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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии
საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

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GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

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WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman (Кириллица)**, для текста на грузинском языке следует использовать **AcadNusx**. Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - <http://www.spinesurgery.ru/files/publish.pdf> и http://www.nlm.nih.gov/bsd/uniform_requirements.html В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректур авторам не высылаются, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or computer-printed on a single side of standard typing paper, with the left margin of 3 centimeters width, and 1.5 spacing between the lines, typeface - **Times New Roman (Cyrillic)**, print size - 12 (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf

In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

**Articles that Fail to Meet the Aforementioned
Requirements are not Assigned to be Reviewed.**

ავტორთა საქურაღებოლ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დაიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx**. შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შედეგის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფხიხლებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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DISEASES OF THE ORAL MUCOSA IN PATIENTS IN THE POST-COVID PERIOD

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Summary.

The impact of SARS-CoV-2 (severe acute respiratory syndrome-related coronavirus-2) on the entire human body causes irreversible changes in all organs and systems. Complications in the form of chronic diseases require the treatment of clinicians in various fields of medicine. Dentists are faced with diseases of the oral mucosa in apparently healthy patients who are not predisposed to them but have undergone COVID-19.

Purpose of the study. To assess the impact of the coronavirus infection (COVID-19) on the course of diseases of the oral mucosa.

We examined 51 patients aged 20 to 75 who had undergone COVID-19 with various diseases of the oral mucosa. The study used clinical and laboratory methods. The features of the clinical course of certain diseases of the oral mucosa were revealed, the dynamics of the local immune defense of the oral cavity in the post-covid period was determined.

Key words. Oral mucosa, COVID-19.

Introduction.

The oral cavity is an open biological system in which there is a constant balance between pathogenic factors and the body's defenses. However, this balance is often under attack. This occurs either due to the rapid multiplication of microorganisms in the oral cavity, or due to the weakening of the factors of general and especially local immune defense [1].

In connection with the spread of a new coronavirus infection, the number of diseases of the oral mucosa developing against the background of COVID-19 is steadily increasing.

SARS-CoV-2 (severe acute respiratory syndrome-related coronavirus-2) salivary gland infections produce large numbers of viruses in salivary gland tissues and secrete them into secretions (Sabino-Silva R, Jardim ACG) [2].

Clinical and post-mortem studies, as well as experimental animal models of SARS-CoV-2, indicate the effect of this infection on the vessels. Damage to the endothelium of blood vessels and thrombosis [1] act as common pathomorphological features of SARS-CoV-2 [3,4].

The assumption that the SARS-CoV-2 virus, which was considered a pathogen of the tissues of the upper and lower respiratory tract, is now supplemented by the idea of pronounced destructive effects on the blood vessels of the whole organism, which causes non-standard and polymorphism of the clinical manifestations of COVID-19 [5,6].

Vascular changes in the lungs occurred early in the development of COVID-19 infection [7]. This vascular pattern of lung injury differs from that in influenza by signs of increased thrombus formation [8].

McGonagle et al. [5,8] also indicate edema of the vascular wall and the presence of an inflammatory infiltrate, pronounced necrosis with hemorrhages and microthrombi of blood vessels, and activation of pulmonary macrophages.

In particular, pathomorphological analysis showed that the presence of the virus in endothelial cells was combined with accumulations of inflammatory cells [9]. This fact suggests that SARS-CoV-2 infection initiates endothelial inflammation throughout the human body and also triggers apoptotic mechanisms, which explains systemic microcirculatory manifestations in various parts of the bloodstream and their clinical manifestations in patients with COVID-19, including in the oral cavity [10]. COVID-19 was more likely to have a poor outcome in patients with comorbid cardiovascular diseases [11,12]. The molecular biological mechanisms of virus invasion involve various pathways of its penetration into the cell and various forms of the development of an inflammatory response involving reactions of innate and acquired immunity.

According to recent studies, COVID-19 is accompanied by the appearance of dental problems in patients: the infection can manifest itself in the form of ulcers, plaques, fungal infections of the oral cavity, cracked lips and tongue, petechial hemorrhages, swollen lymph nodes [13,14]. Such problems may be the result of impaired blood supply and the supply of nutrients to the tissues of the oral cavity, since the coronavirus interacts with cell receptors, damaging the endothelial cells of the vessels of the oral cavity, and in severe cases of COVID-19, hypercoagulability and thrombosis are observed, which leads to impaired microcirculation. The second mechanism is associated with inflammatory reactions in the body that develop during COVID-19 infection. Uncontrolled inflammation, which is accompanied by a sharp increase in the level of cytokines in the blood, can lead to damage to the body's own tissues by immune cells (cytokine storm). In addition, the causes of pathology in the oral cavity may be long-term use of medications prescribed for the treatment of coronavirus [1,9,10].

