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PECULIARITIES OF PERIODONTAL POCKET MICROBIOME IN PATIENTS WITH GENERALIZED PERIODONTITIS IN THE POST-COVID PERIOD

*The oral cavity, like the lungs, is often referred to as the «ecological niche of commensal, symbiotic, and pathogenic organisms,» and the emigration and elimination of microbes between them are constant, ensuring a healthy distribution of saprophytic microorganisms that maintains organ, tissue, and immune homeostasis. The prolonged hospital stays due to COVID-19 complications, cross-infection, oxygenation therapy through the mask or incubation, and long-term intravenous infusions limit the patient's ability to care about the oral cavity, regularly clean teeth, floss interdental, etc., which creates extremely favorable conditions for colonization by aerobic and anaerobic pathogens of the oral cavity and periodontal pockets and leads to the rapid progression of chronic generalized periodontitis in this category of patients in the future. **The goal** of the study was to assess the state of the microbiome of the periodontal pockets of dental patients in the post-covid period. **Methods.** The object of the study was 140 patients with generalized periodontitis of the I and II stages of development in the chronic course (GP), among which 80 patients had coronavirus disease in the closest past. The patients were randomized by age, sex, and stage of GP development. The diagnosis of periodontal disease was established according to the classification by Danilevskyi. The bacteriological material for aerobic and facultative anaerobic microflora and yeast-like fungi was collected from periodontal pockets with a calibrated bacteriological loop and immediately seeded on blood agar. **Results.** Significant qualitative and quantitative changes in the nature of the oral microbiocenosis were observed in patients with GP after the recent coronavirus disease, compared with similar patients who did not suffer from COVID-19. We have noticed almost complete disappearance of bacteria that belong to the transient representatives of the oral microflora such as Neisseria, corynebacteria (diphtheria), micrococci, and lactobacilli. The main resident representatives of the oral microflora, i.e., α-hemolytic Streptococci of the mitis group, were found in all healthy individuals and patients of groups A and C, but in $30.0 \pm 4.58\%$ of patients in group B, α-hemolytic streptococci in the contents of periodontal pockets are present in quantities not available for detection by the applied method (<2.7 lg CCU/mL). In terms of species, Streptococcus oralis and Streptococcus salivarius are more characteris-*

tic in gingival crevicular fluid in healthy individuals (93.8% of selected strains). In 68.4±3.32% of patients in group A, 64.0±3.43% of patients in group B, and 67.5±3.76% of patients in group C, the dominant species were Streptococcus gordonii and Streptococcus sanguinis (p<0.01), which increased pathogenic potential as they produce streptolysin-O, inhibit complement activation, bind to fibronectine, actively form biofilms on the surface of tooth enamel and gum epithelial surface, and can act as an initiator of adhesion of periodontal pathogens. The other representatives of the resident microflora of the oral cavity — Stomatococcus mucilaginosus and Veillonella parvula for the patients of group C are also found in periodontal pockets with a significantly lower index of persistence and minimal population level. In the post-covid period, both the population level and the frequency of colonization of periodontal pockets by Staphylococci and β-hemolytic Streptococci decreases rapidly. For these patient groups, unlike for those that did not suffer from COVID-19, we did not find any case of colonization with Staphylococcus aureus, as well as β-hemolytic Streptococci and Epidermal staphylococcus were also absent. The most characteristic in the post-covid period is a decrease in the proportion of α-hemolytic Streptococci, an increase in the proportion of yeast-like fungi of Candida species, as well as the appearance of a significant number of gram-negative rod-shaped bacteria (Enterobacteria and Pseudomonads). In periodontal patients, the microbial count is approximately 2 orders of magnitude lower than in those with GP who did not suffer from COVID-19 (p<0.05). **Conclusions.** The overpassed coronavirus disease due to intensive antibiotic therapy leads to a marked decrease in the number of viable saprophytic microorganisms in the periodontal pockets of patients with GP. In the post-covid period for the patients with GP, there is a decrease in the level of colonization of periodontal pockets by species of resident oral microflora — α-hemolytic Streptococci, reduction of resident microorganism's species, and almost complete disappearance of transient microflora. On the other hand, the frequency of colonization of periodontal pockets by fungi species, enterobacteria, and pseudomonads significantly increases. There are more expressed disorders in the periodontal pocket's microbiome for the patients with a severe and complicated course of coronavirus disease, such as post-covid pulmonary fibrosis, which requires reconsideration of approaches to therapeutic and pharmacological treatment in this category of patients.

