 44)	Severe (n= 53)	p-value
Gender	Female	36	20(55.6%)	16(44.4%)	0.121
	Male	61	24(39.3%)	37(60.7%)	
Age, year	52.48 ± 12.894		50.36± 12.62	54.27±12.97	0.140
BMI, kg/m	28.63 ± 8.9		27.68±4.26	28.34± 4.33	0.455
IMV	No	92	0 (0)	92 (100)	-
	Yes	5	0 (0)	5 (100)	
NIV	No	88	0 (0)	88 (100)	-
	Yes	9	0 (0)	9 (100)	
Heart disease	No	86	41(47.7%)	45(52.3%)	0.201
	Yes	11	3(27.3%)	8(72.7%)	
Hypertension	No	71	34(47.9%)	37(52.1%)	0.409
	Yes	26	10(38.5%)	16(61.5%)	
Respiratory disease	No	86	39(45.3%)	47(54.7%)	0.995
	Yes	11	5(45.5%)	6(54.5%)	
Diabetes	No	78	38(48.7%)	40(51.3%)	0.178
	Yes	19	6(31.6%)	13(68.4%)	
Kidney failure	No	95	43(45.3%)	52(54.7%)	>0.99
	Yes	2	1(50.0%)	1(50.0%)	
Cancer	No	93	42(45.2%)	31(33.3%)	0.624
	Yes	4	2(50.0%)	2(50.0%)	
Other diseases	No	78	37(47.4%)	41(52.6%)	0.406
	Yes	19	7(36.8%)	12(63.2%)	

Table 2. Comparison of COVID-19 symptoms at the time of hospitalization with follow-up

Symptoms	At the time of hospitalization n (%)	At the time of follow-up n (%)	P- value
Cough	53 (54.63%)	27(27.83%)	0.83
Anorexia	51 (52.57%)	6 (6.18%)	0.68
Fatigue	-	30 (30.93%)	-
Gastrointestinal symptoms	45 (46.39%)	19 (19.58%)	0.008
Chest pain	40 (41.23%)	22 (22.68%)	0.001
Loss of sense of taste	25 (25.77%)	3 (3.09%)	0.162
Shortness of breath	62(63.91%)	70 (72.16%)	0.378

Table 3. Spirometric parameters and 6MWT in COVID-19 patients

Variables	Total mean± SD	Non-severe mean± SD	Severe mean± SD	p-value
FVC	77.14±14.490	77.40±13.28	76.65±15.73	0.805*
FEV1	87.95±67.052	80.21±12.46	81.63±15.79	0.948**
FEV1/FVC	87.03±7.580	86.67±8.15	87.47±7.25	0.616 *
6MWD	461.22±86.663	470.08±74.10	454.04±97.81	0.409*
Heart rate before the test	95.8256±15.542	93.47±14.13	97.54±16.82	0.240*
Heart rate after the test	110.8140±26.21	109.31±26.13	111.52±26.97	0.706*
O2 saturation before the test	93.44± 2.57	94.32±1.97	92.61±2.75	0.002*
O2 saturation after the test	92.76± 3.868	93.24± 6.11	91.50± 4.11	0.125*

* Independent t-test

** Mann-Whitney U test

Table 4. Sleep quality (PSQI total score) and hospital anxiety depression scale (HADS total score) in COVID patients

	PSQ1		HANDS A¶			HANDS D£		
Variable	**Good sleep quality n (%)**	**Low sleep quality n (%)**	**Normal n (%)**	**Borderline n (%)**	**Abnormal n (%)**	**Normal n (%)**	**Borderline n (%)**	**Abnormal n (%)**
Severity								
Non-severe	14(63.6%)	27(37.5%)	18 (39.1%)	10 (47.6%)	13 (54.2%)	23 (52.3%)	12 (35.3%)	6 (46.2%)
Severe	8(36.4%)	45 (62.5%)	28 (60.9%)	11 (52.4%)	11 (45.8%)	21 (47.7%)	22 (64.7%)	7 (53.8%)
P	0.031			0.496			0.326	
Sex								
Female	3 (8.3%)	33 (91.7%)	9 (26.5%)	10 (29.4%)	15 (44.1%)	14 (41.2%)	15 (44.1%)	5 (14.7%)
Male	16 (26.7%)	44 (73.3%)	38 (64.4%)	11 (18.6%)	10 (16.9%)	31 (52.5%)	20 (33.9%)	8 (13.6%)
P	0.029			0.001			0.550	
Age								
Mean ± SD	53.42± 14.531	52.17± 12.617	54.70± 11.723	48.10± 14.275	50.32± 13.680	54.53± 11.739	52.00± 13.700	43.77± 12.833
P	0.709			0.120			0.030	
PSQ1								
Good sleep	-		15 (78.9%)	4 (21.1%)	0	13 (68.4%)	5 (26.3%)	1 (5.3%)
Quality								
Low sleep quality	-		32 (43.2%)	17 (23.0%)	25 (33.8%)	32 (43.2%)	30 (40.5%)	12 (16.2%)
P				0.006			0.129	

