

Evaluation of the Relationship Between Symptoms and Poor Prognosis on Patients Admitted to COVID-19 Outpatient Clinic: Retrospective Cohort Study

COVID-19 Polikliniğine Ayaktan Başvuran Hastaların Semptomları ve Kötü Sonlanım İlişkisinin Değerlendirilmesi: Retrospektif Kohort Çalışma

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ABSTRACT

Aim: To evaluate the relationships between the symptoms of patients admitted to the COVID-19 outpatient clinic and short-term mortality, hospitalization, intensive care unit admission and necessity of mechanical ventilation during hospitalization.

Material and Methods: This retrospective cohort study was conducted at a pandemic clinic. All hospitalized patients and outpatients with positive RT-PCR assay for SARS-CoV-2 were included the study. Demographic parameters, clinical characteristics, vital parameters on admission, outpatient clinic outcomes of each patient were obtained from the hospital computer-based patient data system and analyzed. Primary outcome of this study was determining the relationship between the symptoms of patients admitted to the COVID-19 outpatient clinic and 30-day mortality. The secondary outcomes were hospitalization, intensive care unit admission, and necessity of mechanical ventilation during hospitalization.

Results: A total of 1566 patients with positive results of RT-PCR assay for SARS-CoV-2 were included. The rates of 30-day mortality and hospitalization were 3.6% and 35.1%, respectively. The most common symptoms were cough (56.7%) and fever (33.3%). Cough and shortness of breath associated with short-term mortality, ICU admission and necessity of mechanical ventilation during hospitalization (for cough $P = 0.029$, $P = 0.003$, $P = 0.03$; for shortness of breath $P < 0.001$, $p < 0.001$, and $P = 0.009$, respectively).

Conclusion: The cough and shortness of breath were associated with 30-day mortality, ICU admission and necessity of mechanical ventilation during hospitalization.

Keywords: Coronavirus infections, Dyspnea, Fever, Cough, Prognosis, Turkey

ÖZ

Amaç: COVID-19 polikliniğine başvuran hastaların semptomları ile kısa süreli mortalite, servis yatışı, yoğun bakıma yatışı ve hastanede kalış süresince mekanik ventilasyon gerekliliği arasındaki ilişkiyi değerlendirmek.

Gereç ve Yöntemler: Çalışmamız retrospektif kohort çalışma olarak bir pandemi kliniğinde gerçekleştirildi. SARS-CoV-2 için pozitif RT-PCR testi olan tüm hastanede yatan hastalar ve ayakta tedavi gören erişkin hastalar çalışmaya dahil edildi. Hastanenin bilgisayar tabanlı hasta veri sisteminden her hastanın demografik parametreleri, klinik özellikleri, başvuru sırasındaki vital parametreler, poliklinik sonuçları elde edildi ve analiz edildi. Bu çalışmanın birincil sonlanımı, COVID-19 polikliniğine başvuran hastaların semptomları ile 30 günlük mortalite arasındaki ilişkiyi belirlemektir. İkincil sonlanımları ise, hastanede yatış, yoğun bakıma yatış ve hastanede kalış sırasında mekanik ventilasyon gerekliliğiydi.

Bulgular: SARS-CoV-2 için RT-PCR testinin pozitif sonuçlarına sahip toplam 1566 hasta dahil edildi. 30 günlük mortalite ve hastaneye yatış oranları sırasıyla% 3.6 ve% 35.1 idi. En sık görülen semptomlar öksürük (% 56,7) ve ateş (% 33,3) idi. Kısa süreli mortalite, YBÜ'ye yatış ve hastanede kalış sırasında mekanik ventilasyon gerekliliği ile öksürük ve nefes darlığı ilişkili bulundu (öksürük için $P = 0,029$, $P = 0,003$, $P = 0,03$; nefes darlığı için $P < 0,001$, $p < 0,001$ ve $P = 0,009$ sırasıyla).

Sonuç: Öksürük ve nefes darlığı 30 günlük mortalite, YBÜ'ye yatış ve hastanede kalış sırasında mekanik ventilasyon gerekliliği ile ilişkilidir.

