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Original Article

New regular candidates to the emergency department; lasting symptoms following acute COVID -19 infection: the example of northwestern Syria

Acil Servislerin Yeni Müdavim Adayları; Geçmeyen COVID-19 Semptomları: Suriye'nin Kuzeybatısı Örneği

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Abstract

Background: Symptoms decrease during the first 4-weeks after the onset of COVID -19. The situation of patients whose symptoms persist longer or do not seems to be one of the current research topics. In regions with internal turmoil, such as Northwest Syria, emergency departments that carry the burden of emergency and trauma patients were occupied during the COVID-19 pandemic. This study aimed to investigate the post-discharge symptoms of COVID -19 patients hospitalized by the emergency department in northwestern Syria.

Materials and Methods: Between 07/1/2020 and 01/05/2021, 163 patients who were hospitalized and discharged from the emergency department due to COVID-19 in northwest Syria were included in the study. A questionnaire based on the COVID-19 Yorkshire Rehabilitation Scale was administered to all patients. The obtained data were processed into the data collection form and analyzed with explanatory and comparative statistics.

Results: After they developed COVID-19, we noted decreased dry cough, loss of taste and smell, headache symptoms, and increased fatigue and joint pain symptoms. We found that patients who were re-hospitalized following acute COVID-19 infection received longer treatment and those re-hospitalized patients had increased memory impairment, hoarseness, fatigue, and weakness in the post-COVID-19 period.

Conclusion: We think that symptoms and complaints that do not resolve after COVID -19 may be among the common reasons for admission to the emergency department in the future. Emergency departments need to be better prepared to manage persistent COVID -19 symptoms.

Key words: COVID -19, Emergency department, long COVID, post-COVID, Syria

ÖZ

Amaç: Bu çalışmada Suriye'nin kuzeybatısında acil servisten yatırılan COVID-19 hastalarının taburculuk sonrası devam eden semptomlarının araştırılması amaçlanmıştır.

Gereç ve Yöntem: 1.07.2020-01.05.2021 tarihleri arasında Suriye'nin kuzeybatısında acil servisten COVID-19 nedeniyle yatışı yapılan ve taburcu olan 163 kişiye COVID-19 Yorkshire Rehabilitation Scale anketi baz alınarak hazırlanmış bir anket uygulandı. Elde edilen veriler veri kayıt formuna işlendi ve açıklayıcı ve karşılaştırmalı istatistiksel analizler yapıldı.

Bulgular: Katılımcıların %54.6'sı erkek, yaş ortalaması 52.97∓19.45 yıldı ve %17.8'i COVID-19 nedeniyle yoğun bakımda tedavi görmüştü. COVID-19 enfeksiyonu akut dönemi sonrasında kuru öksürük, tat ve koku duyusu kaybı, baş ağrısı semptomlarında azalma, yorgunluk ve eklem ağrısı semptomlarında ise artış saptandı. COVID-19 enfeksiyonu sonrası yeniden hastaneye başvuran hastaların daha uzun süre tedavi aldıkları ve yeniden yatırılan hastaların COVID-19 sonrası dönemde hafızada zorlanma, ses kısıklığı, yorgunluk ve halsizlik şikayetlerinde artış olduğu tespit edildi.

Sonuç: Suriye'nin kuzeybatısında COVID-19 süreci ile pandemi aciller kurulmuş ve bu aciller üzerinden pandemi süreci tüm yönleriyle yönetilmiştir. Gelecekte COVID-19 sonrası geçmeyen semptom ve şikayetlerin acil servise sık başvuru nedenleri arasına girebileceği ve geçmeyen COVID-19 semptomlarına yaklaşımda acillerin daha hazırlıklı olması gerekebileceğini düşünmekteyiz.

Anahtar Kelimeler: COVID -19, Acil Servis, uzamış COVID, post-COVID, Suriye

Highlights

- Due to the persistent of symptoms after COVID-19, emergency room applications continue to increase.
  - It affects the number of hospitalizations.
  - Post-COVID-19 patients also joined the caravan of those who applied to the emergency department due to exacerbation or complications of common chronic diseases.
  - Emergency services should be prepared for patients whose symptoms continue after COVID-19. Even though we are in conflict zones such as Northwest Syria.
- Patients rehospitalized for persistent symptoms after COVID-19 have 3 hallmarks:
  - They were discharged from the hospital earlier.
  - They have stayed in the hospital longer.
  - One of every two patients was taken to the intensive care unit.

