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Comparison of computed tomography (CT) findings with RT-PCR in the diagnosis of COVID-19 in children

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Abstract

Aim: This study aimed to compare chest computed tomography (CT) findings with reverse-transcription polymerase chain reaction (RT-PCR) test results in children with probable or definitive diagnosis of coronavirus disease 2019 (COVID-19).

Methods: In this retrospective archive study, pediatric patients who were followed up in the hospital with a possible or definitive diagnosis of COVID-19 and who had chest CT at presentation were included. CT scan images of the patients were re-interpreted by a pediatric radiologist and compared with their RT-PCR test results.

Results: Of the total of 89 patients, 33 had negative and 56 had positive RT-PCR tests. The presence of pulmonary lesions and consolidation was statistically significantly higher in the RT-PCR negative group than in the RT-PCR positive group ($p = 0.037$ and 0.001, respectively). Lobe involvement of 0%–25% was higher in the RT-PCR positive group ($p = 0.001$), and lobe involvements of 25%–50% and 50%–75% were significantly higher in the RT-PCR negative group ($p = 0.001$ and 0.005, respectively). Central and perihilar involvement was found to be statistically significant in the RT-PCR negative group ($p = 0.008$ and 0.005, respectively).

Conclusion: Chest CT findings may provide some clues in predicting RT-PCR positivity in children with a probable diagnosis of COVID-19. Lobe involvement percentage of up to 25% is a finding in favor of patients with positive RT-PCR test, whereas 25%–75% lobe involvement, central and perihilar involvement, and consolidation can be interpreted in favor of patients with negative RT-PCR test.

KEYWORDS

computed tomography, COVID-19, RT-PCR

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an acute infectious respiratory system disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which emerged in China in December 2019 and was identified in January 2020. This infection can be transmitted by droplet, contact, or fecal-oral route.[1] Its incidence in children is less than in adults, and it has a milder clinical course. However, studies have reported that children with underlying diseases have a more severe clinical course.[2,3]

Radiological studies conducted in adults with COVID-19 infection have shown that ground-glass opacities (GGOs) and consolidation appearance, usually with peripheral distribution and bilateral multifocal lower lobe dominance, are typical chest computed tomography (CT) examination features.[4] COVID-19 reverse-transcription polymerase chain reaction (RT-PCR) results can be false negative in the early stage of the disease. Since the clinical course of pediatric patients is generally mild and chest radiography does not show all pulmonary lesions, chest CT examination may be necessary to provide supportive information.[5] In previous studies with children, chest

CT findings were defined as similar but milder to the findings in adults. Usually, subpleural GGOs have been reported, and since consolidations with a halo sign are seen in up to 50% of cases, they are considered typical symptoms in pediatric patients. However, in the diagnosis of COVID-19, it has been recommended to evaluate radiological findings together with epidemiological data and RT-PCR results.[5,6]

In this study, it was aimed to reinterpret the CT images of pediatric patients who were followed up in the pediatric clinic with the diagnosis or prediagnosis of COVID-19 by a pediatric radiologist, and to compare the obtained findings with the RT-PCR results. It is thought that the results obtained will contribute to the early and accurate diagnosis of COVID-19 disease in children.

FIGURE 1 An 11-year-old female presented with fever and cough. She had contact with individuals infected with COVID-19 pneumonia in her family. RT-PCR test was negative. There was no pathological finding in thorax CT. Parenchymal region nomenclatures used in the study are shown in the axial thorax CT images of this case: the area around the hilus that constitutes 1/3 of the lung area was named as perihilar lung area (yellow line). The lung parenchyma between the green and yellow lines was accepted as the central area. The area extending from the outer part of the green line to the costal-pleural surface was called the peripheral area. COVID-19, coronavirus disease 2019; CT, computed tomography; RT-PCR, reverse-transcription polymerase chain reaction [Color figure can be viewed at wileyonlinelibrary.com]

2 | MATERIALS AND METHODS

For this retrospective and cross-sectional study, a study permit was obtained from the local ethics committee of Health Sciences University Konya Education and Research Hospital, with the decision numbered 40-32 and dated on February 07, 2020. CT data of the patients were obtained by examining the electronic archive records of the hospital. Children aged 0–18 years who were hospitalized in the COVID-19 clinic with a possible diagnosis of COVID-19 between April 1 and July 31, 2020, who were followed up at least two times with an interval of 48 h, and who had a diagnosis of COVID-19 with a positive RT-PCR test were included in the study. Patients with deficiencies in hospital records and/or laboratory results and with immunodeficiency or any acute, chronic infectious, or inflammatory diseases were excluded from the study.