Keywords: Coronavirus disease (COVID-19), oral microbiome, generalized periodontitis.

The ongoing COVID-19 pandemic, caused by severe acute coronavirus respiratory syndrome (SARS-CoV-2), threatens global health and safety [1]. As by the end of January 2022, the COVID-19 pandemic had infected more than 365 million people worldwide, resulting in more than 5.6 million deaths. The transmission of SARS-CoV-2 usually occurs through respiration or direct contact with droplets and aerosol portions of the body fluids, mainly through coughing and sneezing. When a SARS-CoV-2 particle reaches the nasal cavity, it enters the epithelial cells of the host through the receptor angiotensin-converting enzyme 2 (ACE2), which is present in the lining epithelium of the respiratory, digestive, and oral systems, including oral cavity [2]. The SARS-CoV-2 virus replicates rapidly and is transported to the lower respiratory tract, enhancing pro-inflammatory responses and leading to serious consequences, such as acute respiratory syndrome, organ and system dysfunction,

and progression of chronic diseases, including dystrophic and inflammatory periodontal diseases among dental pathologies. Some of studies have shown that periodontal bacteria are directly involved in systemic inflammation, bacteremia, and pneumonia [3–5]. Patients with severe complications are diagnosed with high levels of inflammatory markers (C-reactive protein, tumor necrosis factor alpha, interleukins 2, 6 and 10) [4], the same markers are recorded with elevated rates in patients with generalized periodontitis [6]. In addition, bacteria present in the oral cavity of patients infected with COVID-19 include high levels of *Prevotella intermedia, Staphylococcus aureus,* and *Fusobacterium nucleatum*, which are usually commensal organisms in the oral cavity [7–9]. The presence of inflammatory or dystrophic-inflammatory processes in the gums and periodontium is associated with a 3.5 times increased risk of hospitalization in the intensive care unit, 4.5 times higher risk of pulmonary

ventilation, and 8,8 times higher risk of patient's death, regardless of other concomitant risk factors [10]. The scientists Golda A., Malek N., and Dudek B. have proved that the persistence of SARS-CoV-2 virus in mucosal epithelial cells from the oral cavity to the respiratory tract increases the adhesion to them of streptococci and pneumococci and inhibits the natural cleansing of these mucous membranes from bacteria and virions, causing complications such as pneumonia and inflammatory lung disease [11].

The oral cavity, like the lungs, is often referred to as an «ecological niche of commensal, symbiotic, and pathogenic organisms», and the emigration or elimination of microbes among them is constant, ensuring a healthy distribution of saprophytic microorganisms, which maintains organ, tissue, and immune homeostasis. But when pathogenic microflora persists in the lung tissue due to coronavirus infection, a lightning inflammatory reaction is formed, with a cytokine storm, i.e., atypical changes in the blood and an imbalance of pathological bacteria in the mouth. As a result, prolonged hospital stays due to COVID-19 complications, cross-infection, oxygenation therapy through the mask or intubation, and long-term intravenous infusions limit the patient's ability to care for the oral cavity, which creates extremely favorable conditions for colonization by aerobic and anaerobic pathogens of the oral cavity and periodontal pockets and leads to the rapid progression of chronic generalized periodontitis. The goal of the study is to assess the state of the microbiome of the periodontal pockets of dental patients in the post-covid period.

