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PULMONARY AND EXTRAPULMONARY POST COVID-19 CHRONIC COUGH

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კოვიდ-19 პანდემიის შემდგომი პულმონარული და ექსტრაპულმონარული ქრონიკული ხველა

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რეზიუმე

ქრონიკული ხველა ერთ-ერთი ყველაზე მნიშვნელოვანი გამოწვევაა პოსტ კოვიდ-19 პანდემიის შემდგომი პერიოდისა, ხოლო მის მართვასთან დაკავშირებული სირთულეები კლინიკური მედიცინის ერთ-ერთი აქტუალური საკითხია. კვლევა მიზნად ისახავს პანდემიის შემდგომი ქრონიკული ხველის პულმონარული და ექსტრაპულმონარული მდგომარეობების იდენტიფიცირებასა და სკრინინგს დასავლეთ საქართველოს პოპულაციაში.

კვლევაში გაერთიანებულია 58 პაციენტი (18 დან 75 წლამდე ასაკის, 34 ქალი და 24 კაცი), პოსტ კოვიდ-19 რესპირაციული სიმპტომებით - გახანგრძლივებული, შემანუხებელი ხველით და სუნთქვის უკმარისობით.

კვლევის დიზაინი: 1) ანამნეზის შეგროვება; 2) სასუნთქი სისტემის ჰიპერ-რეაქტიულობისა და ჰიპერმგრძობელობის შეფასება კომპიუტერული სისტემის მქონე ხელსაწყო Spirolab 3-ის მეშვეობით; 3) ლაბორატორიული მარკერების კვლევა: C რეაქტიული ცილა, Helicobacter pylori; საერთო IgE, D ვიტამინი სისხლის შრატში.

მიღებული შედეგების ანალიზის საფუძველზე გამოიყო ორი ჯგუფი: I ჯგუფში გაერთიანდა 27 (46,5%) პაციენტი პოსტკოვიდური პულმონარული ქრონიკული ხველით, ხოლო II ჯგუფში შევიდა 31 (53,5%) ექსტრაპულმონარული ქრონიკული ხველის მქონე პაციენტი.

ფილტვში და ბრონქში სავარაუდოდ მიმდინარე ობსტრუქციის და/ან რესტრიქციის ხარისხის და შესაბამისად სუნთქვის უკმარისობის სიმძიმის დადგენის მიზნით ჩატარებული კომპიუტერული სპირომეტრიით I ჯგუფში, II ჯგუფისგან განსხვავებით მივიღეთ სპირომეტრული მაჩვენებლების (FEV1; FVC; FEV1/FVC) სარწმუნო ცვლილებები ($p > 0,05$). აქედენ 12 პაციენტს დაუდგინდა შექცევადი ხასიათის ბრონქოობსტრუქცია და მხოლოდ 6 პაციენტს შეუქცევადი ხასიათის. 10 პაციენტში აღინიშნა მსუბუქი და საშუალო სიმძიმის რესტრიქცია. II ჯგუფის სპირომეტრული მაჩვენებლები ნორმის ფარგლებში. სარწმუნო ცვლილებები გამოვლინდა ლაბორატორიული მარკერების მიხედვითაც, როგორცაა: C რეაქტიული ცილა, Helicobacter pylori; საერთო IgE-სა და D ვიტამინი.

კვლევამ შესაძლებლობა მოგვცა სწორი აქცენტებით მოგვეხდინა პულმონარული და ექსტრაპულმონარული გენების ქრონიკული ხველის დიფერენცირება, რაც განსაზღვრავს საბოლოო კლინიკური დიაგნოზის სიზუსტეს და მიზანმიმართულ, ინდივიდუალულობის პრინციპზე დაფუძნებულ მენეჯმენტს.