Anahtar Kelimeler: Koronavirüs enfeksiyonları, Nefes darlığı, Ateş, Öksürük, Prognoz, Türkiye

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Introduction

Until today, many subtypes of coronavirus have caused colds on humans. However, in the last two decades, coronaviruses have caused epidemics such as MERS and SARS that cause severe respiratory failure (1). On December 31, 2019, the new type of coronavirus was found to cause a disease in humans in Wuhan that is a city of Hubei province of China, and the name of the disease was accepted as COVID-19 (2). The name of the pathogen was accepted as SARS-CoV-2. Since there is not enough information about the newly detected SARS-CoV-2, difficulties have been experienced in its treatment and the disease has spread rapidly. Governments around the world have taken measures to stop the spread of the virus (3).

Many predictors such as C-reactive protein, ferritin, and D-dimer have been studied to determine the severity of COVID-19 and reveal its relationship with mortality (1,4). SARS-CoV-2 infection may be asymptomatic or progress with severe respiratory failure. In addition to respiratory symptoms, gastrointestinal symptoms can be seen in patients (4). We speculated that evaluation of relationship between symptoms and severity of disease on patients admitted to COVID-19 outpatient clinic may be helpful to management of the pandemic.

This study sought to evaluate the relationships between the symptoms of patients admitted to the COVID-19 outpatient clinic and short-term mortality, hospitalization, intensive care unit admission and necessity of mechanical ventilation during hospitalization.

Material and Methods

Study design

This retrospective cohort study was conducted at a 672-bed tertiary academic hospital with an annual emergency department census of 438 000 before pandemic. We collected data of the patients who admitted pandemic clinic for COVID-19 symptoms between April 15, 2020 and May 15, 2020 retrospectively.

Study population

Population of our study was patients who admitted to pandemic clinic for COVID-19 between April 15, 2020 and May 15, 2020. Patients with suspected SARS-CoV-2 infection described due to the current guideline of Turkish Ministry of Health prepared for COVID-19 outbreak management and working in the working period (5). Patients who meet the criteria in this guideline, were tested for SARS-CoV-2 infection. Real-time reverse-transcriptase–polymerase-chain-reaction (RT-PCR) was used for diagnosing SARS-CoV-2 infection. Patients who had absent or negative results for SARS-CoV-2 or missing data were excluded from the study. All patients with positive RT-PCR assay for SARS-CoV-2, were included the study. Decisions about the medications and the necessity of hospitalization were made by a team of

emergency physicians, thoracic surgeons, and cardiovascular surgeons according to the COVID-19 Outbreak Management and Working Guideline of the Turkish Ministry of Health. The decision for hospitalization was made regardless of the presence of an inpatient bed. Patients considered to hospitalization were hospitalized to our hospital and they weren't transferred to other hospitals and they were kept waiting until an inpatient bed was available.

Data collection

The data was documented from the computer-based system of our hospital included age, gender, vital parameters on admission, diseases in medical history, smoking status, clinical outcomes for the first 24 hours, and necessity of mechanical ventilation. Symptoms on admission were recorded as fever, cough, sputum, shortness of breath, weakness, muscle-joint pain, loss of taste or smell, headache, sore throat, nausea-vomiting, diarrhea. Diseases in medical history were noted as comorbidities included chronic obstructive pulmonary disease, hypertension, diabetes, coronary artery disease, congestive heart failure and chronic kidney disease. Immunodeficiency state was noted in part of medical history due to according to the presence of immunosuppression. Clinical outcomes for the first 24 hours were filed as discharge, hospitalization, and ICU admission. Systolic blood pressure, diastolic blood pressure, pulse pressure, body temperature, respiratory rate, and pulse oximeter of patients were recorded as vital parameters of patients.

The primary outcome of this study was 30-day mortality after pandemic clinic admission. The secondary outcomes were requirement of hospitalization in hospital services or ICU, and necessity of mechanical ventilation during hospitalization.

Statistical analysis

The categorical data was expressed as number and percentage, and the numerical data was expressed as minimum and maximum values were used for the variables without a normal distribution, whereas the mean \pm standard deviation values were obtained for the normally distributed variables. The independent samples t-test was used to examine normally distributed data. The Mann–Whitney U test and chi-square test were used to compare two groups. Statistical analyses and calculations were undertaken using SPSS program v. 23. The level of statistical significance was accepted as $p < 0.05$.

