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Investigation of Post-COVID-19 Patients' Chronic Symptoms and Clinical Findings

COVID-19 Sonrası Hastaların Kronik Semptom ve Klinik Bulgularının İncelenmesi

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ABSTRACT

Background: The objective of this study was to assess whether multiple relevant symptoms recover following the onset of symptoms in hospitalized and nonhospitalized patients with COVID-19.

Material and Method: In this study, the data of 14 patients who applied to Ankara Polatlı Duatepe State Hospital between May 01, 2020, and May 05, 2021, were confirmed COVID-19 and were hospitalized in the COVID-19 service for 5 to 20 days, and the data of COVID-19 patients 86 stayed at home were analyzed. 79 female and 21 male patients and mean age was 48.65±14.926 (20-82) years were included in the study. Demographic, clinical, radiological, and laboratory records of the patients were reviewed retrospectively.

Results: Of those who had the disease, 42 were mild, 33 were moderate, 14 were severe, and 11 were extremely severe. Of the post-COVID-19 patients who had the disease, 14 had therapy in the hospital and 86 patients had therapy at home. Symptoms seen in post-COVID-19 patients were muscle pain, cough, shortness of breath, loss of taste and smell, fever, nausea, hoarseness, and hair loss, and their frequencies were 70, 60, 51, 51, 49, 46, 40, and 31, respectively. While 34% had one or two symptoms and 56% had three or more.

Conclusion: In hospitalized and nonhospitalized patients with confirmed or suspected COVID-19, multiple symptoms are present, about 5 days after symptoms onset. These suggest the presence of a "post-COVID-19 syndrome", and highlight the unmet healthcare needs in a subgroup of patients with "mild" or "severe" COVID-19.

Keywords: Post-COVID-19 symptoms, CRP, COVID-19

ÖZ

Amaç: Bu çalışmanın amacı, COVID-19'lu hastanede yatan ve hastaneye yatırılmayan hastalarda semptomların başlamasını takiben birden fazla ilgili semptomun iyileşip iyileşmediğini değerlendirmektir.

Gereç ve Yöntem: Bu çalışmada 01 Mayıs 2020 - 05 Mayıs 2021 tarihleri arasında Ankara Polatlı Duatepe Devlet Hastanesi'ne başvuran ve COVID-19 servisinde 5 ila 20 gün yatarak tedavi gören 14 hastanın verileri ve evde kalan 86 COVID-19 hastalarının verileri analiz edildi. Çalışmaya yaş ortalaması 48.65±14.926 (20-82) yıl olan 79 kadın, 21 erkek hasta dahil edildi. Hastaların demografik, klinik, radyolojik ve laboratuvar kayıtları geriye dönük olarak incelendi.

Bulgular: Hastalığı olanların 42'si hafif, 33'ü orta, 14'ü şiddetli ve 11'i aşırı şiddetli idi. COVID-19 sonrası hastalığa yakalanan hastalardan 14'ü hastanede, 86'sı ise evde tedavi gördü. COVID-19 sonrası hastalarda görülen semptomlar kas ağrısı, öksürük, nefes darlığı, tat ve koku kaybı, ateş, bulantı, ses kısıklığı ve saç dökülmesi olup, sıklıkları sırasıyla, 70, 60, 51, 51, 49, 46, 40 ve 31 idi. %34'ünde bir veya iki semptom varken, %56'sında üç veya daha fazla semptom vardı.

Sonuç: COVID-19'u doğrulanmış veya şüphelenilen hastanede yatan ve hastaneye yatırılmayan hastalarda, semptomların başlamasından yaklaşık 5 gün sonra birden fazla semptom mevcuttur. Bunlar, bir "COVID-19 sonrası sendromunun" varlığını düşündürür ve "hafif" veya "şiddetli" COVID-19'lu bir hasta alt grubunda karşılanmamış sağlık hizmeti ihtiyaçlarını vurgular.

