Assessment of Medium-Term Impact of Sars-Cov2 Infection on Pulmonary Function in Albanian Young Adults without Previous History of Respiratory Disease

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Introduction

The COVID-19 pandemic has an increased attention to evaluate the acute, subacute, and long-term consequences in respiratory system. Immediately after COVID-19 breakout, several cohort studies were conducted to evaluate mostly pulmonary parenchyma damage and fibrosis in severe COVID-19. There are reported controversial findings for the association between asthma and severity of COVID-19, whereas allergic rhinitis has a protective effect against severe COVID-19. The inconsistent findings between asthma and the severity of COVID-19 may be due to the different scale of the study in case series, criteria for hospitalization of COVID-19 patients, racial disparities, patient age, severity of asthma, and the condition of asthma control in the patients [1].

Available scientific data support the low expression of ACE2 receptors in airways, due to TH2 inflammation in respiratory tract of allergic subjects, playing a probable protective role toward severe form of COVID-19. Genetic predisposition to any allergic disease was associated with reduced susceptibility to COVID-19, but not clearly with risk of being hospitalized with COVID-19 [2]. On the other side, the real consequences of immune mediation in SARS-COV-2 infection and its role as interchange trigger due to the overstimulation of T cell-mediated immune response in most individuals with highly symptomatic disease, it is largely unknown. It was reported that almost half of adults admitted to hospital due to COVID-19 reported persistent symptoms 6–8 months after discharge. Fatigue and respiratory symptoms were most common, and female sex was associated with persistent symptoms [3]. Risk factors for COVID-19 persistent
symptoms, especially fatigue, were not associated with initial severity [4].

In children, history of allergic respiratory diseases was a risk factor (2.66, 1.04–6.47) for post-COVID-19 condition after 12 months [5]. Although in children and young adults was rarely reported a post-infectious, hyper-inflammatory response following SARS-CoV2 infection [6].

Post-viral bronchial hyper-reactivity syndrome is common after respiratory tract viral infections; however, its prevalence after COVID-19 is unclear. One recent study investigated bronchial hyper-responsiveness in patients with normal baseline lung function but persisting respiratory symptoms. In that study, they are reported only 3.9% of patients who had bronchial hyper-responsiveness after COVID-19, suggesting that as a complication of COVID-19 and indicating a minor role of prior postulated post-viral bronchial hyper-reactivity [7] Another study revealed that 43% of patients with a history of COVID-19 had a positive BCT, but uninfected patients had a significantly higher number (56%) of positive BCT (p = 0.02). The cause of dyspnea in patients with a history of COVID-19 was not associated with bronchial hyper-reactivity. They concluded bronchial hyper-responsiveness in infected people is likely to be caused by an underlying allergy, which may be exacerbated by the disease [8].

Our present study is the first ongoing study in Albanian population to assess pulmonary function effects in moderate-severe post-COVID-19 condition in young adults.

**Aim**

To evaluate the prevalence of compromised pulmonary function in the period 3–6 months post COVID-19 in Albania, in patients under 45 years, without previously known respiratory disease and to correlate any findings with dyspnea perception, clinical and radiological features, including comparison to literature.

**Methods**

This was a prospective cross-sectional study. Patients hospitalized in main tertiary hospital center in Albania, were contacted after hospital discharge to enter in the study. Before initiation Medical Ethical Commission approval and individual informed patient consent was taken. The study has a comparative character for the medium-term prevalence of pulmonary function test changes post-COVID-19. Results have been interpreted both conceptual and critical, to compare and evaluate a series of perspectives on the consequences and factors affection post-COVID-19 pulmonary function among young people in Albania.

**Statistical analysis**

SPSS 25.0 was used to analyze data. Student’s t-test and Mann–Whitney test are used to compare results between groups. A p < 5% was considered statistically significant. Dyspnea was evaluated by visual analog scale (VAS) ranged 0 (none) – 10 (severe dyspnea perception).