Introduction

COVID -19 is a heterogeneous disease affecting the respiratory system and other organs. It has sickened more than 350 million people worldwide, but the pandemic bill does not yet appear to have been met (1). Some survivors of COVID-19 continue to have symptoms, and a new picture, also known as the post-COVID syndrome, is emerging (2).

Acute COVID-19 infection, like other viral infections, may present with symptoms such as fever, fatigue, dry cough, myalgia, and dyspnea (3). Additionally, symptoms such as headache, sore throat, rhinorrhea, gastrointestinal symptoms, conjunctivitis, decreased sense of taste and smell are also common (4). In addition to its routine symptoms, the risk of mortality may increase with the cardiovascular effect of COVID-19 (5).

Generally, symptoms resolve within 4-weeks of starting COVID -19. The situation of patients whose symptoms persist longer or do not resolve, seems to be one of the current research topics. In the literature, COVID -19 symptoms lasting longer than 4-weeks were defined as "long COVID" (6). However, the definition of "long COVID" needed to be expanded as this clinical picture occurred in an increasing number of patients over a long period. Therefore, “ongoing COVID -19” was defined for symptoms lasting between 4 and 12 weeks, and the post-COVID syndrome was defined for symptoms lasting longer than 12 weeks. According to the literature, the most common symptom in more than 40% of patients evaluated as long COVID was found to be fatigue. However, sleep disturbance, dyspnea and cough are other common symptoms, respectively. The prevalence of these symptoms was also found to be more than 25% (7-9).

In northwestern Syria (10), which ranks in the top 5 on the global terror list, the healthcare system has been on the verge of collapse since 2010 due to internal turmoil (11). Since 2016, Turkey has opened hospitals in the region in cooperation with the Turkish Red Crescent. These hospitals started to provide holistic healthcare services under the leadership of emergency services. These hospitals have been converted into pandemic hospitals with the emergence of COVID -19 cases in the region. Applies due to COVID -19 were also handled by pandemic emergency services at these hospitals.

This study aimed to investigate the lasting symptoms after the discharge of COVID -19 patients admitted by the emergency services of the pandemic hospitals in northwestern Syria, where the health care system is in place as part of the humanitarian response.

Materials and Methods

Study Design

This study was conducted with 163 people who applied to the emergency department and were discharged from the pandemic hospital due to COVID-19 in northwest Syria between 01/07/2020-01/05/2021. Participants were given a questionnaire based on the COVID -19 Yorkshire Rehabilitation Scale (C19- YRS). Before the start of the study, ethical approval from the Ethics Committee of Hatay Mustafa Kemal University Non-Interventional Research (date of meetings: 06/05/2021 number of decision: 24), and institutional approval from the relevant hospital administration were obtained. Addition, the study was conducted in accordance with the ethical principles of the Declaration of the World Medical Association of Helsinki.

Selection of participants

In northwest Syria, applications due to COVID-19 have been accepted in the pandemic emergency services. Between 01.07.2020 and 01.05.2021, 3617 patients applied to the pandemic emergency. Patients who were not hospitalized to the pandemic service from these patients were excluded from the study. Among 610 patients who were hospitalized and discharged from the emergency room, 163 patients who came to the hospital for control or applied to the emergency service and volunteered to participate in the study were included in the study. The interviews were conducted face to face with these patients. Patients younger than 18 years, those who presented outside the emergency department, and those whose hospitalization was not due to COVID -19 were excluded from the study.

Obtaining the data

We administered a questionnaire based on C19-YRS to those who agreed to participate in the study [the questionnaire is available free of charge at https://acnr.co.uk/. C19- YRS was created by a multidisciplinary team at the College Hospitals of Leeds, Airedale, and Hull in Yorkshire, England (12). The aim was to assess the long-term symptoms and clinical problems that COVID -19 patients may encounter after discharge. Our survey asked

for general information: the location of the interview, demographic data (age, sex), how many days ago they were admitted to the hospital and whether they were admitted to the service or intensive care unit, the duration of hospitalization, whether they came to the hospital with the recurrent complaints or with the persistent complaints, and whether they were subsequently re-admitted to the hospital. Participants were then asked to rate the severity of shortness of breath, voice, difficulty eating or swallowing, loss of appetite, weight loss, fatigue, distraction, memory difficulties, sadness, and loss of interest complaints before and following COVID -19 using a 10-point Likert scale. They were also asked whether complaints of dry cough, shortness of breath, loss of sense of taste and smell, fatigue, cough with phlegm, sore throat, arthralgias, headache, and nosebleeds occurred during and following the start of COVID -19. We processed the obtained information in a prepared data collection sheet.