Ethics

The ethical approval of the study was gotten from the local ethical committee with the approval number B.10.1. TKH.4.34. H.GP.0.01/119 and Ministry of Health approval has been obtained for our study. We retrospectively reviewed the data documented from the computer-based

hospital information management system. The extracted data were solely clinical material, and it did not include any personal, identifiable information. Therefore, the legal requirement to informed consent was disclaimed.

Results

A total of 6494 patients visited to pandemic clinic during the study period. 4907 patients with suspected infection tested for SARS-CoV-2 with RT-PCR assay. Therefore, for the final analysis, 1566 patients with positive results of RT-PCR assay for SARS-CoV-2 were included. The study flowchart is shown on Figure 1.

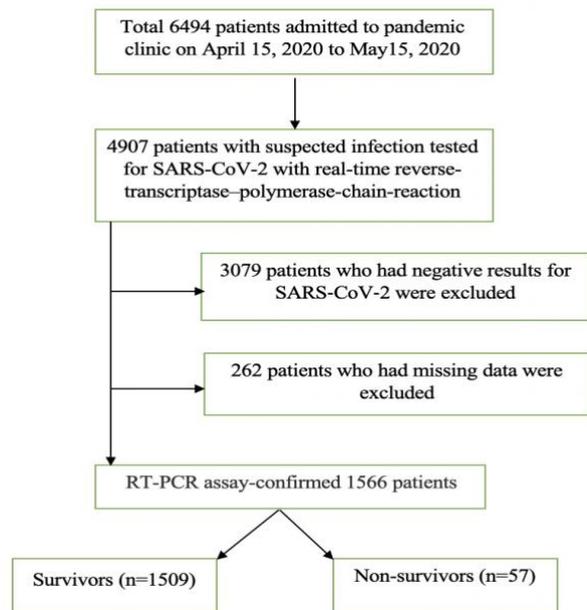


Figure 1. Flowchart of the study

The mean of age and standard divisions of 1566 patients included was 44.22 ± 16.34 (minimum:19, maximum: 89) years and 837 patients (53.5%) were male. A total of 57 patients died within 30-day of admission. The rates of 30-day mortality and hospitalization were 3.6% and 35.1%, respectively. The demographic characteristics, comorbid diseases, symptoms, vital parameters on admission, smoking status, clinical outcomes for the first 24 hours, and necessity of mechanical ventilation are shown in Table 1.

Outcomes

The comparisons of characteristics of the non-survivor and survivor groups are shown in table1. Significant differences were identified between symptoms of survivor and non-survivor groups as; cough (864 versus 27 $P = 0.029$), shortness of breath (351 versus 26, $P = 0.001$), nausea-vomiting (57 versus 7, $P = 0.007$). Significant differences were detected in age (48.9 ± 14.02 versus 81.5 ± 8.69 , $P < 0.001$), chronic obstructive pulmonary disease (30 versus 5, $P = 0.008$), hypertension (178 versus 23, $P < 0.001$), coronary artery disease (38 versus 9, $P = 0.001$), congestive heart failure (9 versus 6, $P < 0.001$), chronic kidney disease (4 versus 4, $P < 0.001$), active malignancy (12 versus 4, $P = 0.002$).

Relationship between the symptoms of SARS-CoV-2 infection and the requirement of hospitalization in clinics or ICU, necessity of mechanical ventilation during hospitalization are shown in Table 2.

Discussion

In this study, we did a comprehensive assessment of the 1566 adult patients with SARS-CoV-2 infection at a pandemic hospital, since the beginning of the outbreak in Turkey, in order to contribute to the limited knowledge base about SARS-CoV-2 cases. All the patients were confirmed with RT-PCR assay for SARS-CoV-2. Our study demonstrated that fever and cough were the dominant symptoms, however cough and shortness of breath associated with short-term mortality, ICU admission and necessity of mechanical ventilation during hospitalization.

