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Original Research

# Evaluation of Pulmonary Functions After Discharge in Pediatric Patients with COVID-19: A Prospective Study

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## Abstract

**Objectives:** The aim of this study was to investigate the pulmonary function of pediatric patients with COVID-19 after recovery.

**Methods:** Pediatric patients aged 5–18 years hospitalized with diagnoses of COVID-19 and discharged with recovery were included in this prospective study. Pulmonary function tests (PFTs) were performed through spirometry.

**Results:** The patient group consisted of 34 children and the control group of 33. The forced vital capacity (FVC%) values of the control and patient groups were 110.62±11.71 and 94.21±13.68 ($p<0.001$), forced expiratory volume in the first second (FEV1%) values were 104.91±6.26 and 98.67±14.93 ($p=0.032$), FEV1/FVC% values were 108.50±8.81 and 101.06±24.89 ($p=0.034$), and forced expiratory flow (FEF) 25–75% values were 106.71±6.68 and 101.85±24.89, respectively ($p=0.286$). However, Spearman correlation analysis revealed moderate negative correlation between length of hospital stay and FEF 25–75% ($r=-0.364$, $p=0.35$).

**Conclusion:** PFTs in pediatric patients after recovery from COVID-19 were abnormal in the present study. The results were significant in terms of the development of mixed-type lung disease. Further long- and short-term studies are now needed for a better understanding of the prognosis in these patients.

**Keywords:** COVID-19, pandemic, pediatrics, pulmonary function test, spirometry

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SARS-CoV-2 was declared a pandemic by the World Health Organization on March 11, 2020.[1] However, uncertainty remains concerning several issues, such as the pathogenesis of COVID-19, the clinical findings, and the course of the disease in adults and children. Adult patients are generally reported to experience more severe disease, while in pediatric patients, the disease is milder and mostly asymptomatic.[2,3] Pulmonary involvement due

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to COVID-19 can cause severe respiratory failure and death.[4] Children have been reported to represent 6–15% of confirmed COVID-19 cases in surveillance studies from various countries.[5-7] Children of all ages can be infected with COVID-19, the most common symptoms being fever, cough, shortness of breath, diarrhea, nausea, abdominal pain, headache, weakness, and fatigue.[7-9] Although the symptoms are reported to be generally milder in pediatric patients compared to adults, cases of children being followed up with severe respiratory failure have also been reported. Sing et al. reported that 18% of pediatric patients in need of intensive care developed acute respiratory distress.[10] However, it is not known exactly how the lungs are affected in the short and long terms after the illness. Abnormalities have been detected at lung imaging of patients diagnosed with COVID-19, and pulmonary fibrosis has been observed in some patients.[11] However, radiological imaging may not correlate with pulmonary function. Huang et al. performed pulmonary function tests (PFTs) after recovery on adult patients diagnosed with COVID-19 and found that these functions were impaired.[12] Our scan of the literature showed that pulmonary functions had been evaluated after COVID-19 in adult patients, but not in children.

The purpose of this study was to investigate the post-recovery pulmonary functions of pediatric patients with COVID-19 using spirometry.

## Methods

### Study Design and Patients

The study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the local ethical committee, before the study commenced (Session 2020, Protocol no. 15, Decision no. 08). The study was carried out between March 2020 and March 2021, in the Department of Pediatrics, Faculty of Medicine, at Kahramanmaraş Sütçü İmam University, a single centered. Pediatric patients aged 5–18 years hospitalized due to diagnosis of COVID-19 and discharged with recovery were included in this prospective study. Patients diagnosed with and treated for COVID-19 based on the WHO diagnostic criteria were invited to the hospital at least 1 month after discharge with recovery.[13,14] Healthy children in the same age group were included as a control group. Written informed consent was obtained from the children's parents. PFTs were performed using a spirometer by a nurse unaware of the study aims. The PFTs results were then compared between the patient and control groups.

Consistent with Dong et al.'s definitions, children with COVID 19 disease were classified as asymptomatic, mild, moderate, severe, or critical on the basis of their clinical status, laboratory data, and chest radiographs.[15] Severe and critical patients were followed up in the pediatric intensive care unit. These patients were excluded from the study after discharge due to comorbidities. Moderately ill patients were hospitalized and followed up in the pediatric clinic. Asymptomatic and mild patients were followed up on an outpatient basis. Patients followed-up with moderate disease were included in the study. Chest radiographs taken during the disease were evaluated retrospectively by two observers (a pediatrician and a radiologist). The demographic characteristics, and clinical and laboratory findings of the patients and the control group were subjected to analysis.

