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Clinical Characteristics of Hospital Follow-up for Patients Hospitalized from SARS CoV-2 (COVID 19) in an Academic Outpatient Internal Medicine Clinic

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Abstract

Background: As of July 2022, there have been more than 91.3 million cases of COVID-19 and nearly 1.03 million deaths in the United States alone. In addition, many people who survived COVID-19 had long-term symptoms, such as fatigue, dyspnea, loss of smell and taste, depression, and anxiety. **Objectives:** The purpose of our study is to evaluate the status of COVID-19 patients who were previously hospitalized. **Methods:** We conducted a single-center retrospective cohort study at Texas Tech University Health Sciences Center and its affiliated University Medical Center under IRB of L21-144. We included all patients hospitalized for COVID-19 and followed up in our Internal Medicine Clinic at any time between April 1, 2020, and April 1, 2021, and reviewed follow-up data for these patients after discharge. **Results:** A total of 128 patients were included; 59 (46%) were men, and 69 (54%) were women with an average age of 59.7 ± 14.8 years. Most of the patients (n = 78, 60.9%) identified their race as Hispanic or Latino origin; the next largest group was Caucasian (n = 29, 22.65%). The average number of days until post-hospitalization follow-up was 36 ± 38 days. The 50% of the patients (n = 64) used telemedicine for follow-up visits. Important comorbidities in these patients included diabetes (n = 84, 65.6%) and hypertension (n = 94, 73.4%). Thirty-four patients (26.6%) reported respiratory symptoms at their follow-up appointments, 24 patients (18.8%) reported constitutional symptoms, 12 patients (9.4%) reported GI symptoms, and 25 patients (19.5%) reported other symptoms, such as paresthesia, lower extremity edema, or psychological symptoms. After hospital discharge, 54 patients had follow-up chest x-rays, and 41 (75.9%) still had abnormal findings consistent with COVID-19 imaging characteristics. Follow-up laboratory tests identified 44 patients (77.2%, 57 tested) with elevated D-dimer levels, 44 patients (78.6%, 56 tested) with high ferritin levels, and 21 patients (35.6%, 59 tested) with elevated troponin T HS levels. **Conclusion:** Long-lasting COVID-19 symptoms in these patients included respiratory symptoms (26.6%), constitutional symptoms (18.8%), GI symptoms (9.4%), and other symptoms, such as paresthesia, lower extremity edema, or psychological symptoms (19.5%). The rate of telehealth follow-up was 50%. Many patients had elevated inflammatory markers that will need follow up to determine the clinical implications.

Keywords
COVID-19, post-COVID-19 syndrome, follow-up

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Introduction

SARS-CoV-2 caused a worldwide COVID-19 pandemic starting in 2020 and is now causing a worldwide endemic infection. The most common symptoms are fever, cough, myalgia, fatigue, headache, dyspnea, sore throat, and diarrhea. In addition, some patients may present with end-organ failure, adult respiratory distress syndrome, shock, acute kidney injury, or even death.[1] Usually these symptoms are

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mild in severity, and patients have been discharged from the hospitals earlier than normal due to shortages of facilities and medical supplies to monitor all COVID-19-positive patients.[2] Hence, these patients may not complete treatment and may have persistent symptoms months after discharge. Several studies have reported persistent symptoms in their previously discharged COVID-19 patients during follow-up clinic visits. For example, Rosales-Castillo et al[3] found that dyspnea and asthenia were common among COVID-19 follow-ups. Huang et al[4] reported that most patients had at least one persistent symptom, namely fatigue, muscle weakness, anxiety, and depression. Furthermore, the newly diagnosed mental illnesses during follow-ups could be due to social distancing from family/friends, recent hospitalizations, or stress and anxiety at baseline.[5] With the increasing awareness of mental health disorders, other studies have also taken a closer look at the association between COVID-19 and psychological consequences, confirming the need to monitor and treat mental illness along with other symptoms.[5,6]

