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EVALUATION OF CONTACTS OF THE PATIENTS WITH NEGATIVE COVID RT-PCR AND THORAX CT FINDINGS COMPATIBLE WITH COVID-19 PNEUMONIA

COVID RT-PCR TESTİ NEGATİF TORAKS TOMOGRAFİSİ COVID-19 PNÖMONİSİ İLE UYUMLU OLAN HASTALARIN TEMASLILARININ DEĞERLENDİRİLMESİ

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Öz

Amaç: Bu çalışmada RT-PCR testi sonucu negatif ancak toraks bilgisayarlı tomografi (BT) bulguları COVID-19 ile uyumlu olan hastaların test sonuçlarını ve bulaştırıcılık durumlarını değerlendirmeyi amaçladık.
Materyal ve Metot: Çalışma kesitsel, tanımlayıcı bir araştırma olarak tasarlandı. Birinci grupta toraks BT COVID-19 pnömonisi ile uyumlu ve RT-PCR testi sonucu negatif olan hastalar ikinci grupta toraks BT COVID-19 pnömonisi ile uyumlu ve RT-PCR testi sonucu pozitif olan hastalar bulunmaktadır. Toplanan veriler SPSS 21.0 yazılım programı ile değerlendirildi. Anlamlılık değeri %5 olarak kabul edildi.
Bulgular: Katılımcıların %54,41'u erkek, %45,59'u kadındı. İki grup arasında temas ortamı, sağlık çalışanı olma ve exitus olma açısından anlamlı bir fark yoktu. Temas sayısı açısından birinci ve ikinci grup arasında fark yoktu. İkinci grupta örnek toplama oranı daha yüksekti. Hastalarla temaslı olan ve RT-PCR testi sonucu pozitif olanların sayısı birinci grupta daha yüksekti.
Sonuç: Hastalar, COVID-19 için negatif RT-PCR test sonuçlarına sahip olsalar bile bulaştırıcıdırlar.

Anahtar Kelimeler: Bilgisayarlı Tomografi, COVID 19, Real Time-PCR

Abstract

Objectives: This study aimed to evaluate the test results of patients whose RT-PCR test result was negative, but thorax CT findings were compatible with COVID-19 and their infectiousness in terms of contacts.
Materials and Methods: The study was designed as cross-sectional, descriptive research. In the first group, thorax CT revealed findings compatible with COVID-19 pneumonia, and the RT-PCR test result was negative. In the second group, thorax CT revealed findings compatible with COVID-19 pneumonia, and the RT-PCR test result was positive. Data collected were assessed with SPSS 21.0 software program. The significance level was accepted as 5%.
Results: Of the participants, 54.41% were male, and 45.59% were female. There was no significant difference between the two groups in terms of contact environment and status of being a healthcare worker and exitus. There was no difference between the first and second groups in terms of the number of contacts. The rate of sample collection was higher in the second group. The number of people who had contact with the patients and positive RT-PCR test results was higher in the first group.
Conclusion: Even if patients have negative RT-PCR test results for COVID-19, they are still infectious.

Keywords: Computerized Tomography, COVID-19, Real Time-PCR.

Introduction

Novel coronavirus disease (COVID-19) that was first defined in 2019 in the whole world is a viral disease which is from the coronavirus family and occurred due to severe acute respiratory syndrome coronavirus. The first case was reported in Wuhan, Hubei, China.[1]

SARS-CoV-2 is a single-stranded, positive-sense and enveloped RNA virus from the coronavirus family.[2]

This novel disease, firstly emerging in China and then spreading all over the world, was declared a pandemic by the World Health Organization (WHO) on the 11th of March, 2020. The fact that it had non-specific symptoms and rapidly caused severe acute lower respiratory tract disease revealed the need for early diagnostic tests.[3]

Although the real-time reverse transcription-polymerase chain reaction (RT-PCR) test is the gold standard test for COVID-19 different tests have been researched as it gives false-negative results.[4]

The most important involvement of COVID-19 is in the lung. Images on thorax computed tomography (CT) of the patient are important for the course of disease, diagnosis and treatment follow-up, and additional complications to develop. As the RT-PCR test, which is the basic method for COVID-19, gives false-negative results in early periods and later, and thorax CT is easy to perform tendency to use thorax CT has increased.[5] Thorax CT was preferred as the screening method in China in the early stages when the epidemic was prevalent. Sensitivities of the tests were compared in a study, and the results revealed that sensitivity of RT-PCR was 71% in the early period and sensitivity of thorax CT was 98%.[6]

Since the risk for infectivity of COVID-19 is a quite high rapid diagnosis of patients is important in terms of finding the source of transmission and close contacts of patients via filiation and applying isolation and treatment plan of patients.

