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Evaluation of Covid-19 cases that applied to the hospital at the first peak of the pandemic

Özlem AKDOĞAN[1,*], Derya YAPAR[1], Kazım ÇEBİ[2], Sertaç ARSLAN[3] Hilal BOYACI[3], Yasemin ARI YILMAZ[3], Pınar TUNÇEL ÖZTÜRK[1], Ünsal SAVCI[4], Hüseyin KAYADİBİ[5, 6] Ayşe YILMAZ[3], Meral GÜLHAN [3], Aysel KOCAGÜL ÇELİKBAŞ[1], Nurcan BAYKAM[1]

[1]Department of Infectious Diseases and Clinical Microbiology, Faculty of Medicine, Hitit University, Çorum, Turkey
[2]Department of Infectious Diseases and Clinical Microbiology, Çorum Erol Olçok Training and Research Hospital, Çorum, Turkey
[3]Department of Chest Diseases, Faculty of Medicine, Hitit University, Çorum, Turkey
[4]Department of Medical Microbiology, Faculty of Medicine, Hitit University, Çorum, Turkey
[5]Department of Medical Biochemistry, Faculty of Medicine, Hitit University, Çorum, Turkey
[6]Department of Medical Biochemistry, Faculty of Medicine, Eskişehir Osmangazi University, Eskişehir, Turkey

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Abstract

Early diagnosis in COVID-19 is essential in terms of treatment and prevention of contagiousness. In this study, we aimed to find an alternative diagnosis method by using fewer laboratory parameters in the early diagnosis of COVID-19 disease by creating a fast, easily accessible, cost-effective index and has a diagnostic accuracy rate of over 90%. All patients over the age of 18 who applied to Hitit University Erol Olçok Training and Research Hospital Emergency COVID Outpatient Clinic with a pre-diagnosis of COVID-19 between March and April 2020 were evaluated retrospectively. Patients were divided into two groups as COVID-19 positive and COVID-19 negative. It was aimed to create a HITIT-19 index by evaluating the cases according to the clinical and laboratory results. Between March and April 2020 (in the first peak of the pandemic), 1586 patients were applied to the Emergency COVID-19 outpatient clinic with a pre-diagnosis of COVID-19. According to COVID-19 RT-PCR, card test, and CT involvement, 285 (13%) patients were diagnosed with COVID-19. PCR was positive in 285 (18%) of 1586 patients, and PCR was negative in 1301 (82%). While 153 (53.7%) of the patients diagnosed with COVID-19 were male and the median age was 45 (28-62.75), 883 (55.7%) of the patients not diagnosed with COVID-19 were male, and the median age was 43 (31-65). Hypertension (HT) was the most common underlying disease in 10.5% of patients applied to the emergency room with a diagnosis of COVID-19, while 38.9% dyspnea and 35.1% fever were the most common symptoms. While 76% of Plaquenil and 58% azithromycin were the most frequently started treatments, 31.4% (28.4% of them were hospitalized in the service, 3% in the intensive care unit) of them hospitalized. It was to create a HITIT-19 index that is fast, easily accessible, cost-effective, and has a diagnostic accuracy rate of over 90% by using laboratory tests. However, we could not achieve this goal due to the low accuracy of the diagnostic tests and the lack of significant change in the laboratory levels of the patients at admission. Considering that the pandemic is continuing rapidly, there is still a need to develop practical diagnostic methods that are easier and cheaper in diagnosis. In this sense, we believe that our study will be a guiding study for other studies that will be designed for diagnostic index studies.

Keywords: Covid-19, early diagnosis, RT-PCR, HITIT-19 index

1. Introduction

SARS-CoV-2 is the cause of a serious pandemic that started in Wuhan City of China in early December 2019 and still has an ongoing impact, affecting the whole world. As of January 9, 2021, 87,589,206 patients and 1,906,606 deaths were reported with laboratory approval, affecting 218 countries worldwide (1, 2).

SARS-CoV-2 is a member of the β coronavirus family and is an enveloped positive strand RNA virus. SARS-CoV-2 acts by attaching to the angiotensin converting enzyme 2 (ACE2) receptor. Since this receptor is found in tissues such as the digestive system, the neurological system and the liver as well as the respiratory system, it also acts by attaching to these tissues (3).