Anahtar Kelimeler: COVID-19 sonrası semptomlar, CRP, COVID-19

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INTRODUCTION

Confirmed COVID-19 case number and death due to coronavirus disease 2019 (COVID-19) should be uptade and referance should be given for example by 22 July 2022, there have been 565.207.160 confirmed cases of COVID-19, including 6.373.739 deaths reported to WHO (1). The clinical spectrum of SARS-CoV-2 infection is wide, encompassing asymptomatic infection, fever, fatigue, myalgias, mild upper respiratory tract illness, severe life-threatening viral pneumonia requiring admission to hospital, and death (2). Physicians are observing persisting symptoms and unexpected, substantial organ dysfunction after SARS-CoV-2 infection in an increasing number of patients who have recovered, as previously observed in the SARS outbreak (3). However, COVID-19 is a new disease and uncertainty remains regarding the possible long-term health sequelae. This is particularly relevant for patients with severe symptoms, including those who required mechanical ventilation during their hospital stay, for whom long-term complications and incomplete recovery after discharge would be expected. Unfortunately, few reports exist on the clinical picture of the aftermath of COVID-19. Instead of aftermath of COVID-19, post-COVID-19 can be used.

Multiple symptoms like fever, cough, fatigue, dyspnoea, headache, diarrhea, nausea, and vomiting, have been reported during the hospital stay (4, 5). About 60 days after the onset of the first COVID-19 symptom, only 13% of the previously hospitalized COVID-19 patients were completely free of any COVID-19-related symptom, while 32% had one or two symptoms and 55% had three or more (6). Next to the hospitalized patients with "severe" coronavirus disease 2019 (COVID-19), millions of people have most probably been infected with SARS-CoV-2 without formal COVID-19 testing and/or medical treatment in the hospital (7, 8). Indeed, COVID-19 testing capacity was not available for patients who initially were considered to have mild signs and symptoms. These patients are classified as having "mild" COVID-19 as they only require home care and the infection is expected to resolve (9). Then again, patients with the so-called "mild" COVID-19 may still complain about persistent symptoms, even weeks after the onset of symptoms. To date, however, only anecdotal evidence is available (6).

This study assessed whether or not multiple relevant symptoms recovered following the onset of symptoms in hospitalized and nonhospitalized patients with COVID-19.

MATERIAL AND METHOD

This study is a retrospective cohort study conducted with patients who had post-COVID-19 symptoms. All patients who applied to Polatlı Duatepe State Hospital with suspected COVID-19 disease between May 01, 2020, and May 05, 2021, and were infected with laboratory-confirmed SARS-COV-2 were included in the study. How did laboratory–corfirmed SARS-COV-2 case idenditfy should be explained for example SARS-CoV-2 real-time reverse-transcription-polymerase chain reaction (rRT-PCR) test positive cases identified as laboratory-confirmed cases. This study was approved by the Siirt University Non-Interventional Clinical Research Ethics Committee (No: 2021/02.01). The data of 100 patients confirmed with post-COVID-19 were studied. The COVID-19 patients participating in the study did not have any additional diseases defined. Demographic, clinical characteristics, and laboratory findings of the patients were obtained from hospital information system records. All data were checked by physicians who are experts in internal medicine and infectious diseases and clinical microbiology. The time from onset of illness to hospitalization was also recorded. All patients participating in this study were laboratory-confirmed COVID-19 patients, and the diagnostic criteria for COVID-19 were based on the positive rRT-PCR tests results.

White blood cell (WBC), lymphocyte (LY), monocyte (MO), neutrophil (NE), eosinophil (EO), basophil (BA), platelet (PLT), urea, creatinine, total and direct bilirubin, alanine transaminase (ALT), aspartate transaminase (AST), sodium (Na), potassium (K), calcium (Ca), C-reactive protein (CRP), and thyroid stimulating hormone (TSH) were determined for each patient. All medical laboratory data were measured by the clinical laboratory of Polatlı Duatepe State Hospital.

Throat-swab specimens obtained from the upper respiratory tract of patients at admission were stored in a viral-transport medium. Total RNA was extracted within 2 hours using the respiratory sample RNA isolation kit. SARS-CoV-2 was examined by rRT-PCR as described previously.

All COVID-19 patients met the following criteria: (a) Epidemiology history, (b) Fever or other respiratory symptoms, (c) Typical CT image abnormities of viral pneumonia, and (d) Positive result of rRT-PCR for SARS-CoV-2 RNA. Furthermore, CT imaging scores were used to quantify the pathological changes in COVID-19 patients.