Statistical Analysis

Statistical analyses of the study were performed using Statistical Package software for Social Sciences version 25.0 for Windows (IBM SPSS Statistics for Windows, version 21.0. Armonk, NY: IBM Corp., USA). The normality assumption was tested with the tests Kolmogorov-Smirnov and Shapiro-Wilk. In addition to these tests, the Kurtosis and Skewness coefficients of the variables were also examined. Explanatory statistics of variables are reported as mean ± standard deviation, median (Min-Max) and n (%). For univariate analyses, the Chi-Square, Fisher's Exact, Fisher-Freeman-Halton exact test, Mann Whitney U and Wilcoxon Sign test were used, depending on the nature of the variables and the availability of assumptions.

Results

The study involved 163 individuals who had applied to the pandemic emergency department and agreed to participate. The mean (±sd) age of the participants was 52.97∓19.45 years, and 89 (54.6%) of the participants were male and 74 (45.4%) were female. The median application time between the diagnosis of COVID-19 and the interview was 21 (min-max: 15-250) days. The median time of application to the emergency department for pandemic post-discharge was 8 (1-150) days. The median length of hospital stay was 7 (1-25) days in the presence of acute COVID-19 infection. Twenty-nine (17.8%) of patients were treated in the intensive care unit due to acute COVID-19 infection. The number of those who applied to the emergency room for treatment due to the persistence of COVID-19 symptoms was 16 (9.8%).

When patients were asked to rate symptoms before and following COVID -19 on a scale of 0-10 (e.g.: none: 0, can't breathe: 10), the mean values obtained and group comparisons before and following COVID -19 are summarized in Table 1.

Table 1. Differences in symptoms before and following COVID -19 (n=163)

	Before COVID-19 Median (Min-Max)	**Following acute COVID-19** Median (Min-Max)	***p****
Shortness of breath	0(0-5)	3(1-10)	<0.001
Change of voice	0 (0-5)	2(1-10)	<0.001
Fatigue during eating and drinking	0(0-5)	2(1-10)	<0.001
Loss of appetite/weight	0(0-4)	3(1-10)	<0.001
Fatigue/weakness	0(0-4)	2(1-10)	<0.001
Distractibility	0(0-8)	2(0-8)	<0.001
Memory strain	0(0-5)	2(0-10)	<0.001
Hoarseness	0(0-7)	2(1-10)	<0.001
Sadness/Loss of interest	0(0-10)	1(0-10)	<0.001

*: Wilcoxon Signed Ranks Test

The frequency and percentages of patients' symptoms during and following acute COVID -19 is shown in Table 2. Following acute COVID -19 infection, patients had a significant decrease in dry cough, loss of taste and smell, headache symptoms, and a significant increase in fatigue and joint pain symptoms ($p < 0.05$).

Table 2. Frequency values of the patients' symptoms during and following COVID -19 (n=163)

	During COVID-19 n, (%)	**Following acute COVID-19 n, (%)**	***p****
Dry cough	127(77.9%)	51(31.3%)	<0.001
Shortness of breath	87(53.4%)	83(50.9%)	0.657
Loss of taste and smell	100(61.7%)	68(41.0%)	0.000
Fatigue	68(41.7%)	85(52.1%)	0.059
Cough with phlegm	67(41.1%)	75(46.0%)	0.372
Throat ache	74(45.4%)	84(51.5%)	0.268
Joint pain	72(44.2%)	91(55.8%)	0.035
Headache	90(55.2%)	70(42.9%)	0.027
Nosebleeds	26(16.0%)	15(9.2%)	0.066

*: Chi-Square test

When examining the radar chart of symptoms (Figure 1), an increase in symptoms of fatigue, cough with phlegm, sore throat, and joint pain was noted following acute COVID-19 infection.
Additionally, 56.3% (n=9) of the patients who were applied to the emergency department with persistent complaints following acute COVID-19 infection (n=16) were patients who had previously received acute COVID-19 treatment in the intensive care unit. We found that those who came to the hospital with complaints that did not improve following the COVID-19 infection stayed longer in the hospital (p=0.034). We found that they received longer treatment (p<0.05). The mean scores of the because of persistent symptoms following acute COVID-19 infection hospitalized patients (n=16) for symptoms before and following COVID -19 are shown in Table 3.