Sociodemographic data, symptoms, clinical findings, and RT-PCR results of the patients were recorded. An experienced pediatric radiologist, who was blinded to the CT reports clinical findings and RT-PCR results made previously by other radiologists, reinterpreted the noncontrast chest CT images obtained from the archive. All CT images were evaluated in terms of the presence of pulmonary lesions, lesion type, pulmonary involvement areas, and maximum lobe involvement percentage. The entire lung parenchyma area was divided into peripheral, central, and perihilar areas in all axial sections. The definition of central and peripheral areas is used to determine the location of the lesions in radiological anatomy. The lung parenchyma area is divided into three regions in axial section CT examination: The 1/3 outer part close to the costal-pleural surface is called the peripheral area. The parenchyma area between the peripheral region and the mediastinum is considered the central area (Figure 1). For adults, peripheral lung tissue is defined as the 3 cm thick area close to the costal-pleural surface. However, there is no metric definition for children. In this study, the 1/3 outer part of the lung close to the costal-pleural surface is the peripheral area; 1/3 of the inner part of the lung between this area and the mediastinum was defined as the central area. In addition, the 1/3 area of the lung parenchyma around the hilus was determined as the perihilar area.[7–9] Lesions were recorded according to their placement in these specified areas. The radiological characteristics of the lesions were recorded as consolidation, GGO, halo sign, vascular fullness, nodule, and fibrosis. (Figures 2–4). Maximum lobe involvement was defined as the percentage expression of the ratio of the total area of the lesion to the total area of the relevant lobe, regardless of the lesion type, in the lobe where the most lesion area was detected in

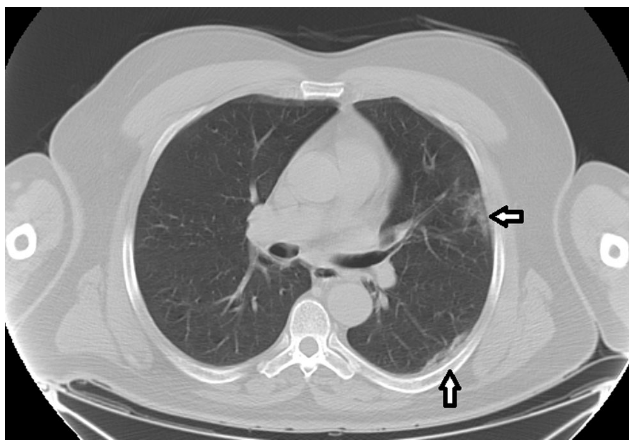

FIGURE 2 A 10-year-old male patient, who was admitted with fatigue and fever and had a positive RT-PCR test, showed involvement in the left upper lobe in the axial plane unenhancement chest CT examination. The lesion with ground glass infiltration (arrows) is located in the peripheral-subpleural location. Less than 25% of the upper lobe is affected. CT, computed tomography; RT-PCR, reverse-transcription polymerase chain reaction

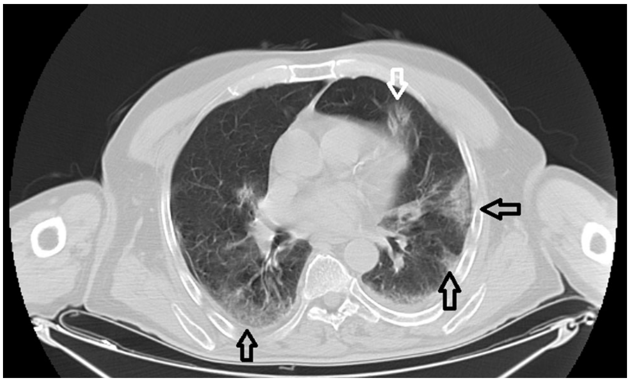

FIGURE 3 In the axial plane CT examination of a 13-year-old male patient with a positive RT-PCR test, who presented with 2-day shortness of breath and fever, subpleural-peripheral (closed arrows) in the upper lobe of both lungs and perimediastinal (open arrow) ground glass infiltration areas in the anterior segment of the left upper lobe are observed. 25%–50% area of both upper lobes is involved. CT, computed tomography; RT-PCR, reverse-transcription polymerase chain reaction

FIGURE 4 RT-PCR test result was negative in a 16-month-old boy with symptoms of fever, restlessness, and shortness of breath. In the unenhanced thorax CT axial image, there was a consolidation lesion located in the central and perihilar area at the upper thoracic level (arrow). This appearance was found to be compatible with the bacterial infective process with the laboratory and clinical findings. The cause of the disease was *Streptococcus pneumonia*. In the left hemithorax, there was a ground glass appearance in the same area. CT, computed tomography; RT-PCR, reverse-transcription polymerase chain reaction

the patient's CT examination. Percentages of involvement were determined with four degrees of involvement: 0%–25%, 25%–50%, 50%–75%, and 75%–100%. A measurement method was not used for this evaluation, the rate of involvement was determined according to the personal experience of the radiologist.