Materials and methods. The objects of the study were 140 patients with generalized periodontitis of the I and II stages of development, chronic course (GP); among them 80 patients had coronavirus disease in the closest past. The patients were randomized by age, sex, and stage of GP development. The diagnosis of periodontal disease was established by the Danilevskyi classification (1994). Protocol group A (n = 40) of examined and treated patients included patients with GP who did not suffer from coronavirus disease. Protocol group B (n = 40) included patients who had coronavirus disease on an outpatient basis and at the time of examination had no post-covid complications. Protocol group C (n = 40) included patients who had coronavirus disease, were treated for it in the hospital conditions, and at the time of examination were in rehabilitation and continued treatment for pulmonary complications. Group H (n=20) included healthy individuals with intact periodontium.

The patients were recruited on the basis of the Ivano-Frankivsk Regional Hospital and City Clinical Hospital No 1 according to the officially approved and signed by the general director petition. The dental examination and collection of periodontal pocket contents for microbiological examination of the patient majority (87.5%) were performed after documented recovery or discharge from the hospital at the Dentistry Center of Ivano-Frankivsk National Medical University, Clinical Hall of Therapeutic Dentistry. The bacteriological material for aerobic and facultative anaerobic microflora and yeast-like fungi was collected from periodontal pockets with a calibrated bacteriological loop and immediately seeded on blood agar.

The bacteria were cultivated using Gold`s method, which allows quantification of microbial contamination [12] and incubated for one day at 37 °C under aerobic and anaerobic conditions (in a hermetically sealed desiccator) in an atmosphere enriched with CO_2. The identification of isolated pure cultures was performed by a set of morphological, cultural, and biochemical properties (sets «STREPTO test 16», «STAPHY test 16», «ENTERO test 24», Lachema, Czech Republic). The evaluation of cultural properties considered the nature of hemolytic Streptococci, plasma coagulase and lecithinase activity of Staphylococci, lactase activity of Enterobacteria, and pigmentation formation.

During the bacteriological study, attention was paid to the presence of the following microorganisms: a-hemolytic Streptococci of the mitis group (*Streptococcus oralis*, *Streptococcus sanguinis*, *Streptococcus gordonii*), b-hemolytic streptococci (group A — *Streptococcus pyogenes*, group G — *Streptococcus dysgalactiae* ssp. *Equisimilis,* and of the anginosus group — *Streptococcus anginosus*, *Streptococcus constellatus*), staphylococci (*Staphylococcus aureus*, *Staphylococcus epidermidis*), and also *Stomatococcus mucilaginosus*, *Veillonella parvula*, *Neisseria* sp., *Corynebacterium* sp., *Bacillus* sp., *Lactobacillus* sp., *Micrococcus* sp., *E. coli* and other types of *Enterobacteria, Pseudomonas* (*Pseudomonas aeruginosa*), and *Candida* species.

In order to characterize the microbiome of periodontal pockets in patients during the initial dental examination, the determined species and spectrum of aerobic, optional anaerobic microflora, as well as quantitative indicators of colonization by microorganisms of each group were established, in particular the population level (PL) — the mass of this habitat colonization; the constancy index (CI) — the frequency of detection of this microorganism in the examined sample of patients (**%**); and the quantitative dominance (efficiency) — the percentage of this microbe relative to the all detected microbial cells in a patient [13].

The control indicators of the oral microbiocenosis characteristics were determined in the study of gingival crevicular fluid collected in the gingival sulcus of intact teeth in healthy persons from group C, group H (see p. 5) who did not suffer from coronavirus disease**,** taking into account the age criteria, and their dental and somatic health accordingly to the criteria of WHO.

The research was carried out in compliance with the basic provisions of the «Rules of ethical principles to scientific medical research with human participation», approved by the Helsinki Declaration (1964‒2013), ICH GCP (1996), EEC Directive No 609 (dated 24.11.1986), orders of the Ministry of Health of Ukraine № 690 from 23.09.2009, No 944 from 14.12.2009, and No 616 from 03.08.2012. In order to participate in the study, all patients signed the form «Voluntary informed consent of the patient to participate in the study». Statistical processing of the obtained data was performed using Microsoft Excel and Statistica software package. The arithmetic mean (M) and its statistical error (m) were used to describe variables with normal distribution. The probability of differences in the mean values for samples with normal distribution was estimated using Student's t-criteria test.

