Out-patient management of patients with COVID-19 on home isolation

Caglayan Merve Ayaz[1], Gulcin Telli Dizman[1], Gokhan Metan[1], Alpaslan Alp[2], Serhat Unal[1]
[1]Department of Infectious Diseases and Clinical Microbiology, Hacettepe University Faculty of Medicine, Ankara, Turkey;
[2]Department of Medical Microbiology, Hacettepe University Faculty of Medicine, Ankara, Turkey

SUMMARY

The rapidly increased number of patients with COVID-19 resulted in the shortage of hospital beds. An outpatient follow-up plan was developed for COVID-19 patients with stable clinical condition and no concomitant diseases. The records of COVID-19 first admission clinic were retrospectively reviewed to identify the COVID-19 patients who were followed on home isolation as outpatients between March 17, 2020 and April 18, 2020 in Ankara, Turkey. Demographic and clinical characteristics of the patients, compliance with isolation rules, re-admission rates, and outcomes were investigated. A total of 41 patients with COVID-19 were followed on home isolation without hospitalization. The median age of the patients was 36 years. Twenty-four (58.5%) of 41 patients were female. Twenty-nine (70.7%) patients were healthcare workers. The most common symptoms at admission were cough, myalgia/arthralgia, and loss of smell and/or taste. Fourteen (34.1%) patients were asymptomatic on the first admission. Anti-viral treatment was given to 27 (65.8%) of 41 patients. Four of 41 patients were readmitted to the outpatient clinic and hospitalized. Three patients had worsening respiratory symptoms and pneumonia was detected in CT scans. One patient was hospitalized because of disseminated herpes zoster infection. Two patients who jeopardized the isolation rules were isolated and monitored at another hospital by provincial health directorate teams. If adequate conditions are provided, follow-up on home isolation seems to be a feasible method in carefully selected patients. However, these patients should be monitored closely by an experienced team during the isolation period.

Keywords: COVID-19, outpatient management, home isolation.

■ INTRODUCTION

An outbreak of a new coronavirus disease was reported in Wuhan, China in December 2019 [1]. The pathogen was identified as a novel enveloped RNA betacoronavirus 2 that has been named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [2]. The first case in Turkey was recorded on 10 March 2020, and then World Health Organization (WHO) announced coronavirus disease 2019 (COVID-19) as a pandemic on 11 March 2020 [3]. A total of 14,560,308 cases had been documented in 216 countries with 607,066 deaths by 19 July 2020. The total number of patients with COVID-19 reached to 219,641 with 5,491 deaths in Turkey on 19 July 2020 [4].

The great majority of patients (80.9%) infected with SARS-CoV-2 had mild disease. On the other hand, 13.8% of the patients had severe disease and required hospitalization with an overall case fatality rate of 2.3% [5]. The shortage of hospital beds for patients who require hospitalization is of concern in case of a rapidly growing number of patients during the pandemic. Considering this potential problem, an outpatient follow-up plan was created in concordance with Ministry of Health guidelines [6].

Herein, we wanted to share our experience about the characteristics and outcomes of COVID-19 patients who were followed as outpatients on home isolation.

Corresponding author
Gökhan Metan
E-mail: gokhanmetan@gmail.com

■ PATIENTS AND METHODS

Hacettepe University Adult Hospital is a 700-bed tertiary care center in Ankara, the capital city of Turkey. The patients with a suspicion of COVID-19 (who do not require respiratory support) at triage points at the main entrances of the hospital and emergency ward were referred to COVID-19 first admission clinic for further evaluation according to the local pandemic plan. A dedicated medical team that was led by an infectious diseases physician obtained detailed epidemiological and medical history. COVID-19 was diagnosed according to WHO interim guidance and the Turkish Ministry of Health COVID-19 guidelines [6].

Combined oropharyngeal and nasopharyngeal swabs were collected to test for SARS-CoV-2 by real-time reverse-transcriptase-polymerase-chain-reaction (RT-PCR). Viral nucleic acid isolation from the samples was achieved by using Bio-Speedy vNAT viral nucleic acid buffer (Bioeksen R&D Technologies Ltd, Turkey). COVID-19 real-time PCR kit (Bioeksen R&D Technologies Ltd, Turkey) was used for the diagnosis in our hospital. A confirmed case of COVID-19 was defined as a patient with a positive PCR result. Only laboratory-confirmed cases were included in this study. The study was approved by the Hacettepe University Non-Interventional Clinical Research Ethics Committee, Ankara, Turkey.