**Time period**

The study has been carried out from October 2021 to October 2022, at least in 1 time slot for each patient at 3–6 months after acute SARS-COV2 infection. The visit included spirometry, anamnestic data, and VAS questionnaire for dyspnea.

**Inclusion criteria**

Post-COVID-19 patients diagnosed by PCR/or serology and CT infiltrations and hospitalized in COVID hospitals in Albania. Age criteria: 18–45 years old.

**Exclusion criteria**

Known respiratory diseases or any concomitant disease that can compromise pulmonary function (e.g. known systemic autoimmune disease), important mental/neurological diseases, active infectious diseases, coronary artery disease/cardiac insufficiency, and active smokers were excluded from the study.

**Study limitations**

We lacked the equipment to perform the body plethysmography to assess more pulmonary function parameters, like TLC (specifically for evaluating the pulmonary restriction), neither bronchial provocation test for bronchial hyper-reactivity, nor the diffusion capacity of the lungs for carbon monoxide (DLCO) for the assessment of the alveolar–blood-barrier thickening and worsening of O2 and CO2 gas exchange. Because of strict exclusion criteria, the number of patients was limited. COVID-19 vaccination and population immunity limited the number of new patients 3–6 months after the study initiation.

**Results**

In the study, 61 patients were included, who fulfilled all criteria, 41 (67.2%) females and 20 (32.8%)
males; mean age 30.6 ± 8.63 years. All included participants had performed chest computed tomography during COVID-19 and had typical infiltrations of pulmonary parenchyma. PCR test for SARS COV-2 was positive in 49 (80.3%) during hospitalization.

The family history for COVID-19 was negative in 9 (14.8%), same severity or more severe in 35 (57.4%).

Spirometry data for pulmonary function resulted: 4 patients (6.56%) with pulmonary dysfunction, among them 1 patient (1.64%) Forced expiratory volume in 1 s (FEV1)/Forced vital capacity (FVC) <75%, with generalized bronchial obstruction and 3 patients (4.92%) with small airway obstruction (bronchial-obstruction), FEF 25–75 <60% (Table 1).

According to criteria classification for disease severity (SpO2 <94% and/or pulmonary infiltrates >50%) 22 (36.06%) had severe COVID-19 (Table 2). Among two groups of COVID severity, resulted statistically significant (p < 0.05), the difference for VAS dyspnea perception reported during 1st month post-COVID-19 after 6 min moderate physical activity and FEV1/FVC (Tiffeneau Index value). The differences were not significant for persistent dyspnea reported during 1st month post-COVID-19 and 3rd–6th month post-COVID-19 in rest and after 6 min of physical activity.

Table 1: Visual analogue scale for dyspnea perception and spirometry data among groups of COVID-19 disease severity

<table>
<thead>
<tr>
<th>Variables</th>
<th>SpO2 during hospitalisation ≤94% in air</th>
<th>SpO2 during hospitalisation &gt;94% in air</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n = 61)</td>
<td>n = 22</td>
<td>n = 39</td>
<td>NA</td>
</tr>
<tr>
<td>Symptoms perception VAS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Persistent dyspnea reported during 1st month post-COVID-19</td>
<td>2.41 ± 2.71</td>
<td>3.43 ± 2.78</td>
<td>0.08</td>
</tr>
<tr>
<td>Persistent dyspnea reported during 3rd–6th month post-COVID-19</td>
<td>1.38 ± 1.95</td>
<td>1.55 ± 1.92</td>
<td>0.38</td>
</tr>
<tr>
<td>Persistent dyspnea reported during 1st month post-COVID-19 after 6 min moderate physical activity</td>
<td>3.54 ± 2.97</td>
<td>5.5 ± 3.12</td>
<td>0.007</td>
</tr>
<tr>
<td>Persistent dyspnea reported during 3rd–6th month post-COVID-19 after 6 min moderate physical activity</td>
<td>2.62 ± 2.7</td>
<td>3.18 ± 2.54</td>
<td>0.22</td>
</tr>
</tbody>
</table>