Results. The observed patients were divided into two groups due to the fundamentally different therapeutic approaches in the treatment for coronavirus infection depending on its severity. Group B included patients who had a mild form of coronavirus disease, were treated on an outpatient basis, and did not have any post covid complications at the time of examination. These patients did not require oxygenation therapy but received tablets of antibiotics (moxifloxacine — 65.0%; cefpodoxime — 17.5%; doxycycline — 17.5%). Group C included patients with moderate to severe coronavirus disease who required inpatient treatment, were in rehabilitation at the examination time, or continued treatment for post-covid pulmonary complications. In the hospital, all patients of this group received oxygenation therapy using oxygen masks, glucocorticosteroids therapy, as well as intensive antibiotic therapy with at least two drugs (ceftriaxone and azithromycine — 37.5%; meropenem and moxifloxacine — 25.0%; cefeloxime, ceftriaxone and moxifloxacin — 12.5%). Significant qualitative and quantitative changes in the nature of the oral microbiocenosis were observed in patients with GP after recent coronavirus disease, compared with similar patients who did not suffer from COVID-19 (Group A). At first, we should pay attention to the marked decrease in the species diversity of microorganisms in the periodontal pockets of patients in groups B and C (Tables 1 and 2).

The oral cavity with its extension into the intestinal tract is the second most massive microbiota of the human body, which plays an important role in the pathogenesis of infectious and viral diseases. Specialized foreign studies have described that pathogenic microorganisms of the lungs and oral cavity can affect the outcome of many infectious diseases by regulating the immunity of the mucous membrane of the host. For example, the intestinal flora can influence the onset and progression of viral infection through the intestinal-pulmonary axis on the one hand, and, on the other hand, the local oral microbiome affected by a viral infection will change the susceptibility and severity of respiratory disease [14]. Accordingly, we have noticed almost complete disappearance of bacteria that belong to the transient representatives of the oral microflora — *Neisseria, Corynebacteria (diphtheria), Micrococci,* and *Lactobacilli.* The main resident representatives of the oral microflora — α-hemolytic Streptococci of the mitis group were found in all healthy individuals and patients of groups A and C, but in $30.0 \pm 4.58\%$ of patients of group B, α-hemolytic Streptococci in the contents of periodontal pockets were present in quantities not available for detection by the applied method (<2.7 lg CCU/mL). In terms of species, *Streptococcus oralis* and *Streptococcus salivarius* are more characteristic in gingival crevicular fluid in healthy individuals (93.8% of selected strains). In $68.4 \pm 3.32\%$ of patients in group A, $64.0 \pm 3.43\%$ of patients in group B, and $67.5 \pm 3.76\%$ of patients in group C, the dominant species were *Streptococcus gordonii* and *Streptococcus sanguinis,* ($p < 0.01$), which have increased pathogenic potential as they produce streptolysin-O, inhibit complement activation, bind to fibronectin, actively form biofilms on the surface of tooth enamel and gum epithelial surface, and can act as an initiator of adhesion of periodontal pathogens [15]. The population level

Table 1. **The population level (lg coefficient of conventional units (CCP)/mL)**
of microorganisms in periodontal pockets of patients with GP after coronavirus disease (COVID-19)