Since there is no vaccine developed against coronavirus disease, precautions taken are mostly for source control and mode of transmission. Filiation is important in this regard.

Filiation means the work or processes performed to determine the sources causing an epidemic. In infectious disease epidemics, finding the first source or contact (filiation) is important. Filiation activities on COVID-19 have meticulously been performed in our country since the 11th of March 2020, when the first index case was detected.

This study aimed to evaluate RT-PCR test results of patients whose RT-PCR test result was negative, but thorax CT findings were compatible with COVID-19 and their infectiousness in terms of contacts.

Materials and Methods

Study design and participants

The study was designed as cross-sectional descriptive research. A total of 136 individuals who were from Kayseri and between the ages of 18 and 86, who had suspected or confirmed COVID-19 and whose consents were obtained were included in the study between 01.05.2020 and 30.05.2020.

Data screening process

This study was conducted with patients who had knowledge of the public health information management system and were followed up by the Kayseri City Hospital pandemic department. We divided the cases into two groups. In the first group, thorax CT revealed findings compatible with COVID-19 pneumonia, and the RT-PCR test result was negative. In the second group, thorax CT revealed findings compatible with COVID-19 pneumonia, and the RT-PCR test result was positive. The study was prospectively designed. Demographic and clinical data of the patients were obtained from public health information systems and computer record systems. The clinical conditions of the patients were classified by their physicians as good, moderate, and severe. Source patients, RT-PCR, and rapid diagnostic test results of the participants and contacts were questioned. Their consent was received via the link sent to their phone. Filiation was performed for patients in both groups. Patients were questioned about the number of contacts, contact histories, and contact environment. Contacts were determined by the declaration of the patients. According to the protocol applied by the Ministry of Health, the patients were first put into isolation by the filiation teams for 14 days. Then RT-PCR test was performed for contact patients with symptoms, old age, and chronic disease, and a Second RT-PCR test was performed on patients at the end of symptoms. This information of the patients was obtained from the Public health information system. Repeated RT-PCR test results of the patients, RT-PCR test results of source patients, and the number of contacts tested with the RT-PCR test were questioned. The data collected were statistically analyzed with SPSS.21 software program.

Statistical Analysis

Descriptive statistics such as mean, standard deviation, minimum and maximum values were calculated for continuous variables, and categorical variables were expressed as numbers and percentiles. Kolmogorov Smirnov test was used to determine whether numerical data of the variables were normally distributed. The relationship between the groups and categorical variables was assessed with the Chi-Square test. Statistically, the significance level in calculations was accepted as 5%, and SPSS 21.0 software program was used for calculations.

Results

A total of 136 patients who were followed up in Kayseri and who were approved to participate in the study were included in our study. Of the patients, 54.41% were male, and 45.59% were female. Age distribution was normal. The mean age was 48.2±18.3. 72.10% of the patients were followed up at Kayseri Research and Training Hospital. The first group consisted of 55.88% of total cases, and the second group consisted of 44.12% (Table 1).

The clinical conditions of the patients were classified as good, moderate, and severe by the treating physicians, and 77.20% had a good course, 19.86% had a moderate course, and 2.94% had a severe course. While the first RT-PCR test result was positive in 44.11% of the patient's second RT-PCR test result was positive in 6.62%. A rapid diagnostic test was performed for the RT-PCR negative group, and the rate of positive results was 19.11%. Of the patients who had contact with a COVID-19 patient, 53.67% had contact in a home environment and 6.61% in a work environment (Table 1).

