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Laboratory changes and parenchymal changes in computed tomography after COVID-19 pneumonia

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ABSTRACT

Aims: Novel coronavirus-2019 (2019-nCoV) has caused a global pandemic. Fort his reason, our study is to determine the variables of thorax tomography findings and laboratory data after COVID-19 pneumonia in cases with severe COVID-19 pneumonia and to detect the findings of possible interstitial lung diseases.

Methods: In this single-center study, 61 consecutive patients were examined. These patients were admitted to the COVID-19 Pandemic Clinic of Malatya Training and Research Hospital between July 15, 2020 and August 28, 2020 and were hospitalized with a diagnosis of COVID-19 pneumonia. Patients were discharged after the illness, and after 6 months, they applied to the outpatient clinic for follow-up. In this study, we compared the changes in laboratory variables and thorax CT scans at the time of diagnosis and 6 months later. Patients were divided into groups 1 and 2. Group 1: patients who were diagnosed with COVID-19 pneumonia at initial presentation and had thorax CT and laboratory parameters at the time of diagnosis and group 2: patients who presented to the outpatient clinic for 6-month follow-up during the postcovid pneumonia period and had control thorax CT and laboratory parameters.

Results: When the laboratory parameters of group 1 and group 2 patients were statistically compared. In addition to the increase in glucose, creatinine, aspartate aminotransferase, alanine aminotransferase, gamma-glutamyl transferase, lactate dehydrogenase, aptt, INR, fibrinogen, neutrophil percentage, mean erythrocyte hemoglobin, albumin, the decrease in calcium, sodium, leukocyte, platelet, hemoglobin, lymphocyte count, erythrocyte distribution range variables were found to be statistically significant ($p<0.05$). In our study, ground glass opacity was seen most frequently in Group 1 Thorax CT and was found in 57 patients. In 10 of these 57 patients, ground-glass opacity was positive on Group 1 and Group 2 Thorax CT, while ground-glass opacity was negative on Group 2 Thorax CT in 47 patients. In 50 patients, consolidation was found on Group 1 Thorax CT and consolidation was positive on Group 1 and Group 2 Thorax CT in 5 patients. The changes in fibrosis, parenchymal band, reticular opacity, traction bronchiectasis, irregular interfaces, ground glass opacity, consolidation, and pulmonary nodule variables in Group 2 Thorax CT were statistically significant ($p<0.05$).

Conclusion: Laboratory data is very important in terms of COVID-19 infection diagnosis, prognosis and guiding treatment. It may be due to the fact that patients with residual abnormalities on control thorax CT after COVID-19 pneumonia were older, had more comorbid diseases, and had severe clinical disease at the time of hospitalization.

Keywords: COVID-19 pneumonia, residual abnormalities on thorax CT, laboratory changes

INTRODUCTION

A virus causing unprecedented outbreaks in communities and hospital resources around the world was detected in December 2019.[1] This virus first emerged in the city of Wuhan in the Hubei province of the People's Republic of China. It was identified as a new coronavirus that is of bat origin, infects humans, causes severe respiratory failure, and poses a serious threat to life. In a short time, it crossed the borders of China and spread all over the world, especially to European countries. This virus was named novel coronavirus-2019 (2019-nCoV), then "Serious Acute Respiratory Syndrome-Coronavirus-2 (namely, SARS-CoV-2)" by the World Health Organization (WHO), and the disease it causes was named

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Corona Virus Disease 2019 (COVID-19). On March 11, 2020, WHO reported that this disease caused a global pandemic and turned into a public health problem threatening the whole world.[2] According to WHO data, as of January 10, 2022, an average of 305 million people were infected with this virus and an average of 5.5 million people died due to COVID-19.[3]

Coronaviruses are single-stranded, positive polarized, and enveloped RNA viruses. Coronavirus is a member of the Coronaviridae family that causes mild respiratory disease in humans. Coronaviruses cause the disease in animals and humans by invading the airways.[4] The disease is usually transmitted by airborne droplet transmission of the virus through aerosols. In addition, it was reported in studies that the virus could also be transmitted by a non-infected individual's contact with the infected individual's belongings, clothes, and any place that the infected individual contacted.[5]

According to preliminary data from China, SARS-CoV-2 infection covers a wide spectrum of clinical forms, including asymptomatic infection, mild upper respiratory tract disease in 81% of these patients, or life-threatening severe viral pneumonia such as acute respiratory failure, sepsis, multiple organ failure and death in those with moderate to severe disease.[6] It was reported that 14% of patients with moderate/severe disease progressed to the severe disease stage, 5% progressed to the severe disease stage with life-threatening multiorgan failure, and the mortality rate was reported to be 50% on average in the severe patient group.[7]

