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Two Months Follow-Up of 139 Unvaccinated COVID-19 Patients Based on Clinical and Imaging Data

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ABSTRACT

Introduction: To understand the effects of COVID-19 vaccines it would be essential to have knowledge about the effects of the disease during the time that vaccines were unavailable. Hence, we tracked the clinical outcomes of Iranian COVID-19 patients during Feb 19th till May 1st 2020 by a longitudinal follow-up study of patients discharged from a university hospital in Iran. **Methods:** Demographic, clinical, and paraclinical data (chest CT scan imaging, and RT-PCR tests) of 139 patients were collected at the admission time. Preliminary clinical, radiological, laboratory, treatment information, and follow up results were extracted and collected from patients' records. **Results:** The mean age of the patients was 60.56±16.32 years. The most common symptoms on admission were dyspnea (79.1%), coughing (77.3%) and fever (73.1%). The common radiological pattern was multifocal patchy ground-glass infiltration. The patients were followed-up for 8 weeks by phone call. During discharge, 24.8% of the patients had no symptoms, the common residue symptoms were weakness and malaise (48.2%), dyspnea (38.7%), coughing (20.4%), hyposmia (18.5%). On week 8, 74.6% of the patients had no symptom. Moreover, 47.14% of CT scan results improved after 4 weeks and 43.39% after 8 weeks. **Conclusion**: Further follow-up studies are required to determine other detrimental illnesses related to the disease and how vaccination against COVID-19 can affect them.

Citation:

INTRODUCTION

Since late December 2019, a group of patients were referred to medical centers worldwide with respiratory symptoms which revealed the emergence of a rapidly-spreading new virus, called SARS-CoV-2 as the cause [1]. Wuhan in China became a place of global attention due to this respiratory illness [2]. The main route of SARS-CoV-2 transmission was suspected to have a zoonotic (animal to human) origin. Bats were identified as the main source of the virus; however, SARS-CoV-2 could be detected in other animals including camels, cattle and cats [3]. The incubation time of SARS-CoV-2 varies in a range of 2-14 days while it may also take up to 19 days [4]. According to the World Health Organization (WHO) report [5], there was around 34'200'000 confirmed cases, 1'020'000 total deaths, and 23'700'000 total recovered globally until October 1st 2020 while Iran with 461'000 confirmed cases ranked 13th among the countries [5]. At that time, based on WHO reports, SARS-CoV-2 mortality rate was 4.4%, compared with 9.6% (SARS) and 34.4% (MERS) which confirmed that SARS-CoV-2 is not as fatal as anticipated initially [6]. It was reported that even after the alleviation of symptoms after therapies, SARS-CoV-2 relapse is still a significant risk [7] and the patients could be virus carriers [8]. The disease known as COVID-19 was declared a pandemic by the WHO, with common clinical manifestations such as fever, coughing, shortness of breath, sputum production, fatigue, sore throat, headache, gastrointestinal symptoms and vomiting [9]. SARS-CoV-2 was reported to affect smell and taste senses in the infected patients as the main COVID-19 neurological manifestations which are known as frequently-reported early symptoms [10, 11]. Computed tomography (CT) imaging of lungs of SARS-CoV-2-infected patients shows subpleural ground-glass opacity as the most common pattern; however, other patterns may be seen, including banding, consolidation, branchial thickening and nodules [12, 13]. Old age and underlying disorders such as chronic obstructive pulmonary

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disease, hypertension, cardiovascular disease, diabetes and obesity may cause the disease to progress quickly to acute respiratory distress syndrome, septic shock, metabolic acidosis, and coagulation dysfunction and even death [14].

To confirm the clinical diagnosis, RT-PCR on nasopharyngeal swabs is applied. Moreover, CT imaging of lungs is a critical complement in conjunction with RT-PCR for diagnosis of the disease [15]. COVID-19 pandemic is an urgent international concern of public health that requires an international coordinated effort to fight against it [16]. The therapeutic options may consist of antiviral drugs and immunomodulators; however, no drugs have so far been specifically approved for SARS-CoV-2 infection treatment. Therefore, repurposing of approved drugs for other conditions has been followed [17]. Previous studies have described the clinical, demographic characteristics, and diagnostic methods of the disease. There are few studies about short-time follow-ups of discharged patients (18-19-20). This cross-sectional study is one of the first reports of COVID-19 patients from Iran that has followed the patients, post-discharge, and also presents the demographic, clinical, and paraclinical characteristics at the admission time. These data are important as they were collected during the time that vaccination against a disease was not available and could be used as a reference for understanding the effects of vaccination on hospitalization and symptoms of COVID-19 patients.