The following criteria were taken into account in the Republic of Turkey Ministry of Health COVID-19 diagnostic manual to determine the probable diagnosis.[10]

I. Household evaluation of epidemiological features

Having a household member hospitalized with a diagnosis of respiratory tract infection within the last 14 days.

Having a household member diagnosed with COVID-19.

Having a household member with fever and cough or respiratory distress with or without fever.

Having a contact history with someone diagnosed with COVID-19.

II. Complaints and symptom findings

Presence of a fever or a measured temperature of 38.0°C or above.

Presence of lung auscultation findings.

Presence of tachypnea.

Presence of a new-onset cough.

Having an oxygen saturation of 92% or lower in room air.

COVID-19 RT-PCR test is requested in the following cases:

The presence of at least one of each of I and II.

The presence of at least two of the II (for each option, the relation to another option cannot be shown).

Presence of two or more people with COVID-19 diagnosis in the same household.

Babies under 9 months of age belonging to mothers diagnosed with COVID-19.

Mothers diagnosed with COVID-19 during pregnancy.

Statistical analysis was performed using the Statistical Package for Social Sciences 18.0 for Windows (SPSS Inc.). Descriptive statistics of the categorical variables were presented as frequencies and percentages, and numerical data without a normal distribution were presented as median and interquartile range (IQR). The Kolmogorov–Smirnov test was used to determine whether the age data were normally distributed or not and the Mann–Whitney *U* test to compare independent groups without normal distribution. The χ^2 test was used to compare the groups in terms of categorical data. All statistical analyses were performed using a two-way hypothesis with a 5% significance threshold and 95% confidence interval.

3 | RESULTS

A total of 89 patients were included in the study. RT-PCR test results were positive in 56 patients and negative in 33. There was no significant difference in terms of gender between the two groups. The median ages of patients with negative and positive RT-PCR were 7 (IQR: 13) and 14 (IQR: 7) years, respectively. The age difference between the two groups was statistically significant (Table 1).

The presence of pulmonary lesions and consolidation were statistically significantly higher in the RT-PCR negative group than in the RT-PCR positive group ($p = 0.037$ and 0.001, respectively). No statistically significant difference was found between the two groups in terms of ground-glass image, halo sign, vascular fullness, and nodule/fibrosis ($p = 0.126$, 1.000, 0.707, and 0.201, respectively; Table 2).

When the two groups were compared according to the maximum lobe involvement percentage, 0%–25% lobe involvement was significantly higher in the RT-PCR positive group than in the RT-PCR

TABLE 1 Baseline characteristics of patients groups

	PCR (−), $n = 33$ (37%)		PCR (+), $n = 56$ (63%)		p
Age (year)	Median: 7 (IQR:13)		Median: 14 (IQR: 7)		0.002[a]
Gender	n	%	n	%	
Female	17	19.1	36	40.4	0.236[b]
Male	16	17.9	20	22.4	

Abbreviations: IQR, interquartile range; PCR, polymerase chain reaction.
[a]Mann–Whitney U test.
[b]χ^2 test.

TABLE 2 Comparison of CT findings according to the lesion image between PCR (+) and PCR (−) groups

	PCR (−)		PCR (+)		
	n	%	n	%	p
Presence of pulmonary lesions					
No	5	5.6	20	22.4	0.037[a]
Yes	28	31.4	36	40.4	
Consolidation					
No	14	15.7	48	53.9	0.001[a]
Yes	19	21.3	8	8.9	
Ground-glass opacity					
No	11	12.3	28	31.4	0.126[a]
Yes	22	24.7	28	31.4	
Halo sign					
No	32	35.9	54	60.6	1.000[b]
Yes	1	1.1	2	2.2	
Vascular fullness					
No	30	33.7	52	58.4	0.707[b]
Yes	3	3.4	4	4.5	
Nodule or fibrosis					
No	31	34.8	47	52.8	0.201[b]
Yes	2	2.2	9	10.1	

Abbreviations: CT, computed tomography; PCR, polymerase chain reaction.
[a]χ^2 tests.
[b]Fisher's exact test.

negative group ($p = 0.001$). Lobe involvements of 25%–50% and 50%–75% were statistically significantly higher in the RT-PCR negative group than in the RT-PCR positive group ($p = 0.001$ and 0.005, respectively). There was no statistically significant difference between the two groups in terms of lobe involvement above 50%–75% and 75%–100% ($p = 0.5281$; Table 3).

