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Thorax Computed Tomography Imaging and Chest X-Rays Results in Children with Different Clinical-Stages of COVID-19

Farklı Klinik Evre COVID-19'u Olan Çocuklarda Toraks Bilgisayarlı Tomografi Görüntüleme ve Göğüs Röntgeni Sonuçlarının Değerlendirilmesi

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Abstract

Objective: Coronavirus disease-2019 (COVID-19) has milder clinical features in children, but information on the association between thoracic imaging and clinical severity of COVID-19 is limited.

Material and Methods: Between March 26th and June 30th, 2020, 982 patients with suspected or confirmed COVID-19, 428 of whom had chest X-rays, were included in the study. Demographic and clinical features, chest X-ray and thoracic computed tomography (CT) imaging results, and clinical severity of the disease were analyzed retrospectively.

Results: Laboratory-proven COVID-19 was detected in 116 (27.1%) patients; 42 (36.3%) had asymptomatic, 60 (51.7%) had mild, 12 (10.3%) had moderate, and two (1.7%) had severe disease. Chest X-rays were abnormal in 12.1% (14/116) of the patients with confirmed COVID-19. Main pathologic findings on chest X-ray were peribranchial thickening (10/14, 71.4%) and ground-glass opacity (GGO) (4/14, 28.6%) in patients with confirmed COVID-19. Thorax CT imaging was performed in 182 (42.5%) patients, 38 (32.7%) had confirmed COVID-19, 39.5% (15/38) of whom had abnormal imaging. Posterior (n= 7), peripheral (n= 7), and both lobe (n= 5) involvement were more prominent. Consolidated GGO (7/38, 18.4%) and bronchial wall thickening (7/38, 18.4%) were the main pathologic CT imaging patterns. Thorax CT images were abnor-

Öz

Giriş: Koronavirüs hastalığı-2019 (COVID-19) çocuklarda daha hafif klinik özelliklere sahiptir. Bu çalışmanın amacı, farklı klinik evrelerdeki doğrulanmış veya şüpheli COVID-19'u olan çocuklarda radyolojik bulguların değerlendirilmesi ve hastalığın şiddetiyle korelasyonunun irdelenmesidir.

Gereç ve Yöntemler: Çalışmaya 26 Mart-30 Haziran 2020 tarihleri arasında doğrulanmış ya da şüpheli COVID-19 hastalığı olan 982 çocuk hastadan akciğer grafi görüntülemesi yapılan 428'i dahil edildi. Hastaların demografik ve klinik özellikleri, akciğer grafisi ve toraks bilgisayarlı tomografi (BT) görüntüleme sonuçları ve COVID-19 hastalığının klinik şiddeti retrospektif olarak incelendi.

Bulgular: Laboratuvarda kanıtlanmış COVID-19 hastalığı 116 (%27.1) olguda tespit edildi; 42 (%36.3)'sinde asemptomatik, 60 (%51.7)'ında hafif, 12 (%10.3)'sinde orta ve ikisinde (%1.7) ise ağır hastalık mevcuttu. COVID-19 tanılı hastaların %12.1 (14/116)'inde akciğer grafisi anormaldi ve akciğer grafisindeki ana patolojik bulgular peribronşial kalınlaşma (10/14, %71.4) ve buzlu cam opasitesi (4/14, %28.6) idi. Toraks bilgisayarlı tomografi görüntülemesi 182 (%42.5) hastaya yapıldı; 38 (%32.7)'ine kesin COVID-19 tanısı konuldu ve %39.5 (15/38)'i anormal görüntülemeye sahipti. Posterior (n= 7), periferik (n= 7) ve her iki lob (n= 5) tutulumu

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mal in 20% (5/25) of the patients with asymptomatic/mild disease, and in 76.9% (10/13) of the patients with moderate/severe disease (χ2= 11.5, Phi= 0.552; p= 0.001).

Conclusion: Chest X-ray and thorax CT imaging were mainly normal in patients with asymptomatic/mild COVID-19 disease. In contrast, thorax CT imaging was abnormal in patients with moderate/severe COVID-19, and CT imaging scores correlated with COVID-19 clinical severity. However, since COVID-19 disease is milder in children, applications involving high amounts of radiation such as thoracic CT imaging should only be applied to selected patients.

Keywords: Children, thorax X-ray, computed tomography, COVID-19

daha belirgindi. Konsolide buzlu cam opasitesi (7/38, %18.4) ve bronş duvar kalınlaşması (7/38, %18.4) ana patolojik BT görüntüleme bulgularıydı. Asemptomatik/hafif hastalığı olanların %20 (5/25)'sinde ve orta/ağır hastalığı olanların %76.9 (10/13)'unda toraks BT görüntüleri anormaldi (χ2= 11.5, Phi= 0.552; p= 0.001).