Tang et al. identified two main types, L and S, based on analysis of 103 genomes of SARS-CoV-2. While the L type is more aggressive and can spread more rapidly, the S type may cause a relatively mild clinical course. L-type is more common and has more mutations (3).

Although the duration of contagion is not known exactly, it can start 1-2 days before the symptomatic period and last up to 14 days following the onset of symptoms. The incubation period is approximately 2-14 days, on average 4-5 days (4). Common symptoms of COVID-19 infection are fever, cough, and dyspnea. In more severe cases, pneumonia, severe acute respiratory infection, kidney failure, and even death may develop. Pneumonia is the most common serious finding of

* Correspondence: akdoganozlem@hotmail.com

the disease. According to the World Health Organization (WHO), COVID-19 clinic is divided into five categories; asymptomatic (test positive, no symptom), mildly symptomatic (difficulty breathing, shortness of breath, or any signs and symptoms without abnormal chest imaging), moderate cases (mild lung involvement detected by clinical evaluation or imaging and> 93% oxygen saturation) severe illness (> 30 respiratory rate / minute, 93% oxygen saturation, partial arterial oxygen pressure to inspired oxygen <300 or lung infiltration> 50%) and critical illness (respiratory failure, septic shock and / or multi-organ failure) (5).

In COVID-19 disease, early diagnosis is important in terms of treatment and prevention of contagiousness. With this study, we aimed to evaluate of COVID-19 cases that applied to the hospital at the first peak of the pandemic and to create an alternative diagnosis method by using some laboratory parameters in the early phase of COVID-19 disease. This index should be fast, easily accessible, cost-effective, and have a diagnostic accuracy of over 90%.

2. Material and Methods

All patients over the age of 18 who applied to Hitit University Erol Olçok Education and Research Hospital Emergency Department "COVID-19 Outpatient Clinic" with the symptoms of COVID-19 between March and April 2020 were evaluated retrospectively. Oropharyngeal and nasopharyngeal swab samples were taken into vNAT™ Transfer Tube in our hospital. Manual RNA extraction was performed in the vNAT™ Transfer Tube. Bio-Speedy SARS-CoV-2 Double Gene RT-qPCR Kit and Bio-Rad CFX96 Real-Time PCR automated system were used for detection of SARS-CoV-2. Patients were divided into two groups as COVID-19 positive and COVID-19 negative according to RT-PCR, antibody-based card test and CT results. All cases were evaluated with clinical findings and laboratory results. Laboratory tests results such as complete blood count, coagulation, fibrinogen, routine biochemistry, D-dimer, venous blood gas, troponin, CRP and procalcitonin; which were taken at the emergency admission of cases were used to create the COVID-19 index for use to evaluate patients. Complete blood count, coagulation, routine biochemistry, D-dimer, fibrinogen, venous blood gas, troponin, CRP and procalcitonin test results were obtained from the automation system of our hospital; Data of clinical findings such as cough, shortness of breath, fever, malaise, weakness, and muscle pain were obtained from the patient files. Clinical data of COVID negative cases could not be accessed.

Hitit University licensed SPSS 23.0 package program was used to create the COVID-19 Index. Demographic and biochemical data were classified as continuous or categorical variables. Kolmogorov Smirnov analysis was used for normality test, and data with Gaussian distribution were presented as mean ± standard deviation, and data without Gaussian distribution were presented as median (25-75 quarters). Comparisons between groups were made using Student's t-test or Mann-Whitney U-test, as appropriate. Categorical variables were compared using the Chi-square test. Univariate and multivariate logistic regression analyzes were used to create a new COVID Index. With this new COVID Index, which was planned to be created, ROC analysis was performed to determine the diagnostic accuracies in the differentiation of COVID-19 patients. P <0.05 was considered statistically significant. The study was approved with the decision of the Ethics Committee of our hospital, dated 12.05.2020 and numbered 240.