COVID-19 is inhaled and the most important site of involvement is the lungs. Therefore, it is very important to demonstrate lung involvement radiologically. Since the diagnosis and treatment of chronic changes and sequelae caused by the virus in the lungs and other organs and laboratory changes will be important parameters in patients with severe disease in the coming months and years, we followed CT and laboratory changes in patients with COVID-19 pneumonia. Although the RT-PCR test is the gold standard for the diagnosis of COVID-19, chest radiography and CT play important roles in the diagnosis, follow-up, and staging of COVID-19 pneumonia.[6-8]

According to the changes in the thorax CT appearance of COVID-19 patients, the disease can be divided into four stages.[8-9]

The early period covers the initial 0-4 days of the disease. Radiologic findings are normal or mild ground-glass opacity (unilateral or bilateral lower lobes, subpleural localization).

The progressive period covers the next 5-8 days. Radiologic findings increase in bilateral, diffuse, multilobar ground-glass opacities with cobblestone appearance and consolidations.

The peak period covers the days 9-13 from the first day. Dense consolidation areas are more prominent. Parenchymal bands may be occasionally seen. Ground-glass and cobblestone appearance may be present.

The regression period covers the 14th day and beyond. In this period, the infection is now under control. Diffuse ground glass opacities may be seen due to regression of consolidation areas. Signs of fibrosis (sequelae fibrotic bands, structural distortion, and traction bronchiectasis) may occur.

This study aimed to evaluate the chronic parenchymal changes and laboratory changes on thoracic CT in patients hospitalized for severe COVID-19 pneumonia infection after 6 months in outpatients who were admitted to the chest diseases outpatient clinic.

METHODS

Ethics

The study was conducted in accordance with the Declaration of Helsinki and approved by the Scientific Ethics Committee of Malatya Training and Research Hospital (Date: 08.07.2020, Decision No: 2020/128). Written informed consent was obtained from all patients that they agreed to participate in the study. The study was supported by İnönü University Scientific Research Projects Coordination (Project No: TSA-2021-2333).

Patients

This study included 61 consecutive patients with severe COVID-19 pneumonia who were hospitalized in the Pandemic Clinic of Malatya Training and Research Hospital between 15.07.2020 and 28.08.2020 and met the inclusion criteria. In this single-center study, between July 15, 2020 and August 28, 2020, patients with a previous diagnosis of COVID-19 infection confirmed by RT-PCR test, whose blood parameters were examined at the time of diagnosis and whose thorax CTs were performed and reported as compatible with COVID-19 pneumonia, and who were clinically and radiologically diagnosed with Covid-19 pneumonia, were selected among the patients who applied to the outpatient clinic in the 6th month of their follow-up. Patients were divided into groups 1 and 2. Group 1; patients who were diagnosed with COVID-19 pneumonia at the first presentation and who had thorax CT and laboratory parameters at the time of diagnosis and group 2: patients who applied to the outpatient clinic for the 6th month control in the postcovid pneumonia period and who had control thorax CT and laboratory parameters.

Clinical/laboratory parameters and demographic data of our patients were recorded. After questioning their backgrounds and physical examinations, thorax CT scans of patients with COVID-19 pneumonia were performed at the time of initial diagnosis. An adult patient with a diagnosis of severe COVID-19 pneumonia was defined as a patient with clinical signs of pneumonia (fever, cough, shortness of breath, rapid breathing) and severe respiratory distress with any of the following parameters: respiratory rate (RR)>30 breaths/minute and resting oxygen saturation <90%, partial oxygen saturation/fraction of inspired oxygen (PaO_2/FiO_2) ≤300 mm Hg.[10]

After non-contrast CT scanning of Group 2 patients, the comparison and interpretation of the radiologic images of Group 1 and Group 2 patients were evaluated by a radiologist with 9 years of experience who was unaware of the clinical history of the patients. The device was a Philips Medical System MX-128-slice multidetector (Koninklijke Philips N.V., Eindhoven, The Netherlands) with 120 kV, 250 mA and 5 mm slice thickness. During thoracic CT scanning, patients were in the supine position and end-inspiration was performed. Image interpretation Thoracic CT images of the patients at the time of diagnosis and a mean of 6 months later were evaluated at the workstation, and images on PACS were evaluated by the same radiologist using the lung window (width, 1000-1500 HU; level, -300 to -500 HU) and mediastinal window (width, 300-400 HU; level, 30-40 HU).

The main CT findings were described using the international standard nomenclature defined by the Fleischner Society Glossary and the peer-reviewed literature on viral pneumonia, using terms such as ground glass opacity (GGO) and consolidation.[11-13] Other findings most frequently evaluated were fibrosis, parenchymal band, reticular opacity, traction bronchiectasis, irregular interfaces, pulmonary nodule and honeycomb.

