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TISSUE DENTAL STATUS AND FEATURES OF PERIODONTAL MICROCIRCULATION IN PATIENTS WITH NEW COVID-19 CORONAVIRUS INFECTION

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ABSTRACT

Severe hemostatic disorders against the background of COVID-19 have a significant effect on the state of dental status. The study aimed to improve the effectiveness of dental care for patients with COVID-19 disease. To study the dental status of patients with COVID-19 undergoing inpatient treatment, to compare the change in saliva pH with the results of SARS-CoV-2 detection in paired nasopharyngeal smears and saliva samples, to study the microcirculation and oxygenation level of periodontal tissues in patients with moderate and severe COVID-19 undergoing inpatient treatment. 194 people were examined, including 112 patients with the new COVID 19 coronavirus infection and 82 comparison group without concomitant pathology. All patients are divided into five age groups according to their recommendations. The complex of examination included assessment of dental status, determination of saliva pH, the study of microcirculation and oxygenation in the periodontium, and on the phalanx of the index finger of the right hand. Analysis of the results of the study shows that when assessing the dental status, the most characteristic complaints were dryness of the oral cavity, ageusia or hypogeusia, anosmia, or hyposmia. Gum bleeding was observed in two older age groups: in patients aged 45-54 years in 20% of cases, in 55-64 years -18.5% of cases. Less than a quarter of the patients complained of hypersensitivity of the teeth. The study of the saliva pH level revealed normal indicators of the acid-base balance of the oral cavity, which did not depend on the results of the PCR test for COVID-19.

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Introduction

Outbreaks of infectious diseases always attract a lot of attention, often paralyzing the work of doctors and forcing science to move forward. All viral infections are also found in the oral cavity [1-4]. The disease caused by the SARS-CoV-2 beta-coronavirus was named COVID-19 and rapidly spread around the world in 2020 [5-9]. Researchers from all over the world have focused all their efforts on studying the course of the disease and developing methods for the treatment of a new infectious disease [10-13]. The main clinical manifestations of COVID-19 are fever, myalgia, cough, shortness of breath, rarely headache, diarrhea, nausea, and vomiting [14-21]. In patients with a severe course, the leading symptom at the beginning of the disease is respiratory failure, which can then progress to multiple organ failure. In prognostic terms, one of the most unfavorable signs is the development of coagulopathies [22-28].

Against the background of viral infection, an immune complex "antigen-antibody" is formed, which leads to damage to the capillary endothelium. At the same time, this process is generalized. The developed septic coagulopathy is accompanied by a rapid release of pro-inflammatory cytokines and activation of the blood clotting system, which leads to the development of disseminated intravascular coagulation (DIC) syndrome [29-33]. In the case of COVID-19 infection, as well as with other infections, DIC syndrome is mainly inflammatory and manifests itself in the form of a systemic inflammatory response

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syndrome. The process of diffuse hemocoagulation is accompanied by the formation of fibrin clots and microthrombs, the occurrence of many hemorrhages with a pronounced violation of microcirculation processes [34-38].
Prevention of infection with the virus in dental practice is very important. This helps to avoid not only fever but also many other dangerous infections [39].
Rapid and accurate diagnostic testing for COVID-19 is essential for monitoring the ongoing pandemic. Currently, the “gold standard” for diagnosing a new coronavirus infection is the detection of SARS-CoV-2 using real-time polymerase chain reaction (RT-PCR) in nasopharyngeal smears. However, the low sensitivity of this test, the risks associated with direct contact of health care provider and patient, lack of nasopharyngeal swabs, and personal protective equipment (PPE) require new diagnostic approaches [40].
The above-mentioned factors of hemostatic disorders cannot but affect the patient's dental status [41-43]. At the same time, there are no publications in the available literature devoted to the study of microcirculation and oxygenation of periodontal tissues in patients with a new coronavirus infection [44].
All this determined the aim and objectives of this study. The study aimed to improve the effectiveness of dental care for patients who have suffered from the disease COVID-19. To reach the aim we worked with main tasks:

– to study the dental status of patients with COVID-19 who are undergoing inpatient treatment;
– to compare the change in saliva pH with the results of SARS-CoV-2 detection in paired nasopharyngeal smears and saliva samples;
– to study the microcirculation and oxygenation level of periodontal tissues in patients with moderate to severe COVID-19 who are undergoing inpatient treatment.