MATERIALS AND METHODS

Ethics Statement

This study was approved by the Islamic Azad University of Medical Sciences Ethics Committee (IR.IAU.PS.REC.1399.036).

Study Design

This Single-Centre, follow-up study performed from Feb 19th till May 1st 2020. In this study, informed consent obtained from included data of 183 confirmed COVID-19 patients from a hospital related to Islamic Azad University in Tehran, based on clinical features, chest CT scan, and RT-PCR collected. COVID-19 diagnosis was based on the Diagnosis and Treatment Program of COVID-19 released by the National Health Commission of CORONA in Iran (initial test result was positive or repeat test results was positive or if there was a high clinical pretest probability of COVID-19). Preliminary clinical, radiological, laboratory, and treatment information was extracted and collected from patients' records. Patients were divided into three groups: mild, moderate, and severe, based on their clinical and imaging characteristics. Severe patients were defined as SpO_2 <90% at rest with room air, lung involvement more than 50%, respiratory rate (11) >30/min, or need for supportive treatments. Moderate patients were defined as SpO_2 90-93% in room air, RR 24-30/min, chest CT involvement more than 25%. Mild patients were defined as SpO_2 >93% in room air, RR<24/min, normal chest CT scan, or <25% involvement. The patients in our study were related to moderate or severe groups.

Discharge criteria were based on the National Health Commission of CORONA in Iran at the time, namely afebrile for at least 2 days, SpO_2 >93% in room air, resolved respiratory symptoms and RR<24/min, and at least 14 days quarantine at home. Out of 83 patients, 30 died at the hospital from COVID-19 and 153 patients were discharged from the hospital. Eleven patients could not be contacted after their discharge, and 3 patients died after their discharge from complication; therefore, were excluded from this study. Finally, 139 COVID-19 patients were included in the study.

Data Collection

Collected data included patient demographic information, travel history within the past 14 days, household contact information, influenza vaccination history, onset symptoms, comorbidities, triage vital signs, initial laboratory tests, initial electrocardiogram results, inpatient medications (including Oseltamivir, Hydroxychloroquine, Lopinavir/Ritonavir, Ribavirin, Sofosbuvir, IV Ig, Corticosteroid, Azithromycin; It should be mention that at the beginning of the epidemic, these drugs were used; however later newer drugs were added. The treatment regimen was according to Iran's national guideline for novel coronavirus infection at the time, supportive treatments (including invasive mechanical ventilation, kidney replacement therapy, hemoperfusion), and outcomes (including the length of stay, discharge symptoms, readmission, and mortality). Radiologic records were obtained from patients' medical records. The onset symptoms and symptoms at discharge were composed of 4 categories: respiratory, gastrointestinal, systemic, and neurologic. The respiratory symptoms included coughing, expectoration, dyspnea, hemoptysis, chest discomfort, pharyngeal pain, rhinorrhea. Gastrointestinal symptoms include diarrhea, nausea, vomiting, loss of appetite, constipation, and abdominal pain; systemic symptoms included fever, myalgia, fatigue, palpitation, backache, malaise and weakness. Neurologic symptoms included hypsomia, taste change, headaches, dizziness and central vascular accident symptoms. Severity of lung involvement was classified based on CT scan criteria to 4 stages: 1: up to 25 %, 2: 26-50 % involvement, 3: 51-75 %, 4: 76-100 % involvements.

Follow-up of the Patients

Patients were followed up every week till eight weeks by phone-calls at weeks 1, 2, 4, 6 and 8. They were asked about the duration of the symptoms, medicines and CT scans taken after their discharge. The obtained information about the symptoms, medication, and CT findings were recorded in a questionnaire form.

Statistical Analysis

Data analysis performed using SPSS version 26. All data of continuous variable were tested for normality using Shapiro–Wilk test. Continuous data are presented as mean ± SD. Categorical outcomes were given as absolute and relative frequencies (%). According to the different data, statistical analysis between groups was analyzed using the ANOVA, or Chi-square or two-sided Fisher's exact test. P<0.05 indicates statistical significance.

RESULTS

Demographics and Baseline Characteristics of COVID-19 Patients

Out of 183 COVID-19 patients admitted to the hospital, 104 were male patients and 79 were female. The age range was from 21 to 96 years old, and the mean age was 60.56±16.32 years. The median age of severe patients (65.10 years) was significantly older than non-severe patients (56.72 years, p<0.05; Table 1).

