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ABSTRACT

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THE IMPACT OF COVID-19 ON ORAL FLUID PROPERTIES: MINERAL POTENTIAL AND ANTIMICROBIAL ACTIVITY IN THE CONTEXT OF DENTAL CARIES RISK

Introduction. Numerous scientific papers have emphasised that COVID-19 should not be considered solely as an acute respiratory viral infection, as this disease can affect not only the respiratory system but also other organs and systems, exerting a complex effect on health and well-being, including the salivary glands and saliva. Considering that teeth are constantly bathed in saliva, the composition and properties of this oral fluid play a significant role in the onset and progression of dental caries, which created the prerequisites for our study.

The purpose of the current study was to evaluate the impact of COVID-19 on the properties of oral fluid – particularly mineral potential and antimicrobial activity – in order to substantiate the risk of dental caries.

Materials and Methods. In accordance with the aims and objectives of the study, 110 patients aged 18 to 35 years were examined and divided into two groups: patients with a history of COVID-19 confirmed by polymerase chain reaction (PCR) test (2 to 6 months prior) and conditionally healthy individuals. The first group was further divided into three subgroups according to the severity of COVID-19, classified by the WHO: mild, moderate, and severe. The objectives were to determine the mineral potential and antimicrobial activity of the oral fluid.

Results. The observed changes in the concentration of calcium-phosphate compounds indicated an imbalance in the mineral metabolism of the oral fluid. The concentrations of calcium and phosphorus were directly associated with disease severity, decreasing progressively from the first to the third subgroup. The lowest values of calcium and phosphorus were recorded in patients of the third subgroup, measuring 1.08±0.034 mmol/L and 2.09±0.074 mmol/L, respectively, with a significant reduction in alkaline phosphatase activity (28.26±4.70 U/L) in this subgroup.

The assessment of the antimicrobial activity of oral fluid revealed that microbial contamination of the oral cavity increased among patients with COVID-19. A pattern similar to that observed for mineral potential was noted in the third subgroup with severe disease, where urease activity was 0.148±0.013 U/mL and lysozyme activity was 77±11 µg/mL. As a result, the dysbiosis index significantly deviated from the normal value of 1, reaching 4.78±0.5, which, based on the interpretation, corresponded to a clinically subcompensated stage.

Conclusions. Based on the conducted studies, it should be noted that patients with a history of COVID-19 are more susceptible to dental hard tissue caries due to a reduction in the natural protective and restorative mechanisms of enamel crystal structure.

Keywords: caries, COVID-19, lysozyme, urease, calcium, phosphorus, demineralisation.

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ВПЛИВ COVID-19 НА ВЛАСТИВОСТІ РОТОВОЇ РІДИНИ: МІНЕРАЛЬНИЙ ПОТЕНЦІАЛ ТА АНТИМІКРОБНА АКТИВНІСТЬ У КОНТЕКСТІ РИЗИКУ РОЗВИТКУ КАРІЄСУ ЗУБІВ

Вступ. На сьогодні численні наукові дослідження підкреслюють, що COVID-19 не можна розглядати лише як гостру респіраторну вірусну інфекцію, оскільки це захворювання здатне уражувати не тільки дихальну систему, а й інші органи та системи, комплексно впливаючи на здоров'я та самопочуття, включно зі слинними залозами та слиною зокрема. Зважаючи на те, що зуби постійно омиваються слиною, склад і властивості цієї ротової рідини відіграють значну роль у виникненні та прогресуванні карієсу зубів, що й створило передумови до проведення нашого дослідження.

Мета справжнього дослідження полягала в оцінці впливу COVID-19 на властивості ротової рідини, зокрема показники мінерального потенціалу та антимікробної активності, задля доведення ризику розвитку карієсу зубів.