### Exclusion Criteria

Patients with chronic diseases such as neurological disease, heart disease, pulmonary hypertension, cystic fibrosis, or immunodeficiency, asthmatic patients, adolescents who were smokers, children unable to perform a PFT (who were unable to blow into the spirometer), children under 5 years old, and patients with mental disability were excluded from the study. Congenital heart disease and pulmonary hypertension were evaluated using echocardiography by a pediatric cardiologist, and patients found to have congenital heart disease and pulmonary hypertension were excluded from the study.

### Spirometry

PFTs were performed using a Zan 100 spirometer (Zan 100, nSpire, Health Inc., Germany) device. Each test was repeated at least 3 times, and the highest values were recorded. Forced vital capacity (FVC), forced expiratory volume in the first second (FEV1), and forced expiratory flow (FEF) between 25% and 75% of FVC (FEF25–75%) were examined in PFTs. A normal child will exhale 80% of his vital capacity within the first second. This value, known as FEV1, was used to determine the state of the major airways. FEF25–75% provides information about the small airways. In terms of pulmonary dysfunctions, a decrease in FEV1 or in FEF25–75% was defined as obstructive airway disease, a decrease in FVC and a normal FEV1/FVC ratio were defined as restrictive lung disease, and a decreased FEV1/FVC ratio with decreased FVC was defined as mixed pulmonary dysfunction.[16-18]

Performing PFTs on patients with COVID-19 are not recommended because the procedure creates a high-risk situation for droplet formation, which might then spread the disease.[19] PFT was, therefore, not performed on our patients during the infection period. It is recommended that PFT be performed after two negative real-time polymerase chain reaction (RT-PCR) tests for SARS-CoV-2 at 24 h intervals on nasopharynx and throat swabs, after symptoms have improved and 30 days after discharge.[19,20] PFTs in the present study were performed after two negative COVID-19 RT-PCR tests were observed and 30 days after discharge.

### COVID-19 PCR Analysis

Nasopharynx and throat swabs of patients were analyzed for COVI-19 PCR using a BIO-RAD CFX96 Real Time System C1000 Touch Thermal Cycler Device and SARS-CoV-2 Double Gene RT-qPCR 1000 Rxn kit.

### Statistical Analysis

Statistical Package for the Social Sciences version 25 software (SPSS) (IBM Corp., Armonk, NY) was used for statistical analyses. The study data are presented as mean, standard deviation, frequency, and percentage distributions. Compatibility with normal distribution was evaluated using the Kolmogorov–Smirnov test. The Chi-square test was used for the analysis of categorical data. The independent sample t-test (Student's t-test) was used to compare normally distributed data and the Mann–Whitney U-test for non-normally distributed data. The Pearson correlation test was used to detect correlations among normally distributed data and the Spearman correlation test was used to detect correlations among non-normally distributed data. The kappa value was checked to measure the agreement between the two observers who evaluated the chest radiographs. $P<0.05$ was considered statistically significant.

## Results

Seventy-six patients who had experienced COVID-19 were screened, 39 of whom were identified as eligible for the study. The others were excluded due to asthma, a history of allergic disease, immunodeficiency, or other underlying diseases. Flowchart is shown in Figure 1. Five patients were also unable to perform the PFTs. Thirty-four patients were able to perform the PFTs and were included in the study. One of the 34 children in the control group was unable to perform the PFTs. Thirty-three healthy children were thus enrolled in the control group. The demographic and clinical characteristics of the children in the study are given in Table 1. No statistical difference between the groups in terms of age or sex ($p=0.24$ and $p=0.54$, respectively). Average length of hospital stay was 7 days (IQR, 9), and the average time after discharge when the PFTs were performed was 49 days (IQR, 36). The chest radiographs of the 34 pediatric patients were retrospectively interpreted by two observers. The chest radiographs of seven children were interpreted as atypical, six being in the form of major airway disease. Other chest radiographs were interpreted as normal. The kappa value was measured to determine the agreement between the two observers who retrospectively interpreted the chest radiographs. The agreement between the two observers was very good (k=0.83), and the Spearman correlation was high ($r=0.849$, $p<0.001$).