3. Results

Between March and April 2020, 1586 patients applied to Hitit University Erol Olçok Education and Research Hospital Emergency Department "COVID-19 Outpatient Clinic with suspicion of COVID-19. According to COVID-19 RT-PCR, card test and CT involvement, 285 (13%) patients were diagnosed with COVID. PCR was positive in 285 (18%) of 1586 patients, and PCR was negative in 1301 (82%) patients. While the typical appearance compatible with COVID-19 in thorax CT was present in 189 (11.9%) cases, card test positivity was detected as 27 (1.7%). The median age of COVID-19 patients was 45 (28-62) and 153 (53.7%) were male, while the median age of patients that negative tests results were 43 (31-65) and 883 (55.7%) of them were male. Hypertension (HT) was the most common comorbidities in COVID-19 cases (10.5%). Other comorbidities are summarized in Table 1. Clinical findings of COVID-19 positive and negative cases are shown in the Table 2.

Table 1. Underlying diseases of Covid-19 negative and positive cases

Underlying Disease	Negative Patients (n=1301)	Positive Patients (n=285)	P
DM	211 (1.2%)	14 (4.91%)	<0.001
HT	399 (30.7%)	30 (10.5%)	<0.001
Cancer	55 (4.23%)	3 (1.05%)	0.010
COPD	61 (4.69%)	5 (1.75%)	0.025
Asthma	76 (5.84%)	6 (2.11%)	0.010
Heart Disease	116 (8.92%)	11 (3.85%)	0.004

DM: Diabetes Mellitus, HT: hypertension, COPD: Chronic Obstructive Pulmonary Disease

Table 2. Symptoms and findings of Covid-19 negative and positive cases

Symptoms and Findings	Negative Patients (n=1301)	Positive Patients (n=285)	*P*
Fever	417 (32.1%)	100 (35.1%)	0.322
Dyspnea	439 (33.7%)	111 (38.9%)	0.095
Cough	732 (56.3%)	49 (17.2%)	<0.001
Sore Throat	215 (16.5%)	14 (4.91%)	<0.001
Fatigue	219 (16.8%)	19 (6.67%)	<0.001
Headache	87 (6.69%)	8 (2.81%)	0.012
Vomit	36 (2.77%)	2 (0.70%)	0.039
Myalgia	82 (6.30%)	8 (2.81%)	0.021
Stomach Ache	27 (2.08%)	0 (0%)	0.009

First laboratory tests result of COVID-19 cases which were evaluated in the emergency department, only the CRP result was found above normal. Other tests results were within normal limits. Laboratory findings are summarized in Table 3. The treatments that initiated for COVID-19 are summarized in Table 4. The most used agents in the treatment were plaquenil (76%), azithromycin (58%), low molecular weight heparin LMWH (42%) and oseltamivir (25%). 31.4% (n=689) of the patients were hospitalized. 91% (n=624) of them were hospitalized in COVID services and 3% (65) in intensive care units. We could not create a COVID-19 index due to the lack of significant changes in the laboratory parameters (ROC analysis, Fig. 1).

Table 3. Laboratory information of Covid-19 cases

	Negative Patients (n=1301)	Positive Patients (n=285)	*P*
WBC (10^9/L)	8.45 (6.77-10.48)	5.82 (4.61-7.19)	<0.001
Neutrophil (10^9/L	5.33 (3.93-7.48)	3.42 (2.67-4.53)	<0.001
Lymphocyte (10^9/L)	1.97 (1.31-2.62)	1.45 (1.05-1.96)	<0.001
Platelet (10^9/L)	239 (199-289)	209 (169-255)	<0.001
AST (U/L)	22 (17-30)	23 (18-32)	0.063
ALT (U/L)	21 (14-33)	20 (15-30)	0.285
LDH (U/L)	195 (164-246)	212 (164-280)	0.009
CK (U/L)	90 (63-138)	78 (53-124)	0.004
D.Dimer (ug/mL)	0.26 (0.10-0.62)	0.29 (0.20-0.63)	0.003
PRO-BNP (pg/mL)	39 (12-176)	44 (15-107)	0.631
Fibrinogen (mg/dL)	341 (280-437)	343 (282-460)	0.626
CRP (mg/l)	5.41 (3.14-31.3)	7.91 (3.14-27.3)	0.744
Procalcitonin (ng/ml)	0.05 (0.03-0.1)	0.13 (0.04-4.3)	<0.001
Ph	7.39 (7.36-7.42)	7.40 (7.38-7.4)	0.001
PCO_2 (mmHg)	43 (39-48)	41 (37-46)	<0.001
Lactate (0.5-2 mmol/L)	1.79 (1.41-2.25)	1.73 (1.45-2.2)	0.451
Hematocrit (%40 - 49.4)	41 (38-45)	40 (38-43)	0.021
RDW (%12–13.6)	35 (13-41)	14 (13-32)	<0.001