We obtained medical records of the patients with laboratory-confirmed COVID-19 infection, between March 17, 2020, and April 18, 2020. Age, occupation as a healthcare worker, smoking history, comorbidities, clinical signs, or symptoms were recorded on admission. The results of the laboratory tests that were performed according to the local guidelines were extracted from the database of the hospital. Laboratory assessments consisted of a complete blood count, neutrophil-to-lymphocyte ratio (NLR), coagulation parameters, assessment of liver and renal functions, measurement of electrolytes, C-reactive protein (CRP), procalcitonin, lactate dehydrogenase, and creatine kinase levels. Multiplex RT-PCR was performed by using the Allplex Respiratory Panel (Seegene, South Korea) to detect any co-existing respiratory viral and bacterial infections. Electrocardiography (ECG) was performed if antiviral therapy with hydroxychloroquine (HQ) was pre-scribed according to the Ministry of Health guidelines.

The number of people sharing the same house, number of COVID-19 tests that were performed in household contacts, number of household contacts with positive PCR results for COVID-19 were also extracted from the medical records of the patients. The decision for outpatient follow-up on home isolation was made according to the severity of clinical presentation, laboratory test results, presence of comorbid conditions, and availability of home isolation. The following recommendations were given to the patients to avoid further diffusion of the virus to household contacts according to the Ministry of Health guidelines:
1) no visitors should be allowed;
2) home patient should stay in rooms apart from others, if possible;
3) patient should wear medical masks if it is necessary to share the same environment with other person(s);
4) the movements of the patient in the house should be limited;
5) patient should use separate bathrooms and toilets, if possible;
6) shared toilets and bathrooms should be well-ventilated and cleaned with diluted bleach;
7) patient should avoid sharing personal items;
8) patient's room should be cleaned with gloves and masks [7].

Patients with concomitant disease or pneumonia, patients older than 60 years regardless of clinical severity, and who declared any obstacles for self-isolation were excluded from the outpatient follow-up plan.

A written informed consent form was obtained from all patients for the statement of compliance with self-isolation. Patients who were included in outpatient follow-up program were called by phone every day for 14 days to evaluate for the presence of new signs and symptoms, medical conditions of family members (any household contact with fever or respiratory symptoms, number of COVID-19 tests were done in household contacts by public health filiation teams, and number of family members positive test results for COVID-19), compliance with isolation rules, and side effects if treatment was started. During the follow-up period, two control PCR tests were recommended at intervals of 24-48 hours after all signs and symptoms were dissolved.

The mean, median values and interquartile ranges (IQR) or simple ranges were calculated for scale variables. Categorical variables were described as counts and percentages. For all statistical analysis, Statistical Packages for the Social Sciences (v17.0 SPSS 24 Inc. Chicago, IL) software was used.

■ RESULTS

A total of 220 patients were diagnosed as COVID-19 between March 17, 2019, and April 18, 2020 in our hospital and 41 (18.6%) of them were followed on home isolation. The median age of the patients was 36.0 years (IQR 25.5-41.5). Twenty-four (58.5%) of 41 patients were female (Table 1). Twenty-nine (70.7%) patients were healthcare workers and 19 (46.3%) patients were current smokers. History of contact with a diagnosed COVID-19 case was documented in all 41 patients. When the history of contact was evaluated, 31 (75.6%) of them were exposed to the virus at work. Twenty-eight (96.5%) of 29 healthcare workers reported to contact with another healthcare worker recently diagnosed as COVID-19 without any personal protective equipment.

Lymphopenia was the most prevalent laboratory finding that was detected in 14 (40.0%) of 35 patients (Table 2). Chest radiography was performed for investigating the presence of pneumonia in 27 (65.8%) patients at the time of admission, however, computed tomography (CT) was performed for all patients. Ground glass opacities were detected in two patients (4.9%) in CT scan. Rest of the patients' CT scans were detected normal.

Multiplex PCR for co-infections with respiratory pathogens was requested from 16 patients. Influenza B was detected in one patient, *Haemophilus influenzae* was detected in 3 patients and *Streptococcus pneumoniae* in one patient. Oseltamivir was initiated to the patient with influenza B co-infection when he was readmitted with fever. However, the patients with co-infection with bacterial pathogens did not have fever or any respiratory symptoms when multplex PCR results became available.