Sonuç: Asemptomatik/hafif COVID-19 hastalığı olanlarda akciğer grafisi ve toraks BT görüntülemesi çoğunlukla normaldi. Buna karşılık, orta/şiddetli COVID-19 hastalarında toraks BT görüntülemesi çoğunlukla anormaldi ve BT görüntüleme skorları COVID-19 klinik şiddetiyle koreleydi. Fakat çocuklarda COVID-19 hastalığı erişkinlere kıyasla daha hafif seyrettiği için toraks BT görüntülemesi gibi yüksek miktarda radyasyon içeren uygulamalar sadece seçili hastalara uygulanmalıdır.

Anahtar Kelimeler: Çocuk, göğüs röntgeni, bilgisayarlı tomografi, COVID-19

Introduction

In December 2019, a new disease called the Coronavirus disease-19 (COVID-19) caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) virus spread worldwide and became a pandemic, changing the lifestyle of people everywhere. In children, SARS-CoV-2 infection causes a mild clinical course compared with adults. Clinical findings usually include absent or mild symptoms of upper respiratory tract infection and mild pneumonia (1-4).

The diagnosis of COVID-19 is made by showing nucleic acid positivity in swabs from the respiratory tract using a real-time reverse transcription-polymerase chain reaction (RT-PCR) assay. However, false-negative results may occur due to the method of sampling, the time of delivery to the laboratory, laboratory conditions, and the non-presence of viruses from where the samples are taken. Recent studies have shown that RT-PCR assays are negative in some patients, but thorax computed tomography (CT) images demonstrate pathologic results (5). Therefore, it is well understood that thorax CT imaging is significant to diagnose and show lung lesions in adults. The overriding common findings on thorax CT imaging are ground-glass opacity (GGO), consolidation, and GGO mixed with consolidation in lesions localized in the periphery, and primarily in the posterior and lower lobes of the lungs (6). However, reports related to chest imaging is limited in children due to the milder clinical course of the disease in the pediatric patient group (7-9). Some publications have shown that lesions are detected on CT images concordant with the clinical severity of COVID-19; in contrast, others have shown CT imaging results incompatible with the clinical severity of the disease (9-10).

In the present study, clinical stage and radiologic findings of COVID-19 pneumonia were investigated in children with laboratory-confirmed and suspected COVID-19.

Materials and Methods

Patients Characteristics

This study was conducted between March 26th and June 30th, 2020, in pediatric patients aged from one month to 18 years in our tertiary hospital. The patients' clinical data were collected retrospectively from hospital charts including age, sex, epidemiologic features, clinical symptoms, duration of hospitalization, the onset date of symptoms, the date from the onset of symptoms to the imaging date, and radiologic imaging results. Patients who underwent chest X-rays and had RT-PCR assays due to suspicion of COVID-19 were included in the study. The patients were then divided as having laboratory-confirmed or suspected (PCR negative) COVID-19. In the same sample, both throat and nasopharyngeal sample swabs for detecting SARS-CoV-2 were taken from patients according to the World Health Organization's advice (11). We used the World Health Organization definition criteria for showing the stages of COVID-19 pneumonia in children (12). We divided the patients into five groups according to the clinical severity of COVID-19: asymptomatic, mild, moderate, severe, critical. Of the 982 patients with suspected and definite COVID-19, 433 had chest X-rays and were included in the study; five patients with artifacts in X-ray were excluded, and the study was completed with 428 patients. The hospital ethics committee approved the study.

RT-PCR Assay

When making a diagnosis of COVID-19, obtaining appropriate samples quickly and using an accurate technique increases the success rate. Combined nasopharyngeal and oropharyngeal swab samples were taken from children with suspected COVID-19 and sent to the medical microbiology laboratory. SARS-CoV-2 was detected using RT-PCR (Bio-Speedy SARS-CoV-2 double Gene RT-qPCR Kit). Specifically, two target genes, including open reading frame 1ab (ORF1ab) and nucleocapsid protein (N), were tested during the RT-PCR assay. At least one swab was collected from each enrolled child.