Some patients with severe COVID-19 infections have had post-COVID multiorgan dysfunction that lasts months after initial infection.[6-8] While short-term follow-up studies have observed fibrotic changes in lungs after infection, studies on long-term consequences are limited. In a single-center prospective cohort study of COVID-19 survivors, persistent chest x-ray abnormalities were observed in 32% of patients at 12 week follow-up.[9] Another study determined that 63% of patients continued to have subtle ground-glass opacities at 4 months follow-up, and 19% had fibrotic lesions.[10] Venous thromboembolism (VTE) is also a common complication associated with COVID-19. However, the risk of VTE after discharge remains unknown, and it is unclear whether post-discharge thromboprophylaxis is beneficial.[11] Engelen et al[12] reported a 0.47% incidence of VTE in COVID-19 survivors after following a cohort of 1877 patients for 2 months.[12] Information on the long-term cardiac injury from COVID-19 infection is still being investigated. Finn et al observed that the higher mortality of COVID-19 was associated with severe cardiac complications like acute myocarditis and cardiomyopathy, and that only 20% of survivors in this study showed left ventricular function recovery at a 12 week follow-up.[13] SARS-CoV-2 causes direct kidney damage as it attaches to the angiotensin-converting enzyme (ACE2) receptors that are highly expressed in the kidney.[8] Available data also suggest a high incidence of kidney disease in patients with COVID-19; however, long-term consequences remain unclear. A study on 143 patients with new-onset kidney disease during COVID-19 hospitalization found that only 9% did not recover from kidney disease after a 4 month follow-up.[14]

In this study, we evaluated a cohort of COVID-19 patients treated at a regional referral center in West Texas for post-COVID-19 clinical characteristics to understand disease sequelae better.

Methods

Study Site

A single-center retrospective cohort study was conducted at Texas Tech University Health Sciences Center and its affiliated University Medical Center (UMC) in Lubbock, Texas. This center serves a large population in West Texas, New Mexico, and Oklahoma.

Subjects

We included adult patients (more than 21 years of age) seen in the Internal Medicine Clinic between April 2020 and April 2021 who had been admitted to the hospital for COVID-19. All patients who were admitted to the hospital during this period and showed up for their clinical appointments in the Internal Medicine outpatient clinic after discharge were included. Data were collected retrospectively from the medical records. We excluded vulnerable subject populations, such as children, prisoners, and pregnant women.

Design and Analysis

A retrospective cohort study was conducted in one center, as identified above. After subjects were identified, their records were retrieved from electronic medical records. The data were collected using a Microsoft Excel datasheet. We collected baseline demographics, including gender, race, ethnicity, chronic medical problems, and information about the use of oxygen, corticosteroids, and mechanical ventilation during hospitalization. Post-hospital follow-up symptoms were also collected from the clinic notes after discharge. In addition, we collected inflammatory markers, including D-dimer, ferritin, and troponin on admission and follow-up. Chest x-rays done at follow-up appointments were compared to the last film done during hospitalization. Persistent and ongoing COVID-related symptoms throughout the follow-up periods were also documented. Descriptive statistical analysis was used for the data. Categorical variable results were reported as numbers and percentages; means, standard deviations (SD), medians, and quartiles 25% and 75% were reported for continuous variables, including BMI at follow up, days until follow up, D-dimer at discharge, ferritin at discharge, troponin T HS, D-dimer level if checked after discharge, ferritin level if checked after discharge, and troponin T HS if checked after discharge. The statistics program in Excel was used for these calculations.

Results

This study included 128 patients with 59 men (46%) and 69 women (54%); the mean age was 59.7 ± 14.8 years. The majority of patients (n = 78, 60.9%) identified their race as Hispanic or Latino origin; the next largest group was Caucasian (n = 29, 22.65%). The average number of days to

Table 1. Showing the Demographic Characteristics of TTUHSC COVID-19 Patients Post-Hospital Follow-up.

Variable	Number N = 128	Percentage (%)
Gender		
Male	59	46
Female	69	54
Patient city		
Lubbock	97	75.8
Others		24.2
Patient state		
Texas	126	98.4
New Mexico	2	1.16
Ethnicity		
Hispanic or Latino or Spanish origin	77	60.1
Race		
Caucasian	29	22.7
Latino/Hispanic	78	60.9
Asians	1	0.8
Black	12	9.4
Others	8	6.3
Comorbidities		
Diabetes mellites	84	65.6
Hypertension	94	73.4
Deceased	4	3.1
Hospital management		
Required supplemental oxygen	80	62.5
Received corticosteroids for COVID treatment	71	55.5
Required mechanical ventilation	11	8.6
Required physical therapy/occupational therapy	21	16.4
Symptoms at follow up		
Respiratory symptoms	34	26.6
GI symptoms	12	9.4
Constitutional symptoms	24	18.8
Others	25	19.5
Telehealth visits (vs In-person)	64	50

