Is the Presence of a Typical Triad of COVID-19 Symptoms (Cough, Dyspnea, and Fever) Enough to Make a Decision About Diagnostic Testing? From the Perspective of an Emergency Department

Tipik Bir COVID-19 Semptom Üçlüsünün (Öksürük, Nefes Darlığı ve Ateş) Varlığı Tanısal Test Yapma Kararı için Yeterli midir? Acil Departmanı Bakış Açısıyla

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ABSTRACT

Objective: The aim of this study is to show the consistence between the recommended guidelines regarding the triad of symptoms—cough, dyspnea, and fever—and the diagnosis of COVID-19.
Methods: A prospective observational study conducted at a tertiary emergency department between April 2, 2020 and May 15, 2020 in Turkey. Detailed patient history, main presenting complaints and imaging findings were recorded. For COVID-19 confirmation, nasopharyngeal RT-PCR was used. The relationship between complaints and COVID-19 test results were analyzed.
Results: Of the 1226, suspected COVID-19 patients, 127 were positive, 471 were negative, and 628 were discharged without any tests. The most common presenting complaints of the COVID-19 positive patients were throat pain (25.2%), dyspnea (15%), cough (22%), malaise and fatigue (11.8%), and fever (8.7%). There was no statistically significant difference between the positive and negative test groups as they had fever (χ^2, p = 0.30), cough (χ^2, p = 0.67) and dyspnea (χ^2, p = 0.14).
Conclusion: Considering that it is difficult to diagnose COVID-19 in emergency settings, testing decision and diagnosis should not depend only on classical symptoms; otherwise, patients with atypical and rare symptoms may be missed. Instead, patient history, clinical status, and radiological findings should be considered together.

Keywords: COVID-19 diagnosis, signs and symptoms, emergency service

ÖZET

Amaç: Bu çalışmanın amacı, semptom üçlüsü (öksürük, nefes darlığı ve ateş) ve COVID-19 tanısına ilişkin önerilen kılavuzlar arasındaki uyumu göstermektir.
Yöntem: Çalışma Türkiye'de bir üçüncü basamak Acil Tıp departmanında 2 Nisan 2020 ve 15 Mayıs 2020 arasında prospektif gözlemsel olarak yapılmıştır. Detaylı hasta hikayesi, ana başvuru şikayeti ve görüntüleme bulguları kaydedilmiştir. COVID-19 doğrulaması için nazofaringeal RT-PCR kullanılmıştır. Şikayetler ve COVID-19 test sonuçları arasındaki ilişki analiz edilmiştir.
Bulgular: COVID-19 şüphesi olan 1226 hastanın 127'si pozitif, 471'i negative saptanmış ve 628'I test yapılmadan taburcu edilmiştir. COVID-19 pozitif hastaların en sık başvuru şikayetleri boğaz ağrısı(%25.2), nefes darlığı(%15), öksürük(%22), halsizlik ve yorgunluk (%11.8) ve ateştir(%8.7). Pozitif ve negatif test grupları arasında ateş (χ^2, p = 0.30), öksürük (χ^2, p = 0.67) ve dispne (χ^2, p = 0.14) olması açısından istatistiksel olarak anlamlı bir fark yoktu.
Sonuç: Acil durumlarda COVID-19'u teşhis etmenin zor olduğu düşünüldüğünde, test kararı ve teşhisi sadece klasik semptomlara bağlı olmamalıdır; aksi takdirde atipik ve nadir semptomları olan hastalar gözden kaçabilir. Bunun yerine hasta öyküsü, klinik durumu ve radyolojik bulgular birlikte değerlendirilmelidir.

Anahtar Sözcükler: COVID-19 tanısı, belirti ve bulgular, acil servis

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INTRODUCTION

After the first case was reported in Wuhan, China, the third novel coronavirus emerged in December 2019. In March 11, 2020, the World Health Organization (WHO) declared COVID-19 as a public health emergency of international concern (1). Similarly, the COVID-19 pandemic in Turkey is part of the ongoing worldwide pandemia.

The first positive COVID-19 case in Turkey was reported by the Turkish Ministry of Health on March 11, 2020 and the first death related to COVID-19 occurred on March 15, 2020. Subsequently, the COVID-19 spread throughout the country, mainly in metropolitan cities (2).