Aphthous lesions, herpetiform lesions, candidiasis, and Kawasaki disease are the most common oral manifestations of COVID-19 disease. But still, one of the most common diseases in the oral cavity in patients who have recovered from coronavirus infection is chronic recurrent aphthous stomatitis [13]. Advanced age and severity of COVID-19 disease appear to be the most predictive factors that predict the severity of oral lesions in these patients. Lack of oral hygiene, opportunistic infections, stress, comorbidities (diabetes mellitus, immunosuppression), trauma (secondary to intubation), vascular abnormalities, and a hyperinflammatory response secondary to COVID-19 may be the most important predisposing factors for development oral lesions in patients with COVID-19 [15].

It can be assumed that the etiological factor in the development of the disease is a violation of cellular and humoral immunity, both local and general. The leading factor in etiopathogenesis is the modulation of the cross-immune reaction, resulting in the formation of aphthae in the oral cavity [9].

The development of dysbiosis is due to antibiotic therapy and, as a result, a violation of the balance of microorganisms in the oral cavity. Dryness in the oral cavity is caused by infectious lesions of the oral cavity by the type of candidiasis [13]. Some patients also had pseudomembranous plaque on the tongue in the form of white plaques. The mucous membrane of the hard palate is sometimes partially hyperemic, enanthems are noted.

The available scattered data on manifestations in the oral cavity observed after a coronavirus infection require further study.

Purpose of the study. Assess the impact of past coronavirus infection (COVID-19) on the course of diseases of the oral mucosa.

Materials and methods. At the clinical bases of the departments of dentistry TDSI, MSMSU, with the permission of the interuniversity ethics committee, a dental examination was carried out on 51 patients (29 women and 22 men) aged 20 to 75 years with various diseases of the oral mucosa. Patients had a history of a coronavirus infection in terms ranging from several days to 6 months. All patients gave voluntary informed consent to participate in the study (Figure 1).

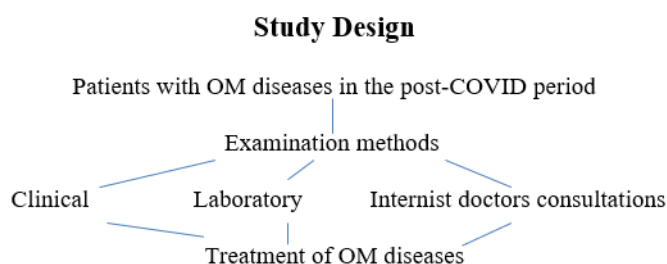


Figure.1. Study Design.

When examining patients, clinical and laboratory methods were used.

Clinical methods. clarification of the patient's complaints and anamnesis; assessment of the dental status included: the state of hygiene of the oral cavity, teeth, periodontal and mucous membranes, the presence and quality of orthopedic structures. The presence of dental deposits was determined by the Green-Vermilion index (OHI-S), the intensity of dental caries was determined by the KPU index. The degree of inflammation in the gums was assessed using the PMA index. When examining the oral mucosa, its color, humidity, signs of edema, the presence and localization of lesions were determined.

To identify concomitant pathology, patients were recommended to consult an endocrinologist, gastroenterologist, immunologist, therapist.

Laboratory studies. 48 patients with a previously transferred and confirmed PCR diagnosis of coronavirus infection COVID-19 took part. 3 patients with severe somatic pathology, primary and secondary immunodeficiency, chronic pathology of the oral cavity with frequent relapses before COVID-19 were excluded from the further study. The oral fluid was taken from patients to determine the level of sIgA in it.

The content of secretory immunoglobulin (sIgA) in the oral fluid was determined by ELISA with a set of test systems Saliva ELISA kit (Euroimmun, Germany) in accordance with the manufacturer's instructions.

We analyzed the duration of the course of the OM disease (from the beginning of the period of primary clinical manifestations to the end of treatment), the terms of rehabilitation after suffering from COVID-19, in which the OM pathology manifested itself. Then, subgroups of patients were formed depending on the duration of the OM disease: the first - up to 7 days, 10 (20.8%) people; the second - up to 14 days, 9 (18.8%); the third - 15–30 days, 25 (52.1%); the fourth - more than 30 days, 4 (8.3%) people.

