



Antiviral Factors of Local Oral Immunity in Patients with Covid-19, Depending on the Course of this Disease

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Abstract: Relevance. Recently, there has been a global pandemic burden due to the transmission of a new coronavirus disease - COVID-19. Since the outbreak in December 2019, COVID-19 has affected more than a dozen million people. According to a study by the World Health Organization, most cases of COVID-19 among people are mild (80%), 20% of infected patients may develop a serious illness. According to some authors, 5% may develop a serious illness and pneumonia, or acute respiratory distress syndrome. In turn, pneumonia associated with lung damage is the main clinical and pathological manifestation of COVID-19. Pneumonia varies from mild to severe, and pathological manifestations range from minor serous exudate to pulmonary edema and diffuse alveolar lesion, which requires the speedy solution of such social, physiological and psychological problems. Instead, the defeat of the SOPR in this infection.

The purpose of the study. To study and evaluate the adaptive mechanism of local immunity in the oral mucosa in severe coronavirus infection (COVID-19), depending on the clinical and immunological features of the course of the disease.

The clinical material for this dissertation work was collected at the hospital No. 2 of the Tashkent district of the Tashkent region, intended for the treatment of patients with COVID-19. Immunological studies were performed at the Institute of Human Immunology and Genomics of the Academy of Sciences of the Republic of Uzbekistan.

A step-by-step examination of patients was carried out to complete the tasks. These include the study of the state of COPD in patients with moderate to severe COVID-19 and the control group without COVID-19.

The examined patients, depending on the severity of COVID-19, were divided into 3 groups:

Group 1 - moderate degree of COVID-19 (n=53);

Group 2 - severe COVID-19, (n=43);

Group 3 - healthy, without COVID-19 (control group, n=22).

The analysis of the sexual characteristics of the examined patients showed: men -57 (48.3%) and women 61 (51.7%) (P>0.05).

In group 1, men were 24 (45.3%), and women 29 (54.7%), in group 2, respectively, men 23 (53.5%) and women 20 (46.5%); in group 3, men made up 10 (45.4%), and women 12 (54.5%).

Immunological studies to determine IFN- α and IFN- γ , IL-1 β cytokines, TNF- α , as well as the immunobiological marker – sIgA in oral fluid were carried out using the ELISA method. The study of the level of proinflammatory and anti-inflammatory cytokines TNF- α , IL-6 and interferons, IFN-

α , IFN- γ of blood serum was carried out by the ELISA method. In both cases, commercial test systems of Vector-Best LLC (Novosibirsk, Russia) were used. The test systems are based on the sandwich method of solid-phase ELISA using horseradish peroxidase as an indicator enzyme. The sensitivity of the method when using these test systems is 2-30 pg/ml [1.3.5.7.9.11.13.15].

The data obtained during the study were statistically processed on a Windows 10 PC using built-in statistical processing functions, including office software. The research materials were subjected to statistical processing using parametric and nonparametric analysis methods. Accumulation, correction, systematization of initial information and visualization of the results were carried out in Microsoft Office Excel 2010 spreadsheets. Statistical analysis was carried out using the IBM SPSS Statistics v.23 (IBM Corporation) program.

The following tasks were set for the implementation of this work: the study of the CPI index, the GI index, the PMA index, the state of COPD with moderate and severe COVID-19 and the control group without COVID-19.

The CPI index was the highest in the 2nd group of patients aged 61-70 years (24 ± 0.41) with a severe degree of COVID-19. In the control and in the 1st group with a moderate degree of COVID-19 at the age of 61-70 years, this indicator was the same (20 ± 1.93) and (20 ± 1.93).

Oral hygiene in both groups with COVID-19 is shown in Table 1, where it is indicated that it was unsatisfactory. At the same time, an abundant amount of soft plaque, supra- and subgingival tartar was observed. It can be assumed that the development of poor oral hygiene is a violation of the balance of oral microorganisms.

