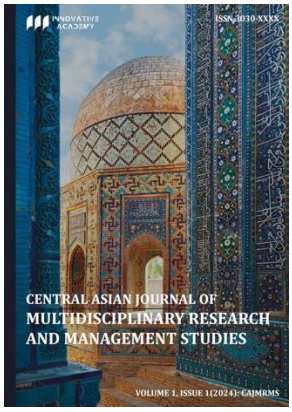

MANIFESTATION OF THE ORAL MUCOSA IN COVID-19

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ABSTRACT

The oral cavity is one of the main gates for coronavirus (SARS-CoV-2); the oral cavity also suffers greatly from this infection, because it is one of the most vulnerable places. In addition, since the salivary glands can serve as a reservoir for viruses and support their release into the external environment, it was concluded that saliva, as a component of oral fluid, can play an important role in the spread of coronavirus infection. This is mainly due to the ACE-2 receptor, which have a high level of expression in the keratinized surface epithelial cells of the oral mucosa, especially in the epithelial cells of the dorsal part of the tongue, tonsils, vocal cords, salivary glands and sinuses, due to which the virus replicates in and causes both oral lesions and oral symptoms mouth After entering the cell, the virus delays the response of the immune system, allowing the infection to progress, and it becomes much more difficult to fight it. Accordingly, due to the relatively high level of COVID-19-associated complications, timely diagnosis of clinical forms, including high-risk patients with prognosis their clinical course and the selection of drug treatment appropriate to the severity of the clinical course remain quite complex and controversial issues. It was emphasized that in some cases oral symptoms may be the initial or only sign of disease, and dentists should take this into account when performing a thorough clinical examination of the oral cavity.

To date, a new strain of COVID-19 has been identified - omicron, which was first identified in South Africa in November 2021, according to WHO, and has been associated with an increase in regional infections. This strain contains more than 30 mutations in the spike protein, which contributed to increased transmissibility compared to previous variants (alpha, beta, gamma, delta), which is confirmed by detection in more than 30 countries of the world and reduced

susceptibility to neutralizing antibodies, including therapeutic monoclonal antibodies [5]. Given the ongoing trend of strain modification, COVID-19 represents an unprecedented, serious medical and social problem for all of humanity that is far from being solved.

Given the continuing trend of strain modification, COVID-19 represents an unprecedented medical and social problem for everyone, which is far from being resolved [3.4].

To date, it has been established that age over 65 years [10], male gender [3], cardiovascular disease [3], diabetes mellitus [7], obesity [3], chronic obstructive bronchitis [7], smoking, lack of oral hygiene [3], tumor disease [11], liver disease [6], opportunistic infections, stress [5], immunosuppression, vasculitis and hyperinflammatory response caused by COVID-19 are predisposing factors for the occurrence of oral lesions in patients in this category [11]. COVID-19 causes a range of oral manifestations, ranging from dry mouth to opportunistic infections. It was emphasized that in some cases oral symptoms may be the initial or only sign of disease, and dentists should take this into account when performing a thorough clinical examination of the oral cavity. Oral ulcers caused by stress may be on the rise among patients due to pandemic-related fears. Also, older age and higher severity of COVID-19 disease are associated with severe damage to the oral cavity [1,2,7]. Moreover, the oral mucosa is very intensively supplied with blood, has a relatively large surface area and is a convenient entry point for penetration and infections into the body, and also serves as a site of colonization and infection by potentially pathogenic microorganisms in the event of infection and weakening of natural immunity. The body's defenses are determined by general and local factors. Local protection is provided by the integrity of the oral mucosa, the microbicidal properties of saliva and lymphoid tissue. The integrity of the oral mucosa is the best physiological barrier to infection. The protective factors of saliva are determined not only by its mechanical properties, but also depend on the biological compounds dissolved in it, which can cause lysis of foreign cells. These substances include lysozyme, which has a bactericidal effect. In addition, saliva contains polymorphonuclear neutrophils, which have high bactericidal activity. Finally, secretory immunoglobulin A (IgA), contained in saliva, is a powerful factor of local protection.

PURPOSE OF THE STUDY

Study of morphological changes in the oral mucosa and taste sensitivity in patients with COVID-19 of varying severity. To draw the attention of doctors to oral manifestations in patients who have had COVID-19, with the aim of an etiopathogenetic approach to the treatment of pathologies of the oral mucosa.

MATERIAL AND METHODS

There were 105 patients under observation (a total of 254 patients), of whom 62 were men and 43 women, aged from 18 to 55 years (average age 41.6±4.7 years). 149 patients were excluded from the study, since 3 of them were under 18 years of age, and 7 were over 55 years of age, 15 were smokers, 30 were severely obese, 1 patient was pregnant, 87 patients had concomitant diseases, 6 refused to provide consent to fill out the questionnaire . All patients had a positive polymerase chain reaction test result for COVID-19. The study design was a cross-sectional questionnaire-based study. This survey contains the following demographic information:

gender, age, weight, height, education level and general health. The questionnaire was divided into two parts:

1) The first part includes the results of an oral hygiene assessment obtained by a group of dentists.