Materials and Methods

We examined 194 people, including 112 patients with a new coronavirus infection COVID-19 and 82 comparison group without concomitant pathology. All patients were divided into five age groups according to who recommendations **(Table 1)**: five COVID groups and five control groups. A study of patients diagnosed with COVID-19 was conducted in a hospital-based on State Budgetary Healthcare Institution “Republican Clinical Hospital for Emergency Medicine” of the Ministry of Health of the Republic of North Ossetia-Alania and State Budgetary Healthcare Institution “Republican Clinical Hospital” of the Ministry of Health of the Republic of North Ossetia-Alania. The condition of the examined patients was assessed as severe or moderate.

Table 1. Age and gender composition of examined people.

Age, years	Patients with COVID-19		Healthy persons	
	Men	Women	Men	Women
18	11	9	9	7
20-24	10	10	8	9
35-44	8	12	8	8
45-54	12	13	7	9
55-64	14	13	8	9

The survey of patients with a new coronavirus infection included a questionnaire to determine the prevalence of:

1. Clinical symptoms of COVID 19, such as hyperthermia, shortness of breath, cough, weakness, myalgia, sore throat, rhinorrhea, nasal congestion, anosmia, hyposmia;
2. Comorbidities;
3. Complaints of pain and burning in various parts of the oral mucosa, dental hyperesthesia, ageusia, dysgeusia, hypo- and hypersalivation, halitosis.

All the subjects were examined for determining the pH of saliva, studying the features of microcirculation and the level of oxygenation in the periodontium and on the phalanx of the index finger of the right hand.

The parameters of microcirculation in periodontal tissues were determined by the laser Doppler flowmetry (LDF) method using a laser analyzer of capillary blood flow LAKK-M (NPP "LAZMA", Russia) equipped with a red and green laser with a wavelength of 0.65 microns and 0.53 microns, and also, a laser output power of at least 0.3 mW. The device is approved for use, registration certificate № 07442-FSR 2010/07442 dated 22-04-2010 (indefinite) and Russian certificate of conformity № ROSS RU. IM02.V11221.
The multifunctional laser diagnostic complex LAKK-M provides simultaneous measurements of tissue perfusion with blood, hemoglobin saturation with oxygen (SO2) in the probed area of the study. Perfusion is estimated by LDF, and SO2 is calculated using the absorption spectroscopy methodology. SO2 is determined based on the different optical properties of the oxygenated (HbO2) and deoxygenated (Hb) hemoglobin fractions contained in the tested volume of blood in the biotissue. To estimate SO2 parameters, we use the difference in recorded signals when probing biotissue in the red and green spectral ranges of wavelengths.

Results and Discussion

Analysis of the data obtained revealed certain patterns. Among all the surveyed patients admitted to the hospital, concomitant diseases were observed in 32.1% of cases, including 10% of patients aged 18 years, 56 % in 45-64 years, and 74.1% in 55-64 years. The structure of General diseases was dominated by hypertension (22.3%), type 2 diabetes (19.4%), and coronary heart disease (16.7%). In 19.4% of cases, there was a combination of hypertension and coronary heart disease. Less frequently, patients examined in the hospital were found to have concomitant diseases such as cholecystitis (5.5%), polyarthritis (5.5%), and others (11.1%). The structure of comorbidities in patients with COVID 19 is shown in **Table 2**.

Table 2. Structure of comorbidities in patients with COVID 19.