It resulted no statistically significant changes between groups for inflammatory markers such as C-reactive protein level, absolute lymphocyte count, and FEV 25–75 or body mass index (BMI). There was a statistically significant change for D-Dimer values. In two groups where present VAS dyspnea perception (≤5) and (>5), no significant correlation was found regarding FEV1/FVC and FEV1/FVC (Tiffeneau Index value), but not significant 3–6 months after COVID-19. This result may indicate an

Discussion

In our investigation in PubMed, Google scholar, and Scopus, few studies have included mainly children and young adults [5] and none of reviewed had strict exclusion criteria for conditions that would affect pulmonary function (comorbidities, smoking, etc).

Published data indicate that spirometric indices appear to be generally well preserved but that a defect in diffusing capacity (DLco) is a prevalent abnormality identified on follow-up lung function; present in 20–30% of those with mild-to-moderate disease; and 60% in those with severe disease [3]. Because of equipment lack, it was impossible to evaluate DLco in our study population.

Studies performed to patients who had COVID in early pandemic during 2020, reported evidence of pulmonary function affection, which is generally improved after 6–12 months, supported by literature review in Table 4 [9], [10].

Our study included patients that had COVID-19 after March 2021 and aligned to many studies conducted 2021–2022 [11], [12] show no significant pulmonary function changes in spirometry data among these patients. The results may be related to less aggressive virus genotype or better treatment approach after 1st year of pandemic.

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Table 3: Body mass index correlation with spirometry data

<table>
<thead>
<tr>
<th>Variables</th>
<th>Normal spirometry</th>
<th>Bronkiolo-obstruction</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>25.97 ± 4.2</td>
<td>24.74 ± 3.35</td>
<td>0.590</td>
</tr>
</tbody>
</table>

BMI: Body mass index.

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improvement in pulmonary function after the 1st month of COVID-19 disease.

Impact of inflammation markers

Elevation in serum inflammatory marker CRP may be indicative of COVID-19 infection severity and mortality and suggested that these parameters may predict COVID-19 severity [13]. Our study resulted no significant change between severity groups and CPR level. D-Dimer is known as an important predictor for severity and mortality of COVID-19 [14]. In 15% of the patients recovered from COVID-19, persistent D-dimer elevation was observed after a median of 3 months following COVID-19. These patients had experienced a more severe COVID and still presented more frequently a lower mean pO2 [13]. Our study resulted a significant change among level of D-Dimer and COVID-19 severity characterized by SpO2 during hospitalization.

Conclusion

The results show that there is minimal change of pulmonary function evaluated by spirometry as pulmonary function test, only in 4 (6.56%) of patients with changes of 6MWD and HRQoL.

Evidence of altered pulmonary function at 3 months of follow-up, as defined by values of FEV1, FVC and/or DLCO < 80% of reference. The most frequent abnormality was reduced DLCO (98 patients (57%), followed by low FEV1 (43 patients (25%)) and low FVC (42 patients (23%)). Improvement of PFTs parameters from 6 months to 1 year after infection.

No evidence that COVID-19 results in impaired spirometric lung function in a population-based sample of young, healthy adults with mild-to-moderate disease.

Spirometry values did not significantly differ between the particular subgroups of the cohort (adults, adolescents, children; infected and noninfected individuals).

Compared to asymptomatic patients, patients with ongoing symptoms were younger and presented a significant lower FVC, TLC and TLCO SB.

Our data suggest that a significant proportion of individuals would develop pulmonary sequelae after COVID-19 pneumonia, regardless of severity of the acute process.

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References

PMid:36647376

PMid:33185910

PMid:34351016

PMid:33382452

PMid:32755212

PMid:32755212

PMid:34322859

PMid:33392056

PMid:36096801

PMid:36188433

PMid:36647376

PMid:3584473

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PMid:34710097

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