Chest Image Acquisition

Chest radiography was acquired as digital radiographs, in the posteroanterior or anteroposterior projection, using the same portable X-ray unit (Mobilett Mira Max, Siemens) in the isolation wards of our department. Thorax CT imaging was performed on a 64-detector CT scanner (Somatom, SIEMENS). Axial images were acquired in supine position from the lung's apex to the costophrenic angle during a single inspiratory breath-hold without intravenous contrast medium. Images were taken using a high-spatial-frequency reconstruction algorithm with 100-110 KVp, mAs (automatic exposure control), 0.8 second rotation time, pitch 1, and reconstructed at 0.6 mm slice thickness with a sharp reconstruction kernel. Axial scans were reconstructed with a slice thickness of 2 mm and reconstruction increment of 0.75 mm to obtain axial, coronal, and sagittal plane images. Lung window setting was -600 Hounsfield units (HU) and a window width of 1500 HU. The estimated effective radiation dose in pediatric patients ranged from 0.7 mSv to 1.1 mSv. For children age under three years or those unable to cooperate, 10% chloral hydrate (5-10 mg/kg) was given orally administered before the scan.

Chest Image Analyses

Chest X-rays and thorax CT images were evaluated independently by two radiologists with five-years and 13-years experience in pediatric thoracic imaging, both of whom were blinded to the clinical data and laboratory indicators. Final decisions were reached by consensus.

Chest X-rays were first evaluated as normal and abnormal, and then abnormal findings were noted. All thorax CT images were reviewed on a standard clinical picture archiving and diagnostic system workstation. The following CT characteristics were evaluated:

1) Location and distribution,

2) CT appearances of lesions, and

3) Extrapulmonary findings.

The anatomic location of lung opacities was noted as right, left, or both lungs. The anterior or posterior predominance of the lesions was recorded. The anatomic distribution of parenchymal lung lesions was classified as peripheral (predominantly involving the outer one-third of the lungs), central/bronchocentric (predominantly involving the inner two-thirds of the lungs), or central/bronchocentric and peripheral. CT appearance of the lung lesion was assessed for the presence of pure GGO, GGO with consolidation, and pure consolidation. GGO was defined as a hazy density increase in the lung with vessel margin preservation, whereas consolidation was opacification with obscured vessel margins (13). CT images were also evaluated for the following characteristics: bronchial wall thickening, consolidation, ground-glass nodule, air bronchogram, tree-in-bud sign, vascular enlargement, halo sign, cobble stoning, subpleural striking, and bronchiectasis. Volume loss of the lung parenchyma at the time of presentation was visually evaluated. Extrapulmonary findings, including pleural effusion, pleural thickening, pericardial effusion, and lymphadenopathy (defined as a lymph node size >10 mm in the short-axis dimension), were also evaluated.

Disease severity, i.e., the extension of pulmonary involvement, was calculated using a semi-quantitative lung severity score. The degree of involvement was classified according to the grading system introduced by Chung et al., each lung lobe was scored from 0 to 5 as none (0%), minimal (1-25%), mild (26-50%), moderate (51-75%), or severe (76-100%). The total CT score ranged from 0 (no involvement) to 20 (maximum involvement), which was the sum of each lobar score (13).

Statistics

Median, first quartile, and third quartile were used to express continuous variables, which were not distributed normally. Differences between the two groups were analyzed using the Mann-Whitney U test, and categorical variables were compared using the Chi-square or Fisher's exact tests. $p< 0.05$ was considered significant. Phi correlation coefficient was used for dichotomous variables in milder (asymptomatic-mild) and severe (moderate-severe) stages of COVID-19 in patients with confirmed disease. Statistical analyses were performed using the SPSS for Windows version 25 software (IBM, Armonk, NY, USA).

Results

Patients' Characteristics

Of the 428 patients with suspected or confirmed COVID-19 who had chest X-rays and RT-PCR, it was positive in 116 (27.1%) patients and negative in 312 (72.9%). Clinical characteristics of the patients and RT-PCR results are shown in Table 1. In the comparison of the median ages of the groups, patients with confirmed COVID-19 were older than patients with suspected COVID-19 (133 vs. 69 months; $p\leq 0.001$). The majority of the patients with confirmed COVID-19 were girls, in contrast to those with suspected COVID-19, who were boys (Table 1). Underlying medical condition was present in 11.6% of the patients; respiratory diseases (n= 20, 4.7%) and neurometabolic disease (n= 7, 1.6%) were the most common, followed by cerebral palsy (n=5, 1.2%). These results were not statistically different between the two groups (p= 0.229). Fever (53.3%), cough (47.9%) and respiratory distress were the most common complaints, followed by throat ache, weakness, and headache. According to the clinical severity of COVID-19, 78 (18.2%) patients had asymptomatic disease, 250 (58.4%) had mild disease, 78 (18.2%) had moderate disease, and 19 (4.4%) patients had severe disease. Three patients whose