Матеріали та методи дослідження. Згідно з метою та завданнями дослідження було проведено обстеження 110 пацієнтів віком від 18 до 35 років, що були розподілені на 2 групи: пацієнти, яким був встановлений діагноз COVID-19 тестом полімеразної ланцюгової реакції (ПЛР-тест) в анамнезі (від 2 до 6 місяців тому), а також умовно-здорові особи. Перша група була розподілена на три підгрупи згідно зі ступенями тяжкості перенесеного захворювання на COVID-19 відповідно до класифікації ВООЗ – легкий ступінь, середній та тяжкий. Були поставлені наступні завдання: визначити мінеральний потенціал та антимікробну активність ротової рідини.

Результати дослідження. Отримані зміни в концентрації кальцій-фосфатних сполук дозволили встановити порушення рівноваги мінерального обміну ротової рідини. Концентрації кальцію та фосфору перебували в прямій залежності від ступеня тяжкості захворювання та знижувалися від першої підгрупи до третьої. Найнижче значення кальцію та фосфору було зафіксовано

у пацієнтів третьої підгрупи та становило 1,08±0,034 та 2,09±0,074 відповідно, при цьому додатково слід звернути увагу на значне зменшення активності лужної фосфатази в цій підгрупі досліджених – 28,26±4,70. Оцінка антимікробної активності ротової рідини дозволила зробити висновки щодо збільшення рівня мікробного обсіменіння ротової порожнини серед пацієнтів, які перехворіли на COVID-19, при цьому аналогічні закономірності, притаманні дослідженню мінерального потенціалу, спостерігалися у третій підгрупі з тяжким ступенем захворювання, де значення уреази становило 0,148±0,013, а лізоциму – 77±11. Як наслідок, індекс ступеня дисбіозу значно відрізнявся від встановлених нормою значення 1, та дорівнював 4,78±0,5, що за інтерпретацією результатів відповідало клінічно субкомпенсованій стадії.

Висновки. На підставі проведених досліджень слід зазначити, що пацієнти, які мали випадок COVID-19 в анамнезі, більш схильні до ураження твердих тканин зубів каріозним процесом через зниження природних механізмів захисту та відновлення кристалічної структури емалі.

Ключові слова: карієс, COVID-19, лізоцим, уреаза, кальцій, фосфор, демінералізація.

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ABBREVIATIONS

COVID-19 – coronavirus disease
PCR – polymerase chain reaction
SARS-CoV-2 – severe acute respiratory syndrome coronavirus 2

INTRODUCTION / ВСТУП

The oral cavity is a complex ecological system, the health of which depends entirely on the interaction of external (social, individual, biological) and internal factors (condition of the mucous membrane, periodontal tissues, composition of bacterial microflora, activity of the local immune system, biochemical and biophysical parameters of saliva) [1]. The WHO Global Report, published in 2024, presented alarming statistics on oral health, pointing to 3–5 billion disease cases worldwide [2]. The Global Burden of Disease research program estimates that about two billion people suffer from untreated permanent tooth decay, making it the most common dental disease [3].

The new coronavirus (SARS-CoV-2), detected in China at the end of 2019, has caused a worldwide pandemic. This virus causes acute respiratory syndrome (COVID-19), which is characterized by potentially fatal interstitial bilateral pneumonia [4, 5].

Numerous scientific studies have emphasized that COVID-19 cannot be considered only an acute respiratory viral infection. Regardless of the presence or extent of lung damage, the SARS-CoV-2 virus can affect other organs and systems [6, 7].

Based on the analysis of the information studied, it can be concluded that coronavirus disease is a multifaceted problem. Its impact extends to the respiratory system and covers a much wider range of lesions, including salivary glands and saliva. Saliva plays a key role in maintaining the homeostasis of the oral cavity and maintaining the balance between the demineralization and remineralization processes, which is extremely important for enamel's high structural and functional resistance.

Considering that teeth are constantly washed with saliva, the composition and properties of this oral fluid play a significant role in the onset and progression of dental caries. Various inorganic (water and electrolytes) and organic (proteins and peptides) components can protect teeth from caries [8]. This protective effect is achieved through several functions, such as clearing food and sugar residues, aggregating and eliminating microorganisms, buffering acids,

maintaining supersaturation of tooth minerals, forming the acquired pellicle, and providing antimicrobial protection [9].