The distribution of findings was defined as peripheral (subpleural), central, or diffuse, depending on which third of the lung they were located in, as well as anterior and posterior, depending on which half of the lungs they were located in.

The semi-quantitative CT severity score proposed by Pan et al.[14] was calculated for each of the 5 lobes according to the degree of anatomical involvement as follows: 0, no involvement; 1, <5% involvement; 2, 5-25% involvement; 3, 26-50% involvement; 4, 51-75% involvement; and 5, >75% involvement. The total CT score was the sum of individual lobar scores ranging from 0 (no involvement) to 25 (maximum involvement). Patients were divided into residual and complete resolution groups based on CT scan images and scores at diagnosis and follow-up CT scans.

Thorax CT findings were evaluated according to radiological patterns such as fibrosis, parenchymal band, reticular opacity, traction bronchiectasis, irregular interfaces, ground glass opacity, consolidation, pulmonary nodule, and honeycomb.

Statistical Analysis

The analysis of the data included in the study was carried out with SPSS (Statistical Program in Social Sciences) 27.0 software. The Kolmogorov-Smirnov Test was used to check whether the data fit the normal distribution. The significance level (p) was taken as 0.05 for comparison tests. Since the variables were normally distributed (p>0.05), the analysis was continued with nonparametric test methods. Paired t-test was used to compare continuous dependent data and a marginal homogeneity test was used to analyze categorical dependent data. Number, percentage, mean, and standard deviation values were used as descriptive values.

RESULTS

Main Characteristics of Patients

A total of 61 patients 34 males (55.7%), 27 females (44.3%), ages <40; 2 (3.3%), 40-60;41 (67.2%), >65; 18 (29.5 %) were included in the study. 6 patients (6/55; 9.8%) were active smokers and 55 patients (55/61; 90.2%) had a history of inactive smoking. The patients who participated in the study consumed alcohol (2/59; 3.3%) and 59 patients (59/61; 96.7%) did not consume alcohol. Patients had known comorbid diseases including hypertension (31/30; 50.8%), type 2 diabetes mellitus (23/38; 37.7%), cardiovascular disease (19/42; 31.1%), neurologic disease (2/59; 3.3%) and obstructive pulmonary disease (14/47; 23%)(Table 1).

The study included 8 patients whose general condition deteriorated in the ward and were admitted to intensive care, 30 patients from the ward, and 23 outpatients. The most common clinical findings Group 2 were shortness of breath, fever, chest pain, cough, myalgia, muscle pain, and fatigue.

One of the inpatients with COVID-19 pneumonia was intubated (1/60; 1.6%) and transferred to the intensive care unit. Follow-up was performed in the intensive care unit. 6 of the patients received non-invasive support (6/55; 9.8%). 38 patients (38/23; 62.3%) received oxygen support. Patients with COVID-19 pneumonia received antiviral agents (59/2; 96.7%), antibacterial agents (54/7; 88.5%), glucocorticosteroids (38/23; 62.3%), low molecular weight heparin (47/14; 77%), aspirin (36/25; 59%) as medical treatment (Table 2).

Table 1. Distribution of demographic variables

Variables	Group	Frequency	Percent
Age (years)	<40	2	3.3
	40-60	41	67.2
	>65	18	29.5
Gender (females, males), n(%)	Female	27	44.3
	Male	34	55.7
Smoker, n(%)	Smoker	6	9.8
	Non-smoker	55	90.2
Alcohol consumption, n(%)	Drinking	2	3.3
	Not drinking	59	96.7
Hypertension, n(%)	Present	31	50.8
	Not present	30	49.2
Cardiovascular disease, n(%)	Present	19	31.1
	Not present	42	68.9
Neurological disease, n(%)	Present	2	3.3
	Not present	59	96.7
Obstructive lung disease, n(%)	Present	14	23.0
	Not present	47	77.0
Diabetes mellitus, n(%)	Present	23	37.7
	Not present	38	62.3