Table 1. Clinical characteristics of patients with laboratory confirmed and suspected COVID-19

Characteristics	Total number	RT-PCR positive	RT-PCR negative	p
Patient number	428	116	312	-
Age, months, median (IQR)	89 (27.2-167)	133 (49.5-177)	69 (22-154)	<0.001
Age group, years, n (%)				
<1	59 (13.8)	9 (7.8)	50 (16)	
1-5	120 (28.1)	23 (19.8)	97 (31.2)	0.001
5-12	111 (25.9)	31 (26.7)	80 (25.6)	
>12	138 (32.2)	53 (45.7)	85 (27.2)	
Sex, n (%)				
Girl	193 (45.1)	62 (53.4)	131 (42)	0.034
Boy	235 (54.9)	54 (46.6)	181 (58)	
Severity of illness, n (%)				
Asymptomatic	78 (18.2)	42 (36.3)	36 (11.5)	
Mild	250 (58.4)	60 (51.7)	190 (60.9)	
Moderate	78 (18.2)	12 (10.3)	66 (21.2)	<0.001
Severe	19 (4.5)	2 (1.7)	17 (5.4)	
Critical	3 (0.7)	0	3 (1)	
Underlying medical conditions, n (%)	50 (11.6)	10 (8.6)	40 (12.8)	
Respiratory system	19 (4.4)	5 (4.3)	14 (4.4)	0.229
Neurometabolic disease	15 (3.4)	3 (2.5)	12 (3.8)	
Clinical features, n (%)				
Fever	228 (53.3)	51 (44)	177 (56.7)	0.019
Cough	205 (47.9)	32 (27.6)	173 (55.4)	<0.001
Respiratory distress	61 (14.3)	6 (5.2)	55 (17.6)	0.001
Gastrointestinal complaint	31 (7.2)	8 (6.9)	23 (7.4)	0.866
Throat ache	22 (5.1)	8 (6.9)	14 (4.5)	0.316
Weakness	23 (5.4)	11 (9.5)	12 (3.8)	0.022
Headache	16 (3.7)	6 (5.2)	10 (3.2)	0.390*
Nasal congestion	5 (1.2)	2 (1.7)	3 (1)	0.616*
Runny nose	7 (1.6)	-	7 (2.2)	0.197
Days from symptoms onset to diagnosis, median, (IQR)	2 (2-3) (n= 423)	2 (1-3) (n= 111)	2 (2-3) (n= 312)	0.101
Hospitalization, n (%)	132 (30.8)	18 (15.5)	114 (36.5)	<0.001
Duration of hospitalization, days, median, n (%)	5 (4-7)	6 (5-7.2)	5 (4-7)	0.270

*Exact test was used to compare the categorical parameters of the patients.

RT-PCR tests were negative were treated in the intensive care unit (ICU) due to critical disease. Median interval from symptom onset to hospitalization was two days [interquartile range (IQR)= 2-3]. Duration of hospitalization was five (IQR= 4-7) days.

Radiologic Findings

All patients (428) had chest X-rays, and 325 (75.9%) were normal (Table 2). Median interval from symptom onset to chest X-ray imaging was two (IQR= 2-3) days. Chest X-ray was normal in 87.9% of the patients with confirmed COVID-19 and 71.5% of patients with suspected COVID-19 (p< 0.001).

Thorax CT imaging was performed in 182 (42.5%) patients, 38 (32.7%) of whom were from among the patients with confirmed COVID-19 and 144 (46.1%) had suspected COVID-19. Median interval from the onset of symptoms to thorax CT

Table 2. Chest radiography results in suspected and laboratory-confirmed patients with COVID-19

	Total	PCR positive	PCR negative	p
Chest radiography, n (%)	428 (100)	116 (100)	312 (100)	-
Normal	325 (75.9)	102 (87.9)	223 (71.5)	<0.001
Abnormal	103 (24.1)	14 (12.1)	89 (28.5)	
Predominant finding on chest X-ray, n/total number of abnormal X-ray (%)				
Peribranchial thickening	64/103 (62.1)	10/14 (71.4)	54/89 (60.7)	0.027
Ground grass opacites	39/103 (37.9)	4/14 (28.6)	35/89 (39.3)	0.013