Depending on the period of rehabilitation in which the ORS pathology was observed, subgroups were formed: the first - up to 1 month, 18 (37.5%) people; the second - from 1 to 3 months, 12 (25%); the third - from 3 to 6 months, 7 (14.6%); the fourth - more than 6 months, 11 (22.9%) people. 12 (25%) patients underwent a course of antibiotic therapy.

The relationship between the change in the local immunity factor in the oral fluid (sIgA level), the duration of the SOR disease and the period of rehabilitation after COVID-19, in which the pathology of the OM was observed, was studied.

Statistical analysis of the study results was performed using the analytical package STATISTICA 10.0 (StatSoft Inc., USA) and Excel, one-sample student t-test and correlation.

According to the results of the examination, the patients were prescribed complex pathogenetic and etiotropic treatment, considering the principles of an individual approach. The general treatment of lesions of the oral mucosa consisted in the appointment of hepatoprotectors, vitamins, antifungal drugs, as well as dietary supplement dihydroquercetin to improve general and local microcirculation. Locally for the treatment of lesions of the mucous membrane, rinsing of the oral cavity with ozonized saline and applications at the site of lesions of dihydroquercetin powder together with sesame oil were prescribed.

Patients were also recommended sanitation of the oral cavity with professional hygiene.

The control group consisted of 28 people without a history of COVID-19, without severe underlying pathology, and without changes in the OM.

Results.

The average age of the examined patients was 43.7 ± 8.5 (M \pm m) years.

The distribution of clinical manifestations on the oral mucosa is presented in (Table 1).

The overwhelming majority of patients who applied for dental care were patients with diagnoses: recurrent aphthous stomatitis - 21 (41.2%) and candidiasis OM - 22 (43.1%). Much fewer patients were diagnosed with lichen planus - 6 (11.8%) and 2 (3.9%) patients with symptoms of necrosis of the oral mucosa.

As a result of a survey of patients, a variety of complaints were identified (Tables 2,3&4).

The main complaint of 90% of the patients who applied was pain in the oral cavity, which sharply increased when eating, in 33% of patients the pain increased even when talking.

In 65% of patients with oral candidiasis, there were complaints of constant burning in the mouth, which was detected in 43.1%

Table 1. Distribution of patients with diseases of the oral mucosa.

| OM pathology | Number of patients |
|-------------------------------|--------------------|
| Recurrent aphthous stomatitis | 21 (41,2%) |
| Candidiasis OM | 22 (43,1%) |
| Lichen planus | 6 (11,8%) |
| Necrosis OM | 2 (3,9%) |

Table 2. Main dental complaints of applied patients.

| Complaints | Number of patients (%) |
|----------------------------|------------------------|
| Pain in the mouth | 90 |
| Bad breath | 90 |
| Dry mouth | 85 |
| Ulcers | 60 |
| Bleeding gums | 28 |
| Burning in the mouth | 27,5 |
| Decreased taste sensations | 51,9 |

Table 3. Psychological complaints of applied patients.

| Complaints | Number of patients (%) |
|--|------------------------|
| Violation of the psycho-emotional status | 38 |
| Cancerophobia | 10 |
| Apathy | 58 |

Table 4. Complaints of applied patients on the part of the respiratory system.

| Complaints | Number of patients (%) |
|--------------------------|------------------------|
| Decreased sense of smell | 51.9 |
| Dyspnea | 35 |

Table 5. Data of examination of the oral cavity.

| Index | Meaning |
|---|--------------|
| The need for oral hygiene | 100% |
| Green-Vermilion Index | 2.1±0.8 |
| Intensity of caries – KPU | 16.7 ±0. 8 |
| RMA index | 34.66 ± 2.23 |
| The presence of orthopedic structures made of dissimilar metals | 8 (15.7%) |
| Confirmed diagnosis of candidiasis (Candida > 103-104 cfu/ml) | 22 (43.1%) |

of patients after bacteriological examination. This amounted to 27.5% of all applied patients.

Dry mouth bothered patients in 85% of cases. 5% of patients complained of shortness of breath even with little physical exertion, and the predominance of mouth breathing, which further aggravated dry mouth. Frequent complaints were also: bad breath (90%).

Some patients (28%) noted the appearance and increased bleeding of the gums and OM after suffering COVID-19.