Concomitant disease	Type 2 diabetes	Coronary heart disease	Hypertensive disease	Coronary heart disease + hypertension	Polyarthritis	Cholecystitis	Other diseases
The frequency of pathology,%	19,4	16,7	22,3	19,4	5,5	5,5	11,1

All patients were admitted to the hospital with hyperthermia of 38.5°C and higher, and the saturation level was below 90%. At the time of the survey, average body temperature was higher in the two older age groups, peaking at 38.5°C in the fourth COVID group. Cough complaints were noted by the vast majority of those examined with a new coronavirus infection. At the same time, dry cough was more often noted: the first COVID group - 80% of patients, the second-75%, the third-95%, the fourth-84%, the fifth-66.6%. Only 12% of patients in the fourth and 18.5% of patients in the fifth COVID groups complained of a wet cough **(Table 3)**.

Table 3. The results of the questionnaire in patients COVID-19 in the hospital

Age, years	Concomitant disease	Average body temperature, ºC (M±m)	Cough			Rhinorrhea, %	Violation of nasal breathing,%	Sore throat, %	Pershenie, %
			dry,%	wet%	none,%				
18	10	37,5±0,1	80	0	20	30	50	30	60
20-24	0	37,8±0,2	75	0	25	0	45	10	50
35-44	0	37,2±0,1	95	0	5	0	55	15	55
45-54	56	38,5±0,1	84	12	4	20	52	36	52
55-64	74,1	38,3±0,2	66,6	18,5	14,9	44,4	59,2	51,8	51,8

The results of the study indicate that rhinorrhea is not the leading clinical symptom of new coronavirus infection. So, in the first COVID group, the runny nose was observed in 30% of patients. In the second and third groups, it did not occur, in the fourth and fifth groups – in 20% and 44.4%, respectively. At the same time, about half of those examined in the COVID groups complained of nasal breathing disorders: the first-50%, the second-45%, the third-55%, the fourth-52%, and the fifth-59.2% **(Table 3)**.

In all age groups with COVID, there was a symptom of sore throat, but its prevalence was not high: in the first – 30%, in the second-10%, in the third-15%, in the fourth-36%, in the fifth – 51.8% of the examined. The sore throat was observed in a larger number of patients with COVID-19. Its prevalence was slightly more than half of the examined patients in each group of the examined **(Table 3)**.

Shortness of breath in patients with a new coronavirus infection COVID-19 on average appeared on day 8 of the disease but was not observed in all the examined patients. At the same time, shortness of breath at rest was observed only in 33.3% of patients over 65 years of age. In two younger age groups, no one complained of shortness of breath when walking, in the third-30%, in the fourth - 32%, in the fifth – 44.4% of the surveyed. Shortness of breath with more pronounced physical activity was observed in 30% of the subjects in the three younger age COVID groups, 44% in the fourth, and 22.3% in the fifth group **(Table 4)**.

Table 4. The results of the questionnaire in patients COVID-19 in the hospital

Age, years	Dyspnea,%				Sweating, %	Weakness, %	Dizziness, %	Pain, %	Changing of stool nature,%	
	none	At rest	At walking	Under load					diarrhea	constipation
18	70	0	0	30	15	80	15	55	35	0
20-24	70	0	0	30	25	90	10	50	25	0
35-44	40	0	30	30	25	100	10	65	10	0
45-54	24	0	32	44	48	100	30	72	0	12
55-64	0	33,3	44,4	22,3	51,8	92,3	40,1	77,8	25,9	31,7

The prevalence of sweating symptoms was 15% in the first COVID group, 25% in the second and third groups, 48% in the fourth group, and 51.8% in the fifth group.