In the first studies at the beginning of the pandemic, cough, fever, and, in the severe cases, dyspnea were thought to be the most common and characteristic symptoms of the disease (3).

As the COVID-19 pandemic started spreading and causing public catastrophes all over the world, the WHO and the United States Centers for Disease Control and Prevention (CDC) recommended clinicians to consider diagnostic testing of people with symptoms of potential COVID-19 infection, including cough, dyspnea, and fever, as well as symptoms of acute respiratory illness. The diagnostic algorithm, developed by the members of Turkish COVID-19 Science Committee under the Turkish Ministry of Health, was presented to all COVID-19 healthcare providers in Turkey (2).

In this study, we aimed to investigate whether the classical triad of COVID-19 symptoms (fever, cough, and dyspnea) is consistent with the decision of the physicians and the real-time reverse transcription polymerase chain reaction (RT-PCR) results at the emergency department (ED). The secondary goal of the study is to describe the demographic characteristics, clinical presentation, medical history, and imaging findings among patients triaged in the ED regarding the COVID-19 diagnostic algorithm recommended by the CDC.

MATERIALS and METHODS

This is a prospective observational study performed at the Gazi University Faculty of Medicine Hospital with 76000 emergency patient admission annually in Ankara in Turkey. In this pandemic, Gazi University Hospital was designated as a pandemic hospital by the local government to treat patients. The data reported are those available between April 2, 2020 and May 15, 2020. With the announcement of pandemic by the WHO, hospitals had planned their own patient flow algorithms. We have also planned a new triage system for the patients suspected of COVID-19. This COVID-19 triage unit was located at a different place outside of the emergency triage. We screened all the consecutive patients for the presence of cough, dyspnea, and fever using the recommended guidelines from the WHO as the main complaints of COVID-19 in this new triage area.

Data Collection

We performed detailed patient history related to clinical signs and symptoms. The type and duration of the signs and symptoms (pain in throat, fever, cough, dyspnea, headache, nasal discharge, anosmia, malaise and fatigue, myalgia, nausea and vomiting, diarrhea), along with a history of close contact with a person who was under investigation for COVİD-19, history of travel, detailed medical history were all collected in the COVID-19 triage area. All suspected COVID-19 patients were then followed up for radiological and laboratory test results.