Table 3. Mean scores of patients hospitalized with persistent symptoms following acute COVID-19 infection, based on their symptoms (n=16)

	Before COVID-19 Median (Min-Max)	**Following acute COVID-19** Median (Min-Max)	**p***
Shortness of breath	1(0-3)	8(1-10)	<0.001
Change of voice	1(0-10)	3(1-10)	<0.001
Fatigue during eating and drinking	1(0-3)	9.5(1-10)	<0.001
Loss of appetite/weight	1(0-3)	7.5(1-10)	<0.001
Fatigue/weakness	1(0-4)	10(1-10)	<0.001
Distractibility	1(0-3)	2(1-7)	<0.001
Memory strain	1(0-3)	3(1-10)	<0.001
Hoarseness	1(0-4)	7(1-10)	<0.001
Sadness/Loss of interest	1(0-4)	4(1-8)	<0.001

*: Wilcoxon Signed Ranks Test

It was determined that patients (n=19) who were due to persistent or recurrent symptoms following acute COVID-19 infection hospitalized after recurrent admissions left the hospital a short time ago and received treatment for a longer period of time ($p < 0.05$). The mean scores of these patients for their symptoms and group comparisons are summarized in Table 4. According to these results, complaints of memory difficulties, hoarseness, fatigue, and weakness increased in hospitalized patients during the post-COVID-19 period ($p < 0.05$).

Table 4. The mean values for the persistent or recurrent symptoms of the patients who were treated at the time of readmission to the hospital (n=19)

	During COVID-19 Median (Min-Max)	**Following acute COVID-19** Median (Min-Max)	**p***
Shortness of breath	3(1-5)	3(1-10)	0.096
Change of voice	2(1-4)	2(1-5)	0.352
Fatigue during eating and drinking	2(1-5)	2(1-4)	0.206
Loss of appetite/weight	3(1-4)	2(1-10)	0.494
Fatigue/weakness	3(1-4)	10(1-4)	<0.001
Distractibility	3(1-8)	3(1-7)	0.914
Memory strain	1(1-4)	4(1-6)	0.016
Hoarseness	1(1-5)	6(2-10)	0.020
Sadness/Loss of interest	1(1-9)	5(1-9)	0.096

*: Wilcoxon Signed Ranks Test

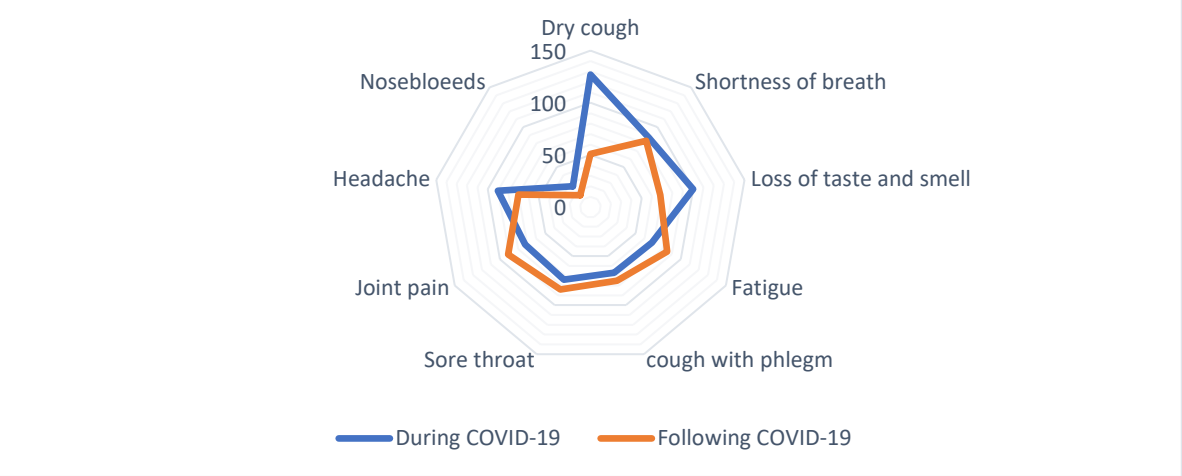

Figure 1. Distribution of patients' complaints during and following COVID -19 (n=163)

Discussion

In regions where there is conflict and turmoil, health care focuses on emergency and trauma patients. However, socioeconomic difficulties and epidemics and their consequences are unknown in these regions.