imaging was two (IQR= 2-4) days. Thorax CT images were abnormal in 39.5% (15/38) and 46.5% (67/144) of the patients with confirmed and suspected COVID-19, respectively, and there was no statistical difference between the groups (p= 0.437). Twenty patients with confirmed COVID-19 had abnormal chest X-ray or thorax CT findings. Nine (45%) of them were over 12 years of age. Thorax CT images were abnormal in six of 38 (15.8%) patients whose chest X-ray was normal; four had moderate clinical stage, and two had mild stage. In the thorax CT results, according to anatomic location and distribution of parenchymal lung lesions, we observed that posterior (n= 26, 14.2%), peripheral (n= 26, 14.2%), and both lobe (n= 26, 14.2%) lung involvements were more prominent (Table 3) (Figure 1). Consolidated GGO (18.4%) and bronchial wall thickening (18.4%) were the main pathologic patterns on CT imaging of the patients with confirmed COVID-19. Cavitation, reverse halo sign, pleural effusion, and pericardial effusion were not detected (Figure 2).

Table 3. Thorax computed tomography findings in patients with suspected or confirmed COVID-19

		Total	PCR positive	PCR negative
Number of thorax CT, n (%)		182 (100)	38 (100)	144 (100)
	Normal, n (%) Abnormal, n (%)	100 (54.9) 82 (45.1)	23 (60.5) 15 (39.5)	77 (53.5) 67 (46.5)
Anatomical localization and distribution of parenchymal lung lesion, n (%)	Bilateral Right Left	26 (14.2) 16 (8.7) 11 (6)	5 (13.1) 4 (10.5) 1 (2.6)	21 (14.5) 12 (8.3) 10 (6.9)
	Peripheric Central Peripheric and central	26 (14.2) 17 (9.3) 20 (10.9)	7 (18.4) 0 3 (7.8)	19 (13.1) 7 (4.8) 17 (11.8)
	Posterior Anterior Anterior and posterior	26 (14.2) 14 (7.6) 16 (8.7)	7 (18.4) 3 (7.8) 0	19 (13.1) 11 (7.6) 16 (11.1)
CT appearance of lessons, n (%)	Bronchial wall thickening	61 (33.5)	7 (18.4)	54 (37.5)
	Consolidation	35 (19.2)	4 (10.5)	31 (21.5)
	GGO and consolidation	33 (18.1)	7 (18.4)	26 (18)
	Ground glass nodule	30 (16.4)	5 (13.1)	25 (17.3)
	GGO	29 (15.9)	5 (13.1)	24 (16.6)
	Air bronchogram	26 (14.2)	4 (10.5)	22 (15.2)
	Tree-in-bud sign	15 (8.2)	1 (2.6)	14 (9.7)
	Vascular enlargement	13 (7.1)	3 (7.8)	10 (6.9)
	Halo sign	13 (7.1)	6 (15.7)	7 (4.8)
	Cobble stoning	11 (6)	2 (5.2)	9 (6.2)
	Subpleural striking	10 (5.4)	4 (10.5)	6 (4.1)
	Bronchiectasis	6 (3.2)	2 (5.2)	4 (2.7)
	Volume loss	5 (2.7)	-	5 (3.4)
Extrapulmonary findings, n (%)	Pleural thickening	1 (0.5)	1 (2.6)	-
	Lymph node (>1 cm)	11 (6)	1 (2.6)	10 (6.9)
Number of involved lobes, n (%)	0 1 2 3 4 5	126 (69.2) 22 (12) 12 (6.5) 11 (6) 5 (2.7) 6 (3.2)	26 (68.4) 7 (18.4) 1 (2.6) 2 (5.2) 1 (2.6) 1 (2.6)	100 (69.4) 15 (10.4) 11 (7.6) 9 (6.2) 4 (2.7) 5 (3.4)
Severity of lobes involved, n (%)	0 1-25% 26-50% 51-75% 76-100%	126 (69.2) 50 (27.4) 4 (2.1) 2 (1) 0	26 (68.4) 11 (28.9) 0 1 (2.6) 0	100 (69.4) 39 (27) 4 (2.7) 1 (0.6) 0