Radiological assessments included chest radiography or computed tomography (CT). The presence of radiological abnormality was determined based on a radiologist's documentation. A confirmed case of COVID-19 was defined by a positive result on the real-time RT-PCR assay of a specimen collected on a nasopharyngeal swab. Only patients whose nasopharyngeal swabs were collected for RT-PCR were included in the statistical analysis. The cases that were sent home for isolation after physical examination without RT-PCR and those under 18 years were excluded. The decision to collect the specimen was made by the physicians according to the complaints and history of the patients.
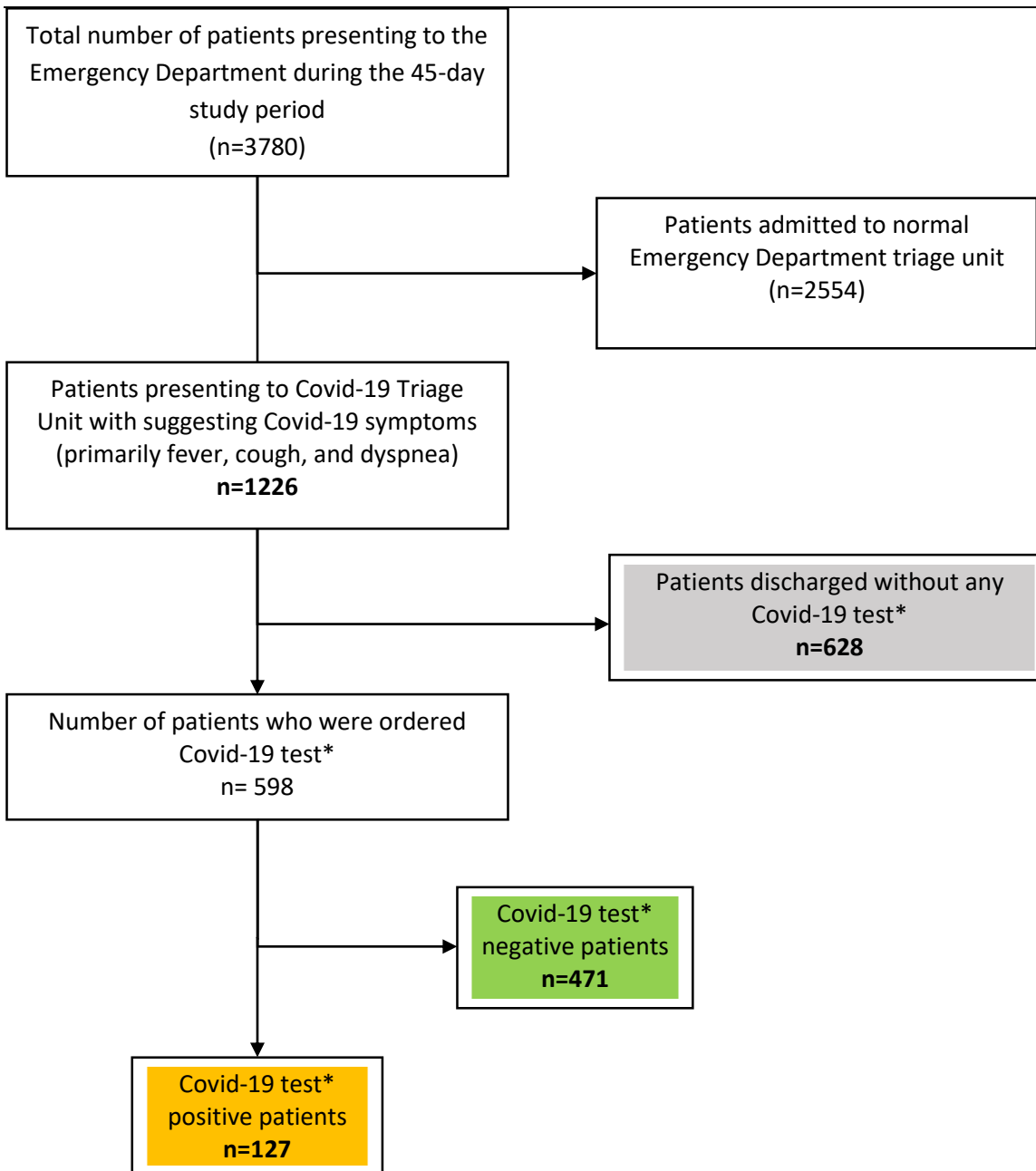
Statistical methods

Categorical variables were described as frequency rates and percentages and compared by, and continuous variables were described using mean, median, and interquartile range (IQR) values. χ^2 test was used to show the relation between complaints, radiological findings, and COVID-19 test results. All statistical analyses were performed using SPSS (Statistical Package for the Social Sciences) version 20.0 software (SPSS Inc., Chicago, IL, USA). Values of $p < 0.05$ were considered statistically significant.

Hospital Head Chief was informed and written study approval was obtained. The study was also recorded by the Turkish Ministry of Health, and reviewed by our Institutional Review Board (09.05.2020/05).

RESULTS

During the study period, 1226 consecutive patients who presented themselves at the COVID-19 triage unit of our ED were included in the study. Of these patients, 127 were confirmed as COVID-19 positive after the RT-PCR test, while 471 were found COVID-19 negative. Of the 1226 patients, 628 were considered non-suspected for COVID-19 and were discharged without administering any diagnostic COVID-19 tests (Figure 1).