The search for molecular indicators of the impact of the new coronavirus disease on oral fluid will allow us to examine this infection from the depths of fundamental biochemical processes and, based on this approach, to identify the most accurate and comprehensive diagnostic criteria that will allow us to optimize the prevention and treatment of caries.

The objective of the paper was to assess the impact of COVID-19 on the properties of oral fluid, in particular mineral potential and antimicrobial activity, in order to prove the risk of dental caries.

MATERIALS AND METHODS

In accordance with the aim and objectives of the study, a total of 110 patients aged 18 to 35 years who sought dental care at the Department of Dentistry, Kharkiv National Medical University, were examined. The patients were divided into two groups: those with a history of COVID-19 confirmed by a polymerase chain reaction (PCR) test 2 to 6 months prior to the study and a control group of conditionally healthy individuals.

The first group was further subdivided into three subgroups based on the severity of COVID-19 according to the WHO classification: mild, moderate, and severe.

The assessment of the mineral potential of oral fluid included the following parameters: calcium (measured by reaction with arsenazo III), phosphorus (measured by reaction with molybdate), and alkaline phosphatase (analyzed using a colorimetric method with a diethanolamine buffer).

The evaluation of antimicrobial activity involved the assessment of lysozyme levels (determined by spectrophotometry according to A.P. Levitsky's modification, based on the measurement of changes in optical density due to the lysis of Micrococcus lysodeikticus cells by lysozyme), urease activity (measured by determining ammonia concentration using Nessler's reagent), and the dysbiosis index (calculated as the ratio of specific urease activity in oral fluid to the specific activity of lysozyme).

Statistical analysis was performed using the Statgraphics Centurion XVI software package, with the calculation of the mean value and its standard error ($M \pm m$). The statistical significance of differences between the obtained data was assessed using the Student's t-test (at a significance level of $p \leq 0.05$).

Calcium and phosphorus are essential components for maintaining strong and healthy teeth, as their presence in saliva and plaque plays a crucial role in the processes of demineralization and remineralization. It has been demonstrated that the levels of calcium and phosphorus in saliva and plaque are inversely proportional to the incidence of caries, with high concentrations of calcium in saliva providing a protective effect against caries [10, 11]. Our study revealed a significant decrease in the mineral potential of saliva, with a marked decrease in the indicators corresponding to the severity of COVID-19 (Table 1).

Table 1 – Indicators of Mineral Metabolism in Oral Fluid among the Examined Patients

Study Parameters	Main Group			Control Group (n = 20)
	Mild Form (n = 26)	Moderate Form (n = 42)	Severe Form (n = 22)	
Total Ca, mmol/l	1.42±0.049*	1.23±0.044*	1.08±0.034*	1.88±0.054
P (inorganic), mmol/l	2.63±0.109*	2.24±0.057*	2.09±0.074*	3.95±0.212
Alkaline phosphatase, U/l	63.25±4.52**	45.32±3.45*	28.26±4.70*	75.15±5.75

Notes:

*1. * – statistical significance of the difference in the studied indicators compared to the control group of healthy individuals. *p < 0.001*

*2.** – statistical significance of the difference in the studied indicators compared to the control group of healthy individuals. *p < 0.05*

The data presented in the table show that the observed changes in the concentration of calcium-phosphorus compounds indicate an imbalance in the mineral metabolism of the oral fluid. This imbalance may serve as an additional factor contributing to the development of a cariogenic environment in the oral cavity. Furthermore, the reduced concentration of alkaline phosphatase negatively impacts the mineralization process, rendering enamel less resistant to acids, thereby increasing the risk of caries,

particularly in individuals with other risk factors, such as poor oral hygiene, inadequate nutrition, or conditions leading to decreased enamel mineralization.