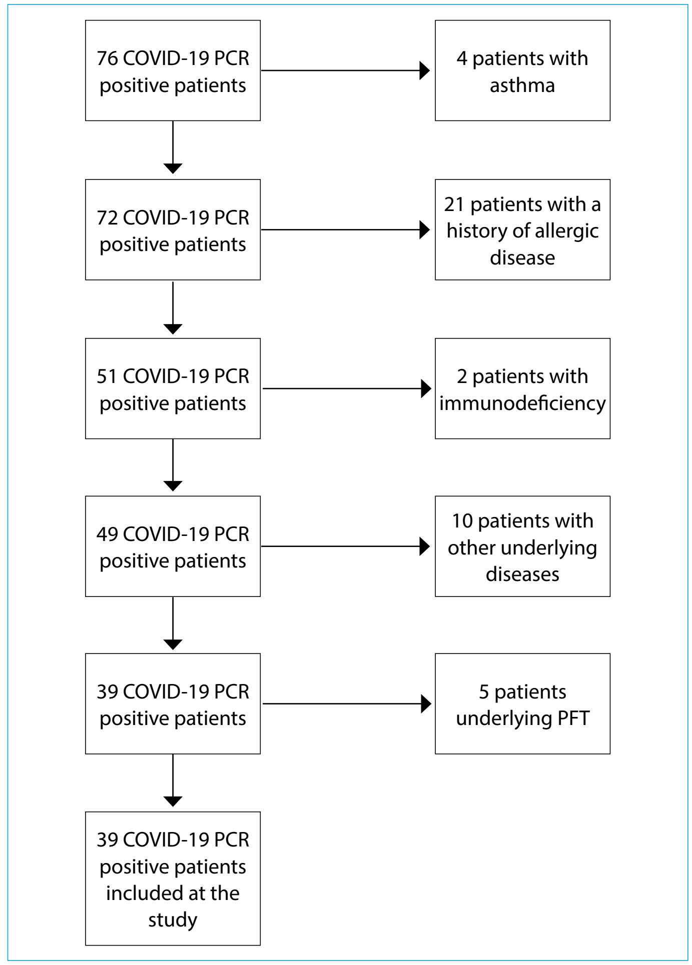


**Figure 1.** Flowchart of COVID-19 PCR positive patients.

**Table 1.** Demographic and clinical data of patients

| | Patient (34) | Control (33) | p |
|---|---|---|---|
| Age (year) | 12.7±3.12[a] | 11.98±2.37 | 0.241 |
| Sex (female:male) | 18:16 | 15:18 | 0.540 |
| Height (cm) | 158.5±17.03[a] | 158.71±11.31 | 0.903 |
| Weight (kg) | 51.7±16.59[a] | 54.91±10.77 | 0.364 |
| Length of hospital stay (days) | 7 (9)[b] | | |
| Time of PFT after discharge (days) | 49 (36)[b] | | |

[a](mean ±SD); [b](median (IQR); PFT: Pulmonary function test.

The FVC% values of the control and patient groups were 110.62±11.71 and 94.21±13.68, respectively, the difference being statistically significant ($p<0.001$). FEV1% values were 104.91±6.26 and 98.67±14.93 in the control and patient groups, with a difference between them of $p=0.032$. FEV1/FVC values also differed significantly between the control and patient groups, at 108.50±8.81 and 101.06±24.89, respectively (p=0.034).

The FEF 25–75% value of the patient group was lower than that of the control group, although the difference was not significant (101.85±24.89 and 106.71±6.68, respectively, p=0.286) (Table 2). Negative correlation was found between length of hospital stay and FEF 25–75% (r=–0.364, p=0.035). All patients were evaluated by a pediatric cardiologist, and those with pulmonary hypertension and congenital heart disease were excluded from the study.