Routine blood samples were collected from Group 1 and Group 2 patients. Variables related to COVID-19 pneumonia, acute and 6 months after the acute period were statistically compared. The increase in glucose (mg), creatinine (mg/dL), aspartate aminotransferase (AST) (IU/L), alanine aminotransferase (ALT) (IU/L), gamma glutamyl transferase (GGT) (IU/L), lactate dehydrogenase (LDH) (IU/L), aptt, inr, fibrinogen (mg), neutrophil percentage (%), mean erythrocyte hemoglobin (MCH) (pg) was statistically significant (p<0.05). The decrease in albumin (g/dl), calcium (mg/dl), sodium (Na) (mEq/L), leukocyte, platelet, hemoglobin, lymphocyte count, erythrocyte distribution range variables was statistically significant (p<0.05). However, the increase in urea (mg/dl), creatine kinase (CK) (u/l), ckmb (u/l), protein (g/dl), potassium (k)(mmol), c-reactive protein (CRP)(mg/dl), troponin (ng/ml), platelet distribution range (pdw)(%) was not statistically significant (p>0.05). The decrease in alkaline phosphatase (ALP)(ıu/l), total bilirubin (t.bil)(mg/dl), direct bilirubin (d.bil)(mg/dl), d-dimer (mcg/ml), hematocrit (%), neutrophil count (mcl), mean erythrocyte hemoglobin concentration (MHC)(g/dl), mean erythrocyte volume (MCV)(fl), plateletcrit, mean erythrocyte volume (MCV) was not statistically significant (p>0.05) (Table 3).

When the thorax CT of 61 patients was analyzed, 19 patients (19/61) showed complete resolution of lung findings, while 42 patients (42/61) had residual findings in their lungs. Patients were divided into Group 1 and Group 2. In our study, ground-glass opacity was seen most frequently in Group 1 Thorax CT (Figure 1). In 57 (100%) patients, ground-glass opacity was found and in 4 (100%) patients ground-glass opacity was not observed. Of these 57 patients, 10 (18%) were positive for

Table 2. Distribution of disease-related variables

Variable	Group	Frequency	Percent
Intensive care ward	Intensive care	8	13.1
	Service	30	49.2
	Outpatient	23	37.7
Fire	Present	9	24.6
	Not present	46	75.4
Chest pain	Present	21	34.4
	Not present	40	65.6
Cough	Present	21	34.4
	Not present	40	65.6
Shortness of breath	Present	42	68.9
	Not present	19	31.1
Muscle pain	Present	27	44.3
	Not present	34	55.7
Fatigue	Present	36	59.0
	Not present	25	41.0
Pulmonary function test	Present	48	78.7
	Not present	13	21.3
Invasive	Present	1	1.6
	Not present	60	98.4
Noninvasive	Present	6	9.8
	Not present	55	90.2
Oxygen support	Present	38	62.3
	Not present	23	37.7
Antiviral agent	Present	59	96.7
	Not present	2	3.3
Glucocorticosteroid	Present	38	62.3
	Not present	23	37.7
Antibacterial	Present	54	88.5
	Not present	7	11.5
Low molecular weight heparin	Present	47	77.0
	Not present	14	23.0
Aspirin	Present	36	59.0
	Not present	25	41.0

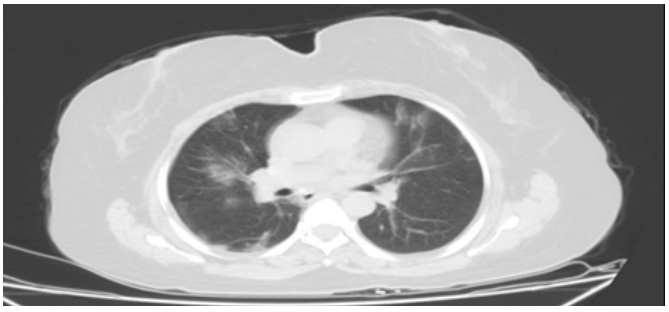

Figure 1. Thoracic computed tomography shows bilaterally located ground-glass opacities

ground-glass opacities in Group 1 and Group 2 Thorax CT, while 47 (82%) were negative for ground-glass opacities in Group 2 Thorax CT. While 4 (100%) of these 4 patients had no ground-glass opacity on Group 1 Thorax CT, 1 (25%) of them had ground-glass opacity on Group 2 Thorax CT, and 3 (75%) had no ground-glass opacity (Table 4). In 50 patients (100%), consolidation was found on Group 1 Thorax CT and no consolidation was observed in 11 patients. Of these, 5 (10%) had positive consolidation on Group 1 and Group 2 Thorax CT, while 45 (90%) had negative consolidation (Figure 2). Consolidation was not seen in Group 1 and Group 2 Thorax CT in these 11 patients (100%) (Table 4).