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┌─────────────────────────────┐
│ Total number of patients    │
│ presenting to the           │
│ Emergency Department during │
│ the 45-day study period     │
│ (n=3780)                    │
└─────────────────────────────┘
            │
            │────────────────────►┌─────────────────────────────┐
            │                     │ Patients admitted to normal │
            │                     │ Emergency Department triage │
            │                     │ unit                        │
            │                     │ (n=2554)                    │
            │                     └─────────────────────────────┘
            ▼
┌─────────────────────────────┐
│ Patients presenting to      │
│ Covid-19 Triage Unit with   │
│ suggesting Covid-19 symptoms│
│ (primarily fever, cough,    │
│ and dyspnea)                │
│ n=1226                      │
└─────────────────────────────┘
            │
            │────────────────────►┌─────────────────────────────┐
            │                     │ Patients discharged without │
            │                     │ any Covid-19 test*          │
            │                     │ n=628                       │
            │                     └─────────────────────────────┘
            ▼
┌─────────────────────────────┐
│ Number of patients who were │
│ ordered Covid-19 test*      │
│ n= 598                      │
└─────────────────────────────┘
            │
            │────────────────────►┌─────────────────────────────┐
            │                     │ Covid-19 test* negative     │
            │                     │ patients                    │
            │                     │ n=471                       │
            │                     └─────────────────────────────┘
            ▼
┌─────────────────────────────┐
│ Covid-19 test* positive     │
│ patients                    │
│ n=127                       │
└─────────────────────────────┘
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* Covid-19 diagnostic test is a Real time Reverse Transcription-Polymerase Chain Reaction (rT-PCR) kit.

Figure 1. Patients' Flow Chart

Among the 127 COVID-19 positive patients, 59.8% were men, and the mean (± SD) age was 41.5 ± 15.9 years (median: 38; IQR: 30–50; range: 18–85 years). Of the total, 12.6% were over 65 years and 59.1% were younger than 40 years.

Most of the patients presented to the ED between 12 noon and midnight (61.4%) and 9.4% of them used prehospital emergency medical systems. After the temperature and other vital signs were obtained, 70.0% of the patients were examined at the fast track unit of COVID-19, while 22% of the patients who needed emergency medical treatment such as oxygen, bronchodilator treatment, etc., were isolated in special emergency rooms.

Upon investigation of the travel history and contact with ill persons, it was found that 7 (5.5%) patients had a history of national travel and 3 (2.4%) of international travel.

About recent contact with a person known to have been ill, 20 patients (15.7%) reported that the contact was at home and 19 patients (15%) reported that the contact occurred at work. The nearby contact persons of patients were either their spouses (5.5%) or their friends (3.1%).

At the COVID-19 triage area, the most common complaints of the COVID-19 positive patients regarding ICD-10 symptoms codes were pain in throat (32 (25.2%)) with R97.0, dyspnea (19 (15%)) with R06.0, cough (28 (22%)) with R05, malaise and fatigue (15 (11.8%)) with R53, fever (11 (8.7%)) with R50.9, and headache (6 (4.7%)) with R51. Detailed demographic characteristics of all the consecutive patients related to the different patient groups (i.e., COVID-19 test positive, COVID-19 test negative, and non-suspected patients discharged from the ED) are provided in Table 1.

Table 1. The demographic data and common complaints of study patients admitted to COVID-19 Triage Unit

	COVID-19 test Positive	COVID-19 test Negative	Patients without test
	n = 127	n = 471	n = 628
Age			
Mean ± SD	41.5 ± 15.9	41.0 ± 15.6	41.8 ± 16.7
Median (min-max)	38 (18–85)	38 (18–91)	39 (19–94)
Gender (n, %)			
Male	76 (59.8%)	259 (55%)	368 (58.6%)
Female	51 (40.2%)	212 (45%)	260 (41.4%)
Presenting complaints (n, %)			
Pain in throat (R97.0)	32 (25.2)	109 (23.1)	215 (34.2)
Cough (R05)	28 (22.0)	99 (21.0)	85 (13.5)
Dyspnea (R06.0)	19 (15.0)	88 (18.7)	107 (17.0)
Malaise and fatigue (R53)	15 (11.8)	46 (9.8)	32 (5.1)
Fever (R50.9)	11 (8.7)	50 (10.6)	55 (8.8)
Headache (R51)	6 (4.7)	23 (4.9)	32 (5.1)
History of travel (n, %)			
Inside country	7 (5.5)	16 (3.4)	24 (3.8)
Outside country	3 (2.4)	4 (0.8)	13 (2.1)
History of contact (n, %)			
At home	20 (15.7)	57 (12.1)	44 (7.0)
At work	19 (15.0)	61 (13.0)	40 (6.4)
Medical history			
Diabetes mellitus	11 (8.7)	30 (6.4)	31 (4.9)
Hypertension	19 (15.0)	48 (10.2)	77 (12.3)
Coronary artery disease	15 (11.8)	26 (5.5)	41 (6.5)
Asthma	9 (7.1)	34 (7.2)	25 (4.0)
COPD	4 (3.1)	15 (3.2)	32 (5.1)
Smoking	28 (22)	115 (24.4)	142 (22.6)