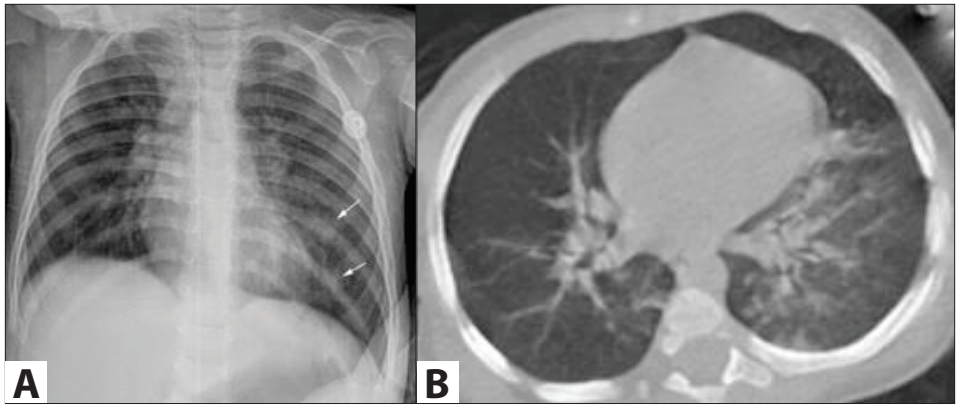

Figure 1. Two-year-old female with Coronavirus disease, two days after symptom onset. **(A)** Chest X-ray (CXR) shows bilateral perihilar peribronchial wall thickening with ground glass opacities in the left lung (arrows). **(B)** Axial and **(C)** coronal CT images obtained one day after the CXR displays bilateral bronchial wall thickening with ground-glass opacities and consolidation, predominantly in the left lower lobe.

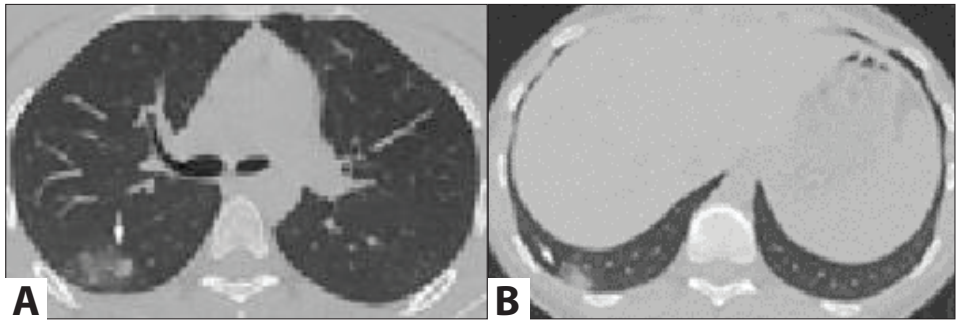

Figure 2. Sixteen-year-old female with Coronavirus disease, four days after symptom onset. **(A)** Axial CT image shows peripheral ground-glass opacities with consolidation in the right lower lobe, upper segment (arrow). **(B)** Axial CT image at the lower level displays pulmonary nodule with peripheral ground-glass opacity (halo sign) in the right lower lobe, posterior basal segment.

Table 4. The clinical stage and radiological patterns of COVID-19 pneumonia of the patients

RT-PCR positive						
	Asymptomatic	**Mild**	**Moderate**	**Severe**	**Critical**	**Total**
Number of chest X-ray, n (%)	42 (100)	60 (100)	12 (100)	2 (100)	-	116 (100)
Normal Abnormal	38 (90.5) 4 (9.5)	56 (93.3) 4 (6.7)	6 (50) 6 (50)	2 (100) -	- -	102 (87.9) 14 (12.1)
Number of Thorax CT, n (%)	6 (14.3)	19 (31.6)	12 (100)	1 (50)		38 (32.7)
Normal Abnormal	6 (14.3) -	14 (23.3) 5 (8.3)	2 (16.7) 10 (83.3)	1 (50) -	- -	23 (19.8) 15 (12.9)
RT-PCR negative						
	Asymptomatic	**Mild**	**Moderate**	**Severe**	**Critical**	**Total**
Number of chest X-ray, n (%)	36 (100)	190 (100)	66 (100)	17 (100)	3 (100)	312 (100)
Normal Abnormal	33 (91.7) 3 (8.3)	159 (83.7) 31 (16.3)	25 (37.9) 41 (62.1)	5 (29.4) 12 (70.6)	1 (33.3) 2 (66.7)	223 (71.5) 89 (28.5)
Number of thorax CT, n (%)	7 (19.4)	65 (34.2)	54 (81.8)	15 (88.2)	3 (100)	144 (46.1)
Normal Abnormal	6 (16.7) 1 (2.7)	50 (26.3) 15 (7.9)	16 (24.2) 38 (57.6)	5 (29.4) 10 (58.8)	- 3 (100)	77 (24.6) 67 (21.5)

The evaluation of clinical stage and radiologic patterns of COVID-19 pneumonia are shown in Table 4 for both patient groups. In the moderate-severe group, the pathologic findings on chest X-ray were detected in 42.8% (6/14) and thorax CT images were abnormal in 76.9% (10/13) of the patients with confirmed COVID-19. The severity score of thorax CT imaging was significantly higher in the moderate-severe clinical group compared with the asymptomatic-mild groups among patients with confirmed COVID-19 (p= 0.013). In patients with confirmed COVID-19, the number of lobes with lesions was remarkably higher with a moderate-severe clinical stage compared with an asymptomatic-mild clinical stage (at least one lobe with lesions in 8/13 patients with moderate-severe clinical stage, in contrast to 4/25 in patients with asymptomatic-mild clinical stage of the disease) (p= 0.005).