Groups of microorganisms	Control Healthy (n=20)	Patients with GP		
		Group A (did not suffer from COVID-19), (n=40)	Group B (COVID-19 outpatient without complications), (n=40)	Group C (COVID-19 inpatient, postcocious pulmonary fibrosis), (n=40)
α-hemolytic *Streptococcus* sp.	5.68 ± 0.24	6.0 ± 0.20*	5.26 ± 0.18†	4.45 ± 0.18*/†
β-hemolytic *Streptococcus* sp.	2.70 ± 0.03	3.99 ± 0.15*	0*/†	0*/†
Staphylococcus aureus	3.35 ± 0.18	4.33 ± 0.19*	0*/†	0*/†
Staphylococcus epidermidis	3.62 ± 0.15	3.99 ± 0.17	4.00 ± 0.28	0*/†
Stomatococcus mucilaginosus	3.49 ± 0.22	3.81 ± 0.19	3.74 ± 0.25	3.00 ± 0.05†
Veillonella parvula	3.76 ± 0.24	4.07 ± 0.24	3.85 ± 0.13	3.70 ± 005
Lactobacillus sp.	3.60 ± 0.12	4.70 ± 0.15*	0*/†	0*/†
Neisseria sp.	3.57 ± 0.31	3.70 ± 0.20	0*/†	0*/†
Micrococcus luteus	0	3.54 ± 0.18*	0†	0†
Corynebacterium sp.	3.00 ± 0.03	4.16 ± 0.20*	0*/†	0*/†
Bacillus sp.	2.00 ± 0.03	0*	0*	0*
E. coli	0	3.70 ± 0.12*	5.00 ± 0.13*/†	0†
Pseudomonas aeruginosa	0	0	0	4.70 ± 0.05*/†
Candida sp.	0	3.63 ± 0.22*	3.85 ± 0.25*	4.23 ± 0.16*/†

Note: * — $p < 0.05$ in comparison with the control; † — $p < 0.05$ when compared with patients of group A.

of α-hemolytic Streptococci in patients with GP who did not have COVID-19 (group A) is quite high — 6.70 ± 0.20 lg CCU/mL. In patients with GP after coronavirus disease, it decreases in proportion to its severity and intensity of broad-spectrum antibiotic therapy: in group B — up to 5.26 ± 0.18 lg CCU/mL ($p < 0.05$), in group C — up to 4.45 ± 0.18 lg CCU/mL ($p < 0.01$) (Table 1). The other representatives of the resident microflora of the oral cavity, *Stomatococcus mucilaginosus* and *Veillonella parvula,* for the patients of group C are also found in periodontal pockets with a significantly lower index of persistence and minimal population level (Tables 1, 2).

After coronavirus disease (groups B and C), both the population level and the frequency of colonization of periodontal pockets by *Staphylococci* and β-hemolytic Streptococci decrease rapidly. For these groups, unlike patients from group A, we did not find any case of colonization by *Staphylococcus aureus,* as well as β-hemolytic Streptococci. Epidermal *Staphylococcus* is also absent in the periodontal pockets of patients in group C.

The *Enterobacteria* species, in particular *E. coli* (population level 3.70 ± 0.12 lg CCU/mL, persistence index $2.40 \pm 1.21\%$) was found only in isolated cases in the oral cavity of group A patients. In patients of group B both the mass and frequency of colonization of periodontal pockets by *Escherichia coli* are significantly higher (population level 5.00 ± 0.13 lg CCU/mL, $p < 0.05$, persistence index $23.5 \pm 2.84\%$, $p < 0.01$). We diagnosed for some patients of group C a fairly high level of periodontal pockets colonization by *Pseudomonas aeruginosa* (population level 4.70 ± 0.05 lg CCU/mL, persistence index $7.5 \pm 1.22\%$, $p < 0.05$ in comparison with group A). The *Enterobacteria species* and *Pseudomonas* do not belong to the resident microflora of the oral cavity, and their presence indicates an extremely unsatisfactory hygienic condition.

Table 2. **Persistence index (%) in periodontal microbiocenoses of patients with GP after coronavirus disease (COVID-19)**