51.9% of the observed patients complained that can be attributed to the long-term consequences of the presence of the COVID-19 virus in the human body - a decrease in the sharpness of smell and taste.

38% of patients experienced disturbances in their psycho-emotional status, in particular, stress after suffering a coronavirus infection, fear of re-infection.

Frequent complaints (58%) were apathy, fatigue, decreased attention, chronic fatigue. In 10% of patients who had frequent recurrences of lesions of the oral mucosa, carcinophobia was expressed.

When collecting an anamnesis, it turned out that 45% of the observed patients were treated in covid hospitals. There were also those patients who self-medicated (22%).

Based on the initial examination of the oral cavity in patients, it was revealed (Table 5): all examined (100%) needed oral cavity sanitation; the Green-Vermilion index was 2.1+0.8; the KPU index was 16.7; PMA index reached 34.66±2.23; the presence of orthopedic structures made of dissimilar metals was detected in 8 (15.7%) patients; detection of Candida fungi in an amount exceeding 103-104 CFU / ml.

When examining the oral cavity on the mucous membrane of the lips, gums, cheeks, soft palate, pharynx and tongue, various elements of the lesion were revealed (Table 6 and Figures 2,3,4,5&6): single and multiple aphthae ranging in size from 5 to 10 mm with an erythematous corolla and yellow-white fibrinous plaque (in 41.2% of patients), erosions (5.9%), ulcers (5.9%), plaque (92%), necrosis of the OM, papules (11.8%).

In some (45%) cases, aphthae, erosions merged, forming extensive lesions of the oral mucosa.

Lesions of the oral mucosa were more common in patients in the early stages of rehabilitation (up to 1 month after COVID-19), and less frequently in patients whose rehabilitation period exceeded 30 days.

According to the results of the advisory opinions of related specialists, concomitant somatic pathology was confirmed in all patients: chronic gastrointestinal diseases were observed in 17

Table 6. Manifestations on the oral mucosa.

| OM pathology | Number of cases, % |
|------------------------|--------------------|
| Language furnishing | 92 |
| Aphthae | 41.2 |
| Papules | 11.8 |
| Erosion | 5.9 |
| Ulcers | 5.9 |
| Necrosis | 3.9 |
| Bleeding hematomas COR | 1.9 |

Table 7. The level of sIgA in oral fluid in patients depending on the period of rehabilitation after suffering COVID-19.

| No | Terms of rehabilitation | sIgA level, µg/ml, Me (LQ – UQ) | Reliability |
|----|---------------------------------|---------------------------------|--|
| 0. | Control (n=28) | 326.9 (175.7–551.7) | p ₀₋₁ =0.016; |
| 1. | Before one months (n=18) | 849.0 (497.6–1403.9) | p ₀₋₂ =0.013 p ₀₋₃ >0.05; |
| 2. | From one before 3 months (n=12) | 851.9 (468.8–1037.3) | p ₀₋₄ >0.05 p ₁₋₂ >0.05; |
| 3. | From 3 before 6 months (n=7) | 328.0 (143.8–428.9) | p ₁₋₃ =0.006 p ₁₋₄ =0.004; p ₂₋₃ =0.028 |
| 4. | More 6 months (n=11) | 230.0(193.6–372.6) | p ₂₋₄ =0.032; p ₃₋₄ >0.05 |

p0-x - significance of differences between groups
Multiple testing has not been done

Table 8. The level of sIgA in oral fluid in patients depending on the duration of the disease.

| No. | The timing of the disease | sIgA level, $\mu\text{g/ml}$, Me (LQ – UQ) | Reliability |
|-----|---------------------------|---|-----------------------------------|
| 1. | 7 days (n=10) | 438.1 (193.6–628.9) | $p_{1-2}=0.043$; $p_{1-3}=0.038$ |
| 2. | 8–14 days (n=9) | 635.2 (421.5–746.2) | $p_{1-4}=0.004$; $p_{2-3}>0.05$ |
| 3. | 15-30 days (n=25) | 828.2 (266.4-1206.5) | $p_{2-4}=0.019$; $p_{3-4}>0.05$ |
| 4. | more thirty days (n=4) | 1476.8 (865.0-2156.1) | |

p_{0-x} - significance of differences between groups
Multiple testing has not been done



Figure.2. Candidal lesion of the tongue after suffering Covid-19.



Figure.3. Necrotic changes in sky after suffering Covid-19.



Figure.4. Inflammation and necrosis of the mucous membrane of the lower surface of the tongue and the floor of the mouth.