TABLE 3 Comparison of pulmonary CT findings according to the percentage of maximum lobe involvement between PCR (+) and PCR (−) groups

	PCR (−)		PCR (+)		
	n	%	n	%	p
0%–25%					
No	28	31.4	28	31.4	0.001[a]
Yes	5	5.6	28	31.4	
25%–50%					
No	20	22.4	52	58.4	0.001[b]
Yes	13	14.6	4	4.5	
50%–75%					
No	25	28.1	54	60.7	0.005[b]
Yes	8	8.9	2	2.2	
75%–100%					
No	33	37.1	54	60.7	0.528[b]
Yes	0	0	2	2.2	

Abbreviations: CT, computed tomography; PCR, polymerase chain reaction.
[a]χ^2 tests.
[b]Fisher's exact test.

In the comparisons made according to the localization areas of the lesions, it was found that central and perihilar involvements were higher in the RT-PCR negative group ($p = 0.008$ and 0.005, respectively). There was no significant difference between the two groups in terms of peripheral and diffuse involvement ($p = 0.074$ and 1.000, respectively; Table 4).

4 | DISCUSSION

Early diagnosis of COVID-19 disease, which has become a pandemic in a short time, and causes significant morbidity and mortality, is important in terms of disease control, spread prevention, and effective treatment. Epidemiological history and clinical findings are generally used to define possible cases.[10] The gold standard method used for diagnosis today is the RT-PCR test, which enables the detection of viral ribonucleic acid belonging to SARS-CoV-2. Throat swabs, sputum, lower respiratory tract secretions, stool, and blood samples are used for screening. However, the kit quality, different sampling methods, and various sample handling problems decrease the sensitivity of the RT-PCR test. In addition, the time required to complete the test poses a problem for the early treatment and control of the disease.[11–14]

Epidemiological studies and clinical observations have revealed that COVID-19 has a lower prevalence in children and young adults than in adults, and it is more likely to have a mild or asymptomatic course.[15] In a study, it was shown that children constitute 1%–5% of

TABLE 4 Comparison of pulmonary CT findings according to the area of involvement between PCR (+) and PCR (−) groups

	PCR (−)		PCR (+)		
	n	%	*n*	%	*p*
Central					
No	24	26.9	53	59.6	0.008[b]
Yes	9	10.1	3	3,4	
Peripheral					
No	9	10.1	26	29.2	0.074[a]
Yes	24	26.9	30	33.7	
Perihilar					
No	25	28.0	54	60.7	0.005[b]
Yes	8	8.9	2	2.2	
Common					
No	31	34.8	52	58.4	1.000[b]
Yes	2	2.2	4	4.5	

Abbreviations: CT, computed tomography; PCR, polymerase chain reaction.

[a]χ^2 tests.

[b]Fisher's exact test.

the cases of COVID-19 diagnosis so far, the disease is milder than adults, and deaths are rare.[16] Dong et al.[17] reported that of 2143 children between 1 and 18 years old who were diagnosed with COVID-19, 4% had asymptomatic, 90% mild or moderate, and 5% severe symptoms. In our study, the average age of the RT-PCR positive group was two times higher than that of the RT-PCR negative group, regardless of gender, showing that the prevalence of COVID-19 is higher in older children.

COVID-19 disease, along with being a systemic viral infection, mainly affects the respiratory system, and lung involvement is the most important cause of mortality and morbidity associated with this disease. The severity level of the infection is generally determined by the degree of lung involvement. Clinical and radiological findings related to pulmonary involvement are one of the determining factors especially for symptomatic patients in determining the level of clinical severity in children.[18]

Today, chest CT is used as a common and routine tool in diagnosing and monitoring COVID-19. Studies conducted so far have revealed that COVID-19 pneumonia has typical chest CT imaging features.[4,19] However, the fact that CT findings such as GGO and bilateral involvement, which are usually associated with COVID-19 pneumonia, are not specific for COVID-19 and can be seen in other viral pneumonia makes its diagnosis controversial, especially in cases where other respiratory infections are more common.[20] Poortahmasebi et al.[21] in a systematic review including 28 scientific articles comparing the diagnostic value of chest CT scan with RT-PCR test revealed that chest CT scanning should be used in symptomatic and hospitalized patients and recommended RT-PCR as the first-step diagnostic tool in the diagnosis of COVID-19.