Given that dental caries is a prevalent disease caused by specific bacteria, primarily *Streptococcus mutans*, the activity of oral defense mechanisms is crucial for preventing carious lesions [12]. As a cationic protein, lysozyme facilitates bacterial aggregation and adhesion, and activates bacterial autolysins that degrade bacterial cell walls [13]. It is important to note that a decrease in the immunological and antimicrobial properties of oral fluid leads to an increase in the concentration of urease, which correlates with the excessive growth of opportunistic microflora [14], since urease is not produced by somatic cells but is synthesized by opportunistic and pathogenic bacteria.

The results of the relevant studies are presented in Table 2.

Table 2 – Urease and Lysozyme Activity, and Degree of Dysbiosis in Oral Fluid among the Examined Patients

Study Parameters	Main Group			Control Group (n = 20)
	Mild Form (n = 26)	Moderate Form (n = 42)	Severe Form (n = 22)	
Lysozyme Activity, U/ml	110±10***	89±12**	77±11*	137±8
Urease Activity, μkat/l	0.096±0.011*	0.131±0.012*	0.148±0.013*	0.055±0.002
Degree of Dysbiosis, U	2.17±0.3*	3.66±0.2*	4.78±0.5*	1±0.01

Notes:

*1. * – statistical significance of the difference in the studied indicators compared to the control group of healthy individuals. *p < 0.001*

*2.** – statistical significance of the difference in the studied indicators compared to the control group of healthy individuals. *p < 0.01*

*3.*** – statistical significance of the difference in the studied indicators compared to the control group of healthy individuals. *p < 0.05*

As shown by the data in the table, urease activity in patients with COVID-19 was higher than in the group of conditionally healthy individuals, indicating an increase in microbial contamination of the oral cavity. Notably, lysozyme activity was reduced in patients with a history of COVID-19.

A typical consequence of increased urease activity and decreased lysozyme activity was an elevated degree of dysbiosis. This suggests a disruption in the balance of the normal microbiota, likely due to a deficiency in local nonspecific immunity.

Based on the aforementioned findings, the following **conclusions** were drawn:

1. The systematization of the results obtained from the examined patients revealed higher mean urease activity in the first group compared to the second group, indicating increased microbial colonization, as reflected in the dysbiosis index.

2. Patients with COVID-19 also exhibited reduced lysozyme activity, confirming the impairment of local nonspecific oral immunity.

3. The assessment of the mineral metabolism of oral fluid revealed significant differences in the concentrations of key inorganic components, particularly calcium and phosphorus, as well as the activity of mineral homeostasis regulators such as alkaline phosphatase, especially in the context of severe COVID-19, which may contribute to the development of a cariogenic situation and subsequent enamel demineralization.

PROSPECTS FOR FUTURE RESEARCH / ПЕРСПЕКТИВИ ПОДАЛЬШИХ ДОСЛІДЖЕНЬ

The results obtained in this study should be considered when planning treatment and preventive measures for patients with COVID-19, who represent a special group with an increased risk of caries development. A deeper understanding of the onset and progression of hard tissue damage could provide a basis for the development of more effective treatment methods, which represents a key direction for further research.

AUTHOR CONTRIBUTIONS / ВКЛАД АВТОРІВ

Diasamidze ME – writing the manuscript, conception and design of the study, interpretation of the results. Diasamidze ED – data collection and curation, manuscript revision.

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None.

CONFLICT OF INTEREST / КОНФЛІКТ ІНТЕРЕСІВ

The authors declare no conflict of interest.

COMPLIANCE WITH ETHICAL STANDARDS / ВІДПОВІДНІСТЬ ЕТИЧНИМ СТАНДАРТАМ

The publication of the study data was conducted in accordance with the principles of the Declaration of Helsinki. The study was approved by the Ethics and Bioethics Committee of Kharkiv National Medical University, Protocol No. 8, dated 06.10.2021.

ARTIFICIAL INTELLIGENCE DISCLOSURE / ВИКОРИСТАННЯ ШТУЧНОГО ІНТЕЛЕКТУ

The authors confirm that no artificial intelligence-based technologies were utilized in the writing or editing of the manuscript.

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