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Table 1. Demographics and comorbidities findings of COVID-19 patients

Characteristics	Total	Non-severe	Severe	P-value
Demographic				
Age (Mean ±SD)	60.56±16.32	56.72±16.3	65.10±14.8	0.00
Female	79 (43.2%)	42 (53.2%)	37 (46.8%)	0.825
Male	104 (56.8%)	57 (54.8%)	47 (45.2%)	
Weight (Mean±SD)	74.73±13.77	77.39±12.56	71.50±14.5	0.005
Height (Mean±SD)	179.48±125.37	169 ±8.88	192.24±186.32	0.226
BMI (Mean±SD)	26.33±4.56	27.07±3.85	25.45±5.21	0.020
Comorbidities				
Over weight	84 (48.3%)	54 (64.3%)	30 (35.7%)	0.024
Hypertension	84 (46.2%)	36 (42.9%)	48 (57.1%)	0.005
ASA use	63 (35.4%)	27 (43.5%)	35 (56.5%)	0.027
Diabetes	61 (33.5%)	30 (42.9)	31 (50.8%)	0.339
Cardio and cerebrovascular disease	56 (30.8%)	21 (38.2%)	34 (61.8%)	0.004
Hyperlipidemia	21 (12%)	10 (47.6%)	11 (52.4%)	0.443
Flu vaccination	18 (11.6%)	11 (61.1%)	7 (38.9%)	0.807
Respiratory system disease	17 (9.3%)	5 (29.4%)	12 (70.6%)	0.032
Corticosteroid therapy	13 (7.3%)	5 (38.5%)	8 (61.5%)	0.228
Hematologic disorder	11 (6%)	4 (36.4%)	7 (63.6%)	0.215
Autoimmune disease	11 (6%)	3 (27.3%)	8 (72.8%)	0.065
Immunosuppressing drugs	10 (5.6%)	3 (30%)	7 (70%)	0.109
Chronic liver disease	7 (3.8)	3 (42.9%)	4 (57.1%)	0.541
Chemotherapy	6 (3.4%)	3 (50%)	3 (50%)	0.822
Malnutrition	6 (3.3%)	0	6 (100%)	0.750
Malignant tumor	5 (2.7%)	3 (60%)	2 (40%)	0.799
Hyperthyroid	4 (2.3%)	2 (50%)	2 (50%)	0.777
Hypothyroid	11 (6.3%)	5 (45.5%)	6 (54.5%)	
Splenectomy	2 (1.1%)	0	2 (100%)	0.120
HIV	0	0	0	-
Pregnancy	0	0	0	-

The most common onset symptom was exertional dyspnea (79.1%), followed by coughing (77.3%), and fever (73.1%) (Table 2).

The mean duration of the inpatient was 7 days. Patients admitted to ICU were 63 (34.4%) while 99 (54.1%) of patients were in the non-severe group and 84 (45.9%) of them were in the severe group. The mean duration of treatment (days of treatment), was 9.04±4.6 days in total. The most common medication used for the patients was the combination of Hydroxychloroquine and Azithromycin. This combination was used with other antiviral drugs. The mortality rate was 33 (18%), 30 (16.39%) death was related to COVID-19 in the hospital, and 3 after the discharge, related to complications of COVID-19. There was a significant correlation between age and mortality rate (*P*= 0.00). We observed that deceased patients were older (mean age among dead patients was 74.09±14.9, compared with alive patients with mean age 57.28±13.8). Moreover, there was a significant correlation between low blood pressure (*P*=0.001), overweight (*P*= 0.052), cardio- and cerebrovascular disease (*P*= 0.00), and malnutrition (*P*= 0.02) with mortality rate.

Most of the patients had comorbidity diseases; the most common of them were overweight 84(48.3%), hypertension 84 (46.2), diabetes mellitus 61(33.5%), chronic cardiovascular disease 56(30.8%) and respiratory disease 17(9.3%). Hypertension and cardiovascular diseases in severe patients were significantly more than in non-severe patients; however, the overweights in non-severe patients were more than in the severe patients group. (Table1). Considering the laboratory tests, haemoglobin was significantly lower in the severe patients than the non-severe patients. Blood urea nitrogen (BUN), creatinine, and lactate dehydrogenase (LDH) were significantly higher in the severe patients than the non-severe patients (Table 3).

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Table 2. Onset symptoms of COVID-19 patients