Figure.5. LP of the oral mucosa after suffering Covid-19.



Figure.6. Bleeding due to dental trauma erosion on the mucosa of the back of the tongue in a patient who has had Covid-19.

(33%) patients, endocrine diseases (type II diabetes mellitus) - in 6 (12%) people, diseases of the cardiovascular system - in 9 (18%) patients, 20 (39%) people suffered from hypertension.

The median amount of secretory immunoglobulin (sIgA) in oral fluid in post-COVID-19 patients (n=48) was 592.67; 254.23–944.39 $\mu\text{g/ml}$ (Me; LQ–UQ), which is statistically significantly higher than in the control group (n=28) 326.94; 175.72–551.76 $\mu\text{g/ml}$ ($p<0.05$) (Table 7).

During the rehabilitation of patients after suffering COVID-19 up to 1 month, the level of sIgA in the oral fluid was 849.0 (497.6–1403.9) $\mu\text{g/ml}$, $p_{0-1}=0.016$; during the rehabilitation period from 1 to 3 months, the level of sIgA slightly increased and amounted to 851.9 (468.8–1037.3) $\mu\text{g/ml}$, $p_{0-2}=0.013$, $p_{1-2}>0.05$; in the rehabilitation period from 3 to 6 months, the sIgA level dropped markedly and amounted to 328.0 (143.8–428.9) $\mu\text{g/ml}$, $p_{0-3}>0.05$, $p_{1-3}=0.006$, $p_{2-3}=0.028$; during the rehabilitation period of more than 6 months, the sIgA level continued to decrease and amounted to 230.0 (193.6–372.6) $\mu\text{g/ml}$, $p_{0-4}>0.05$, $p_{1-4}=0.004$, $p_{2-4}=0.032$, $p_{3-4}>0.05$.

Depending on the duration of the ORS disease in patients with COVID-19, the level of sIgA in the oral fluid was increased for 7 days compared to the control group and amounted to 438.1 (193.6–628.9) $\mu\text{g/ml}$. If patients applied 8-14 days after the onset of the ORS disease, a statistically significant increase

in secretory IgA was observed in the oral fluid 635.2 (421.5-746.2) $\mu\text{g/ml}$ ($p_{1-2}=0.043$); after 15-30 days, the level of sIgA increased significantly and amounted to 828.2 (266.4–1206.5) $\mu\text{g/ml}$ ($p_{1-3}=0.038$, $p_{2-3}>0.05$); in terms of more than 30 days from the onset of the disease, the OM level of sIgA was significantly increased and amounted to 1476.8 (865.0–2156.1) $\mu\text{g/ml}$ ($p_{1-4}=0.004$, $p_{2-4}=0.019$; $p_{3-4}>0, 05$) (Table 8).

Depending on the timing of the disease in patients with COVID-19, a statistically significant increase in secretory IgA levels was observed after seven days ($p = 0.043$; $p = 0.038$; $p = 0.004$) and increased until the 30th day from the onset treatment ($p>0.05$; $p=0.019$; $p>0.05$).

Discussion.

The COVID-19 pandemic has largely changed our understanding of the processes occurring in the body as a result of viral aggression. However, there is still much unclear in the pathogenesis of various disorders caused by SARS-CoV-2 infection and affecting almost all organs and systems. As for the pathology of the oral mucosa, directly or indirectly associated with coronavirus infection, there is still a lot of work to be done. So far, it is only clear that we are faced with a new pathology that requires detailed study in the context of interdisciplinary interaction of specialists in order to solve urgent diagnostic and treatment problems due to the variety of clinical variants of SARS-CoV-2 infection and post-COVID disorders.

Our study found that before COVID-19, none of the patients included in the study had pathology of the ROP. A study by Gherlone EF, Polizzi E, Tetè G, et al. (2021), which included patients hospitalized due to COVID-19, showed that lesions of the oral cavity are detected in 83.9% of patients 3 months or more after discharge [16].

An analysis of the data obtained in our study made it possible to establish that the incidence of OM lesions in patients was different at different stages of rehabilitation after undergoing COVID-19.

Frequent complaints from patients in our study were: bad breath. This is consistent with the results obtained by Yu.A. Makedonova et al. (2021) [17]. The appearance of ulcers on the mucous membrane of the cheeks and lips was observed in 60% of cases. Many researchers describe similar symptoms in the post-COVID period [18,19].