Anti-viral treatment was given to 27 (65.8%) of 41 patients. The most preferred drug was HQ in 25 patients and two patients with non-severe pneumonia was treated with a combination of HQ plus azithromycin plus oseltamivir. The patient with concomitant influenza B infection was treated with hydroxychloroquine plus oseltamivir. Side effects of drugs were seen in 6 (23.1%) patients but no intervention was needed. Side effects during treatment included symptoms of hypoglycaemia in 3 patients, palpitations in 2 patients, and nausea in one patient. Treatment was continued in two patients with palpitations, control ECG was not performed, and their complaints improved in their follow-up.

Table 1 - Demographic and clinical characteristics of the patients.

Characteristic	All patients (No 41)
Age (median) (years)	36.0 (IQR 25.5-41.5)

Gender
  Female
  Male
	
	24 (58.5%)
	17 (41.5%)

Healthcare worker	29 (70.7%)
History of contact with a diagnosed COVID-19 case	41 (100.0%)

Location of contact
  At work
  At home
	
	31 (75.6%)
	10 (24.4%)

Current smoking	19 (46.3%)
Comorbid diseases	2 (4.9%)
Hypothyroidism Familial Mediterranean Fever and asthma	1 1
Asymptomatic on the first admission	14 (34.1%)
Symptoms	
Fever (body temperature ≥ 37.5°C)	4 (9.8%)
Cough	16 (39.0%)
Myalgia/arthralgia	15 (36.6%)
Headache	3 (7.3%)
Sore throat	5 (12.1%)
Loss of smell and/or taste	12 (29.3%)
Runny nose	1 (2.5%)
Nasal congestion	3 (7.3%)
Postnasal drip	3 (7.3%)
Hoarseness	1 (2.4%)
Dyspnoea	2 (4.9%)
Nausea/vomiting	3 (7.3%)
Diarrhoea	3 (7.3%)
Skin rash	1 (2.4%)

Table 2 - Laboratory findings on admission.

Laboratory findings	Number of tested patients (%)
Anaemia (for women <12 g/dL, for men <13 g/dL)	4/35 (11.4%)
Leukopenia (<4000 per mm³)	3/35 (8.6%)
Leucocytosis (>10000 per mm³)	1/35 (2.9%)
Lymphocytopenia (<1500 per mm³)	14/35 (40.0%)
Thrombocytopenia (150,000 per mm³)	3/35 (8.6%)
CRP (>0.8 mg/dL)	10/33 (30.3%)
Procalcitonin (>0.05 ng/dL)	1/14 (7.1%)
Ferritin (>500ng/ml)	0/21 (0.0%)
Creatine kinase (≥200 U/L)	2/13 (15.4%)
Lactate dehydrogenase (≥250 U/L)	0/14 (0.0%)
Creatinine (>1.2 mg/dL)	0/20 (0.0%)
Alanine aminotransferase (> 35 IU/L)	1/16 (6.3%)
D-dimer (≥0.5 mg/L)	0/21 (0.0%)
Elevated or decreased fibrinogen	0/14 (0.0%)
Positive respiratory virus panel	1/16 (6.3%)
Positive respiratory bacterial panel	4/16 (25.0%)

The median duration improvement of initial symptoms was 5.0 days (IQR 2.25-8.50) for cough, 4.0 days (IQR 3.0-8.0) for myalgia/arthralgia and healing loss of smell and taste was 4.0 (IQR 3.0-5.75). A total of 14 (34.1%) patients were asymptomatic on the first admission. However, 7 (50%) patients showed signs and symptoms attributable to COVID-19 during the 14-day follow-up. Seven out of 14 patients completed the follow-up period at home without any symptoms.

Four of 41 patients were readmitted to the outpatient clinic and hospitalized. Three patients had worsening respiratory symptoms and pneumonia was detected in CT scans. One patient was hospitalized because of disseminated herpes zoster infection. They were discharged in good condition after successful therapy. Two patients who jeopardized the isolation rules were detected by Public Health Services of Ministry of Health and isolated at another hospital.

COVID-19 PCR was repeated in 36 (87.8%) patients. The median duration was 10.5 days (IQR 7.25-13) from admission to achieve first negative control COVID-19 PCR in 36 (87.8%) patients and the second negative control COVID-19 PCR was achieved in the median duration of 12 days (IQR 8.75-14) in 34 (82.9%) patients.