Onset symptoms				
Exertional dyspnea	144 (79.1%)	73 (50.7%)	71 (49.3%)	0.051
Cough	140 (77.3%)	74 (52.9)	66 (47.1%)	0.358
Fever	133 (73.1%)	68 (51.1%)	65 (48.9%)	0.145
Malaise(weakness)	113 (63.1%)	55 (48.7%)	58 (51.3%)	0.033
Loss of appetite	111 (62.4%)	59 (53.2%)	52 (46.8%)	0.394
Myalgia	104 (58.8%)	57 (54.8%)	47 (45.2%)	0.719
Chest pain	96 (53%)	45 (46.9%)	51 (53.1%)	0.025
Vertigo	87 (48.6%)	51 (58.6%)	36 (41.4%)	0.386
Dry mouth	80 (47.6%)	45 (56.3%)	35 (43.8%)	0.710
Biphasic symptom	71 (41%)	38 (53.5%)	33 (46.5%)	0.573
Vomiting	68 (38%)	37 (54.4%)	31 (45.6%)	0.850
Nausea	67 (37.4%)	36 (53.7%)	31 (46.3%)	0.743
Chest rale	62 (34.4%)	19 (30.6%)	43 (69.4%)	0.00
Shortness of breath	62 (34.3%)	20 (32.3%)	42 (67.7%)	0.00
Chill	61 (34.3%)	31 (50.8%)	30 (49.2%)	0.352
Diarrhea	61 (34.1%)	40 (65.6%)	21 (34.4%)	0.047
Sweating	54 (31.4%)	27 (50%)	27 (50%)	0.211
Sore throat	55 (30.4%)	25 (45.5%)	30 (54.5%)	0.099
Smell reduction	51 (30.4%)	30 (58.8%)	21 (41.2%)	0.932
Taste reduction	51 (30.4%)	30 (58.8%)	21 (41.2)	0.932
Headache	47 (26.4%)	26 (55.3%)	21 (44.7%)	0.966
Abdominal pain	35 (19.6%)	21 (60%)	14 (40%)	0.534
Sputum	23 (12.7%)	7 (30.4%)	16 (69.6%)	0.012
Low blood pressure	23 (12.6%)	11 (47.8%)	12 (52.2%)	0.499
Common cold symptom	20 (12.6%)	12 (60%)	8 (40%)	0.884
Joint pain	10 (5.6%)	5 (50%)	5 (50%)	0.728
Bloody sputum	10 (5.5%)	5 (50%)	5 (50%)	0.759
Eye redness	4 (2.2%)	3 (75%)	1 (25%)	0.416
Skin bruise	3 (1.7%)	1 (33.3%)	2 (66.7%)	0.447

Table 3. laboratory test findings of COVID-19 patients.

Laboratory findings				
WBC	8235.70±4449.36	7658.03±3977.11	8926.09±4890.85	0.057
Neutrophil	6024.85±3927.7	5830.58±3589.93	6255.54±3927.76	0.456
Platelet	205167.2±112503.5	193266.3±84803.5	219390.2±219390.2	0.121
Lymphocyte	1502.9±1024.6	1450.4±647.5	1565.3±1344.02	0.462
Hemoglobin	13.19±2.40	13.76±2.23	12.52±2.43	0.00
CRP	1.47±0.815	1.38±0.88	1.58±0.71	0.105
ESR	38.15±22.46	35.40±23.45	41.60±20.81	0.092
ALT	53.74±74.81	47.27±58.86	61.31±89.82	0.247
AST	48.55±61.55	41.72±38.58	56.54±80.11	0.137
ALP	214.14±134.09	191.51±100.08	240.01±161.60	0.036
FBS	142.45±65.63	140.09±70.68	144.56±61.29	0.723
BS	146.95±74.66	145.10±66.80	149.12±83.45	0.755
CPK	215.19±351.74	179.56±326.36	255.98±376.9	0.188
BUN	21.17±17.12	17.72±14.35	25.18±19.18	0.004
LDH	525.84±253.2	466.44±221.8	595.8±270.9	0.001
Cr	1.36±0.6	1.25±0.45	1.49±0.71	0.007
Ca	9.01±0.89	9.07±1.07	8.96±0.66	0.560
P	3.24±0.97	3.31±1.02	3.17±0.99	0.528
INR	1.1±0.13	1.11±0.13	1.09±0.12	0.406
BC	0.01±0.096	0.02±0.1	0	0.257
UA	0.12±0.366	0.09±0.229	0.16±0.365	0.264
UC	0.05±0.209	0.02±0.152	0.07±0.25	0.334
PT	13.70±0.935	13.75±0.85	13.64±1.02	0.536
PTT	35.88±6.4	35.67±5.4	36.09±7.29	0.709
Procalcitonin	4.06±18.27	7.76±28.3	1.41±2.44	0.311
Vitamin D3	34.14±20.69	35.11±18.98	32.85±22.96	0.553
D diameter	2302.96±2313.51	1577.13±1366.59	3061.77±2842.12	0.030
Amylase	72.09±56.85	78.50±61.24	62.99±50.69	0.440

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Lipase	62.79±62.02	76.42±71.59	41.73±37.15	0.152
Troponin	296.88±2012.8	25.12±32.45	549.22±2787.2	0.244

Complications

Sixty percent of all patients reported no complications. The most common complication among all was ARDS (10.5%; and the most essential cause of death) followed by bacterial pneumonia, ataxia, CVA, COPD, hepatitis, and pancreatitis with the same percentage of 2 (2.1%). Abdominal adenitis, GI bleeding, quadriplegia, hyperpigmentation, left hand paresis due to axillary neural plexus, and zona each in one patient. Hepatitis and bacterial pneumonia were observed only in the severe group of COVID-19 patients. Among them, hyperpigmentation, left-hand paresis, zona, and pancreatitis were cured at week 2 of the follow-up.