WBC:White blood cell, AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase, LDH: Lactate Dehydrogenase, CK: creatine kinase , PRO-BNP: pro b-type natriuretic peptide, CRP: C-Reactive Protein, PCO2: Partial Carbon Dioxide Pressure, RDW: Red cell distribution width

Table 4. Treatments initiated for COVID-19

Treaments Started	n (%)
Plaquenil	217 (76.1%)
Azithromycin	165 (57.9%)
LMWH	119 (41.8%)
Oseltamivir	72 (25.3%)
Vitamin C	68 (23.9%)
Favipiravir	61 (21.4%)
Ceftriaxone	40 (14.0%)
Steroid	11 (3.86%)
Tosilizumab	4 (1.4%)

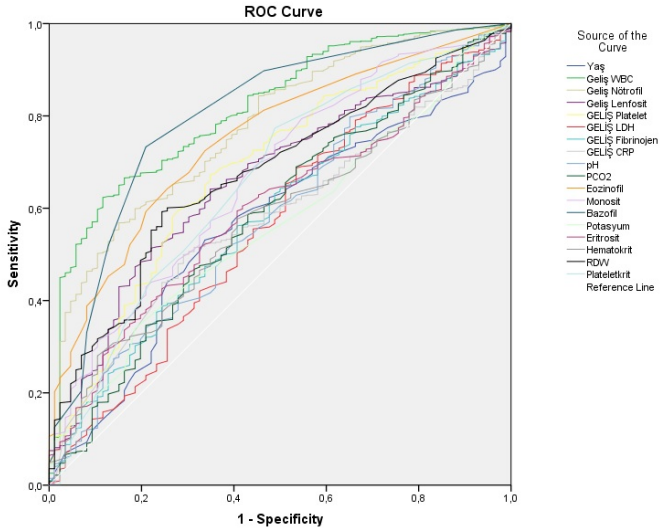

Fig. 1. ROC analysis

4. Discussion

Turkey was also affected by COVID-19, which caused a global public health problem by affecting the whole world. The diagnosis of COVID-19 is based on epidemiological history, clinical symptoms, RT-PCR, thoracic CT and antibody-based card test (6). In our country, according to the Ministry of Health COVID-19 diagnosis and treatment guideline, definitive diagnosis of the COVID- 19 based on real-time reverse transcription polymerase chain reaction (rRT-PCR) positivity (7). It is reported in the literature that the RT-PCR test used in the diagnosis of COVID-19 has high specificity (8) and a low sensitivity rate (9). Although the sensitivity rate of the test is not clear, it is estimated to be around 45–97% (10-12). Because the sample is taken in the early or late period, mutations, low viral load may cause the test to be negative (10). RT-PCR was obtained from all 1586 patients applied to our Emergency Department "COVID-19 Outpatient Clinic". The PCR results of 285 (18%) cases were positive. This was a very low value compared to the literature. It was thought that this result may be caused by the excessive number of applies due to COVID-19 anxiety and panic in both physicians and patients at the beginning of the pandemic.

Typical CT findings are diagnostic in patients until RT-PCR results are available (12). RT-PCR should be repeated to avoid the isolation and misdiagnosis of patients with typical CT findings and negative RT-PCR results. It has been reported that the missed diagnosis of COVID-19 by CT is low (3.9%) (13). CT positivity was reported as 64% in the study of Kostaoğlu et al. (12). In our study, on thoracic CT, typical appearance compatible with COVID-19 was present in 189 (11.9%) cases. This low rate can be explained by the fact that almost all patients were referred to the Emergency Department COVID-19 Outpatient Clinic for both retraction and diagnostic purposes due to the concern of COVID-19, the high rate of thoracic CT scans, and most of the patients presenting to the emergency COVID-19 outpatient clinic with panic.