There was no difference between the groups in terms of age. There was no difference between the first and second groups in terms of the median number of contacts (p=0.182). The median number of RT-PCR tests performed for contacts of the second group was higher (p=0.022). The median number of positive RT-PCR test results was higher in the first group (p=0.010) (Table 2).

The number of Rapid Diagnostic Tests performed was higher in the first group, and 33.34% of the first group had positive results (p=0.022). The number of source patients reached was higher in the second group, and the number of positive RT-PCR test results of samples collected from source patients was higher (p=0.022). There was no significant difference between the two groups in terms of contact environment and status of being a healthcare worker and exitus (p=0.21, p=0.068, and p=0.401, respectively).

Table 1. General Characteristics of the Participants

Gender		**number (%)**
Female		62 (45.59)
Male		74 (54.41)
Groups		
Group 1	Positive CT, Negative PCR	76 (55.88)
Group 2	Positive CT, Positive PCR	60 (44.12)
Clinical Condition of the Cases		
Good		105 (77.20)
Moderate		27(19.86)
Severe		4 (2.94)
Source of Disease		
Locally acquired		135 (99.26)
Overseas-acquired		1 (0.74)
Patient RT-PCR		
Positive		60 (44.11)
Negative		76 (55.89)
Rapid Diagnostic Test		
Positive		26 (19.11)
Negative		24 (17.64)
Sample not collected		86 (63.25)
RT- PCR Test Result of Source Patients		
Positive		32 (23.52)
Negative		4 (2.94)
Not found		100 (73.52)
Contact Environment		
Home Environment		73 (53.67)
Work Environment		9 (6.61)
Home+Work Environment		11 (8.08)
Other		43 (31.61)