The second part contains data on the severity of COVID-19, which was obtained through a telephone call

All patients underwent a daily visual examination of the oral cavity, registration and assessment of the characteristics of the clinical course of the disease, the severity of temperature, and symptoms of intoxication.

RESEARCH RESULTS

During the examination, changes in the oral mucosa were detected in 91 patients (86.6%) (see Table 3.1), which echoes the literature data.

It is worth noting that 13 (12.4%) patients had hemorrhagic manifestations on the buccal mucosa, and the history of this disease was not burdened. In addition , there were pinpoint hemorrhages on the mucous membranes of the lips and cheeks. Cyanosis of the lips was also detected in these patients. The color of the oral mucosa varied from the usual pale pink tint to cyanotic due to the appearance of different levels of vascular pattern on the mucous membrane of the inner surface of the lips.

Pigmentation in the area of gum attachment to the upper and lower jaw was found in 45 (42.8%) patients, while in 5 (4.7%) pigmentation was observed in the area of the hard palate. Also, lentigo, a brown spot caused by the accumulation of melanin, raised above the surface of the mucous membrane of the upper and lower lips, was detected in 13 (12.3%) patients.

Mycological culture analysis was performed in all cases and was positive in 6.6% of patients (n = 7) . Other manifestations of the mucous membrane were aphthous stomatitis in 10.5% of patients (n = 11) and mucositis in 5.7% (n = 6). 8.5% of the patient (n = 7) complained of glossalgia, which consists of a burning sensation of the tongue or the entire oral mucosa.

In addition, the most common manifestation of changes in the mucous membrane of the tongue was pronounced angular cheilitis, consisting of inflammation of the corners of the mouth, characterized by the formation of cracks, crusts and redness of the mucous membrane of this area of the mouth in 26 (24.7%) patients.

Particular attention was drawn to transient U-shaped papillitis , identified in 15 patients (14.3%), while edema of the tongue was detected in 8 patients (7.6%). Inflammatory disease of the tongue, characterized by glossitis with focal depapilation, was observed in 5 patients (4.7%).

Plaque of the mucous membrane of the tongue was detected in 90 patients (85.7%), the color of which varied from white to light cinnamon and brown. At the same time, the plaque was easily removed by scraping, and evenly expressed papillae were noted over the entire surface of the tongue.

Changes in the oral mucosa in hospitalized patients with COVID-19 (n=105)

Types of change	n (%)
Changes in the oral mucosa	91 (86.6)
Plaque of the mucous membrane of the tongue	90 (85.7)
Parageusia	64 (60.9)
Pigmentation in the area of gum attachment to the upper and lower jaw	45 (42.8)
Angular cheilitis	26 (24.7)
U-shaped papillitis	15 (14.3)
Hemorrhagic manifestations on the buccal mucosa	13 (12.4)
Lentigo	13 (12.4)
Aphthous stomatitis	11 (10.5)
Glossalgia	7 (8.5)
Swelling of the tongue	8 (7.6)
Oral candidiasis	7 (6.6)
Mucositis	6 (5.7)
Pigmentation of the hard palate	5 (4.7)
Glossitis with focal depapilation	5 (4.7)
Dysfunction of the olfactory organ	
Parosmia	85 (81)

Anosmia	11 (10.5)

Perversion of taste sensitivity, the appearance of taste sensations in the absence of a corresponding stimulus - parageusia was determined in 60.9% of patients (n = 64), which was often combined with complaints of distorted perception of smells - parosmia in 81% of patients (n = 85) after 5 days of observation. In addition, 10.5% (n = 11) of patients had a lack of smell perception - anosmia.

According to the results of a questionnaire survey of data on the initial state of the oral cavity, 84 (80%) patients had a severe severity of COVID -19, while a mild severity was found in 21 patients (20%)

Correlation between oral health and severity of COVID-19 (n=105)

Oral health status		**Severity of COVID -19**		***R***
		Severe degree	**Lightweight degree**	
Bad condition	n	62	1	<0.001
	%	73.8%	4.7%	
Satisfactory	n	17	17	
	%	20.2%	80.9%	
good	n	5	3	
	%	5.9%	14.2%	
General indicator	n (%)	84 (80%)	21 (20%)	

According to the analysis, severe COVID-19 shows a statistically significant association with poor oral health ($p < 0.001$). Accordingly, patients with good oral health were found to have a significantly lower incidence of severe COVID-19 disease.

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The relationship between the clinical course of morbidity and the initial state of oral health in the first and second weeks of observation

$p<0.001$

Analysis of subgroups according to the severity of COVID-19 showed that patients with initial good, satisfactory, and poor oral hygiene conditions had a mild course in 79.4%, 17.4%, 3.2% of cases in the first week of observation, respectively. Patients with initial good, satisfactory, and poor oral hygiene conditions developed a severe course in 9.1%, 25.7%, 65.2% of cases in the first week of observation, respectively.