Radiologic patterns were compared among patients with confirmed COVID-19. Chest X-rays were abnormal in 7.8% (8/102) of patients with an asymptomatic-mild clinical stage and in 42.8% (6/14) of patients with moderate-severe clinical stage (χ^2= 14.2, Phi= .350; p< .001). Abnormal thorax CT images were significantly more common with moderate-severe clinical stage than in asymptomatic-mild clinical stages (5/25 asymptomatic-mild vs. 10/13 moderate-severe) (χ^2= 11.5, Phi= .552; p= .001).

Discussion

This present study focused on investigating the clinical severity of COVID-19, chest imaging of children with laboratory-confirmed and suspected COVID-19. Although 982 patients were admitted to our tertiary hospital, 428 (43.5%) underwent radiological imaging and were included in our study. Approximately one-third of the patients had laboratory-confirmed COVID-19 disease, similar to Dong et al.'s study (2).

Chest X-ray is the first-line imaging for the diagnosis of pneumonia in children. Nevertheless, there are few studies on the effectiveness of chest X-rays with COVID-19 pneumonia in children (10,14,15). Consistent with the literature, we found that chest X-ray images were mostly normal (87.9% vs. 71.5%, respectively) in patients with confirmed and suspected COVID-19 (14,16-18). Interestingly, the predominant abnormality in chest X-ray was peribranchial thickening in patients with confirmed COVID-19, in contrast to the suspected patients in which the predominant abnormality was GGO. Although not specific, GGO is an expected finding in COVID-19 pneumonia; we detected GGO appearance in more patients in the suspected group. In the study of Biko et al., the authors have found that chest X-rays demonstrated no abnormalities related to COVID-19 pneumonia in 67% of patients (9). Some studies have shown that pathologic chest X-ray imaging was more common in children with COVID-19 pneumonia than normal images (10). In the study of Caro-Dominguez et al., peribranchial wall thickening was the prominent abnormality of chest X-rays and detected in 58% of patients with COVID-19 (10). In the study of Das et al. GGO and GGO with consolidation were the main pathologic appearances in chest X-ray, which were detected in about 10% of patients (15). In our results, peribronchial wall thickening, although the main pathologic appearance on chest X-ray, was detected in only 12% of patients with laboratory-confirmed COVID-19.

As mentioned in our study, thorax CT images were abnormal in almost half of the patients and there was no statistically difference for abnormal CT counts between patients with confirmed and suspected COVID-19. Peng et al. have shown that nearly half of their patients had abnormal thorax CT images (19). Contrary to our study, some reports have shown a high rate of lesions on CT images in children. Ma et al.'s study has shown that thorax CT images were abnormal in nearly 85% of patients (16). When we divided the patients according to the clinical severity of COVID-19 pneumonia, the thorax CT images were abnormal in nearly 90% of patients with confirmed COVID-19 and 60% in patients with suspected disease with moderate-severe clinical stages. In asymptomatic and mild clinical stages, thorax CT images were mainly normal, as in other studies (14,17,20). In a study that compared chest radiography and thoracic CT imaging in pediatric COVID-19 pneumonia, approximately 20% (11/56) of patients had pathologic results on chest X-ray, and approximately half (26/56) of the patients had lesions on thoracic CT images (15). In the same way, we found pathologic results on chest X-ray in 12% (14/116) of confirmed COVID-19 patients but in 40% (15/38) of thoracic CT scans. Das et al. have found lesions on CT scans in 26.8% (15/56) of the patients that could not be seen on chest X-rays (15). In our study, lesions that were not detected on chest X-rays were observed in thorax CT imaging in 15.7% (6/38) of patients. Five of six patients had GGO with consolidation on CT imaging, all of whom had mild CT severity scores. These results show that thorax CT imaging is not superior to chest radiography in children.