the post-hospitalization follow-up was 36 ± 38 days. Notable findings included a 50% rate (n = 64) of telehealth visits, a 65.6% rate (n = 84) of diabetes, and a 73.4% rate (n = 94) of hypertension. A total of 26.56% of patients (n = 34) reported respiratory symptoms at their follow-up appointments, 18.75% of patients (n = 24) reported constitutional symptoms, 9.37% of patients (n = 12) reported GI symptoms, and 19.5% of patients (n = 25) reported other symptoms, such as paresthesia, lower extremity edema, or psychological symptoms. After discharge, 54 patients had follow-up chest x-rays, and 41 (75.9%) still had abnormal findings consistent with COVID-19 imaging characteristics. Follow-up laboratory tests at the clinic visit included the following results: 77.2% (44/57) had elevated D-dimer levels, 78.6% (44/56) had elevated ferritin levels, and 35.6% (21/59) had elevated troponin T HS levels (See Tables 1 and 2).

Discussion

Persistent COVID-19 symptoms are an important concern for COVID-19 patients and their healthcare providers, especially with rising vaccine hesitancies.[15,16] Prolonged but poorly understood sequelae can be physically and psychologically troubling to patients. Furthermore, managing these symptoms is challenging for healthcare workers. In response, special COVID clinics have been developed to specifically address patients with COVID sequelae or symptoms likely attributed to COVID-19 illness.[17] Management at these visits varies, but special attention has been paid to symptoms, imaging, and the persistence of biomarkers related to acute COVID-19 infection.[18] Several studies have assessed these factors in post-COVID patients, with some including follow-up several months post-discharge or resolution of symptoms.

Table 2. BMI, Time to Follow-up, and D-dimer, Ferritin, and Troponin in COVID-19 Patients at Hospital Discharge and Follow-up Visit.

Variable	Mean	SD	Median	Q1; Q3
BMI at follow up (kg/m$^{2)}$	34	11	33.0	27.9; 38.2
Days until follow up	36	38	20	14; 42
D-dimer at discharge (ng/mL)	1241	1209	899	437; 1168
Ferritin at discharge (ng/mL)	715	620	580	283; 829
Troponin T HS at discharge, ng/L	119	494	11	7; 26
D-dimer level if checked after discharge (ng/mL)	1425	928	991	572; 1722
Ferritin level if checked after discharge (ng/mL)	682	364	706	256; 1001
Troponin T HS if checked after discharge (ng/L)	51	48	23	9; 84

Abbreviations: BMI, body mass index; Q1, first quartile, Q3, third quartile; SD, standard deviation.

The main biomarkers that have been associated with COVID-19 illness and can predict outcomes include C-reactive protein, neutrophilia, and various cytokines.[19] However, the predictive value of many biomarkers is still unclear. For example, D-dimer has been associated with disease severity and in-hospital mortality.[20] However, Valerio et al noted the limitations of studies associating D-dimer levels with outcomes in acute COVID-19 patients due to small sample sizes and concluded that, in isolation, D-dimer levels have limited prognostic value. Other authors have noted the discrepancy in studies of biomarkers, suggesting that different study methods may contribute to the observed heterogeneity.[21] D-dimer, troponin, and ferritin remain important laboratory parameters associated with coagulation and/or inflammation.

Cardiovascular complications have been observed in acute and convalescent COVID-19 patients. A systematic review by Xie et al[22] showed that patients with COVID-19 are at increased risk of incident cardiovascular disease, including cerebrovascular disorders, dysrhythmias, ischemic and non-ischemic heart disease, pericarditis, myocarditis, heart failure, and thromboembolic disease after the first 30 days of infection regardless of the acute phase of COVID-19. D-dimer, a marker for clot formation, has been elevated in both acute and convalescent COVID-19 patients, suggesting that D-dimer may predict COVID-19 prognosis. Several studies have found elevations of D-dimer in post-COVID-19 patients, typically in the 20% and 30% range, and average D-dimer elevations are typically under 500 ng/mL at follow-up, although levels as high as 2350 ng/mL have been observed.[23-27] Convalescent D-dimers were significantly elevated in patients requiring hospital admission and older than 50 years.[23] The elevated D-dimer levels found in this study (1425 ± 928 ng/mL) are much higher than those typically observed at follow-up and is comparable to admission D-dimer levels (1241 ± 1209 ng/mL) in these patients. These results support previous observations that an elevated D-dimer occurs in acute COVID-19 infections and indicate that in certain subsets of patients (such as those with higher inpatient D-dimer levels or more severe disease), D-dimer levels may remain noticeably high well after discharge.