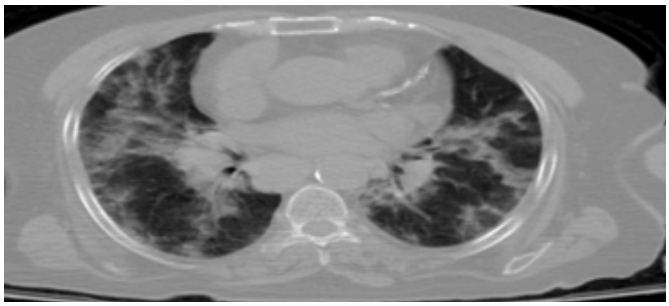

Figure 2. Thoracic computed tomography shows multifocal, segmental, patchy, mostly lower lobe and peripheral localized, irregularly circumscribed consolidations

DISCUSSION

SARS-CoV-2 is a highly contagious and high-mortality viral pneumonia caused by a novel coronavirus of unknown origin. Nearly 4 years after the COVID-19 pandemic, the long-term effects of post-COVID-19 pneumonia on patients have become a popular research topic. As the long-term effects of coronavirus agents that caused the pandemic in previous years have been proven, it has started to be thought that COVID-19 infection may also have the potential to have a permanent effect on patients. So far, there are very few studies in the literature investigating radiologic findings in the lung after COVID-19 pneumonia. In this study, we aimed to evaluate the pulmonary findings of post-COVID-19 pneumonia in the 6th month with CT and to reveal the risk factors that cause these abnormalities, as well as to analyze the variables in laboratory parameters.

In this study, we observed 61 patients diagnosed with COVID-19 pneumonia. In our study, we observed that patients diagnosed with COVID-19 pneumonia were more likely to be male. We also determined that hypertension and diabetes were the most common comorbidities in patients hospitalized with COVID-19 pneumonia. The most common symptoms observed in post-COVID-19 pneumonia patients were chest pain, cough, shortness of breath, myalgia, and fatigue. Fatigue, myalgia, and shortness of breath are frequently reported in other studies.[15-16]

The main routine tests ordered for COVID-19 patients included complete blood count (CBC), tests investigating coagulation and fibrinolysis cascades (PT, aPTT, and D-dimer), and parameters associated with inflammatory biomarkers (ESR, CRP, ferritin and procalcitonin). These blood parameters are used in acute COVID-19 disease and are useful in chronic inflammation.[17] Increased CRP, ferritin, LDH, and fibrinogen levels were also observed in our patients during acute COVID-19 disease. This allowed us to prove that COVID-19 disease is an inflammatory disease by using these markers in our study.

Since the heart, kidneys, and liver, which are our vital organs, are severely affected by the virus and cause deterioration including organ failure, analyzing biochemical parameters is an appropriate way to evaluate the functional activities of these organs.[18] In our study, despite an increase in Glucose, Creatinine, AST, ALT, GGT, LDH, APTT, INR, Fibrinogen, Neutrophil percentage, MCH parameters, a decrease was

Table 3. Comparison of changes in parameters over time

Variables	Group 1	Group 2	p
	Mean±sd	Mean±sd	
Glucose(mg)	160.8±97.52	132.38±59.82	0.029*
Urea(mg/dl)	38.45±21.98	37.51±19.2	0.679
Creatinine(mg/dl)	1.04±1.14	0.98±1.01	0.045*
AST(IU/L)	41.71±40.16	21.43±9.98	<0.001*
ALT(IU/L)	36.2±32.48	26.49±17.02	0.021*
ALP (IU/L),	74.62±22.23	78.67±19.34	0.086
GGT(IU/L)	47.57±31.95	34.58±38.65	0.010*
LDH (U/L)	373.8±251.18	236.9±72.2	<0.001*
CK (U/L),	114.9±77.83	114.67±76.01	0.985
CK-MB (U/L),	23.35±17.7	21.89±37.69	0.786
T.bil(mg/dl)	0.53±0.28	0.55±0.28	0.642
D.bil(mg/dl)	0.22±0.11	0.23±0.1	0.347
Protein(g/dl)	7.21±0.91	7.17±0.88	0.715
Albumin(g/dl),	3.4±0.53	3.92±0.68	<0.001*
Calcium(mg/dl)	8.56±0.67	9.11±0.53	<0.001*
Sodium(mEq/L)	135.7±3.88	138.34±2.83	<0.001*
Potassium(mmol)	4.53±0.57	4.46±0.5	0.336
Crp (mg/dl)	5.51±6.39	0.66±1.16	<0.001*
Troponin(ng/ml)	0.11±0.04	0.11±0.03	0.597
Ferritin (ng/ml)	455.29±573.42	146.02±231.89	<0.001*
NT-proBNP(pg/mL)	401.05±451.53	284.55±935.51	0.36
Procalcitonin(µg/l)	0.15±0.25	0.16±0.22	0.749
Aptt(sec)	25.88±3.79	22.38±3.85	<0.001*
Inr	1.14±0.17	0.8±0.2	<0.001*
Fibrinojen (mg/dl)	429.25±111.65	326.63±105.53	<0.001*
D-dimer (mcg/ml)	0.8±0.9	0.89±1.63	0.663
Leukocyte, $x10^3$/L	7.29±3	8.4±2.52	0.009*
Platelet($x10^3$/L)	249.11±98.63	284.3±82.98	0.011*
Hemoglobin(g/dL)	13.08±1.86	13.43±1.95	0.022*
Hemotokrit(%)	40.26±4.99	40.85±6.39	0.389
Neutrophil count(mcl)	5.09±2.97	5.2±2.44	0.797
Lymphocyte count(mcl)	1.75±1.7	2.49±0.92	0.004*
Neutrophil percentage(%)	68.19±13.98	59.6±11.66	<0.001*
Lymphocyte percentage(%)	23.54±11.91	29.35±10.26	0.001*
Mean erythrocyte hemoglobin (MCH)(pg)	26.82±2.49	27.33±2.53	0.004*
Mean erythrocyte hemoglobin concentration (MCHC)(g/dl)	32.41±1.5	32.55±1.58	0.344
Mean erythrocyte volume (MCV) (fl)	83.03±6.02	83.96±5.36	0.055
Erythrocyte distribution range (RDW) (%)	13.99±1.63	14.42±2.43	0.019*
Plateletcrit	0.26±0.1	0.29±0.08	0.052
Platelet distribution range (PDW) (%)	11.97±1.81	11.74±1.89	0.342
Mean platelet volume(MPV)(fL)	10.3±0.8	10.32±1.03	0.851