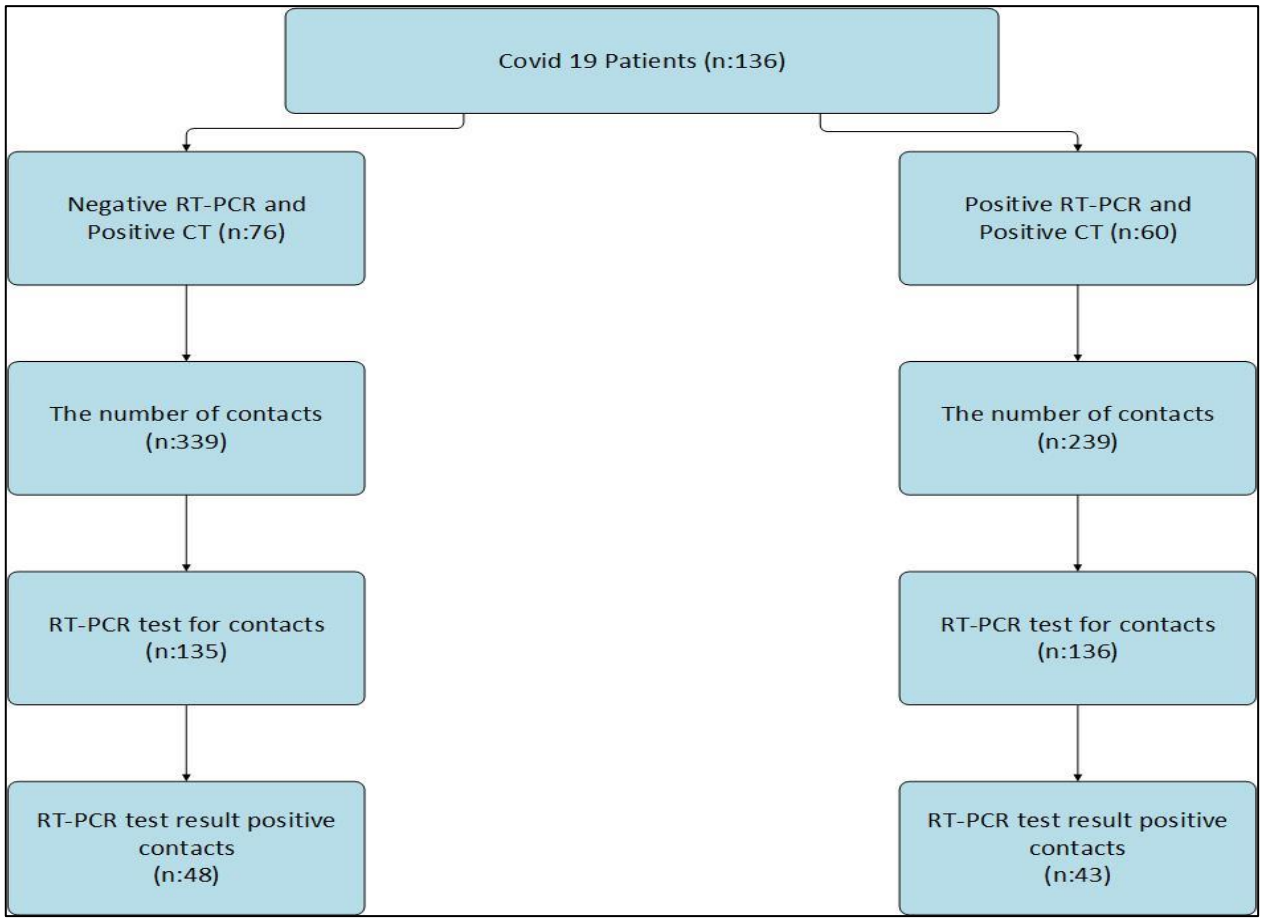

Figure 1. Algorithm

Table 2. Evaluation of the Two Groups

	CT (+) PCR (-) (Group 1)	**CT (+) PCR (+) (Group 2)**	***p***
Age (mean±SD)	50±18.4	45.8±17.9	0.185
Number of Contacts [median(min-max)]	4 (1-21)	4 (0-16)	0.182
RT-PCR tests for Contacts [median(min-max)]	0 (0-16)	1 (0-8)	**0.022**
Contacts with Positive RT-PCR Test Result [median(min-max)]	0 (0-15)	0 (0-4)	**0.010**

Table 3. Comparison of the Groups

		CT (+) PCR (-) Group 1 Number (%)	CT (+) PCR (+) Group 2 Number (%)	*p*
Gender	Female	35 (56.45)	27(43.55)	0.555
	Male	42 (56.75)	32 (43.25)	
Clinical Condition	Good	60 (57.14)	45 (42.86)	0.953
	Moderate	15(55.55)	12(44.45)	
	Severe	2 (50.00)	2 (50.00)	
RT-PCR of Patients	Positive	0 (0.00)	60 (100.00)	**<0.001**
	Negative	76 (100.00)	0 (0.00)	
RT-PCR of Source Patients	Positive	15 (46.90)	17 (53.13)	**0.022**
	Negative	0 (0.00)	4 (100.00)	
	Not found	62 (62.00)	38 (38.00)	
Contact Environment	Home Environment	42 (57.53)	31 (42.47)	0.211
	Work Environment	6 (66.66)	3 (33.34)	
	Home+Work Environment	3 (27.27)	8 (72.73)	
	Other	26 (60.46)	17 (39.54)	
Healthcare Worker	Yes	2 (25.00)	6 (75.00)	0.068
	No	75 (58.59)	53 (41.41)	
Exitus	Yes	1 (33.34)	2 (66.76)	0.401
	No	76 (57.14)	57 (42.86)	

Discussion

In this study, the infectiousness of patients who had negative RT-PCR test results and thorax CT findings compatible with COVID-19 was found higher than that of patients who had positive RT-PCR test results and thorax CT findings compatible with COVID-19.

SARS-CoV-2 belonging to novel coronavirus family was declared a pandemic by WHO and originated from Wuhan in 2019 and is an agent of acute lower respiratory tract infection.[7,8]

It was reported that just as symptoms such as fever, cough, shortness of breath, fatigue, and headache could be seen in this coronavirus disease which is a new infection source, it may totally have an asymptomatic course. Two main modes of transmission have been mentioned for COVID-19 so far: aerosol and droplet transmission that has an important role in the spread of the disease.[9,10]

Early diagnosis is crucial due to the strong infectivity of the disease. The most important way to prevent the disease from spreading within the society is early diagnosis and isolation of patients diagnosed early and their contacts from other healthy individuals.[11]

The risk for transmission from an infected person differs according to the type and duration of exposure, use of preventable precautions, and possible individual factors (e.g., virus amount in respiratory secretion). In studies, hospitals, long-term healthcare facilities, domestic life with passenger liners, and places where there are social or business meetings were determined as places with a high risk of transmission.[12,13,14] In our study, the household transmission was found higher among infection's modes of transmission, which was consistent with other studies.