INTRODUCTION. Cough is one of the important post-pandemic challenge of 21 century and with them associated management difficulties are an active issue in clinical medicine. Post-pandemic chronic cough is globally prevalent across all age groups. This disorder is challenging to treat because many pulmonary and extra pulmonary conditions can present with chronic cough, and cough can also be present without any identifiable underlying cause or be refractory to therapies that improve associated conditions. Post-pandemic patients are just more aware of coughing. Lingering, nagging

cough persists. For many, it's a six-to-eight-week cough. For others, it can last up to 100 days [1,2,3,10]. The airway reactivity increased after recovery from COVID-19 in individuals who did not have severe illness [4,5,6]. The impact of COVID-19 on pulmonary function or airway reactivity is established. As cough reflex is determined by interaction of the nervous system with immune system, persistent dysregulation of one or both of these systems may lead to chronic cough hypersensitivity. This may explain the difficulties associated with post-pandemic cough. Various environmental and host factors, such as respiratory infection, air pollutants, occupational irritants, allergens, eosinophils or refluxate, can sensitize and trigger cough and are potential risk factors for chronic cough [4].

Infection with respiratory viruses (such as rhinovirus or severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)) is a common cause of acute cough and is usually self-limiting, but post-infectious cough may persist for months in some individuals. Common pulmonary causes of chronic cough in non-smokers with normal chest X-rays and spirometry are corticosteroid-responsive cough such as eosinophilic conditions, including cough variant asthma, non-asthmatic eosinophilic bronchitis and atopic cough [8,9]. Extrapulmonary conditions are also commonly associated with cough, including GERD and upper airway cough syndrome (previously called 'post-nasal drip syndrome') due to rhinitis or rhinosinusitis [10]. Indeed, cough variant asthma, eosinophilic bronchitis, upper airway cough syndrome and GERD account for 51–92% of cases of adult chronic cough globally [10].

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 all the patients with persistent cough [3,5].

Based on the above, the presented study is aimed at screening and identifying some pulmonary and extrapulmonary conditions which are reason of post pandemic chronic cough in West Georgian population.

METHODS. 58 patients (18 to 75 years of age, 34 women and 24 men) who were referred to the National Institute of Allergology, Asthma & Clinical Immunology with post-COVID-19 conditions, especially with respiratory complications – long-term, dry, lingering cough, shortness of breath, for further diagnosis and problem management, were involved in the study.

The research design included: 1) collection of anamnesis - via a specially designed questionnaire for collecting the medical history; 2) assessment of airway hyperreactivity and hypersensitivity performed by a modern, computerized spirometer - Spirolab 3; 3) studying and analysis of laboratory markers, such as: C-reactive protein, *Helicobacter pylori*, total IgE, Vitamin D3.

RESULTS. Based on the analysis of medical history, of airway hyperreactivity and hypersensitivity performed by a modern, computerized spirometer - Spirolab 3 and of specific laboratory markers the patients were divided into two groups: 27 (46,5%) patients with pulmonary chronic cough were involved in group I, and 31 (53,5%) patients with extrapulmonary chronic cough - in group II, respectively.

Reliable changes ($p > 0.05$) in the spirometric parameters (FEV1; FVC; FEV1/FVC) were observed in the I group after computerized spirometry 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 II groups. PEF < 70% peak expiratory flow was reduced in 22 (81%) patients with pulmonary chronic cough, compared to the norm. Mild-moderate-severe obstruction were observed in 18 (66%) patients, 12 cases from this obstruction were reversible and only 6 irreversible. Mild-moderate restriction was observed in 11 (40%) of cases. In the II group patients, the spirometric indicators varied within the norm.

Since the main clinical symptoms of I group patients were a dry, lingering chronic cough and respiratory failure with difficulty in expiration and/or inspiration, allergological status was evaluated, and an increase in the level of the allergomarker total IgE was revealed ($M \pm m = 318.5 \pm 21.45$ (norm < 100) in 13 (48%) of I group patients, while among the patients of II group it was fixed in 8 (25%).

Based on the analysis of laboratory markers the obtained results showed that C-reactive protein was increased in 23 (85%) cases of patients from I group and only in 11 (35%) patients from II group with extrapulmonary chronic cough.

In addition, detection of *Helicobacter pylori* showed an increase in the level of this marker in 19 (61%) patients from II group, while in the patients of the I group, changes in the above-mentioned marker were revealed only in 4 (14%) cases.