sd: standard deviation, p: significance of paired t-test,
The change between measurements was found to be statistically significant at the level of *p<0.05.

Table 4. Comparison of changes in thoracic tomography

Variable	Group	Group 1	Group 2	Total	p
		Present n (%)	Not Present n (%)		
Fibrosis	**Present**	1(100%)	14(23%)	15(25%)	**0.001***
	Not present	0(0%)	46(77%)	46(75%)	
Parenchymal band	**Present**	2(50%)	24(42%)	26(43%)	**0.001***
	Not present	2(50%)	33(58%)	35(57%)	
Reticular opacity	**Present**	0(0%)	11(19%)	11(18%)	**0.013***
	Not present	2(100%)	48(81%)	50(82%)	
Traction bronchiectasis	**Present**	1(50%)	7(12%)	8(13%)	**0.034***
	Not present	1(50%)	52(88%)	53(87%)	
Irregular interfaces	**Present**	0(0%)	11(18%)	11(18%)	**0.001***
	Not present	0(0%)	50(82%)	50(82%)	
Frosted glass opacity	**Present**	10(18%)	1(25%)	11(18%)	**0.001***
	Not present	47(82%)	3(75%)	50(82%)	
Consolidation	**Present**	5(10%)	0(0%)	5(8%)	**0.001***
	Not present	45(90%)	11(100%)	56(92%)	
Pulmonary nodule	**Present**	2(100%)	9(15%)	11(18%)	**0.003***
	Not present	0(0%)	50(85%)	50(82%)	
Honeycomb	**Present**	0(0%)	2(3%)	2(3%)	0.564
	Not present	1(100%)	58(97%)	59(97%)	

n; frequency, %; percent, p; significance of Marginal Homogenity Test, *p<0,05; The change between measurements was found to be statistically significant

observed in Albumin, Calcium, Sodium, Leukocyte, Platelet, Hemoglobin, Lymphocyte count, Erythrocyte distribution range variables at the time of COVID-19 pneumonia diagnosis. These parameters were statistically significant. In a study, white blood cell (WBC), lymphocyte, neutrophil, hemoglobin (HB), and platelet (PLT) values were found to be significantly lower.[19] Clinical laboratory data are indisputably important in the diagnosis of COVID-19 patients and the evaluation of the severity of the disease. In addition to clinical findings, biochemical parameters contribute to the distinction between severe and mild COVID-19 infection and the clinical decision to hospitalize patients. Thus, it is provided in conditions where patients can be differentiated such as hospitalization and/or intensive care unit admission, and more opportunities are provided to patients who need it.

In our study, glucose (mg), creatinine (mg/dL), aspartate aminotransferase (AST) (IU/L), alanine aminotransferase (ALT) (IU/L), gamma glutamyl transferase (GGT) (IU/L) were the control blood values after 6 months, The decrease in lactate dehydrogenase (LDH) (IU/L), APTT, INR, fibrinogen (mg), neutrophil percentage (%), mean erythrocyte hemoglobin (MCH) (pg) was found to be statistically significant ($p<0.05$). The increase in albumin (g/dl), calcium (mg/dl), sodium (Na) (mEq/L), leukocyte, platelet, hemoglobin, lymphocyte count, erythrocyte distribution range variables were found to be statistically significant ($p<0.05$).