Characteristics of Chest CT Scans on Admission and After Discharge

During the follow-up period, only 53 (29%) discharged patients underwent chest CT. At the time of admission; all of the patients had chest CT scan, 1.1% had a normal chest CT scan at the admission. Meanwhile, 23% showed more than 50% multifocal patchy ground-glass infiltration in both lungs as the most common radiologic pattern, (19.7%) patients had 40% involvement of both lungs with the subpleural ground-glass pattern, 13.1% showed 30% involvement both lungs, 16.9% presented with 25% involvement of both lung, 8.2% had less than 25% lung involvement and 2.2% had more than 75% involvement of both lungs. The lower lobes were the most frequently involved lobes. Pure ground-glass opacity was the most common pattern. During the follow-up period, 47.14% of patients had complete chest CT recovery at week four, 43.39% of cases showed complete chest CT recovery at week eight, 9.43% of chest CT scans showed 20% -40% fibrosis. There was a significant correlation between lung damage confirmed by CT scan at admission and shortness of breath, chest rales. No significant correlation could observe between disease severity and the CT scan severity; during the follow up period, complete recovery in severe group 9(28.1%) and non-severe group 23(71.9%) and partial recovery in severe patients 9(42.9%), and in non-severe patients 12(57.1%). There was a correlation between severity and lung recovery.

Follow-up Symptoms of COVID-19 After Discharge

The observational study of patients' symptoms at discharge showed; 24.8% of patients did not have any symptoms, but weakness (48.2%), dyspnea (38.7%) and cough (20.4%), smell reduction 25(18.5%), loss of appetite 12(8.8%), sweating 11(8%), taste reduction 10(7.3%), and chest pain 10(7.3%) were the most frequent symptoms among other patients. After the first week of follow-up, no symptom be observed in 25.7% of patients, but at this time, weakness/malaise, dyspnea, cough, and smell reduction as common symptoms be observed in the rest of patients. During the second week of follow up, 35.5% of patients showed no symptoms, and the common residue symptoms were weakness/malaise (35.5%), dyspnea (29.7%), cough (13.8%), and smell change (13.8%). At week four of follow up after discharge, 59.4% of patients had no symptoms, while weakness/malaise (19.6%), dyspnea (18.8%), cough (5.8%), and smell change (5.1%) were the common symptoms in the rest. At week six after discharge, 73.9% of patients reported no symptoms; however, some of patients reported weakness/malaise (10.9%), dyspnea (11.6%), cough (2.9%), and smell reduction (2.9%) as common symptoms. On week eight of follow up, 74.6% of patients did not have any symptoms, dyspnea (11.6%), weakness/malaise (11.6%), cough (2.6%), and smell change (2.2%) be observed in the rest of patients. It is worth mentioning that, the severe group showed higher percentages of reported symptoms than non-severe patients. The most prolonged symptoms were weakness/malaise and dyspnea during follow up period, however; other symptoms are observed too, but with low rate (Table 4). After discharge two patients showed symptoms of relapse, and admitted to the hospital; three patients died because of complication of COVID-19 mhs_alijani@yahoo.com (one from quadriplegia, two from bacterial pneumonia).

Table 4. A) Follow up symptoms of COVID-19 discharged patients.