Chest CT findings are typical and high diagnostic value for COVID-19 in adults. A meta-analysis by Bao et al. who included 13 adult studies found that the CT positive rate of COVID-19 was 89.76%, and typical CT findings were GGOs (83.31%), GGO with mixed consolidation (58.42%), interlobular septal thickening (48.46%), and air bronchograms (46.46%).[22] Another meta-analysis that evaluated 1099 adult patients found the sensitivity rate to be 86.2%.[23] Ai et al.[24] compared the CT scan results of 1014 adult patients, who underwent RT-PCR test, to determine the value and consistency level of chest CT scan in the diagnosis of COVID-19. They reported that the sensitivity and specificity of chest CT scan to suggest COVID-19 were 97% and 25%, respectively. In our study, the sensitivity and specificity rates of CT scanning in the RT-PCR positive group were 40.4% and 22.4%, respectively, which is significantly lower than in adults. Interlobular septal thickening and bronchogram were not reported in any of our patients.

Systematic reviews and meta-analyses performed on children with previous COVID-19 revealed the role of chest CT scanning in diagnosing children with positive RT-PCR tests. In a meta-analysis of 48 studies that examined 5829 pediatric patients, the rate of normal chest CT scan was 41%, and the GGO rate was 36% in cases with RT-PCR positivity.[25] In another meta-analysis, which included 7780 patients and 131 studies from 26 countries, these rates were reported as 18.9% and 32.9%, respectively.[26] The most common chest CT scan abnormality reported in these studies is bilateral GGOs. Duan et al.[27] reported that chest CT findings were atypical and milder in children diagnosed with COVID-19 than in adults, and they recommended that chest CT scan should be performed as little as possible and at low doses due to the risk of radiation. In our study, the negative and GGO rates of chest CT scanning were 22.4% and 31.4%, respectively. The results of our research are in line with previous studies. The reason for the higher negative rates of chest CT scan in children than in adults may be that pediatric patients experience milder or asymptomatic disease.

Xia et al.[5] examined chest CT findings of 20 pediatric patients with positive RT-PCR test and found no abnormalities in the chest CT scan of four (20%) patients. The same study also found a halo sign with consolidation in 10 (50%) patients, GGO in 12 (60%), and small nodules in 3 (15%). In our study, the consolidation rate in RT-PCR positive children was low than in the earlier study, and it was significantly higher in patients with negative RT-PCR test. Although the rates of GGOs, halo marks, and small nodules were low, RT-PCR was not different from negative patients. The difference between our research and other studies in the literature is that the chest CT findings of patients who met the epidemiologically and clinically possible case definition but had negative RT-PCR test were compared with those of who had positive RT-PCR test in terms of the abovementioned CT findings. Our results show that CT scanning features, although not typical as in adults, may be useful in predicting RT-PCR test positivity in children.

In children with a possible diagnosis of COVID-19, the predictive value of chest CT findings for RT-PCR positivity is not as typical as in adults. The possible reason is that children have milder or asymptomatic disease than adults and CT findings are atypical. However, up to 25% lobe involvement is significant for RT-PCR positive patients, whereas 25%–75% lobe involvement, central and perihilar involvement, and consolidation can be interpreted in favor of RT-PCR negative patients. Future studies that have a similar methodology and will include more cases can make important contributions to the early diagnosis and treatment of children with a prediagnosis of COVID-19 by chest CT scanning.

5 | LIMITATIONS OF THE STUDY

This study has some limitations. One of them is that other disease factors were not detected in negative RT-PCR test cases. For this purpose, the determination of viral agents from respiratory tract samples by RT-PCR and comparison of these results with CT findings will further strengthen the clinical and radiological interpretation of the diagnosis. The other limitation of the study is that the radiological evaluation was performed by a single pediatric radiologist.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

Zafer Bağcı: conceptualization (lead); data curation (equal); formal analysis (lead); investigation (lead); methodology (lead); project administration (lead); resources (lead); supervision (lead); validation (equal); writing original draft (lead); writing review and editing (lead). **Avni Merter Keçeli**: conceptualization (supporting); data curation (equal); formal analysis (supporting); investigation (supporting); methodology (supporting); project administration (supporting); resources (supporting); supervision (supporting); validation (equal); writing original draft (supporting); writing review and editing (supporting).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available in [repository name e.g "figshare"] at https://doi.org/10.1002/ppul.25426, reference number [reference number].

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