In the second week of observation, in the group of patients who had an initial poor state of oral hygiene, the deterioration was significantly higher in 73.8% of cases than in patients with a good initial state of oral hygiene (5.9%) ($p<0.001$). Also, patients with a satisfactory initial state of oral hygiene experienced a deterioration in the clinical course in the second week in 20.3% of cases, which is significantly lower than in patients with an initial poor state of oral hygiene ($p < 0.001$). Accordingly, in the second week of hospitalization, a mild course of the disease was observed in patients with good, fair and poor oral health in 80.9%, 14.4% and 4.7% of cases.

Clinical recovery at weeks four and six of clinical follow-up was significantly more common in COVID-19 patients with poor baseline oral health (41.2% and 48.4%, respectively) compared with patients with good baseline oral health (8 .9% and 5.3%, respectively) ($p<0.001$). The period of rapid recovery (at the 2nd week of observation) was significantly more often observed in COVID-19 patients with initial good oral health (85.8%) according to compared with baseline poor oral health (10.4%) ($p<0.001$).

Clinical recovery of patients with a satisfactory state of oral health was noted before two weeks of clinical observation in 56.8% of cases, compared with four weeks (33.4%) and six weeks (9.8%) observations of patients in this category.

Secondary endpoint study. The relationship between the initial state of oral health and the period of clinical recovery. **$p <0.001$

It is worth noting that a negative correlation was established between the initial state of oral health and the period of clinical recovery of patients with COVID-19 ($p <0.001$, $r = -0.614$)

Correlation between the initial state of the oral cavity and the period of clinical recovery (n=105)

Parameter		Clinical recovery period
Initial oral health status	*r*	-0.614
	P	0.001
	n	105

Impact of COVID-19 severity on clinical recovery (n=105)

Secondary study endpoint			Severity of COVID -19		*R*
			Severe degree	**Lightweight degree**	
Clinical recovery period	6 weeks	n	42	2	<0.001
		%	50.0%	9.5%	
	4 weeks	n	35	4	
		%	41.6%	19.0%	
	2 weeks	n	7	15	
		%	8.3%	71.2%	
General indicator		n (%)	84 (80%)	21 (20%)	

The rate of delayed clinical recovery in the sixth week of clinical follow-up was significantly higher in the group of severe patients with COVID-19 (50.0%) compared to the group of patients with mild clinical course (9.5%).

Clinical recovery in the second week of observation was observed 7 times more often in the group of COVID-19 patients with a clinically mild course (71.2%) compared to the group of

patients with a severe course (8.3%) (p <0.001), when in the fourth week week of observation in the group of COVID-19 patients with a mild clinical course, clinical recovery was found in 19.0% of cases, and in the group of patients with a severe course this figure was 41.6% (p <0.001).

CONCLUSION.

A high level of damage to the oral mucosa was detected in 91 (86.6%) patients. 13 (12.4%) patients had hemorrhagic manifestations on the buccal mucosa, and the history of this disease was not burdened. There were also pinpoint hemorrhages on the mucous membranes of the lips and cheeks, and cyanosis of the lips. The color of the oral mucosa varied from the usual pale pink tint to cyanotic due to the appearance of different levels of vascular pattern on the mucous membrane of the inner surface of the lips. Pigmentation in the area of gum attachment to the upper and lower jaw was found in 45 (42.8%) patients, in 5 (4.7%) patients pigmentation was observed in the area of the hard palate. Lentigo, a brown spot resulting from the accumulation of melanin, rising above the surface of the mucous membrane of the upper and lower lips, was present in 13 (12.3%) patients. Mycological culture analysis was positive in 7 (6.6%) patients. Other mucosal manifestations were aphthous stomatitis (10.5%) and mucositis (5.7%). 8.5% of the patient complained of glossalgia, which consists of a burning sensation of the tongue or the entire oral mucosa. In addition, the most common manifestation of changes in the mucous membrane of the tongue was pronounced angular cheilitis, consisting of inflammation of the corners of the mouth, characterized by the formation of cracks, crusts and redness of the mucous membrane of this area of the mouth in 26 (24.7%) patients. Particular attention was drawn to transient U-shaped papillitis, detected in 15 (14.3%) patients, while 8 (7.6%) had swelling of the tongue. Inflammatory disease of the tongue, characterized by glossitis with focal depapilation, was observed in 5 (4.7%). Plaque on the mucous membrane of the tongue, the color of which varied from white to light cinnamon and brown, was diagnosed in 90 (85.7%). The plaque was easily removed by scraping. Papillae of uniform severity were also noted over the entire surface of the tongue. Perversion of taste sensitivity, the appearance of taste sensations in the absence of a corresponding stimulus - parageusia - was determined in 60.9% of patients. Often this symptom was combined with complaints of distorted perception of odors - parosmia - in 81% of patients. In addition, 10.5% of patients had no perception of smell - anosmia.

CONCLUSIONS.

1. A high level of manifestation in the form of damage to the oral mucosa (oral manifestation) indicates the highest expression of ACE-2 receptors in the oral cavity, which requires special attention in organizing dental treatment and preventive consultations with patients.

2. Active treatment of oral diseases and compliance with all clinical recommendations developed by the European Federation of Periodontology helps prevent the oral-vascular-pulmonary spread of the COVID-19 virus.

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