SARS-CoV-2 is a highly contagious pathogen that causes respiratory tract infection especially pneumonia in infected patients (6). Most SARS-CoV-2 infections are either asymptomatic or result in only mild disease. Nevertheless, in an important proportion of infected persons, the infection leads to a respiratory illness requiring hospital care (4,6). Moreover, some authors expressed their concerns about exceeding install capacity of the hospitalization (7,8).

The patients in our study presented with respiratory symptoms similar to those of patients described in recent studies (9-11). In this study, cough was the most common symptom, approximately half of patients had cough symptoms. Only one third of the patients has fever or history of fever in admission and one third of the patients in our study had shortness of breath. Approximately 10% of the infected patients may initially show gastrointestinal symptoms such as diarrhea, abdominal pain, and vomiting, making it difficult to distinguish SARS-CoV-2 infections from other common diseases. In our study, gastrointestinal symptoms were uncommon, as recent studies. Loss of taste or smell was one of the rarest symptoms, interesting there was no mortality in patient group with loss of taste or smell. In the current literature, patients with severe pneumonia findings, acute respiratory distress syndrome, sepsis, and shock are defined as serious diseases for COVID-19 (12-15). Clinical process in severe disease is as shortness of breath on fifth day after the first symptom, hypoxia on the seventh day, acute respiratory distress syndrome on the 8th-10th days (16). The presence of shortness of breath and cough at the beginning of the disease was associated with mortality and the necessity of an intensive care unit admission and mechanical ventilation in the later period (17). Similar to the current literature, in our study, cough and shortness of breath associated with short-term mortality, ICU admission and necessity of mechanical ventilation during hospitalization.

Variables	Total n=1566	Survivor n=1509	Non-survivor n=57	p values
Age, years	44.22±16.34	43.21±15.57	70.96±13.36	<0.001
Gender				0.087
Male	837 (53.5%)	801 (53.1%)	36 (63.2%)	
Female	728 (46.5%)	707 (46.9%)	21 (36.8%)	
Clinical outcome for the first 24 hours				<0.001
Discharge	993 (63.4%)	993 (65.8%)	0	
Hospitalization	550 (35.1%)	516 (34.2%)	34 (59.6%)	
ICU admission	23 (1.5%)		23 (40.4%)	
Comorbidities				
Chronic obstructive pulmonary disease	35 (2.2%)	30 (2%)	5 (8.8%)	0.008
Hypertension	201 (12.8%)	178 (11.8%)	23 (40.4%)	<0.001
Diabetes	153 (9.8%)	143 (9.5%)	10 (17.5%)	0.045
Coronary artery disease	47 (3%)	38 (2.5%)	9 (15.8%)	<0.001
Congestive heart failure	15 (1%)	9 (0.6%)	6 (10.5%)	<0.001
Chronic kidney disease	8 (0.5%)	4 (0.3%)	4 (7%)	<0.001
Active malignancy	16 (1%)	12 (0.8%)	4 (7%)	0.002
Immunodeficiency state	3 (0.2%)	2 (0.1%)	1 (1.8%)	0.105
Smoking status				0.158
Smoker	49 (3.1%)	49 (3.2%)	0	
Nonsmoker	1517 (96.9%)	1460 (96.8%)	57 (100%)	
Frequency of symptoms				
Fever	522 (33.3%)	499 (33.1%)	23 (40.4%)	0.255
Cough	888 (56.7%)	864 (57.3%)	24 (42.1%)	0.029
Sputum	44 (2.8%)	41 (2.7%)	3 (5.3%)	0.213
Shortness of breath	377 (24.1%)	351 (23.3%)	26 (45.6%)	<0.001
Weakness	285 (18.2%)	280 (18.6%)	5 (8.8%)	0.078
Muscle-joint pain	238 (15.2%)	233 (15.4%)	5 (8.8%)	0.192
Loss of taste or smell	111 (7.1%)	111 (7.4%)	0	0.014
Headache	130 (3.8%)	129 (8.5%)	1 (1.8%)	0.041
Sore throat	158 (10.1%)	154 (10.2%)	4 (7%)	0.652
Nausea-vomiting	64 (4.1%)	57 (3.8%)	7 (12.3%)	0.007
Diarrhea	74 (4.7%)	71 (4.7%)	3 (5.3%)	0.512
Vital parameters				
Systolic blood pressure	120 (80-200)	120 (88-192)	130 (80-200)	0.523
Diastolic blood pressure	72 (45-118)	72 (50-118)	71 (45-104)	0.905
Pulse pressure	85 (35-180)	84 (53-144)	97 (35-180)	0.002
Body temperature	36.5 (35-39)	36.5 (36-36.7)	37.1 (35.9-39)	0.005
Respiratory rate	20 (14-38)	20 (14-30)	23 (17-38)	0.091
Pulse oximeter	97 (84-100)	96 (84-100)	90.5 (88-96)	0.745
Necessity of mechanical ventilation				
Mechanically ventilated	38 (2.4%)	0	38 (66.7%)	<0.001