Follow-up imaging and pulmonary function tests should be performed in patients with clinically suspected residual disease. We performed thorax CT imaging and pulmonary function tests in our patients.

On control thorax CT scans, 19 patients showed complete resolution of lung findings, while 42 patients had residual findings in the lungs. These residual findings may be due to the severity of the disease clinic at the time of hospitalization (i.e. respiratory rate >30 breaths/min, severe respiratory distress or oxygen saturation <90% in room air, diffuse bilateral ground glass opacities and multifocal segmental, patchy consolidations on thorax CT, i.e. severe respiratory failure and pneumonia).Pneumonia is a common and serious condition in patients with COVID-19 infection and increases the risk of mortality. Although the early clinical manifestations of the disease are well known, it is not clear what kind of sequelae it will leave in the lungs in the long term in patients who have severe pneumonia and survive. Currently, there is no consensus on the frequency and methods of monitoring pulmonary complications that may occur in patients with COVID-19 pneumonia. Radiologic improvement occurs in the early period in most patients. It has been reported that the ideal time for early control is the second week after discharge.[20] In a study investigating the findings 3 months after discharge of 55 patients treated for COVID-19 for long-term follow-up, it was reported that symptoms persisted in 64% of patients and radiological abnormalities in 71%.[21] In our study, lung findings showed complete resolution in 31% of the patients, while 68% had residual findings in the lungs. In our study, ground-glass appearance and consolidations were the most common residual radiological abnormality findings in the lungs at 6 months. When the radiologic course of COVID-19 pneumonia was observed in other studies, the most common tomographic findings at the beginning were bilateral subpleural ground-glass appearance and consolidation in the lower zones.[22-23]

In this study, the presence of middle-aged and elderly patients, radiologically and clinically severe pneumonia in our patients, and underlying diseases such as hypertension, type 2 diabetes mellitus, neurological diseases, and obstructive pulmonary disease were thought to be the reasons for the higher incidence of fibrosis and parenchymal bands. In other studies, the patient's age, severity of the disease, bacterial superinfection, duration of intensive care unit stay, presence of underlying lung disease, and extremely high levels of inflammation markers may be effective

factors in the development of lung fibrosis in patients with COVID-19 pneumonia.[24-25]

In our study, fibrosis (15/46; 25%), parenchymal band (26/35; 43%), reticular opacity (11/50; 18%), traction bronchiectasis (8/53; 13%), pulmonary nodule (11/50; 18%) were observed in Group 2 patients. Subpleural and parenchymal bands are linear striations seen mostly during the healing process. The reticular pattern is a pathological process of the pulmonary interstitium and is characterized by interlobular septal thickening and prominent intralobular striations. They are thought to be mostly sequelae of fibrosis. The presence of traction bronchiectasis is usually thought to be a consequence of fibrosis. However, recent studies have shown that reversible bronchiectasis may occur in cases of severe infection and inflammation and has been named pseudobronchiectasis.[26]

Although pleural pathologies such as pleural effusion and focal pleural thickening have been reported on a case basis, they are rare findings. The presence of pleural fluid is considered a poor prognostic marker.[8] In other studies, airway changes such as endobronchial mucus plug, bronchiectasis, bronchiolectasis, and bronchial wall thickening may also be observed in COVID-19 cases. Opacities of the lung parenchyma with a diameter ≤3 cm are defined as nodules. Nodules are a common finding in viral pneumonia. In studies, it has been reported to be observed in 6-8% of COVID-19 cases.[8]

In Group 2, sequel fibrotic bands, which are one of the signs of fibrosis, and ground-glass opacity, which appears to be the most common (Figure 3 and Figure 4), were examined. There are insufficient studies and evidence on the prevention and treatment of lung fibrosis that may develop after COVID-19 pneumonia.[27-28]

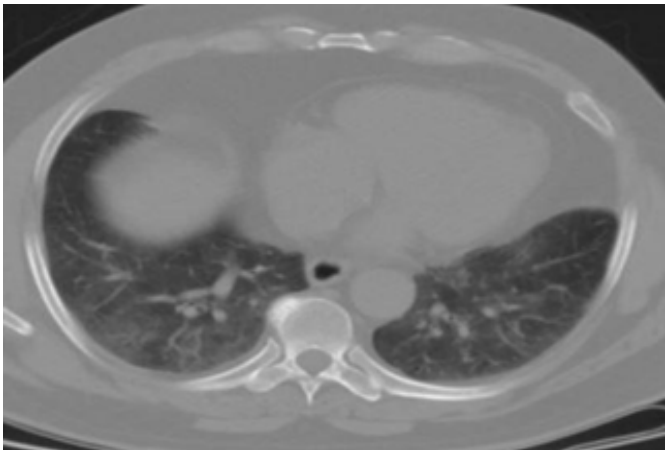

Figure 3. Bilateral irregular limited ground-glass opacities and fibrotic bands located mostly in the lower lobe and periphery on thoracic computed tomography