Post-COVID-19; COVID-19 symptoms in patients with diagnosed defined as a longer duration. Syndromes; fever, cough, shortness of breath, loss of taste and odor, hair loss, nausea, muscle pain, and hoarseness (10-12).

Statistical Analysis

For the statistical evaluation of the results obtained, SPSS (Statistical Package for Social Sciences, Chicago, Illinois, USA) 22.0 package program was used. In the evaluation of the results, descriptive values were expressed as number (n), percentage (%), mean, and prevalence value Standard deviation (SD). Student t-test and chi-square test were used to compare categorical variables. $p<0.05$ were considered statistically significant.

RESULTS

In this study, out of 100 post-COVID-19 patients sampled for the diagnosis of laboratory findings were female, 79 (79%) were 21 (21%) male, and the mean age was 48.65±14.926 (20-82) years (**Table 1**).

Table 1. The demographic evaluation and post-COVID-19 grade

Female/Male	79/21
Age (years)	48.65±14.926
Strong	14
Severe	11
Middle	33
Mild	42
Hospital	14
House	86

In our study, the CRP and TSH were found to be higher than the reference ranges (**Table 2**). In our study, the hemogram parameters unchange comparase to the reference ranges (**Table 3**).

Table 2. Laboratory parameters (mean±SD)

Parameters	Post-COVID-19 (n= 100)	Reference range
Urea (mg/dL)	30.823±13.756	17-43
Creatinine (mg/dL)	0.678±0.198	0.67-1.17
TBil (mg/dL)	0.605±0.295	0.3-1.2
DBil (mg/dL)	0.111±0.049	0-0.2
ALT (U/L)	23.578±17.029	0-50
AST (U/L)	20.905±8.334	0-50
Na (mmol/L)	138.797±2.417	136-146
K (mmol/L)	4.484±0.345	3.5-5.1
Ca (mg/dL)	9.533±0.328	8.8-10.6
CRP (mg/dL)	0.655±1.692	0-0.5
TSH (mIU/L)	2.262±2.678	0.4-4

T Bil-Total bilirubine, D Bil-Direct bilirubine, ALT-Alanine transaminase, AST-Aspartate transaminase, Sodium-Na, Potassium-K, Calcium-Ca, CRP-C-reactive protein, TSH-Tiroit stimulating hormone

Table 3. Hemogram parameters (mean±SD)

Parameters	Post-COVID-19 (n= 100)	Reference range
WBC 10^3/mL	6.612±1.766	4-10
LY 10^3/mL	2.166±0.668	1-5
MO 10^3/mL	0.445±0.129	0.2-1.5
NE 10^3/mL	3.796±1.302	2-8
EO 10^3/mL	0.168±0.107	0-0.7
BA 10^3/mL	0.034±0.029	0-0.25
PLT 10^3/µL	258.989±66.259	150-500

WBC-White blood cell, LY-Lymphocyte, MO-Monocyte, NE-Neutrophil, EO-Eosinophil, BA-Basophil, PLT-Platelet

Of those who had the disease, 42 were mild, 33 were moderate, 14 were severe, and 11 were extremely severe. Of the post-COVID-19 patients who had the disease, 14 had it in the hospital and 86 had it at home Table 1. Symptoms seen in post-COVID-19 patients were muscle pain, cough, shortness of breath, loss of taste and smell, fever, nausea, hoarseness, and hair loss, and their frequencies were 70, 60, 51, 51, 49, 46, 40, and 31, respectively **Table 4**. While 34% had one or two symptoms and 56% had three or more.