Some of the patients examined by us noted the appearance and increased bleeding of the gums and ORS after suffering COVID-19, which is consistent with the results of many other researchers who mention vesiculobullous lesions [16,18]. Including in the studies of Z.S. Khabadze et al. (2020) a similar symptom was observed in 13% of patients. Although these researchers talk about hemorrhages only on the OM [14].

More than half of the patients we observed presented complaints that can be attributed to the long-term consequences of the stay of the COVID-19 virus in the human body - a decrease in the sharpness of smell and taste. The results obtained are consistent with the results of other researchers [13,14,18,19].

The occurrence of complaints of dry mouth after suffering COVID-19 in our study is also confirmed by other researchers [14,16-18]. Many researchers describe the addition of a fungal infection in the post-COVID period [18,19]. The authors who

conducted similar studies [13] confirmed the diagnosis of candidiasis in 61% of cases, which is significantly more than in our studies (43%).

When examining the oral cavity on the mucous membrane of the lips, gums, cheeks, soft palate, pharynx and tongue, we revealed various elements of the lesion: single and multiple aphthae with an erythematous corolla and yellow-white fibrinous plaque, erosion, ulcers, plaque, necrosis of the OM, papules. The presence of many described elements of OM lesions is also confirmed by other researchers [18,19].

Most of the observed elements of OM lesions are accompanied by an inflammatory process. The mechanism of the inflammation process is enhanced by a large number of pro-inflammatory cytokines, for example, IL-6, IL-1, chemokines (IL-8), etc. Clinical manifestations of functional insufficiency of internal organs in COVID-19 are accompanied by an increase in the level of inflammatory cytokines, in particular, interleukin 6 (IL-6), which plays a key role in the development of the cytokine storm. IL-6 mediates a wide range of inflammatory changes that cause disturbances in the structural and functional organization of blood vessels [5].

IL-6 has a pleiotropic effect on acquired immunity by stimulating the production of antibodies by B cells, including sIgA. Normally, inflammation is regulated by anti-inflammatory cytokines, and disruption of the regulatory balance leads to significant destruction of one's own tissues [9]. sIgA, the predominant mucosal immunoglobulin, is considered the main specific defense mechanism in the oral cavity. One of the important components of the complex mechanism of innate immunity is neutrophils, when activated by pathogenic or opportunistic microorganisms, a wide range of anti-inflammatory cytokines is secreted.

In our study, we found that with prolonged persistence of the virus in the body, the level of sIgA in the oral fluid increases, and even after the end of COVID-19 treatment, the level of immunoglobulin remains high. However, a longer period of rehabilitation of patients leads to a gradual decrease in the sIgA index to values and slightly lower than those of the control group. Depending on the duration of the course of the disease, OM in Patients with COVID-19, the level of sIgA in the oral fluid increased compared to the control group. The increase in the level of sIgA was the more significant, the longer the OM disease lasted.

The revealed changes, as shown in our studies and in the studies of other authors [13,14,16], may be not only the result of the direct action of the virus. These changes may be based on changes in the oral microbiome due to the use of antibiotics, as well as such aggressive manipulations as intubation, tracheostomy, non-invasive mechanical ventilation.

Conclusions.

Thus, in the post-COVID period, patients often experience pain in the oral cavity, constant burning and dry mouth, bad breath, and they often need oral hygiene. Oral mucosal lesions are more common in patients in the early stages of rehabilitation (up to 1 month after COVID-19) than in the later period. The level of sIgA in the oral fluid remains elevated for a long time after treatment with COVID-19, then decreases, but may increase

with an increase in the duration of the course of the onset of the OM disease. All this determines the special tasks of dental care for patients in the post-COVID period.

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Резюме.

Воздействие SARS-CoV-2 на весь организм человека вызывает необратимые изменения во всех органах и системах. Осложнения в виде хронических заболеваний нуждаются в лечении клиницистов различных областей медицины. Стоматологи сталкиваются с заболеваниями слизистой оболочки полости рта у практически здоровых пациентов, не предрасположенных к ним, но перенесших COVID-19.

Цель исследования. Оценить влияние перенесенной коронавирусной инфекции (COVID-19) на течение заболеваний слизистой оболочки рта.

Обследованы 51 больных в возрасте от 20 до 75 лет, перенесших COVID-19, с различными заболеваниями слизистой оболочки рта. В исследовании использовались клинические и лабораторные методы. Выявлены особенности клинического течения отдельных заболеваний слизистой оболочки рта, определена динамика местной иммунной защиты полости рта в постковидный период.