Groups of microorganisms	Control Healthy (n = 20)	Patients with GP		
		Group A (did not suffer from COVID-19) (n = 40)	Group B (COVID-19 outpatient without complications) (n = 40)	Group C (COVID-19 inpatient, post COVID pulmonary fibrosis) (n = 40)
α-hemolytic *Streptococcus* sp.	100.0	100.0	$70.0 \pm 4.58^{*/\dagger}$	100.0
β-hemolytic *Streptococcus* sp.	6.3 ± 4.42	$25.7 \pm 6.03^{*}$	$0^{\dagger}$	$0^{\dagger}$
Staphylococcus aureus	12.5 ± 6.04	$22.4 \pm 5.60^{*}$	$0^{*/\dagger}$	$0^{*/\dagger}$
Staphylococcus epidermidis	31.3 ± 8.46	28.9 ± 6.12	$26.6 \pm 3.13^{*}$	$0^{*/\dagger}$
Stomatococcus mucilaginosus	56.3 ± 9.06	53.5 ± 3.14	$43.7 \pm 4.02^{*/\dagger}$	$5.0 \pm 0.86^{*/\dagger}$
Veillonella parvula	43.8 ± 8.72	$64.3 \pm 3.42^{*}$	$18.4 \pm 3.63^{*/\dagger}$	$7.5 \pm 1.22^{*/\dagger}$
Lactobacillus sp.	12.5 ± 6.04	$6.4 \pm 2.04^{*}$	$0^{*/\dagger}$	$0^{*/\dagger}$
Neisseria sp.	18.8 ± 7.13	$29.4 \pm 6.33^{*}$	$0^{*/\dagger}$	$0^{*/\dagger}$
Micrococcus luteus	0	$13.9 \pm 3.33^{*}$	$0^{\dagger}$	$0^{\dagger}$
Corynebacterium sp.	12.5 ± 6.04	$24.1 \pm 5.71^{*}$	$0^{*/\dagger}$	$0^{*/\dagger}$
Bacillus sp.	12.5 ± 6.04	0^{*}	0^{*}	0^{*}
E. coli	0	2.40 ± 1.21	$23.5 \pm 2.84^{*/\dagger}$	0
Pseudomonas aeruginosa	0	0	0	$7.5 \pm 1.22^{*/\dagger}$
Candida sp.	0	$28.6 \pm 5.47^{*}$	$35.6 \pm 3.03^{*/\dagger}$	$47.5 \pm 3.24^{*/\dagger}$

Note: * — $p < 0.05$ in comparison with the control; † — $p < 0.05$ when compared with patients of group A.
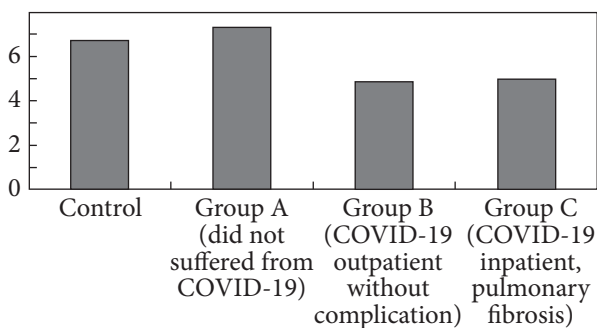
Fig. 1. The total number (lg CCU/mL) of viable aerobic and facultatively anaerobic microorganisms in the contents of periodontal pockets of patients with GP in the post-covid period

Approximately in one third (28.6 ± 5.47%) of the group A patients, we have found fungi of the *Candida* species (mainly *C. albicans*, single strains of *C. tropicalis*, *C. lusitaniae,* and *C. kefir*) in the contents of periodontal pockets, with an average population level of colonization 3.63 ± 0.22 lg CCU/mL. At the same time, none

of the examined healthy people were diagnosed with yeast-like fungi in the amount of ³ 2.7 lg CCU/mL (sensitivity limit of the applied method) in the gingival crevicular fluid. For the patients with GP in the post-covid period, both the incidence of *Candida* species in the contents of periodontal pockets and the mass of their colonization increased significantly in proportion to the severity of coronavirus disease and the mass of corticosteroid and antibiotic therapy: in group B, persistence index was 47.5 ± 3.24%, population level equaled 3.85 ± 0.25 lg CCU/mL, and in group C, the persistence index was 35.6 ± 3.03% and the population level equaled 4.23 ± 0.16 lg CCU/mL, ($p < 0.05$, compared to the patients of group A).