Almost all patients with diagnosed COVID-19 infection had a General weakness: in the first group, 80% of the examined patients, in the second – 90%, in the third and fourth groups – all, in the fifth – 92.3%. A small number of patients complained of dizziness **(Table 4)**. Pain of various localization, mostly of moderate-intensity was noted by a large number of patients with COVID (the first group – 55%, the second - 50%, the third - 65%, the fourth – 72%, the fifth - 77.8%). At the same time, myalgia was most often observed - 35.6% in the structure of pathology in all patients.

Complaints from the gastrointestinal tract consisted mainly in the presence of loose stools (35% - I gr., 25% - II gr., 10% - III gr., 25.9% - V gr.). Constipation was observed only in 12% of patients aged 45-54 years and 37.1% - in the 55-64 year group.

One of the main symptoms was the loss of smell. Thus, in all age groups, anosmia occurred in more than half of the patients (70% - I gr., 65% - II gr., 65% - III gr., 64% - IV gr., 66.7% - V gr.).

The assessment of dental status in a hospital was carried out in a limited format, due to the lack of necessary conditions for a full-fledged examination **(Table 5)**. The results allowed us to draw certain conclusions. In all groups of patients with a new coronavirus infection, there was a symptom of partial or complete loss of taste, but its frequency was slightly lower than the symptom of anosmia (50% - I gr., 40% - II gr., 40% - III gr., 56% - IV gr., 55.5% - V gr.). The nature of salivation in several patients was pathological. Hyposalivation was observed with the following frequency: the first age group- 40%, the second - 50%, the third - 50%, the fourth - 64%, the fifth - 77.8%. Gum bleeding was observed only in two older age groups: in patients aged 45-54 years in 20% of cases, in 55-64 years -18.5% of cases. Patients did not complain of burning and paresthesia of the oral mucosa except for 28% of those examined in the IV age COVID group. The number of patients had increased sensitivity of hard dental tissues, the prevalence of which was lower in older age groups (25% - I gr., 25% - II gr., 20% - III gr., 16% - IV gr., 11.1% - V gr.). None of the examined patients had any pathological changes in the oral mucosa. Bad breath was observed in 8 % of patients aged 45-54 years and 11.1 % - in 55-64 years.

Table 5. The dental status of patients with the new COVID-19 coronavirus infection.

Age, years	Loss of smell,%	Loss of taste,%	Dryness in the mouth,%	Bleeding gums,%	Burning and paresthesia of the oral mucosa,%	Hypersensitivity of the teeth,%	Pathological changes in the mucous membrane of the oral cavity, %	Halitosis, %
18	70	50	40	0	0	25	0	0
20-24	65	40	50	0	0	25	0	0
35-44	65	40	50	0	0	20	0	0
45-54	64	56	64	20	28	16	0	8
55-64	66,7	55,5	77,8	18,5	0	11,1	0	11,1

The results of the study revealed normal values of the acid-base balance in the oral cavity, regardless of the presence of a positive or negative PCR test for the presence of a new coronavirus infection **(Table 6)**.

Table 6. State of acid-base balance in patients COVID-19 PCR + and PCR –

Index	Age, years				
	18	20-24	35-44	45-54	55- 64
the pH of saliva at COVID +	6,4	6,5	6,1	6,5	6,6
the pH of saliva at COVID –	6,3	6,5	6,0	6,4	6,7

Significant hemostatic disorders characteristic of the new COVID-19 coronavirus infection certainly have an impact on the condition of periodontal tissues. Analysis of the results of laser Doppler flowmetry in COVID and control groups revealed certain features of microcirculation. The integral index of microcirculation in the periodontium and on the phalanx of the finger in patients with COVID-19 was significantly lower than in patients of the control groups. The value of this indicator on the finger in comparison with periodontal disease was slightly reduced both in the COVID groups and in the control group. According to LDF data, periodontal the microcirculation index increased slightly with age in both patients with COVID-19 and controls. All of the above indicates a violation of perfusion of periodontal tissues with blood in patients with a new coronavirus infection. Analysis of microcirculation on the phalanx of the finger showed lower indicators, which may be due to the initially better vascularization of periodontal tissues. It is difficult to explain the periodoxic increase in the microcirculation index in the periodontium with age, but this phenomenon may be associated with the presence of venous congestion and an increase in the number of red blood cells per unit volume of the studied tissues.