The first complaints of the patients were pain in throat 30 (23.6%), malaise and fatigue 18 (14.2%), dyspnea 16 (12.6%), fever 11 (8.7%), and headache 5 (3.9%). As the complaints were asked individually with duration, 45.7% had pain in throat (median: 3; IQR: 2–5), 29.9% dyspnea (median: 3; IQR: 2–7), 34.6 % cough without sputum (median: 3; IQR: 2–7), 22.8% headache (median: 2; IQR: 1-4), 29.9% fever (median: 2; IQR: 1–4).

The uncommon complaints were pain in joint (3.1%), unspecified chest pain (3.1%), headache (4.7%), and anosmia (1.6%). Of these patients, 2 (1.57%) had rhinorrhea and anosmia together. Documented fever was present in 12.5% of the patients on presentation at the triage unit. 19 (15%) had hypertension, 15 (11.8%) had coronary artery disease, 11 (8.7%) had diabetes mellitus, 9 (7.1%) had asthma, and 4 (3.1%) had COPD (Table 1). 28 patients (22%) were current or former smokers. 14.2% of the COVID-19 positive patients had presented themselves previously to another hospital, 11% had provided nasal swab, and 2.4% had taken chloroquine pills as prophylaxis before coming to our institution.

Chest radiographs were obtained for 91 (71.7%) patients on ED admission. Only 3 (2.4%) of the radiographs showed pulmonary opacities. Among COVID-19 positive patients, 19 (14.9%) patients had neither chest radiograph nor CT, and for 17 patients, CTs were obtained directly without X-rays.

A computed tomographic scan (CT) of the chest was obtained for 48 (37.8%) patients; 11 (8.7%) of the scans showed ground glass opacities, 10 (7.9%) showed pulmonary nodules, 10 (7.9%) showed atelectasis, 5 (3.93%) showed consolidation, and 3 (2.36%) showed thickened pleura.

Of the 127 patients with positive COVID-19 test, 50 (39.4%) were discharged with instructions for self-isolation at home, 73 (57.4%) were admitted to COVID-19 isolated hospital service and 4 (3.1%) were admitted to critical care unit. The length of stay at the ED was 1 hour in 42.5% and 3 hours in 32.3% of the COVID-19 positive patients. The reasons for the longer stay for some of the patients were obtaining the CT and consultation from other departments.

Patients with positive and negative test results were evaluated based on common complaints. There was no statistically significant difference between the groups as they had fever (χ2, p = 0.30), cough without sputum (χ2, p = 0.67) and dyspnea (χ2, p = 0.14). Patients with COVID-19 positive and negative tests were grouped as mild and severe groups according to their presenting complaints. Among the COVID-19 positive patients, 14 patients (11%) were in the mild group and 6 patients (4.7%) were in the severe group. There was no statistically significant difference between the groups (χ², p = 0.09, p = 0.19, respectively) according to the severity of the symptoms (Table 2).

Table 2. The relationship between COVID-19 test results and common presenting complaints

Common Symptoms	COVID-19 negative	COVID-19 positive	Total	P values
	n (%)	n (%)		
Fever	118 (75.6)	38 (24.4)	156	0.305
Cough	153 (77.7)	44 (22.3)	197	0.671
Dyspnea	176 (82.2)	38 (17.8)	214	0.144
Fever + cough	33 (70.2)	14 (29.8)	47	0.140
Fever + cough + dyspnea	13 (68.4)	6 (31.6)	19	0.260

Pearson χ², row percent

Among the thorax CT findings, ground glass opacity is defined as an important finding in COVID-19 positive patients. After evaluating the reports of the patients, no statistically significant difference between groups was found if they had mild or severe complaints (χ^2, p = 1.0) (Table 3).