## Discussion

A PFT is the most objective means of assessing pulmonary function in the evaluation of lung diseases.[16] Huang et al. found a decrease in the FEV1/FVC ratio and a decrease in diffusion capacity in the early convalescent phase in adult patients with COVID-19 pneumonia.[12] Fumagelli et al. stated that the disease basically resulted in a restrictive pattern based on PFTs applied after resolution of COVID-19.[21] Lv et al. reported restrictive ventilation disorder and increased small airway disease in critically ill adult patients at the respiratory function test.[22]

To the best of our knowledge, the present study is the first to investigate PFTs of pediatric patients after COVID-19. The disease usually progresses differently in children and adults. The low FVC% (p<0.001), FEV1% (p=0.032), and FEV1/FVC% (p=0.034) values in the present study may be significant in terms of showing that mixed-type pulmonary dysfunction can develop in previously healthy pediatric COVID-19 patients. While a restrictive pattern has been observed in adult patients, a mixed-type pattern was observed in pediatric patients in the present study. In addition, analysis revealed moderate negative correlation between length of hospital stay and FEF25–75%, FEF25–75% decreasing as the duration of hospitalization increased. FEF25–75% yields information about obstructions in the medium and small diameter bronchi. As the degree of restrictive diseases increases, indirect decreases can be observed in FEF25–75% values.[23] The present study is significant in showing that lung function worsens in pediatric patients as the length of hospitalization due to COVID-19 increases.

**Table 2.** Evaluation of percentage values of pulmonary function tests between pediatric COVID-19 patients and the healthy control group

| | Control | Patient | p |
|---|---|---|---|
| FVC | 110.62±11.71 | 94.21±13.68 | <0.001 |
| FEV 1 | 104.91±6.26 | 98.67±14.93 | 0.032 |
| FEV 1/FVC | 108.50±8.81 | 101.06±24.89 | 0.034 |
| FEF25-75 | 106.71±6.68 | 101.85±24.89 | 0.286 |

Statistics: Independent samples t-test. FVC: Forced vital capacity; FEV1: Forced expiratory volume in the first second; FEF25–75: Forced expiratory flow between 25% and 75% of FVC.

Data concerning computed tomography (CT) findings of COVID-19 pneumonia in children are very limited. The American Pediatric Radiology Association recommends that another imaging method be employed instead of tomography in children, and that if its use is absolutely essential, it should be performed in line with the principle of "ALARA" (As Low as Reasonably Achievable).[22,24] Our patients did not undergo CT except in case of medical necessity. Follow-up thoracic CT can be used to evaluate the development and/or occurrence of fibrotic lung disease in patients with persistent changes in PFTs after the resolution of acute infections.[25]

A structured reporting style involving four categories, typical, indeterminate, atypical, and negative, was created for plain radiography for COVID-19 in children.[25] The chest radiographs of the 34 children in the present study were retrospectively interpreted by two observers. The chest radiographs of seven children were interpreted as atypical, six of these involving large airway disease. According to the current data, COVID-19 is milder in children than in adults. When the chest radiographs of the patients are evaluated, although COVID-19 seems to affect the upper airways in children, the lower PFTs in the patient group are important in terms of showing that the lungs are also affected.

Kara et al. evaluated patients followed up with pneumonia from a cardiac perspective during active infection and suggested that even mild pneumonia may affect the cardiovascular system.[26] In the present study, patients were evaluated in terms of heart diseases before PFTs, and no significant cardiac pathology was determined in any cases. This may be due to the patients being evaluated after recovery.

The limitations of the study include the small number of patients, the lack of CT due to the radiation risk, and the lack of long-term follow-up. More extensive long- and short-term studies are now needed for a better understanding of the prognosis in pediatric patients.

## Conclusion

The results of the respiratory function tests performed after COVID-19 in pediatric patients in this study showed that the effects of the disease were significant in terms of the development of mixed-type lung disease. In addition, although there was no significant difference between FEF25 and 75% values in the patient and control groups, the decrease in FEF25–75% as the duration of hospital stay increased may be meaningful in terms of worsening of lung functions in later years.

### Disclosures

**Ethics Committee Approval:** Ethical approval was obtained from the local ethical committee, before the study commenced (Session 2020, Protocol no. 15, Decision no. 08). The study was carried out between March 2020 and March 2021, in the Department of Pediatrics, Faculty of Medicine, at Kahramanmaraş Sütçü İmam University, a single centered.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** None declared.

**Authorship Contributions:** Concept – S.I., S.G., M.Y.O.; Design – S.İ., S.G., U.U.G.; Supervision – S.G., U.U.G.; Materials – B.K, M.K.K., S.D., S.Y.; Data collection &/or processing – B.K, M.K.K, S.D., S.Y.; Analysis and/or interpretation – S.İ, S.G., M.Y.O.; Literature search – S.I., U.U.G., S.Y., M.Y.O, B.K., M.K.K., S.D.; Writing – S.I., U.U.G.; Critical review – S.I., S.G., U.U.G.

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