	Discharge				**1 weeks after discharge**				**2 weeks after discharge**			
	Total N (%)	**Non severe N (%)**	**Severe N (%)**	***P*-value**	**Total N (%)**	**Non severe N (%)**	**Severe N (%)**	***P*-value**	**Total N (%)**	**Non severe N (%)**	**Severe N (%)**	***P*-value**
No symptom	34 (24.8)	24 (70.6)	10 (29.4)	0.4	35 (25.7)	23 (65.7)	12 (34.3)	0.8	49 (35.5)	28 (57.1)	21 (42.9)	0.1
Weakness (malaise)	66 (48.2)	46 (69.7)	20 (30.3)	0.2	66 (48.5)	46 (69.7)	20 (30.3)	0.2	49 (35.5)	34 (69.4)	15 (30.6)	0.3
Exertional dyspnea	53 (38.7)	30 (56.6)	23 (43.4)	0.1	50 (36.8)	29 (58)	21 (42)	0.2	41 (29.7)	24 (58.5)	17 (41.5)	0.3
Scanty cough	4 (2.9)	2 (50)	2 (50)	0.5	4 (2.9)	2 (50)	2 (50)	0.5	3 (2.2)	2 (66.7)	1 (33.3)	0.5
Chest pain	10 (7.3)	6 (60)	4 (40)	0.7	9 (6.6)	6 (66.7)	3 (33.3)	0.8	8 (5.8)	6 (75)	2 (25)	0.5
Smell reduction	25 (18.5)	15 (60)	10 (40)	0.6	25 (18.4)	15 (60)	10 (40)	0.5	19 (13.8)	12 (63.2)	7 (36.8)	0.8
Sweating	11 (8)	6 (54.5)	5 (45.5)	0.4	11 (8.1)	6 (54.5)	5 (45.5)	0.4	10 (7.2)	5 (50)	5 (50)	0.3
Taste reduction	10 (7.3)	5 (50)	5 (50)	0.3	10 (7.4)	5 (50)	5 (50)	0.3	7 (5.1)	5 (71.4)	2 (28.6)	0.6
Loss of appetite	12 (8.8)	8 (66.7)	4 (33.3)	0.8	12 (8.8)	8 (66.7)	4 (33.3)	0.8	7 (5.1)	4 (57.1)	3 (42.9)	0.3
Cough	28 (20.4)	18 (64.3)	10 (35.7)	0.9	26 (19.1)	16 (61.5)	10 (38.5)	0.7	19 (13.8)	13 (68.4)	6 (31.6)	0.7

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Weight loss	2 (1.5)	2 (100)	0	0.2	2 (1.5)	2 (100)	0	0.2	2 (1.4)	2 (100)	0	0.2
Sputum	3 (2.2)	3 (100)	0	0.1	3 (2.2)	3 (100)	0	0.1	1 (0.7)	1 (100)	0	0.4
Diarrhea	4 (2.9)	3 (75)	1 (25)	0.6	4 (2.9)	3 (75)	1 (25)	0.8	4 (2.9)	3 (75)	1 (25)	0.6
Dry mouth	4 (2.9)	4 (100)	0	0.1	4 (2.9)	4 (100)	0	0.1	4 (2.9)	4 (100)	0	0.1
Abdominal pain	4 (2.9)	4 (100)	0	0.1	4 (2.9)	4 (100)	0	0.1	4 (2.9)	4 (100)	0	0.1
Palpitation	3 (2.2)	3 (100)	0	0.1	3 (2.2)	3 (100)	0	0.1	3 (2.2)	3 (100)	0	0.1
Myalgia	1 (0.7)	0	1 (100)	0.1	1 (0.7)	0	1 (100)	0.1	1 (0.7)	0	1 (100)	0.1
Vertigo	2 (1.5)	1 (50)	1 (50)	0.6	2 (1.4)	1 (50)	1 (50)	0.6	1 (0.7)	0	1 (100)	0.1
Anxiety	2 (1.5)	1 (50)	1 (50)	0.6	2 (1.5)	1 (50)	1 (50)	0.6	2 (1.4)	1 (50)	1 (50)	0.6
Back pain	2 (1.5)	1 (50)	1 (50)	0.6	1 (0.7)	0	1 (100)	0.1	1 (0.7)	0	1 (100)	0.1
Headache	2 (1.5)	1 (50)	1 (50)	0.6	2 (1.5)	1 (50)	1 (50)	0.6	1 (0.7)	1 (100)	0	0.4