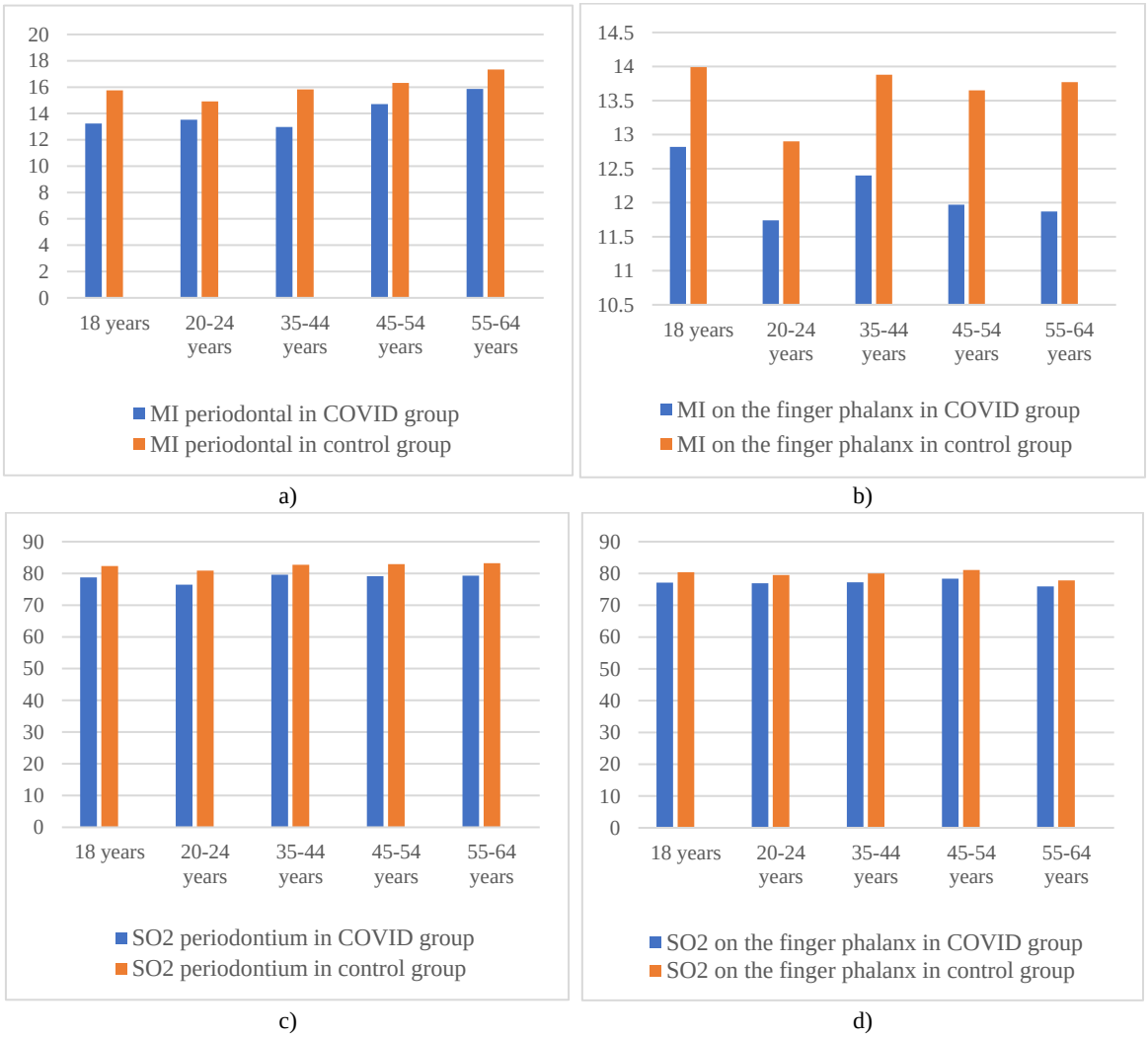

Figure 1. Results of study: a) Periodontal microcirculation index (MI) according to LDF data in patients with COVID-19 and healthy individuals; b) Microcirculation index (MI) on the finger phalanx according to LDF data in patients with COVID and the control group; c) Level of hemoglobin oxygen saturation (SO2) in the periodontium in patients with COVID-19 and control groups; d) Level of hemoglobin oxygen saturation (SO2) on the finger phalanx in patients with COVID-19 and control groups.

The capabilities of the lack-M device allow us to evaluate the hemoglobin saturation with oxygen in the studied tissues. Thus, in patients with COVID-19 in comparison with the control in all age groups, the level of saturation in both the periodontium and the phalanx of the finger were lower. At the same time, the values of the indicator did not have age dynamics. Tissue saturation on the finger phalanx was lower than in periodontal disease in all groups of patients.

Analysis of the results of the study allows us to judge certain patterns in the clinical symptoms of new coronavirus infection, including those inherent in dental pathology. We were not able to detect changes in the oral mucosa in the form of hemorrhagic rashes, despite the presence of several publications from our colleagues with information about similar symptoms in patients with COVID-19.

According to the data obtained, complaints of General weakness and dry cough, which were noted by the vast majority of the examined patients, play a leading role in the structure of General symptoms. More than half of the patients complained of difficulty in nasal breathing, the pain of various localization, more often myalgia, and a feeling of tickling in the throat. The prevalence of symptoms such as sweating, sore throat, and dizziness increased with age and occurred in about half of patients with COVID-19 aged 55-64 years. Less than a third had a stool disorder in the form of diarrhea. The prevalence of concomitant diseases increased with age, which was observed in 74% of patients aged 54-65 years. Rhinorrhea was not the most common clinical sign, but it occurred in a third of patients in the first COVID group and almost half of the fifth. The increase in body temperature was inherent in almost all patients. Its average values at the time of the survey increased with age from 37.2-37.8 in the first three age groups to 38.5 and 38.3 in the fourth and fifth, respectively.

