

# Analysis of the Diagnostic Markers in Patients with Post-COVID-19 Disorders

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DOI: 10.52340/GBMN.2023.01.01.22

## ABSTRACT

**Background:** The post-COVID complications have turned out to be an urgent problem. Most patients suffered from dry, lingering cough of assault character, shortness of breath, sweating, weakness, fatigue, and other symptoms and signs. There is a need to study the functional status of the respiratory system and provide permanent monitoring of laboratory markers among patients with post-COVID-19 disorders.

**Objectives:** The study aimed to evaluate the functional status of the respiratory system and laboratory markers among Georgian patients with post-COVID-19 disorders.

**Methods:** 157 patients (18 to 75 years of age, 88 women and 69 men) with post-COVID-19 disorders were involved in the study and evaluated according to the following plan: (i) collection of anamnesis; (ii) assessment of the functional state of external respiration performed by a modern, computerized spirometer - Spirolab 3; (iii) analysis of laboratory markers, such as D-dimer, coagulogram, C-reactive protein (CRP), procalcitonin, interleukin-6 (IL-6), total IgE and vitamin D. Based on the obtained results, the patients were distributed among two groups: 101 (64%) patients with post-COVID-19 respiratory disorders in study group I, and 56 (36%) patients without post-COVID-19 disorders - in control group II.

**Results:** No reliable changes ( $p < 0.05$ ) in the spirometry parameters (FEV1; FVC; FEV1/ FVC) were observed in the study group. PEF < 70% peak expiratory flow was reduced in only 43 (42%) patients, compared to the norm. Mild restriction and irreversible obstruction were observed in 25 (24%) cases. In the control group, the spirometry indicators varied within the referral ranges. Among the correlogram markers, fibrinogen concentration was increased in most cases, namely in 51 (50%) patients. In addition, in 35 (34%) of 157 patients studied, a slight increase in the DD marker was revealed ( $218.5 \pm 2.45$  (norm < 200)); It should be emphasized that the increase in CRP was observed in 16 (15%) patients involved in this study; Only 2 (1.9%) patients with complicated respiratory changes showed a slight increase in procalcitonin levels. Detection of interleukin-6 showed an increase in the level of this marker in 38 (37 %) patients, while in the patients of the control group, changes in the markers mentioned above were revealed in single case: fibrinogen level in 4 (7%); DD - 9 (16%); CRP - 2 (1.9%); procalcitonin - 2 (1.9%); Interleukin-6 - in 5 (8.9%), respectively. The allergy marker total IgE was revealed in 34 (33%) of the studied patients, while among the control group patients, it was fixed in 12 (21%). Vitamin D insufficiency was detected in 31 (31%) patients, deficiency in 35 (35%), and normal level in only 34 (34%) patients, respectively. In contrast, in the control group, insufficiency was detected only in 11 (19.7%), deficiency in 15 (26.8%), and norm in 30 (53.5%) patients.

**Conclusions:** The study has shown the necessity of monitoring laboratory biomarkers such as vitamin D, IL-6, and total IgE, as well as conducting computerized spirometry in patients with post-COVID-19 respiratory disorders.

**Keywords:** post-COVID-19 disorders; laboratory markers.

## BACKGROUND

The post-COVID-19 disorders have become an urgent problem. In this regard, the long-term course of post-COVID (Long COVID) condition was particularly emphasized. Most patients suffered from dry, lingering cough of assault character, shortness of breath, sweating, weakness, fatigue, and other organic changes.<sup>1</sup> The mentioned complaint persists for a long time and is sometimes the cause of human social discomfort.<sup>2,3</sup> Despite the relevance of the issue, so far, in the medical literature, studies on breathing functional changes have yet to be found. Spirometry data statistical analysis in different populations of patients with post-COVID-19 respiratory complications was rarely conducted.<sup>4</sup>

The aforementioned has raised the need for studying the functional status of the respiratory system, conducting

computer spirometry, as well as providing permanent monitoring of laboratory markers in clinical medicine among patients with COVID-19 disorders.<sup>4,5</sup> Unfortunately, studies in this direction are scarce, while the issue's relevance is acute. Therefore, based on the above, the presented study is aimed to evaluate the functional status of the respiratory system and inflammatory blood markers.

## METHODS

157 patients (18 to 75 years of age, 88 women and 69 men) referred to the National Institute of Allergology, Asthma & Clinical Immunology with post-COVID-19 disorders, especially with respiratory symptoms (long-term, dry, lingering cough, shortness of breath, and discomfort in the scapular area), were involved in the study and distributed



among two groups: 101 (64%) patients with post-COVID-19 respiratory disorders in study group I, and 56 (36%) patients without post-COVID-19 disorders - in control group II.