¶- HADS anxiety

£- HADS depression

Table 5. The Spearman correlation test assessing the association of spirometric characteristics with on-admission laboratory parameters

		C-reactive protein	Lactate dehydrogenase	D-Dimer	Ferritin	Lymphocyte	Leukocyte count
FVC	R	-0.259	0.022	-0.072	0.111	0.094	-0.067
	P-value	0.070	0.894	0.694	0.566	0.498	0.629
FEV1	R	-0.230	0.041	-0.011	0.129	0.017	-0.140
	P-value	0.108	0.803	0.951	0.504	0.900	0.313
FEV1/FVC	R	0.180	0.157	0.169	-0.198	-0.040	0.150
	P-value	0.211	0.340	0.354	0.302	0.777	0.280

DISCUSSION

The present study describes data from 97 COVID-19 patients within three months after infection with SARS-CoV-2. Patients with COVID-19 experience symptoms such as cough, anorexia, fatigue, gastrointestinal symptoms, chest pain, shortness of breath, and loss of sense of smell and taste. Our data documented no significant differences between the severity of illness and symptoms in follow-up. Older patients had lower oxygen saturation levels. Many studies show that age is a risk factor in COVID-19 infection (15-18). The immune system changes with age, which seems responsible for the increased risk of tissue damage and inappropriate response to infections (19). It is, therefore, no surprise that older patients had more critical conditions.

In follow-up, our study showed that the corona symptoms did not show significant differences between those with severe versus non-severe disease courses. However, it was surprising that a remarkable proportion of the patients who complained of corona-related symptoms remained within three months after the infection. For example, more than 70% of the patients suffered from shortness of breath. Almost all symptoms improved at follow-up, but a statistically significant decrease was limited to gastrointestinal symptoms and chest pain.

There is a high angiotensin-converting enzyme 2 (ACE2) expression in the gastrointestinal tract, and some COVID-19 patients showed gastrointestinal symptoms during the disease and even at follow-up. Different studies reported that 3.6%-11.4% of patients with COVID-19 suffer from gastrointestinal disorders (20, 21). Zhao et al. presented a rate of 30.91% of gastrointestinal symptoms among COVID-19 patients followed for three months. Multiorgan involvement and virus virulence have been notified as the risk factors for the long-term persistence of the symptoms (6).

In a review study on COVID-19 patients, chest pain was presented in a wide range of 1.7% to 33.9% in different countries (22). Similarly, high levels of ACE2 expression in myocytes and the detection of coronavirus RNA in the myocardium have contributed to the etiology of chest pain in COVID-19 (23, 24). Accordingly, scientists have hypothesized that probably, chest pain occurs due to myocyte damage or an inflammatory process in the pleura (25, 26). Further studies are recommended to determine why gastrointestinal symptoms and chest pain were the only symptoms that recovered significantly.

We observed no difference between those with severe and non-severe COVID-19 comparing FVC, FEV1, FEV1/FVC, and 6MWD; however, generally, the period of 6MWT is less among those with a severe course of the disease. Controversial outcomes have been presented in the literature (8). In the Lv et al. study, FVC and FEV1 were higher in non-severe patients, but FEV1/FVC showed no difference between the two groups (27). Another study in Switzerland reported statistical differences in FVC, FEV1, FEV1/FVC, and 6MWD among severe and mild/moderate patients at a 4-month follow-up (18). Follow-up at different times, dissimilar designs, and various samples may explain different study results.

We found significantly better sleep quality among those with non-severe COVID-19 infection, while the other psychological parameters did not differ. In agreement with the current study, Jiang et al. documented that patients with severe and moderate symptoms experienced more sleep problems than patients with mild symptoms. They reported that older adults were more likely to have sleep disorders (28).

In the present study, age was a risk factor for depression following COVID-19 incidence. A study in Italy supported our results regarding the association of gender with poorer sleep quality in females. In that study, sleep problems were lower in men, while age did not affect sleep quality and the incidence of post-COVID-19 anxiety or depression. Sex and age appeared to be risk factors for anxiety in Casagrande's study (29). In a study in China, sex was not significantly associated with sleep quality, anxiety, and depression. Older participants experienced a better mood condition(30). Different questionnaires to assess

sleep quality, anxiety, and depression, diversity in the sample populations, and methods in the various studies made the comparison difficult.

Anxiety was remarkably associated with sleep quality in the current study. Extensive research has evidenced the importance of quality sleep in anxiety and depression. Poor sleep quality adversely affects health status and immune response (31-33).

CONCLUSION

Our results revealed that approximately 70% and 55% of COVID-19 patients have corona symptoms and abnormal pulmonary function test (PFT) three months after recovery, regardless of their infection severity. However, no significant differences were found between those with severe versus non-severe disease courses. Besides, sleep quality was considerably affected by the severity of the disease and was directly associated with the post-COVID-19 mood of the patients. Accordingly, it seems necessary to consider and control the long-term consequences of COVID-19 even if the disease was not severe.

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Conflict of interest

No Conflict of interest

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