The sensitivity and specificity of typical symptoms of COVID-19 positive results are shown in Table 4. The sensitivity of pain in throat is 45.7 (95% CI 36.8 to 54.7) and specificity of fever, cough and dyspnea is 97.2 (95% CI 95.3 to 98.5) (Table 4).

Table 3. The relationship between COVID-19 test results and radiological findings

	CT-Ground glass opacity absent n (%)	CT-Ground glass opacity present n (%)	Total	P values
Fever + cough	20 (76.9)	6 (23.1)	26	1.000
Fever + cough + dyspnea	8 (72.7)	3 (27.3)	11	1.000

Pearson χ^2, row percent

Table 4. The diagnostic accuracy of typical symptoms for COVID-19 positive results

Complaints	Sensitivity % (95% CI)	Specificity % (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Dry cough	34.7 (26.4–43.6)	67.5 (63.1–71.7)	1.07 (0.8–1.4)	0.97 (0.84–1.11)
Dyspnea	29.9 (22.1–38.7)	62.3 (58.1–67.0)	0.80 (0.60–1.07)	1.12 (0.98–1.28)
Fever	29.9 (22.1–38.7)	74.9 (70.8–78.8)	1.19 (0.88–1.63)	0.94 (0.83–1.06)
Pain in throat	45.7 (36.8–54.7)	56.0 (51.4–60.6)	1.04 (0.84–1.29)	0.97 (0.81–1.16)
Headache	22.8 (15.9–31.1)	72.2 (67.9–76.2)	0.82 (0.58–1.17)	1.07 (0.96–1.19)
Fever and cough	11.0 (6.2–17.8)	92.9 (90.3–95.1)	1.57 (0.87–2.85)	0.96 (0.90–1.02)
Fever, cough, and dyspnea	4.7 (1.7–10)	97.2 (95.3–98.5)	1.71 (0.66–4.41)	0.98 0.94–1.02)

DISCUSSION

This study showed that COVID-19 diagnostic algorithms recommended by the CDC and WHO were not proper for the diagnosis of COVID-19 regardless of whether the patients exhibited COVID-19 pneumonia or COVID-19 viral upper respiratory tract infections. Patients with symptoms similar to those of COVID-19 confirmed patients were discharged with instructions for self-isolation at home.

The symptoms recommended by the CDC and WHO were not very helpful in the diagnosis of COVID-19. In fact, our results show that the COVID-19 positive patients had symptoms similar to those in non-specific, systemic viral infections.

It was also observed that there was no change in diagnosis irrespective of whether tests were performed on the patients. In such a situation, the primary goal should be focused on identifying patients who need urgent medical treatment. This situation was handled with the recommended CDC algorithm. However, the fact that more than half of the patients in our study, for example, were not tested and therefore not diagnosed with COVID-19 may have been instrumental in the spread of the disease.

COVID-19 infection seems to cover a wide clinical spectrum from asymptomatic patients, mild upper respiratory tract illnesses, and severe pneumonia, to even death (4). All the viruses that cause severe acute respiratory syndrome-associated coronavirus (SARS-CoV), Middle East respiratory syndrome-associated coronavirus (MERS-CoV), and COVID-19 are categorized within the family Coronaviridae (3). The symptoms of these viral diseases as well as those of seasonal influenza seem to be similar, which makes it difficult to diagnose them with certainty. However, fever and cough were defined as dominant and gastrointestinal symptoms as uncommon among COVID-19 patients, which differs in viral tropism as compared with SARS-CoV, MERS-CoV, and seasonal influenza (1). Although dyspnea, cough, and fever were reported as the main complaints of the disease and the cornerstone of testing at the beginning of this pandemic, it was later noticed that even patients without these symptoms might test positive for COVID-19.

COVID-19 was mainly reported for the 30–65 age group (5). Li et al. reported the median age of the patients as 59 years (range: 15–89 years) with 56% being male (6). In our study, the median age was 38 (range: 18–85 years) and 59.8% were male, which is compatible with the literature.

In a cohort study, the most common presenting symptoms were fever, cough without sputum, and dyspnea. Few patients had noticeable upper respiratory tract and intestinal signs and symptoms (8).