The following evaluations were performed in both groups of patients:

- Collection of anamneses via a specially designed questionnaire;
- Assessment of the functional state of external respiration performed by a modern, computerized spirometer - Spirolab 3;
- Analysis of inflammatory markers, such as D-dimer, coagulogram, C-reactive protein (CRP), procalcitonin, and interleukin-6 (IL-6) using chemiluminescent immunoassay;
- Analysis of the total IgE and vitamin D blood concentrations.

The correlation (interval) coefficient *r* was used for the statistical data analysis. A statistical significance was taken as *p*<0.05.

**RESULTS AND DISCUSSION**

Based on the analysis of obtained results, the patients were divided into two groups: 101 (64%) patients with post-COVID-19 disorders were involved in the study group I, and 56 (36%) patients without post-COVID-19 disorders - in control group II, respectively. No reliable changes (*p*<0.05) in the spirometry parameters (FEV1; FVC; FEV1/ FVC) were observed in the study group after computerized spirometry was performed to determine the degree of possible obstruction and/or restriction in the lung and bronchus and, consequently, the severity of respiratory failure, compared to the control group. PEF < 70% peak expiratory flow was reduced in only 43 (42%) patients, compared to the norm. Mild restriction and irreversible obstruction were observed in 25 (24%) cases. In the control group, the spirometry indicators varied within the referral ranges. Based on the analysis of the obtained results after diagnostics using an automated computer system in patients with post-COVID respiratory complications, among the correlogram markers, fibrinogen concentration was increased in most cases, namely in 51 (50%) patients. Continuous monitoring of the coagulogram showed that, despite intensive treatment, a high level of fibrinogen concentration persisted for a long time.

In addition, in 35 (34%) of 157 patients studied, a slight increase in the DD marker was revealed (218.5 ±2.45 (norm < 200)); It should be emphasized that the increase in CRP was observed in 16 (15%) patients involved in this study; Only 2 (1.9%) patients with complicated respiratory changes showed a slight increase in procalcitonin levels. Detection of interleukin-6 showed an increase in the level of this marker in 38 (37 %) patients, while in the patients of the control group, changes in the markers mentioned above were revealed in single case: fibrinogen level in 4 (7%); DD - 9

(16%); CRP - 2 (1.9%); procalcitonin - 2(1.9%); Interleukin-6 - in 5 (8.9%).

Since the main clinical symptoms of the study group patients were a dry, lingering cough and acute respiratory failure with difficulty in expiration and/or inspiration, allergological status was evaluated. An increase in the allergy marker total IgE was revealed in 34 (33%) of the studied patients, while among the patients of a control group, it was fixed in 12 (21%).

In addition, vitamin D monitoring revealed that in study group I, vitamin D insufficiency was detected in 31 (31%) patients, deficiency in 35 (35%), and normal level in only 34 (34%) patients, respectively, while in the control group, insufficiency was detected in 56 patients, without post-COVID complaints only in 11 (19.7%), deficiency in 15 (26.8%), and normal in 30 (53.5%) patients, respectively (Tab.1).

TABLE 1. Laboratory markers in patients with post-COVID-19 disorders

	Group I (n=101) Abs. (%) m±sd	Group II (n=56) Abs. (%) m±sd	p-value
D-dimer	35 (34.6) 218.5±2.45	9 (16) 105,6±1,69	<0.05
C-reactive protein	26 (25.7) 10±2,5	2 (1.9) 3±0.23	>0.05
Procalcitonin	2 (1.9) 0.42±0.05	2 (1.9) 0.39 ±0.03	>0.05
Interleukin-6	38 (37.4) 7.5±0.25	5 (8.1) 4.5±0.55	<0.05
Total IgE	34 (33.6) 170±4.56	12 (21.4) 85±2.45	<0.05

Abbreviations: Group I, patients with post-COVID-19 disorders; Group II, patients without post-COVID-19 disorders; m±sd, mean±standard deviation.

The statistical analysis revealed a high correlation between laboratory markers among patients with post-covid respiratory complications in the study group. Statistical analysis indicated a high correlation between vitamin D, total IgE in the blood (r=0.4), and D dimer (r=0.5). The interleukin 6 levels correlated to varying degrees with the above indicators. In particular: with vitamin D (r=0.4), Fibrinogen concentration in the blood (r=0.6), and D dimer (r=0.5).

**CONCLUSIONS**

The study has shown the necessity of monitoring inflammatory blood markers, vitamin D, IL-6, and total IgE and conducting computerized spirometry in patients with post-COVID-19 respiratory symptoms and signs.

The obtained results will be of great value to preventing post-covid complications and active disease management planning, especially for patients with post- covid disorders. In addition, the study results are also exciting and meaningful, not just scientific sense but from a clinical perspective as well.

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