B) Follow up symptoms of COVID-19 after discharge **.**

	4 weeks after discharge				**6 weeks after discharge**				**8 weeks after discharge**			
	Total *N (%)*	**Non severe N (%)**	**Severe N (%)**	***P*-value**	**Total N (%)**	**Non severe N (%)**	**Severe N (%)**	***P*-value**	**Total N (%)**	**Non - severe N (%)**	**Severe N (%)**	***P*-value**
No symptom	82 (59.4)	56 (68.3)	26 (31.7)	0.2	102 (73.9)	66 (64.7)	36 (35.3)	0.9	103 (74.6)	65 (63.1)	38 (36.9)	0.5
Weakness (malaise)	27 (19.6)	18 (66.7)	9 (33.3)	0.7	15 (10.9)	12 (80)	3 (20)	0.1	16 (11.6)	13 (81.3)	3 (18.8)	0.1
Dyspnea	26 (18.8)	14 (53.8)	12 (46.2)	0.2	16 (11.6)	9 (56.3)	7 (43.7)	0.4	16 (11.6)	10 (62.5)	6 (37.5)	0.8
Scanty cough	2 (1.4)	1 (50)	1 (50)	0.6	2 (1.4)	1 (50)	1 (50)	0.6	2 (1.4)	1 (50)	1 (50)	0.6
Chest pain	5 (3.6)	3 (60)	2 (40)	0.8	3 (2.2)	2 (66.7)	1 (33.3)	0.9	3 (2.2)	2 (66.7)	1 (33.3)	0.5
Smell reduction	7 (5.1)	5 (71.4)	2 (28.6)	0.6	4 (2.9)	2 (50)	2 (50)	0.5	3 (2.2)	2 (66.7)	1 (33.3)	0.5
Sweating	6 (4.3)	3 (50)	3 (50)	0.4	3 (2.2)	2 (66.7)	1 (33.3)	0.9	3 (2.2)	3 (100)	0	0.1
Taste reduction	4 (2.9)	3 (75)	1 (25)	0.6	3 (2.2)	2 (66.7)	1 (33.3)	0.9	2 (1.4)	1 (50)	1 (50)	0.6
Loss of appetite	4 (2.9)	3 (75)	1 (25)	0.6	2 (1.4)	1 (50)	1 (50)	0.6	2 (1.4)	1 (50)	1 (50)	0.6
Cough	8 (5.8)	4 (50)	4 (50)	0.3	4 (2.9)	2 (50)	2 (50)	0.5	4 (2.9)	2 (50)	2 (50)	0.5
Weight loss	1 (0.7)	1 (100)	0	0.4	1 (0.7)	1 (100)	0	0.2	2 (1.4)	2 (100)	0	0.2
Sputum	0	0	0	-	0	0	0	-	0	0	0	-
Diarrhea	2 (1.4)	1 (50)	1 (50)	0.6	1 (0.7)	1 (100)	0	0.4	1 (0.7)	1 (100)	0	0.4
Dry mouth	4 (2.9)	4 (100)	0	0.1	2 (1.4)	2 (100)	0	0.2	2 (1.4)	2 (100)	0	0.2
Abdominal pain	1 (0.7)	1 (100)	0	0.4	1 (0.7)	1 (100)	0	0.2	1 (0.7)	1 (100)	0	0.4
Palpitation	2 (1.4)	2 (100)	0	0.2	2 (1.4)	2 (100)	0	0.2	2 (1.4)	2 (100)	0	0.2
Myalgia	0	0	0	-	0	0	0	-	0	0	0	-
Vertigo	1 (0.7)	1 (100)	0	0.4	0	0	0	-	0	0	0	-
Anxiety	2 (1.4)	1 (50)	1 (50)	0.6	2 (1.4)	1 (50)	1 (50)	0.6	2 (1.4)	1 (50)	1 (50)	0.6
Back pain	1 (0.7)	0	1 (100)	0.1	0	0	0	-	0	0	0	-
Headache	1 (0.7)	1 (100)	0	0.4	1 (0.7)	1 (100)	0	0.4	1 (0.7)	1 (100)	0	0.4

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DISCUSSION

Based on our knowledge, this study is the first longitudinal follow up study about COVID-19 patients in Iran. Here, we followed-up and assessed clinical characteristics, laboratory findings, chest CT imaging results, mortality rate and complications data during admissions and hospitalizations of Iranian COVID-19 patients up to two months during the time that COVID vaccination was not available. Our aim was to understand the possible outcome of COVID-19 recovered patients and determine if they have any other detrimental illnesses by longitudinal analysis to safeguard their life as a reference for future related studies. In summary, 183 patients were admitted to a university hospital in Tehran. The total mortality rate of the patients (33(18%) after their discharge and 30(16.39%) during hospitalization). Finally, 139 discharged patients were included in the study. The mean age of these patients was 60.56±16.32 years, and in terms of gender, 79 (43.2%) were women and 104 (56.8%) were men. The most common underlying disease were overweight 84 (48.3%), hypertension 84 (46.2%), diabetes 61 (33.6%), and cardiovascular diseases 56 (30.8%). The most common onset symptoms were dyspnea 144 (79.1%), coughing 140 (77.3%), fever 133(73.1%), malaise 113(63.1%), myalgia 104(58.8%) and loss of appetite 111(62.4%). A number of patients had more severe symptoms than others (Table 2).