Table 1. Baseline characteristics of enrolled patients and comparison of characteristics between the survivor group and non-survivor group

Symptoms of SARS-CoV-2 infection	Intensive Care Unit Admission			Necessity of Mechanical Ventilation			Hospitalization requirement		
	No	Yes	p value	No	Yes	p value	Outpatients	Inpatients	p value
Fever	516 (33.4)	6 (26.1%)	0.458	507 (33.2%)	15 (39.5%)	0.416	302 (30.4%)	220 (38.4%)	0.001
Cough	882 (57.2%)	6 (26.1%)	0.003	873 (57.1%)	15 (39.5%)	0.030	553 (55.7%)	335 (58.5%)	0.286
Sputum	43 (2.8%)	1 (4.3%)	0.483	43 (2.8%)	1 (2.6%)	0.946	22 (2.2%)	22 (3.8%)	0.061
Shortness of breath	361 (23.4%)	16 (69.6%)	<0.001	361 (23.6%)	16 (42.1%)	0.009	196 (19.7%)	181 (31.6%)	<0.001
Weakness	285 (18.5%)	0	0.014	283 (18.5%)	2 (5.3%)	0.036	164 (16.5%)	121 (21.1%)	0.023
Muscle-joint pain	236 (15.3%)	2 (8.7%)	0.561	234 (15.3%)	4 (10.5%)	0.417	156 (15.7%)	82 (14.3%)	0.458
Loss of taste or smell	111 (7.2%)	0	0.402	111 (7.3%)	0	0.085	85 (8.6%)	26 (4.5%)	0.003
Headache	130 (8.4%)	0	0.251	130 (8.5%)	0	0.061	98 (9.9%)	32 (5.6%)	0.003
Sore throat	158 (10.2%)	0	0.159	156 (10.2%)	2 (5.3%)	0.317	114 (11.5%)	44 (7.7%)	0.016
Nausea-vomiting	60 (3.9%)	4 (17.4%)	0.013	58 (3.8%)	6 (15.8%)	<0.001	28 (2.8%)	36 (6.3%)	0.001
Diarrhea	73 (4.7%)	1 (4.3%)	0.931	71 (4.6%)	3 (7.9%)	0.351	44 (4.4%)	30 (5.2%)	0.470

Table 2. Relationship between the symptoms of SARS-CoV-2 infection and the requirement of hospitalization in clinics or ICU, necessity of mechanical ventilation during hospitalization

Limitations

The main limitations of this study are its retrospective nature and small sample size. Less biased results can be obtained with prospective studies. However, our study is important because it compares hospitalized and outpatients. Another limitation of our study is that our study had single-center observational design, and therefore the results cannot be generalized to other healthcare institutions.

Conclusion

In this study, we concluded that the cough and shortness of breath associated with 30-day mortality, ICU admission and necessity of mechanical ventilation during hospitalization.

Conflict of Interest: The authors declare no any conflict of interest regarding this study.

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Authors' Contribution: All authors contributed for conception, design of the study, data collection, data analysis, and assembly. The manuscript was written and approved by all authors.

Ethical Statement: Ethical approval for this study was obtained from Umraniye Training and Research Hospital Ethics Committee with the approval number B.10.1.TKH.4.34. H.GP.0.01/119
All authors declared that they follow the rules of Research and Publication Ethics.

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