Vitamin D (such as marker of immunomodulation) monitoring revealed that in I group patient with pulmonary chronic cough, vitamin D insufficiency was detected in 8 (31%) patients, deficiency in 10 (35%) and normal level in only 9 (34%) patients, respectively, while in the II group, insufficiency of vitamin D was detected in 6 (19.3%), deficiency in 10 (32.2%), and norm in 15 (48.5%) patients, respectively (Table N1).

Cough monitoring tools have been useful to evaluate the efficacy of cough medicines. Owing to differences in the pathology, the organs involved and individual patient factors, treatment of chronic cough is progressing towards a personalized approach, and, in the future, novel ways to endotype patients with cough may prove valuable in management.

Table N1. Analyzing the Laboratory Markers in Patients with Post-COVID chronic cough condition

Indicators	* I Study Group n=27			II Control Group n= 31			P value (Confidence Interval)
	Abs.	%	(M±m)	Abs.	%	(M±m)	
C-reactive protein (CRP)	23	85	22±2,5	11	35	10±0.23	>0,05
Total IgE	13	48	370±4.56	8	25	125±2,45	<0,05
Vitamin D	18	66	19±2.35	16	51	25±1,65	>0,05
<i>Helicobacter pylori</i>	4	14	0,7±0,16	19	67	1,5±0.76	<0,05

* I Group – Patient with pulmonary chronic cough; II Group - Patient with extrapulmonary chronic cough

Screening for chronic cough is not carried out in clinical practice. How screening could be done and whether it would lead to clinical benefit is unclear. Screening patients with chronic respiratory disease may be beneficial as cough is often overlooked during clinical evaluation. Moreover, early identification may improve the quality of life (QOL) of patients and possibly avoid over-treatment by specifically targeting cough. One simple screening method is a numerical rating scale that assesses cough severity and ascertains the duration of cough [10].

CONCLUSION. Screening the general population could identify patients with respiratory disorders such as COPD, asthma, lung cancer and smoking-related chronic bronchitis at an earlier stage. The most important diagnosis is that of lung cancer, where development of a cough may be the first symptom, particularly in a smoker. Whether non-smoking-related chronic cough is preventable is unknown. A greater understanding of the mechanism of cough, particularly cough hypersensitivity, is needed.

The obtained results will be of great value to prevent post-covid chronic cough, to establish causes of hyper reactivity and hypersensitivity of airway and active planning of disease management, especially to patients with post-covid conditions. In addition, the study results are also interesting and meaningful not just scientific sense but from clinical perspective as well. Consequently, researches are actively keep continuing in this direction worldwide.

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SUMMARY

Chronic cough is one of important post Covid-19 challenge of 21 century and with them associated management difficulties are an active issue in clinical medicine. The presented study is aimed at screening and identifying some pulmonary and extrapulmonary conditions which are reason of post Covid-19 pandemic chronic cough in West Georgian population.

58 patients (18 to 75 years of age, 34 women and 24 men) were involved in the study. The research design included: 1) collection of anamnesis 2) assessment of airway hyperreactivity and hypersensitivity by a modern, computerized spirometer - Spirolab 3; 3) studying and analysis of laboratory markers, such as: C-reactive protein, Helicobacter pylori, total IgE, Vitamin D3. Based on the analysis of results patients were divided into two groups: 27 (46,5%) patients with pulmonary chronic cough were involved in group I, and 31 (53,5%) patients with extrapulmonary chronic cough - in group II, respectively. Reliable changes ($p > 0.05$) in the spirometric parameters (FEV1; FVC; FEV1/FVC) were observed in the I group after computerized spirometry 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 II groups. In the II group patients, the spirometric indicators varied within the norm. With studying and analysis of laboratory markers, such as: C-reactive protein, Helicobacter pylori, total IgE, Vitamin D3 was found the statistically significant changes between the patients from both groups. In addition, the study results are also interesting and meaningful not just scientific sense but from clinical perspective as well. Consequently, researches are actively keep continuing in this direction worldwide.

Keywords: Spirometry, Post covid-19 pandemic, chronic cough, Helicobacter pylori