Taghizadeh et al. have reported in 2020 that early clinical symptoms of COVID-19 might mimic the common cold features; therefore, appropriate diagnosis and isolation of the patients will help to reduce further transmissions [21]. Jun Chen et al. have reported in 2020 that fever has occurred in 235 (94.3%) of the patients [22]. Fever has been proposed as the most common symptom among mild to moderate cases, observed in all studies. Dyspnea has been reported as a marker of severe disease [23]. In our study, symptoms during admission were nearly the same as the other studies. For instance, dyspnea was the most common symptom while coughing was recognized as the second most common one. The most common radiological pattern in our study was multifocal patchy ground-glass infiltration of both lungs (42 patients; 23%). The patients were followed every other week, up to eight weeks by phone calls as shown in Table 4. The majority of symptoms decreased within two to three weeks; however, a few continued for four to eight weeks. Wang and colleagues have shown their study that residual symptoms such as coughing (29.01%), expectoration (6.11%) and chest tightness (6.11%) were still visible at discharge time while they consistently diminished, 2-3 weeks after the recovery [24]. Payus and coworkers in a literature review on neurological involvement in SARS-CoV-2 infections have found that patients with COVID-19 can be affected by neurological symptoms that could be divided into central nervous system involvements (e.g., headache, dizziness, altered mental state, and disorientation, seizures, stroke, flaccid paraparesis, corticospinal weakness, and even coma) and peripheral nervous system involvements (e.g., anosmia and hypogeusia) [18]. Fiani et al. in a review of neurological sequelae of COVID-19 have reported that in Wuhan, China, 36.4% of the severe infections were accompanied with neurological symptoms (19), including ANE, meningitis, hemorrhage, vertigo, cephalgia, impaired consciousness, seizures, ataxia, and acute cerebrovascular disease and damage to the thalamus. In our study, we observed hyposmia (30.4%), taste damage (30.4%), vertigo (48.6%) and rarer cases of CVA and convulsion (1 case), CVA and right-side hemiplegia (1 case), Guillain-Barre Syndrome (1 case), cerebellar ataxia, paraplegia (1 case), and left-hand paresis due to axillary neural plexus (1 case).

Mazrouei et al. have reported acute pancreatitis as a complication of COVID-19 who recovered in two weeks [20]. Hadi et al. have described two relative patients with pancreatitis as a complication of COVID-19 that was admitted to ICU (25). We observed two cases of acute hepatitis with SARS-CoV-2 infection that one was a carrier of HbsAg but not reactivation of HBV who died during hospitalization while the liver function test of another patient became normal when discharged. Wander and colleagues have reported a COVID-19 case as acute hepatitis [26]. Another remarkable result of this study was that after discharge, one of patients after the recovery showed hyperpigmentation in his face. It has also been reported that two Wuhan phsicians who have recovered from severe OVID-19 infection have exhibited altered facial pigmentation which could be due to abnormal liver functions. However in our study, the liver function test of a COVID-19 patient was normal during 8 weeks follow-up and hyperpigmentation disappeared. As we described in Table 4, the majority of symptoms significantly have been diminished at the end of follow up and 74.6% of the patients left without symptoms (more in non-severe patients than the severe patients. Zhang and coworkers have assessed1673 cured patients with COVID-19 in a follow-up study in two different fever clinics. Their results have shown that patients had no fever, sore throat, dyspnea, and cough and all symptoms disappeared at a three-weeks follow-up [27].

Carotti *et al*. have reported that the lung CT-imaging hallmarks of COVID-19 are a bilateral distribution of ground-glass opacities with or without consolidation in the posterior and peripheral lung; however, the predominant findings in later phases include consolidations, linear opacities “crazy-paving” pattern “reversed halo” sign and vascular enlargement (30). In our study, pure ground-glass opacity was the common radiologic pattern, as 23% of the patients showed more than 50% multi patchy ground glass infiltration in both lungs. In the follow-up period of this study, 47.14% of the patients had complete chest CT recovery at week four while 43.39% of the cases showed complete chest CT recovery at week eight and 9.43% of chest CT scans showed 20-40% fibrosis at the end of follow up period. No significant correlation could be observed between the disease severity and the CT scan severity during the follow up period. However, we observed a correlation between the severity of the disease and the lung recovery.

Dou et al. have described serial CT-imaging features in discharged COVID-19 patients from January 28th till February 26 of 2020 regarding two cases who have shown nearly complete recovery during four weeks [31]. Huang et al. have reported that there were 40 non-severe cases and 17 severe cases in a follow up study of 57 patients in which 31 patients (54.3%) had abnormal CT findings and abnormalities had been detected in the pulmonary function tests in 43 (75.4%) of the patients [32]. In our study, most of the symptoms and complications recovered during follow up period.

In conclusion, the results of our study showed that most patients recover if the discharge criteria are met. We suggest that patients be followed-up since a certain number of the patients may die after their discharge due to COVID-19 complications or the relapse of the symptoms. Among the limitations of this study the following could be mentioned. A number of patients died before their pertinent information could be recorded and few did not remember the time of recovery from their symptoms. The psychological aspects of the patients

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were also missing. In many COVID-19 patients, fear and psychological problems may exacerbate their symptoms. Moreover, some of the patients are not willing to take a second CT scan because of the radiation side effects.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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