Discussion. The changes in the coefficients of microorganisms' quantitative dominance in different groups of patients testify to the violation of quantitative relationships among different participants in the periodontal pocket's mi-

Table 3. **The coefficient of quantitative dominance in periodontal microbiocenoses (%) in different groups of periodontal patients after coronavirus disease**

Groups of microorganisms	Control Healthy (n = 20)	Patients with GP		
		Group A (did not suffer from COVID-19) (n = 40)	Group B (COVID-19 outpatient without complications) (n = 40)	Group C (COVID-19 inpatient, post COVID pulmonary fibrosis) (n = 40)
α-hemolytic *Streptococcus* sp.	94.77 ± 2.24	97.07 ± 0.61	64.96 ± 11.30	82.50 ± 4.86
β-hemolytic *Streptococcus* sp.	0.01 ± 0.0003	0.08 ± 0.03	0	0
Staphylococcus aureus	0.22 ± 0.08	0.55 ± 0.32	0	0
Staphylococcus epidermidis	6.53 ± 1.41	0.73 ± 0.35	5.22 ± 3.94	0
Stomatococcus mucilaginosus	4.59 ± 2.72	0.33 ± 0.12	3.25 ± 1.39	9.83 ± 5.00
Veillonella parvula	0.32 ± 0.17	0.72 ± 0.13	2.14 ± 1.33	1.52 =0.93
Lactobacillus sp.	0.12 ± 0.03	0.12 ± 0.03	0	0
Neisseria sp.	3.01 ± 1.29	0.26 ± 0.14	0	0
Micrococcus luteus	0	0.01 ± 0.004	0	0
Corynebacterium sp.	0.11 ± 0.03	0.37 ± 0.28	0	0
Bacillus sp.	0.07 ± 0.01	0	0	0
E. coli	0	0.21 ± 0.08	19.42 ± 8.24	0
Pseudomonas aeruginosa	0	0	0	5.18 ± 3.17
Candida sp.	0	0.59 ± 0.26	5.1 ± 3.95	3.27 ± 0.11

Note: * — $p < 0.05$ in comparison with the control; † — $p < 0.05$ when compared with patients of group A.

crobiocenoses (Table 3). The most characteristic in the post-covid period is the decrease in the proportion of α-hemolytic Streptococci, the increase in the proportion of yeast-like fungi, as well as the appearance of a significant number of gram-negative rod-shaped bacteria *(Enterobacteria* and *Pseudomonas* species).

The influence of coronavirus infection and its treatment using different protocols on the microflora of periodontal pockets is clearly described with the help of the total microbial count (Fig. 1).

For the periodontal patients in the post-covid period, it is about 2 orders lower compared with those who did not suffer from COVID-19 (p<0.05). In our opinion, the main reason for this is intensive and not entirely justified antibiotic therapy, which during the 1–2 waves of the COVID-19 epidemic was provided by the existing treatment protocols because of fear of secondary bacterial pneumonia. Even in the mild course of coronavirus disease, patients of group B received oral broad-spectrum antibiotics, namely fluoroquinolones of the third generation, cephalosporins, and tetracyclines.

The overpassed coronavirus disease due to intensive antibiotic therapy leads to a marked decrease in the number of viable saprophytic microorganisms in the periodontal pockets of patients with GP. In the post-covid period for the patients with GP, there is a decrease in the level of colonization of periodontal pockets by species of resident oral microflora, i.e., α-hemolytic Streptococci, reduction of resident microorganisms'species and almost complete disappearance of transient microflora. On the other hand, the frequency of colonization of periodontal pockets by fungi species, enterobacteria, and pseudomonads significantly increases. There are more expressed disorders of the periodontal pocket's microbiome for the patients with severe and complicated course of coronavirus disease, such as post covid pulmonary fibrosis, which requires reconsideration of approaches to therapeutic and pharmacological treatment in this category of patients.