In a survey conducted through social media, it was found that 26% of people who had COVID -19 had painful symptoms (13). When meta-analyses were examined, muscle and joint pain were present in 35% to 50% of all COVID -19 cases (14), and these symptoms were observed to persist in 1 in 4 patients after treatment for COVID -19 (15). In our study, in accordance with the literature, it was found that approximately half of the patients had joint pain both during and following acute COVID-19 infection. In general, joint pain seems to be one of the most common complaints following acute COVID-19 infection.

A review of the literature shows that 5% to 20% of COVID -19 cases complain of sore throat and that sore throat usually persists after other symptoms of infection have resolved. (14,16) Painful necrotic and aphthous ulcers reported in patients may contribute to changes in taste and smell in addition to sore throat (14). In our study, we observed that almost half of the patients suffered from sore throats. Conditions such as poor oral hygiene and tobacco use may cause this symptom more frequently in Syria, where socioeconomic status is poor.

Zayet et al. (15), found that 74% of patients with persistent symptoms after COVID -19 had a loss of smell, and 31.5% had a loss of taste. While in our study, 61.7% of patients suffered from a loss of taste and smell at the beginning of COVID -19, this rate decreased to 41.0% after COVID -19, and it is one of the most common symptoms that persist in parallel with the literature. The loss of taste and smell likely affects the quality of life of patients with COVID -19.

The rate of depression after COVID -19 varies from 11% to 28% in the literature (16). In studies conducted in Turkey, it has been shown that COVID-19 and related effects cause psychiatric effects in healthcare workers and also in pregnant women (17,18,19). Some studies also reported cases of psychosis (20). Women and individuals with previous psychiatric disorders are more psychopathologically affected by COVID-19. However, depression and anxiety symptoms are reported more frequently in individuals with a shorter length of hospital stay (21). In our study, we observed an increase in sadness and loss of interest in patients readmitted to the hospital with unresolved symptoms. COVID-19 can affect the emotional states of patients who experience social isolation and have difficulties in the treatment process. It may have caused further distress and loss of interest in patients who felt inadequately treated and did not receive adequate medical care after re-hospitalization. It has been shown that social and economic factors increase the tendency to depression in patients following acute COVID-19 infection (22-24). It is reasonable to assume that the social and economic difficulties associated with poverty and the inability to cope with it, especially in northern Syria, may lead to depression in the current patient population after COVID -19.

A literature review shows that during COVID -19, headaches occur in 11% to 40% of cases. In our study, we noted headaches in about half of the patients. While headache is one of the ongoing symptoms like other pain, patients with chronic headaches may also be triggered by COVID -19. While cerebrovascular events due to thromboembolic conditions can be seen with COVID -19, subcortical changes have also been noted in some brain MRIs. Associations with various diseases, such as Parkinson's disease and post-flu psychosis, were found in the 1918 Spanish flu (14). COVID -19 has not yet completed its impact, can leave many lasting traces, and what we learn from this infection can influence the rest of our lives (25). Because of the conditions in the northern Syria's region, few advanced neurologic examination tests are available. However, it is suspected that patients with headaches may have other associated symptoms or may have neurologic problems in the future.

In our study, we observed an increase in memory difficulties, distractibility, sadness, and loss of interest between the onset of COVID -19 and later hospitalizations. Cognitive impairment was observed in 67% of patients presenting to the neurology outpatient clinic in Germany after COVID -19, whereas depressive symptoms were observed in 65% (25). In addition to the neuropsychiatric findings, the meta-analysis by Jennings et al. (8), found that the rate of fatigue in ongoing COVID -19 was 43%. In our study, consistent with the general literature, fatigue was observed in more than half of the participants. According to neuroinflammatory models, the hypothalamic paraventricular nucleus is affected in severe infections, and the persistence of fatigue is a effect of severe infections, along with neuropsychiatric effects (26). In areas of civil turmoil, as in the regions where our study was conducted, emergency services may provide the closest contact with patients. Once such complex neuropsychiatric syndromes are identified, it would likely be more beneficial for patients to be referred by any emergency department that provides initial evaluation and medical attention. Of course, it is known that it is more convenient in terms of cost effectiveness to establish post covid polyclinics where routine control and rehabilitation of these patients can continue. however, the regional conjuncture does not allow this.