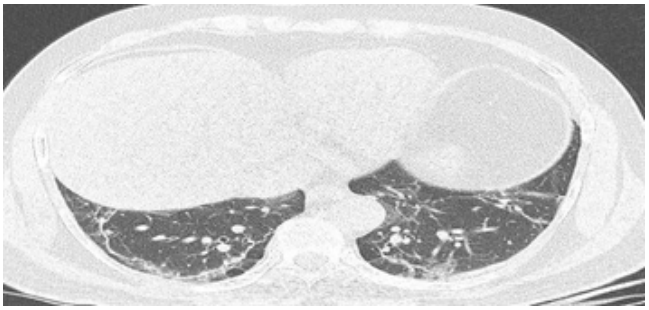

Figure 4. Bilateral fibrotic bands with irregular borders located mostly in the lower lobe and periphery on thoracic computed tomography

The frequency of long-term complications in COVID-19 pneumonia is not yet clear. However, the phylogenetic similarities of SARS-CoV-1 and SARS-CoV-2 viruses and the fact that Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) pneumonia caused by these viruses show very similar clinical, radiologic, and pathologic features with COVID-19 pneumonia suggest that the risk of progression may also be similar.[29]

Although long-term studies on COVID-19 pneumonia are insufficient, permanent damage to the lung parenchyma is expected to be observed in some patients with COVID-19 pneumonia, as seen in SARS and MERS infections. Organized pneumonia, fibrotic bands, reticulation, and honeycomb appearance have been described among CT findings in follow-up.[30]

Limitations

Limitations of our study include that our study was a single-center study. To evaluate the diagnostic power in terms of COVID-19, the initial laboratory values of the patients at the outpatient clinic were taken into account and changes in laboratory parameters during hospitalization were not monitored. Furthermore, laboratory results may have been affected by bacterial co-infections. In addition, the retrospective study design may have led to a high rate of cases with residual abnormalities in the lungs, especially considering that more symptomatic patients presented to the hospital in the post-COVID-19 pneumonia period. Again, due to the retrospective nature of the study, selecting patients with thorax CT at the time of diagnosis and control CT imaging 6 months later led to a decrease in the number of patients. The lack of patients with ARDS/critically severe pneumonia, adequate intensive care, and mechanical ventilation in our study patients provides a limitation to our study. Another limitation was the lack of long-term follow-up of the patients. Long-term follow-up of these patients is needed to understand how much of the findings seen on control CT reflect true fibrosis.

CONCLUSION

In patients who were followed up for 3-6 months after COVID-19 pneumonia, 19 (31%) of 61 patients admitted to the hospital showed complete resolution of pulmonary findings, while 42 (69%) had residual findings in the lungs. Patients with residual abnormalities were older (>40 years of age), had more comorbid diseases (especially HT, DM, CAD, obstructive pulmonary disease), had a severe clinical picture of the disease at the time of hospitalization, i.e. respiratory rate >30 breaths/min, severe respiratory distress or oxygen saturation <90% on room air, severe respiratory failure due to the presence of diffuse bilateral ground-glass opacities and multifocal segmental, patchy consolidations on thorax CT, and severe pneumonia.

Laboratory data is very important in diagnosing COVID-19 infection, prognosis, and guiding treatment. It can be difficult to say that any one blood value may be important in follow-up.

The most common findings in the lungs of patients diagnosed with COVID-19 pneumonia are ground-glass opacity and consolidation. The most common radiologic findings seen on follow-up thorax CT 3-6 months later were ground-glass opacity and consolidation.

There is insufficient evidence on whether fibrosis will develop in the lungs in patients followed up after COVID-19 pneumonia, and if so, whether this fibrosis will affect the patient's quality of life, performance, respiratory functions, whether long-term follow-up should be done, and whether serious clinical consequences such as idiopathic pulmonary fibrosis and findings similar to fibrotic lung disease with severe fibrosis findings on thorax CT will occur.

There is no consensus on how often patients should be followed up after COVID-19 pneumonia. It is also known that radiologic resolution of COVID-19 pneumonia may take a long time.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was conducted in accordance with the Declaration of Helsinki and approved by the Scientific Ethics Committee of Malatya Training and Research Hospital (Date: 08.07.2020, Decision No: 2020/128).

Informed Consent

Informed written consent form was obtained from the patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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