The median number of household contacts of the patients were 3.0 (IQR 0.5-3.0). On admission, all family members of 6 (14.6%) patients had been already diagnosed as COVID-19. COVID-19 PCR was performed for 18 patients' household contacts based on information that was collected by phone call during 14-day self-isolation at home. The 14 (42.4%) of 33 household contacts were tested for screening but the remaining 19 (57.6%) of them had symptoms that were attributed to COVID-19. PCR detected SARS CoV-2 in 12 household contacts of patients. The household contacts suffered for a symptom in median 4.5 days (IQR 2.25-7.0) after the index case was identified.

■ DISCUSSION

The ideal way of controlling an outbreak with a rapidly disseminating respiratory pathogen is the isolation of the patients at healthcare facilities under appropriate respiratory precautions. However, this would result with the shortage of beds for the patients who require respiratory support. Turkish Ministry of Health released a guideline for COVID-19 patients who can self-isolate at home [7]. We have implied these recommendations in our daily practice for patients with mild symptoms. We offered hospitalization for the two patients with pneumonia, but they have declined for social reasons. The rate of anxiety and depression is high related to COVID-19 pandemic. Self-isolation at home (a well-known environment with family support) can help to overcome the psychological problems. However, this can introduce the risk of spread SARS-CoV-2 to household contacts. Daily follow-up by phone calls which included the review of clinical situation of the patient with reminding the principles of self-isolation kept our strategy as safe as possible. Telemedicine is a growing area during COVID-19 pandemic [8]. Also, the public health teams were already on ground for filiation and their efforts are invaluable to detect COVID-19 in household contacts.

In our cohort, most of the patients with COVID-19 were healthcare workers. Although this was a depressing situation, it was safe to follow-up them on home isolation. Many healthcare

workers are known to be infected during pandemic [9, 10]. Transmission between healthcare workers was detected as a major problem in our cohort, and 28 (96.5%) of 29 healthcare workers had contact with another healthcare worker infected by SARS COV-2 in our study. This situation may have been caused by asymptomatic or pre-symptomatic healthcare staff with a lack of compliance with social isolation precautions. The dynamics of transmission of COVID-19 between healthcare workers are complex. Recently, the increasing number of healthcare staff with COVID-19 was found to be related to the COVID-19 activity in the society [11].

The most common laboratory findings were high CRP and lymphopenia in our patients that were similar to other studies [12-14]. Co-infections with *H. influenzae*, *S. pneumoniae,* and influenza B were detected in 5 (33.3%) patients by multiplex PCR. Studies have shown that co-infections may be seen with COVID-19. In a review study evaluating co-infections reported that 8% of patients had fungal/bacterial co-infection during hospital admission [15]. In another study involving 115 COVID-19 PCR positive patients, viral pathogens were detected in 20% of patients [16]. The rate of co-infection can vary according to the sampling strategy and methods that are used to test respiratory samples. As PCR is a very sensitive method, it should be kept in mind that positive PCR may not mean an active infection if there are no symptoms as we experienced in our study.

A total of 33 household contacts were tested for screening or when symptoms occurred and 12 (36.4%) of them were detected as positive. The rising question is "Who was the initial source of COVID-19 at home?". Since the incubation period of COVID-19 can be as long as 14 days, it is difficult to judge on the transmission of SARS-CoV-2 between patients and household contacts. There were 4.5 (median) days (IQR 2.25-7.0) between detection of the index case and the appearance of household contacts' symptoms. Studies show that there may be household transmission of SARS-CoV-2 and the median incubation period was estimated to be 4.3 days (IQR 3.4-5.3) [17, 18]. Ensuring isolation of infected patients at home, rapid investigation of contacts, closely monitoring family members, and testing household contacts immediately are the most important points to prevent the household transmission.

Control SARS-CoV-2 PCR was performed in 36 patients and the first negative control test result was noted at median 10.5 days (IQR 7.25-13). Ministry of Health guidelines recommended two consecutive negative PCR to terminate isolation at the beginning of the pandemic, but this recommendation was changed to 14 days isolation without any control PCR tests except healthcare staff. The patients can remain PCR positive longer than 14 days but viable virus was not detected in clinical samples beyond 10 days [19].

The outpatient follow-up program ended with the introduction of a dormitory as a treatment centre by the Provincial Health Directorate of Ankara. Mild or asymptomatic cases were transferred to this centre for isolation. The effectiveness of such community treatment centre derived from a dormitory with strict isolation and active surveillance has been reported, recently (20).

Our study was limited with the low number of patients from a single centre. However, our findings showed that self-isolation at home may be an alternative to manage mild cases or asymptomatic patients when applied with careful and close observation.

Conflict of interest
None

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