Table 1 Indicators of the hygienic index in patients with moderate and severe COVID-19 and healthy individuals, $M \pm m$

Age of patients	GI					
	1-group, n=53		2- group, n =43		3- group, n =22	
	n	M \pm m	n	M \pm m	n	M \pm m
up to 40 years old	19	3,20 \pm 0,04*	3	3,60 \pm 0,10** x	2	1,29 \pm 0,34
41-50	18	3,30 \pm 0,15*	6	3,80 \pm 0,24** x	4	1,39 \pm 0,31
51-60	15	3,50 \pm 0,15**	7	4,50 \pm 0,38** x	8	1,42 \pm 0,37
61-70	1	3,60 \pm 0,20**	27	4,90 \pm 0,19** x	8	1,70 \pm 0,29
Total	53	3,33 \pm 0,07**	43	3,79 \pm 0,78** x	22	1,46 \pm 0,18

Note: * - reliability of differences in relation to control (* - $P < 0.05$; ** - $P < 0.001$); x - reliability of differences between moderate and severe COVID-19.

The assessment of the GI index was very poor in patients of group 2 with severe COVID-19 at the age of 51-60 years (4.5 ± 0.38) and 61-70 years (4.90 ± 0.19). In patients of group 1 with moderate COVID-19, this indicator was high at the age of 51-60 years (3.5 ± 0.15) and 61-70 years (3.6 ± 0), and in the control group, the highest rate was also in patients aged 61-70 years, which was (1.7 ± 0.29).

It should be noted that all patients with COVID-19 had periodontal diseases in 100% of cases. Depending on the severity of COVID-19 and the age of the patient, the phenomena of gingivitis and periodontitis were noted.

From the table. 2 It can be seen that the PMA index score was unsatisfactory in group 2 patients with severe COVID-19 aged 51-60 years (62.00 ± 1.73) and 61-70 years (72.00 ± 1.29).

Table 2. PMA index in patients with moderate to severe COVID-19 and healthy individuals, $M \pm m$, %

Age of patients	PMA					
	1- group, n =53		2- group, n =43		3- group, n =22	
	n	M \pm m,%	n	M \pm m,%	n	M \pm m,%
up to 40 years old	19	45,00 \pm 1,05**	3	54,00 \pm 1,73** x	2	25,00 \pm 3,30
41-50	18	50,00 \pm 1,11**	6	60,00 \pm 1,88** x	4	26,75 \pm 1,44

51-60	15	55,00±1,23**	7	62,00±1,73** x	8	29,70±0,54
61-70	1	55,00±0,00**	27	72,00±1,29** x	8	30,00±1,35
Total	53	49,72±6,11**	43	58,7±11,28** x	22	28,84±0,67

Note: * - reliability of differences in relation to control (** - $P < 0.001$); x - reliability of differences between moderate and severe COVID-19.

In group 1 with a moderate degree of COVID-19, this indicator was high and the same at the ages of 51-60 and 61-70 years (55,00±1,23; 55,00±0,00), in patients of the control group, aged 51-60 and 61-70 years, this indicator was good (29,70±0,54; 30±1,35).

Data The indicators are more clearly shown in Fig. 2, where significant differences between the groups of patients and healthy were clearly observed ($P < 0.001$), in addition, significant differences between both groups of patients are visible ($P < 0.001$). Thus, when assessing the CPI index, the CPI index was the highest in patients of the 2nd group of patients aged 61-70 years with severe COVID-19. In the control group and in the 1st group with a moderate degree of COVID-19 at the age of 61-70 years, this indicator was the same. In group 2 patients with severe COVID-19, due to the absence of teeth and wearing prostheses in this group of examined patients, the indicator was high. When determining the hygienic index, the GI index was very poor in group 2 patients with severe COVID-19 aged 51-60 years and 61-70 years. In group 1 patients with moderate COVID-19, this indicator was high at the age of 51-60 years and 61-70 years, and in the control group, the highest indicator was also in patients aged 61-70 years [2.4.6.8.10.12.14.16.18].

When determining the PMA index, the indicator was unsatisfactory in patients of group 2 with severe COVID-19 at the age of 51-60 years and 61-70 years. In group 1 with a moderate degree of COVID-19, this indicator was high and the same at the age of 51-60, 61-70 years, in patients of the control group, aged 51-60 and 61-70 years, this indicator was good, which indicates the absence of an inflammatory process in the control group.