Table 4. COVID-19 syndromes

Syndromes	Existent n (%)	Absent n (%)
Fever	49 (49%)	51 (51%)
Cough	60 (60%)	40 (40%)
Shortness of breath	51 (51%)	49 (49%)
Loss of taste and odor	51 (51%)	49 (49%)
Hair loss	31 (31%)	69 (69%)
Nausea	46 (46%)	54 (54%)
Muscle pain	70 (70%)	30 (30%)
Hoarseness	40 (40%)	60 (60%)

DISCUSSION

Since the pandemic continues, there are limited data on clinical and prognostic factors in patients with COVID-19. COVID-19 is a highly infectious respiratory disease that leads to decreased respiratory, physical, and psychological function in affected patients (13). Patients' symptoms widely vary; from asymptomatic to severe (14). As COVID-19 is highly infectious, the patients are isolated in order to limit the spread of SARS-CoV-2. This leads to a significant reduction in social interactions, as a consequence of which the patients feel lonely and isolated (15). The mechanism causing pneumonia is particularly complex. It seems that the infection can elicit an excessive immune response in the host. COVID19 in some cases elicits a response generally known as a 'cytokine storm' (16).

In some cases, moreover, patients suffer from an extensive lung tissue inflammation. The main cytokine in this 'storm' is interleukin 6 (IL-6). IL-6 is produced by activated leukocytes and acts on a large number of cells and tissues. IL-6 assists in B cell differentiation. Many patients remain to lie in the intensive care unit for a longer period of time. Patients often remain in one position for several hours, which may lead, due to critical illness, to dysphagia, muscle weakness, myopathy, and neuropathy, as well as to reduced mobility (17) due to muscle weakness. It may also result in walking problems potentially affecting patients' daily activities. In the post-infection period, patients may experience persistent pulmonary, musculoskeletal, neurological, cardiac, and psychological problems (18).

In our study, we demonstrated that the serum CRP and TSH levels were higher than the reference ranges.

While many studies have shown the onset of subacute thyroiditis (SAT) after certain infections, including COVID-19, few studies have demonstrated the relationship between COVID-19 and over the hypothyroidism (19).

Chen et al. demonstrated that TSH lower than the normal range was present in 56% (28/50) of the patients with COVID-19. The levels of TSH and serum total triiodothyronine (TT3) of the patients with COVID-19 were significantly lower than those of the healthy control

group and non-COVID-19 pneumonia patients. The more severe the COVID-19, the lower the TSH and TT3 levels were, with statistical significance. The degree of the decreases in TSH and TT3 levels was positively correlated with the severity of the disease. The total thyroxine (TT4) level of the patients with COVID-19 was not significantly different from the control group. All the patients did not receive thyroid hormone replacement therapy. After recovery, no significant differences in TSH, TT3, TT4, free triiodothyronine (fT3), and free thyroxine (fT4) levels were found between the COVID-19 and control groups (20).

Huang et al. found that fatigue or muscle weakness, sleep difficulties, and anxiety or depression were common, even 6 months after symptom onset. Huang et al. also found that being a woman and severity of illness were risk factors for persistent psychological symptoms (21). Female SARS survivors had higher stress levels and higher levels of depression and anxiety (22). In a 3-month follow-up survey of 538 COVID-19 patients, it was found that physical decline or fatigue, post-activity polypnoea, and alopecia were more common in women than in men. The underlying mechanism of the psychiatric consequences of COVID-19 is likely to be multifactorial and might include the direct effects of viral infection, the immunological response, corticosteroid therapy, ICU stay, social isolation, and stigma (23).

In our study, we demonstrated that of those who had the disease, 42 were mild, 33 were moderate, 14 were severe, and 11 were extremely severe. Of the post-COVID-19 patients who had the disease, 14 had it in the hospital and 86 had it at home. Symptoms seen in post-COVID-19 patients were muscle pain, cough, shortness of breath, loss of taste and smell, fever, nausea, hoarseness, and hair loss, and their frequencies were 70, 60, 51, 51, 49, 46, 40, and 31, respectively. While 34% had one or two symptoms and 56% had three or more.

CONCLUSION

As a result, In previously hospitalized and nonhospitalized patients with confirmed or suspected COVID-19, multiple symptoms are present about 5 days after symptoms onset. This suggests the presence of a "post-COVID-19 syndrome" and highlights the unmet healthcare needs in a subgroup of patients with "mild" or "severe" COVID-19. Further studies are required for randomized clinical trials may help confirm in confirming the results and hypotheses.

ETHICAL DECLARATIONS

Ethics Committee Approval: This study was approved by the Siirt University Non-Interventional Clinical Research Ethics Committee (No: 2021/02.01).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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