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ОСОБЛИВОСТІ МІКРОБІОМУ ПАРОДОНТАЛЬНИХ КИШЕНЬ
У ХВОРИХ НА ГЕНЕРАЛІЗОВАНИЙ ПАРОДОНТИТ У ПОСТКОВІДНОМУ ПЕРІОДІ

Ротову порожнину, подібно до легень, часто називають «екологічною нішею коменсальних, симбіотичних та патогенних організмів», а еміграція та елімінація мікробів між ними є постійною, що забезпечує здоровий розподіл сапрофітних мікроорганізмів, який функціонує у збереженні гомеостазу органів, тканин та імунітету. Внаслідок коронавірусної інфекції в легеневій тканині персистує патогенна мікрофлора, формується блискавична запальна реакція, з цитокіновим штормом та нетиповими змінами крові, і виникає дисбаланс патологічних бактерій у роті. **Мета дослідження** — оцінити стан мікробіому пародонтальних кишень стоматологічних хворих у постковідному періоді. **Методи.** Об'єктом дослідження стали 140 хворих на генералізований пародонтит I та II ступеня розвитку і хронічного перебігу (ГП), серед яких 80 пацієнтів, які перехворіли коронавірусною хворобою в легкому, середньому та важкому її прояві. Пацієнтів рандомізовано за віком, статтю та ступенем розвитку ГП. Матеріал для бактеріологічного дослідження на предмет виявлення аеробної і факультативно-анаеробної мікрофлори та дріжджоподібних грибів забирали з пародонтальних кишень відкаліброваною бактеріологічною петлею і негайно висівали на кров'яний агар за методом Голда. **Результати.** У пацієнтів із ГП після нещодавно перенесеної коронавірусної хвороби спостерігалися істотні якісні і кількісні зміни характеру мікробіоценозу вмісту пародонтальних кишень порівняно з аналогічними пацієнтами, які не хворіли на COVID-19. Нами виявлено практично повне зникнення бактерій, які належать до транзиторних представників мікрофлори ротової порожнини — нейсерій, коринебактерій (дифтероїдів), мікрококів, лактобацил. Домінуючими видами були *Streptococcus gordonii* та *Streptococcus sanguinis* (p < 0.01), які володіють підвищеним патогенним потенціалом — продукують стрептолізин-О, гальмують актива-

цію комплементу, зв'язуються з фібронектином, активно формують біоплівки як на поверхні емалі зубів, так і на поверхні епітелію ясен, а також можуть ініціювати адгезію пародонтопатогенних мікроорганізмів. Інші представники резидентної мікрофлори ротової порожнини — *Stomatococcus mucilaginosus* та *Veillonella parvula* у пацієнтів із ГП після стаціонарного лікування коронавірусної хвороби та на фоні постковідних ускладненьтакож виявляються у пародонтальних кишенях з достовірно меншим індексом постійності і при мінімальному популяційному рівні. У постковідному періоді різко зменшується як популяційний рівень, так і частота колонізації пародонтальних кишень пацієнтів стафілококами і β-гемолітичними стрептококами. У них, на відміну від пацієнтів, які не хворіли на коронавірусну хворобу, нами не виявлено жодного випадку колонізації золотистим стафілококом, а також β-гемолітичними стрептококами. У пародонтальних кишенях пацієнтів цієї групи відсутній також епідермальний стафілокок. Найбільш характерними у постковідному періоді є зменшення частки α-гемолітичних стрептококів, збільшення частки дріжджоподібних грибів, а також поява істотної кількості грам-негативних паличкоподібних бактерій (ентеробактерій та псевдомонад). У пародонтологічних пацієнтів в постковідному періоді мікробне число приблизно на два порядки менше, ніж у осіб із ГП, які на COVID-19 не хворіли (p < 0.05). **Висновки.** У пародонтологічних хворих у постковідному періоді спостерігається зниження рівня колонізації пародонтальних кишень представниками видової резидентної оральної мікрофлори — α-гемолітичними стрептококами, зменшення видової різноманітності мікроорганізмів та практично повне зникнення представників транзиторної мікрофлори. Збільшується масивність і частота колонізації пародонтальних кишень дріжджоподібними грибами, ентеробактеріями і псевдомонадами. Більш виражені порушення мікробіому пародонтальних кишень характерні для пацієнтів з важким та ускладненим перебігом коронавірусної хвороби, такими як постковідний легеневий фіброз, що потребує переглянути підходи до терапевтичного та фармакологічного лікування у такій категорії хворих.

Ключові слова: коронавірусна хвороба (COVID-19), мікробіом ротової порожнини, генералізований пародонтит.