Different studies have validated the typical CT findings in adults including bilateral pulmonary parenchymal GGO and GGO with consolidative pulmonary opacities, sometimes with a rounded morphology with predominant distribution in the lungs' posterior and peripheral distributions (13,21). Lesion distribution along the bronchovascular bundles is less common in adults (13,21). GGO, which is alveolar edema, exudation, and bleeding secondary to inflammation, may be observed mainly on thorax CT imaging (13,22). In our study, as mentioned in the literature, non-specific abnormalities were detected (pure GGO and/or consolidation) and distributed with a bilateral, posterior, and peripheral predominance

(14,16,18,23). Pure GGO, a combination of GGO with consolidation, and ground-glass nodules were seen in similar numbers in thorax CT imaging. In the review of Zhen et al. GGO was detected in 107 (26.4%) of 406 cases in thorax CT, whereas in our study, GGO and consolidation were detected in 33 (18.1%) patients, ground-glass nodule was observed in 30 (16.4%) patients, and pure GGO was found in 29 (15.9%) patients (24). Notably, the most pathologic finding was bronchial wall thickening in patients with suspected disease, which is non-specific for COVID-19 pneumonia. It might detect most viral infections.

In our study, 45% of the patients were girls, but there were statistically more girls in the confirmed COVID-19 group (%53 vs. %42). Karbuz et al. have found that 49% of confirmed COVID-19 patients were girls, similar to another study in which 43% were girls (3,25). Another study has also confirmed that the girl rate is lower than the boy rate (26). Also, in this study, patients with COVID-19 were separated into two groups: those with and without pneumonia. The researchers observed that the rate of girls was lower in the pneumonia group (50% vs. 43%). According to what is currently known, males are more severely affected by COVID-19 than females. In our study, the confirmed COVID-19 group contained more girls than the suspected COVID-19 group. This could be because patients with suspected COVID-19 had a more severe disease course.

In the present study, we examined the CT image severity score and clinical severity of COVID-19 pneumonia in children. Pathologic thorax CT imaging was observed in nearly 90% of the patients with a moderate-severe clinical stage in patients with laboratory-confirmed COVID-19. In contrast, due to the asymptomatic and milder clinical-stage, thorax CT imaging was mostly normal. There was a strong correlation between the disease's clinical severity and the severity score of thorax CT imaging in patients with confirmed disease. Also, pure GGO, bronchial wall thickening, bronchiectasis, ground-glass nodule, halo sign, crazy paving pattern, and GGO with consolidation were significantly more common with moderate-severe clinical-stage in patients with confirmed COVID-19. However, although with diagnostic accuracy, thorax CT scans have some limitations, such as artifacts due to the short and fast breath and fast pulse in children, high radiation exposure, and the need for sedation, restricting the routine use of CT scans in children.

Thorax CT imaging was frequently performed in approximately one-third of the patients with confirmed COVID-19 and almost half of the suspected cases. In the early phase of the pandemic, the exact course of the disease in children was unknown, some fear and anxiety might have created the need for clinicians to perform more examinations, causing the patients to be screened even with mild symptoms. Also, in the early stages of the epidemic, RT-PCR assays resulted within 1-2 days due to the possibly large number of suspected COVID-19 patients and problems with the kit supply; today it results in 2-4 hours. Besides, our hospital is a pandemic center, and the physicians who treated the patients in the first wave were in heterogeneous groups, which caused unnecessary examinations. Later on, COVID-19 was observed to have a slighter clinical course in children compared with adults, then more homogeneously trained teams were commissioned to follow up patients' examinations. Accordingly, unnecessary investigations were prevented. During the study period, 982 patients were admitted to our hospital with suspected COVID-19, and CT imaging rates accounted for nearly 20% of all patients with suspected and laboratory-confirmed COVID-19. Given that only patients with chest radiography were included in the study, the CT imaging rates may be relatively higher as a result.

This study has limitations. First, we excluded patients who did not undergo chest X-ray. We did not check children for other viral infections using multiplex respiratory virus assays. Children with COVID-19 may have other concurrent viral or bacterial infections that could confuse imaging findings. However, our study's outstanding feature is the high number of children with laboratory-confirmed or suspected COVID-19.

Conclusion

This study focused on the clinical severity and radiologic characteristics of pediatric patients with suspected or confirmed COVID-19. COVID-19 progressed with mostly mild clinical course and mostly normal radiologic imaging results in children. In contrast, thorax CT imaging was mostly abnormal in patients with moderate-severe COVID-19, and CT imaging scores were correlated with COVID-19 clinical severity. However, very few patients had severe and critical COVID-19, so it would be more appropriate to apply radiological imaging for a small number of selected patients.

Ethics Committe Approval: Ethics committee approval for the study was obtained from the Health Sciences University Tepecik Training and Research Hospital Clinical Research Ethics Committee (Decision no: 2020 8-16, Date: 08.07.2020).

Informed Consent: Patient consent was obtained.

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