After a while, antibodies (IgM, IgG, IgA) develop in those who recovering from the disease. Antibody response usually begins to occur after 4-7 days of illness. Since antibody positivity occurs approximately after the 10th day of the disease, serological tests should be performed after this day (14). The sensitivity and specificity of serological tests vary according to the test technique, the specificity of the antibody examined, the duration of symptoms at the time of collection, and the immune competence of the individual (10). Li et al. Reported the sensitivity of these tests as 88.7% and the specificity as 90.6% (15). Similarly, in another study conducted in Thailand, 98% sensitivity and 98-100% specificity rates were reported (16). In our study, card test positivity was detected as 27 (1.7%). The test positivity rate was low because our cases were in the early stages of the diseases.

While Baloch et al. (17) reported that the median age was 56 and 54.3% were male, the median age was reported to be 62 in the study of Jin et al. (18). 59% of the cases were male and the mean age was 52 in the study of Kostakoglu et al. (12). Wan et al. was reported the average age of patients as 47 years (19). In our study, 55.7% of our cases were male and the average age of our cases was 45 and it was like the literature.

In the study of Jin et al., 37% were reported to have at least one comorbidity (18). In the study of Kostaoğlu colleagues, the most common comorbidity was hypertension (12). In a study conducted in Iran, diabetes, chronic respiratory disease, and hypertension were the most common comorbidities (20). Wan et al. reported that 32% of their patients had a comorbidity and the most common of them were hypertension (10%), diabetes (9%), cardiovascular disease (5%) and malignancy (3%) (19). In our study, hypertension (11%), diabetes (5%) and heart disease (4%) were the most common comorbid diseases in patients diagnosed with COVID-19 and were like the literature.

Baloch et al. reported the most common symptoms as 98% fever, 76% cough and 44% myalgia (17). The most common symptoms in the study of Jin et al. were 95% fever and 65% cough (18). In our study, dyspnea (39%) and cough (17%) were the most common symptoms. Since our study consisted of patients applied to the emergency department, that is, it did not include only hospitalized patients, our rates were expected to be lower than in the literature.

Laboratory findings include leukopenia, lymphopenia, thrombocytopenia, transaminases, increased CK, LDH, ferritin, and fibrinogen (7,21). Wan et al. reported the mean leukocyte mean 5.4×10^9 / L, lymphocyte mean 1.1×10^9 / L, platelet mean 158×10^9 / L, coagulation parameters were normal in almost all patients, mean creatine kinase 82.2U / L, mean LDH 320 U / L reported the mean CRP of 10.5 mg / L and the mean procalcitonin as 0.11 ng / Ml (19). In our study, the mean laboratory parameters of the patients who were evaluated in the emergency department were within normal levels, but statistically significant differences were found between two groups.

There are many different approaches and guidelines for effective drug therapy in the treatment of COVID-19 patients in the first peak of pandemic. There is no specific treatment with proven safety and efficacy. Remdesivir, which is one of the agents used in treatment, is licensed for the treatment of COVID-19, while chloroquine phosphate, favipravir, lopinavir / ritonavir, and remdesivir are among the recommended drugs (7,22). LMWH (enoxaparin) is also recommended for prophylaxis due to the predisposition to venous and arterial thromboembolic events by various mechanisms in the course of COVID-19 disease (7). Wan et al. initiated 100% antiviral therapy (catheter and interferon), 44% antibacterial therapy, and 26% corticosteroid therapy (19). Our treatment experience in the first two months was 76% plaquanil, 58% azithromycin, 42% LMWH and 25% oseltamivir.

While planning this study, our aim was to use laboratory tests such as complete blood count, coagulation, routine biochemistry, D-dimer, fibrinogen, venous blood gas, troponin, CRP, and procalcitonin to create a COVID 19 index which is fast, easily accessible, cost-effective, and diagnostic accuracy rate of over 90%. However, we could not achieve this goal due to the low accuracy of diagnostic tests and the lack of significant change in the laboratory values of the patients at admission.

Considering that the pandemic is continuing rapidly, there is still a need to develop practical diagnostic methods that are easier to diagnose. In this sense, we believe that our study will be a guiding study for other studies that will be designed for diagnostic index studies.

Conflict of interest

None to declare.

Acknowledgments

None to declare.

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