In December 2019, it was reported that common symptoms were 98% fever, 76% cough without sputum, and 55% dyspnea (5). Dyspnea and cough were reported as the most common symptoms on admission in another study (9). Zhou et al. reported the most common symptoms as fever, cough, sputum production, and malaise (4). In our study, pain in throat, cough, dyspnea, and malaise and fatigue were the most common presenting symptoms of COVID-19 positive patients. Fever was the fifth common symptom, while headache, anosmia, chest pain, and joint pain were uncommon symptoms.

At the beginning of 2020, Guan et al. reported that fever is frequently the main and the first symptom, which can be seen with or without other symptoms (5). In another study, it was reported that 90% of the patients infected with COVID-19 had fever (10). However, in the later studies, it was mentioned that in COVID-19, fever might not be seen more frequently than in SARS-CoV and MERS-CoV infections, which may lead to missing of afebrile patients (1). Bhatraju et al. reported that 50% of the patients had documented fever when they came to the hospital and emphasized that using fever as diagnostic criteria may delay diagnosis (9). In our study, 87.4% of COVID-19 positive patients were reported without fever when they presented themselves to the ED.

In a review by Pascarella et al, about 80–90% of cases were defined with mild or asymptomatic clinical state and the rest with dyspnea and extensive radiological involvement of lung parenchyma (11). Dyspnea was reported in 18 patients (13.3%) by Wan (12). We also reported it as a complaint in 15% of COVID-19 diagnosed patients.

In a cohort study of 508 patients, total loss of smell was reported in 64% and loss of taste in 60% of the patients (13). In another study, smell or taste alterations were reported in 64.4% of the patients (14). In a prospective study of 1788 patients from Australia, 2.2% of patients suffered from both smell and taste problems, with 3.1% smell loss alone and 4.1% taste loss alone (15). In our study, 2 (1.6%) patients complained about anosmia as the main complaint. Anosmia is not as frequent as we believed. Some of the patients defined anosmia with nasal congestion or rhinorrhea together. Therefore, it is difficult to distinguish patients with olfactory involvement from the others.

Patients with the diagnosis of COVID-19 may present with flu-like symptoms, and it is difficult to differentiate them from other respiratory diseases (11). Chen et al. reported 5 (5%) patients with pain in throat and 4 (4%) with rhinorrhea as upper airway symptoms (16). Our patients defined pain in throat as the most common complaint and none of the COVID-19 positive patients at the ED presented rhinorrhea as the main complaint.

It was an interesting finding that rhinorrhea—one of the typical symptoms of coronavirus infections—did not appear in any of the patients.

Myalgia or fatigue was reported in 44 (32.5%) patients as one of the most common and diarrhea in 18 (13.3%) patients as rare symptoms by Wan (12). We too found malaise and fatigue as a common symptom; however, none of our COVID-19 positive patients had diarrhea.

It was difficult to diagnose the disease because of the variability in symptoms and imaging findings. The performed chest CT scans showed mostly ground-glass opacity and bilateral shadowing in some areas. On the first presentation, radiological abnormalities were not stated in clinically 2.9% of severe and 17.9% of non-severe patients (1). Multifocal bilateral ground-glass opacities or consolidation is defined as common with round, triangular, and linear shapes. Cavitation, nodules, pleural effusions are rare (17). Bernheim et al. reported that 56% of patients who obtained CT in the first two days had normal CT (18). In our study, among the COVID-19 positive patients' chest CT images, the most common findings were ground-glass opacity, nodules, and atelectasis. As most of our patients had mild symptoms, the number of pathological chest CT was less. Because the clinical findings were nonspecific and rare, some of our patients were discharged without any radiological study.

CONCLUSION

Given that the signs and symptoms of COVID-19 can mimic other upper respiratory viral infections, it may be difficult to diagnose the disease in the context of history. Although specificity of these symptoms look higher in patients presenting with the typical triad of COVID-19 symptoms, they may still yield negative test results, and clinicians may miss other patients who do not exhibit the classical symptoms. Based on the findings of this study, we have come to the conclusion that symptom-dependent diagnostic strategies should not be designed strictly. Moreover, if the patients do not present clinical indications for hospital admission, self-isolation at home and follow up instructions may be advised by the emergency department.

Conflict of interest
No conflict of interest was declared by the authors.

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