All groups of patients had true physiological and true pathological halitosis. Halitosis in men was less common than in women. Almost every second patient (52%) who were examined noted the appearance of ulcers on the cheeks. At the same time, patients complained of pain during conversation, the act of chewing, swallowing and when eating. Against this background, patients noted a decrease in appetite, loss of body weight, some even refused to eat because of severe pain during meals. (Figures 8 and 9). Table 3.6 shows that in the control group, halitosis at the age of up to 40 years of $n=2$, the occurrence was in 1, in 41-50 years of $n=4$ patients, it was observed in 2. At the age of 51-60 years out of $n=8$, it was 4, in patients aged 61-70 years out of $n=8$ patients, the incidence was also 4. In 1 group of patients with a moderate degree of COVID-19 at the age of 40 years out of $n=19$, the incidence was 4. In patients aged 41-50 years, the incidence of $n=18$ was 8, at the age of 51-60 years from $n=15$, it was 5, and in patients aged 61-70 years from $n=1$ patients, the incidence was 1. In the 2nd group of patients with severe COVID-19 under the age of 40 years of $n=3$ patients, the occurrence was 2, at the age of 41-50 years from $n=6$, the occurrence was 4, in the age group 51-60 from $n=7$, the occurrence was in 6, at the age of 61-70 years from $n=27$, it was 23.

In 1 group of patients with moderate degree of COVID-19, candidiasis was not observed in patients under the age of 40, at the age of 41-50 years, the incidence of $n=18$ was 9, at the age of 51-60 years from $n=15$, it was 5, in patients aged 61-70 years from $n=1$ patients, the incidence was 1. In the 2nd group of patients with severe COVID-19 under the age of 40, out of $n=3$ patients, the occurrence was 1, at the age of 41-50 years out of $n=6$, the occurrence was 5, in the age group 51-60 out of $n=7$, the occurrence was 5, at the age of 61-70 years out of $n=27$, was 20.

Oral signs and symptoms associated with COVID-19 are known to include taste disorders, non-specific mouth ulcers, desquamative gingivitis, petechiae and coinfections such as candidiasis and many others. In this regard, the purpose of this work was to evaluate the study of violations of adaptive local immunity of the oral cavity in COVID-19 patients, as well as to assess the state of systemic immunity with the study of the main pro-inflammatory and anti-inflammatory blood cytokines.

It is known that the key mechanism of COVID-19 progression is immunological mechanisms, which occupy one of the primary places in the course and progression of COVID-19. Thus, the immune system of the mucous membrane is the largest component of the entire immune system, which has evolved to protect the main sites of the infectious threat: the mucous membranes [17.19.21.22.23].

First, the result of a study of violations of the adaptive mechanisms of local immunity of the oral cavity in persons with moderate and severe COVID-19 will be presented. Thus, the concentrations of humoral factors of local immunity in the oral fluid were studied. SIDA has been studied, which plays an important protective function in the cascade development of anti-infective protection and may partially determine the effectiveness of the final, effector reactions of humoral local immunity for inactivation and elimination of viral antigens.

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Conclusion.

1. Clinical examination of the oral cavity revealed that the CPI index score was highest in 3 groups of patients aged 61-70 years (24 ± 0.41) with severe COVID-19. The assessment of the hygiene index was very low in the 3rd group of patients with severe COVID-19 at the age of 51-60 years (4.5 ± 0.38) and 61-70 years (4.90 ± 0.19). When determining the PMA index, the indicator was also unsatisfactory in group 3 patients with severe COVID-19 aged 51-60 years (62.00 ± 1.73) and 61-70 years (72.00 ± 1.29).
2. It is shown from the SOPR studies that halitosis was not observed in the control group. A large percentage of the occurrence of halitosis 53.49%, candidiasis 46.5%, petechiae 44.19%, HRAS 62.79% and xerostomia 58.14% was at the age of 61-70 years also in the group with severe COVID-19. In the 2nd group of patients with moderate COVID-19 in the age index of 41-50 years, the incidence of halitosis was 5.79% higher than in the 3rd group. At the age of 41-50 and 51-60 years, the percentage of HRAS was high in the 2nd group of patients (16.98%).

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