Troponin is routinely used as a biomarker for cardiac injury in suspected myocardial infractions and has been associated with acute coronary events in both acute and convalescent patients. Troponin has been shown to be a predictor of mortality[28] in acute COVID-19. One study associated elevated troponin with fatigue among patients with long-COVID. Troponin may continue to be elevated at follow-up in patients who had acute cardiac injuries during admission for COVID-19.[29] Troponin has been used to indicate cardiac injury in acute COVID-19, although its usefulness as a predictor of long-term cardiac pathology is unclear. For example, a study of 148 patients post-discharge found that elevated troponin levels did not predict myocarditis or non-ischemic LGE at follow-up.[30] At a 6 month follow-up, one study noted that troponin elevation was not associated with the persistence of symptoms.[31]

Follow-up imaging is essential to monitor recovery or the development of new complications, particularly in pulmonary and cardiovascular systems. Chest x-rays are usually the most common follow-up imaging due to the respiratory component of COVID-19, the ease of acquisition, and the relatively low radiation exposure. Some studies have reported that chest x-rays in some post-COVID patients have persistent or increasing infiltrates. Rates of abnormal radiographs in post-COVID-19 patients vary. One study reported a 14% (15/110) rate of abnormal chest radiographs at 8 to 12 weeks post admission, whereas another study noted 100% abnormal chest radiographs at the same interval.[32,33] Some patients had more abnormal chest radiographs at their follow-up clinic visits; a prior study found that 9% had increased chest x-rays abnormalities at follow-up.[24] The utility of follow-up radiographs in post-COVID patients has been questioned; however, since fibrosis may persist in many patients during the post-COVID phase, serial chest x-rays provide a good method to monitor recovery.[34]

Persistent symptoms in patients who have been discharged or have cleared the COVID-19 infection have been reported, and a new diagnosis of the post-COVID syndrome has been developed. Many studies have assessed symptoms in convalescent COVID-19 patients. A large meta-analysis and systematic review found that constitutional symptoms, such as fatigue and weakness (28%, 95% CI: 18-39) and arthro-myalgia (26%, 95% CI: 8-44) were common, as was dyspnea (18%, 95% CI: 13-24).[35] We also observed that respiratory and constitutional symptoms were the most common symptoms. Of note, GI symptoms are an infrequently studied post-COVID complication. However, one study noted an increased development of functional gastrointestinal disorders at 6 months post-infection compared to controls.[36]

This study has several limitations. First, the study was done in one center and is not generalizable. Follow-up was not performed at uniform intervals, but this is a limitation inherent to most retrospective post-COVID studies. Not all patients who were admitted to the hospital came to their follow up appointments in the clinic. Larger studies will be needed to identify trends and reach conclusions, especially about biomarkers. Longer follow-up periods will be required to characterize the type and duration of post-COVID symptoms better. In addition, levels of D-dimer, ferritin, and troponin were not tested in all patients at follow-up, and testing may have been biased toward those with higher levels while inpatients or with cardiovascular complications.

The strengths of this study include the measurement of D-dimer, ferritin, and troponin biomarkers that are of interest in COVID-19 research but frequently not measured in studies of post-COVID-19 patients. In addition, more than half of the included patients received post-hospitalization x-rays. Finally, a significant portion of patients in this cohort was Hispanic or Latino, a group that has experienced a disproportionate impact from COVID-19.[37]

Conclusion

Long-lasting symptoms of COVID-19 include respiratory symptoms (26.6%), constitutional symptoms (18.8%), GI symptoms (9.4%), and other symptoms, such as paresthesia, lower extremity edema, or psychological symptoms (19.5%). Telehealth was used in 50% follow-up visits (n = 64) and provides a convenient and safe way for patient follow-up. Comorbidities in these patients included diabetes (n = 84; 65.6%) and hypertension (n = 94; 73.4%); these patients may need more frequent follow-up to make certain their chronic disorders remain stable. In addition, many patients had elevated inflammatory markers. Future studies should examine symptoms and biomarkers at extended follow-up times, and this should become more feasible as additional time elapses for patients with post-COVID symptoms. Standardized questionnaires might also be used to assess the constellation of post-COVID symptoms more uniformly.

Declaration of Conflicting Interests

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Ethics statement

The study was approved by the Texas Tech University Health Sciences Center Institutional Review Board (IRB #: L21-144).

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