In our study, more than half of the patients who came to the hospital with complaints that did not improve following the COVID-19 infection was treated in the intensive care unit. Those treated in the intensive care unit were hospitalized more frequently when they were applied to the hospital again. Also, the average length of treatment in hospital in acute COVID-19 time was longer for patients who were re-hospitalized because of persistent or recurrent COVID-19 symptoms than for those who were not hospitalized because of persistent or recurrent COVID-19 symptoms. This may have resulted in the need to seek medical attention again, depending on the presence of persistent symptoms or progress of comorbidities, even if the treatment of the critically ill had been completed in the hospital. For this reason, the people and institutions that provide health care must be prepared for this situation, especially in the follow-up of patients treated in the intensive care unit and the emergency services.

Hospitalization may be required for patients with symptoms that do not resolve after COVID -19. Therefore, a thorough examination should be done in the emergency department.

The most common GIS symptom in COVID-19 patients is anorexia, and symptoms such as nausea, vomiting, diarrhea, gastrointestinal bleeding, and abdominal pain have also been noted. It has even been noted that at the onset of COVID-19, gastrointestinal symptoms may occur even before fever or other symptoms of COVID-19 (27, 28). In another review, it was observed that weight and appetite loss have been complained in ongoing COVID -19 (8). In our study, we showed that weight and appetite loss complaints increased after the disease. The aforementioned GIS symptoms and decreased sense of taste and smell suggested that appetite loss may increase. The nutritional deficiency of patients living in difficult conditions due to socioeconomic problems is already a problem. As mentioned in our study, it can be assumed that weight loss may increase with COVID-19 and accompanying medical problems. Even if the COVID-19 treatment is completed, there may be an increase in recurrent emergency applications with such comorbidities that may arise with COVID-19.

Complaints of cough, shortness of breath, sore throat, and hoarseness were persistent symptoms in our study as well as in the literature (15). In our study, the complaints of dyspnea were prevalent. The effects of polluted air in conflict areas and increased tobacco use in underdeveloped societies may exacerbate respiratory symptoms with COVID -19. Although some studies have shown that tobacco users do not suffer more COVID -19 than nonsmokers (29), there are insufficient data on persistent symptoms. The overlap of these respiratory illness with other respiratory illness or symptoms may increase the emergency department and ICU admissions. In Bangladesh, one of the socioeconomically similar countries, shortness of breath is shown as one of the main problems of hospitalizations both during and following acute COVID-19 infection. Moreover, one-third of the patients still had shortness of breath 2 months later (30). Looking at developed countries, it was found that in countries such as France and Italy, 40% of patients suffer and continue to suffer from shortness of breath. The incidence of respiratory tract diseases may vary depending on climate and air pollution. However, the uncertainty of how long the symptoms of dyspnea last and the difficulty of emergency care and medical management of these patients indicate that the costs of COVID-19 are and will be high. In addition to conditions such as chronic obstructive pulmonary disease and asthma, complaints of shortness of breath that do not resolve after COVID -19 appear to be among the reasons for emergency department routine applications.

Conclusion

In northwestern Syria, pandemic emergency departments were established for the COVID -19 pandemic, and the pandemic process was managed by these departments in all aspects. In this study, the persistent symptoms of COVID-19 after discharge of COVID-19 patients hospitalized from the emergency room were investigated. It was observed that the patients applied to the emergency service due to the persistence of the symptoms and their hospitalizations were repeated. Possibly, symptoms and complaints that do not resolve following COVID-19 and exacerbation of comorbidities of COVID-19 will become reasons for routine emergency department applications; and patients with such complaints will become new regulars of emergency departments. We believe this research will help improve the preparedness of emergency departments in dealing with persistent COVID-19 symptoms.

Limitation

Because of in regions where civil turmoil and terrorism are prevalent, the inability to reach elderly patients who have completed acute COVID -19 treatments in the hospital is a limitation of our study. The lack of telephone or other means of communication with Internet options for socioeconomic reasons makes it difficult to reach patients or their relatives.

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