RT-PCR test used to diagnose patients, rapid antibody test, and thorax CT used in diagnosis, treatment, and follow-up of complications are of great importance.[15] In some studies, the sensitivity of the RT-PCR test was found lower than that of thorax CT, which was reported to be due to the health personnel collecting the sample.[9] Assessment of thorax CT in patients infected with COVID-19 should be supported with the clinical condition of the patient. CT image assessed with clinical findings of the patient is commented as a typical image for COVID-19 or image compatible with COVID-19.[16] In our study, thorax CT findings of all the patients were typically compatible with COVID-19 pneumonia.

Although the RT-PCR test has been the standard method for the diagnosis of COVID-19 infection, these real-time PCR test kits have several limitations. High rates of false-negative results have been reported. A correct and rapid test method was immediately needed to prevent transmission of the virus, provide timely treatment for patients, and rapidly detect a large number of infected patients and asymptomatic carriers. The rapid diagnostic test covered these expectations.[17] In our study, rapid antibody tests of patients with thorax CT findings compatible with COVID-19 and negative RT-PCR test results were highly positive during their follow-up, which is similar to results in the literature. The high positivity of rapid antibody tests of patients who had negative RT-PCR test results suggests that the RT-PCR test may result in false-negative in the early period.

In a study by Yang et al., it was stated that throat swabs collected for the RT-PCR test might be affected by being collected in different periods of time and collecting techniques.[18] Collecting technique and time in our study may have been effective in patients who had thorax CT findings compatible with COVID-19 but negative RT-PCR test result.

It was reported in the studies by Corman et al. that contacts of cases who had negative RT-PCR test results developed symptoms later on and that both the cases and contacts should be followed up even if their RT-PCR tests were negative.[19] In our study, although the number of contact patients of both groups was similar RT-PCR positivity rate of contact patients of the RT-PCR negative group was higher. This suggests that RT-PCR negative patients among the cases have virulence load and infectiousness as much as RT-PCR positive cases.

In some studies, it was observed that asymptomatic cases had an important infective role in the spread of the disease.[6,20] On thorax CT of asymptomatic cases, 50% had typical images such as ground-glass opacities. On the following days, symptoms occurred in 20% of these cases.[21]

In our study, the clinical condition of the patients with the negative RT-PCR test result and thorax CT findings compatible with COVID-19 was proportionally better, and the infectiousness of patients in this group was higher. Lack of symptoms or better clinical conditions in patients may have delayed the diagnosis. Therefore, late diagnosis may have increased the infectivity.

Limitations

This study has some limitations. One of them is that it provides limited information about the whole world as it was performed with a specific sampling group. Another limitation is that CTs were assessed by a single radiologist. Another important limitation is that RT-PCR tests were affected by the work experience of healthcare personnel who collected the samples.

Conclusion

It was concluded that patients with the negative RT-PCR test result and thorax CT findings compatible with COVID-19 were as infectious as patients with the positive RT-PCR test result and that the RT-PCR positivity rate of their contacts was high. It was also concluded that filiation had an effective role in fighting against the epidemic and limited its spread and that patients who had negative RT-PCR test results should be re-tested. We think that filiation should be performed for patients who had negative RT-PCR test results but who had thorax CT findings compatible with COVID-19 in order to lower infectivity.

Ethical considerations

Our study was designed in accordance with the principles of the Helsinki Declaration and regulation of patient rights and approved by the clinical research ethics committee of Kayseri Research and Training Hospital with the date of 11.06.2020 and the number of 74.

Conflict of interest

The authors declare no conflict of interest.

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