When assessing the dental status, the most characteristic complaints were dry mouth, ageusia or hypogeusia, ANO-or hyposmia. However, these symptoms were not typical for all patients with COVID-19. Gum bleeding was observed in two older age groups: in patients aged 45-54 years in 20% of cases, in 55-64 years -18.5% of cases. Less than a quarter of patients complained of dental hyperesthesia, the prevalence of which decreased with age, which can be explained, perhaps,

by the deposition of replacement dentin in the dental pulp in older patients. The study of the saliva pH level revealed normal indicators of the acid-base balance of the oral cavity, which did not depend on the results of the PCR test for COVID-19. Studies of blood flow characteristics have revealed severe violations of blood supply to periodontal tissues in patients with COVID, which is confirmed by a decrease in the microcirculation index in all age groups. The detected changes in blood flow are confirmed by the obtained indicators of hemoglobin oxygen saturation (SO2), which were also significantly lower in patients with a new coronavirus infection.

Conclusion

Given the currently available data on severe violations in the hemostatic system in patients with a new coronavirus infection COVID-19, the data obtained during our study on the state of microcirculation and oxygenation of periodontal tissues are of great practical importance. The revealed changes in the microcirculatory bed cannot but affect the further functioning of periodontal tissues with the development of numerous complications. Thus, the results of the study revealed several completely new and significant factors in the pathogenesis of dental pathology. This suggests a high risk of developing pathological processes in the periodontal and other organs of the oral cavity in patients with COVID-19 in the near and long term, which dictates the need to develop preventive measures aimed at preventing them.

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