

# Functional State of Local Immune Status in the Inflammatory Process in the Upper Respiratory Tract in Patients Infected with COVID-19

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**Abstract** In the period from 2020-2021, we examined COVID-19 infected 53 patients who applied to the infectious diseases department of the Bukhara Regional Infectious Diseases Medical Center. Of these, 32 people suffered from acute rhinosinusitis and 21 people-acute purulent tonsillitis. All patients underwent a standard examination: clarification of complaints and anamnestic data. Examination of the upper respiratory tract organs was carried out according to the generally accepted scheme. We also studied the indicators of local immunity of the mucous membranes of the upper respiratory tract using immunohistochemical studies with antibodies to T-helper lymphocytes (CD4 +), suppressor T-lymphocytes (CD8 +) and B-lymphocytes (CD20) in patients of different groups. Indicators of local immunity of the mucous membrane of the nasal cavity and pharynx in the first two weeks of the acute process correspond to an adequate response of local immunity to an infectious agent; the third week is characterized by an imbalance of local immune protection, which indicates a high activity of the inflammatory process, which is a milestone in the course of the disease.

**Keywords** Acute rhinosinusitis, Acute tonsillitis, T-lymphocytes, B-lymphocytes

## 1. Relevance

The body's defenses are determined by systemic and local factors. Local protection is provided by the integrity of the mucous membrane of the VDP (upper respiratory tract) of the oral cavity, the microbicidal properties of saliva and lymphoid tissue. The integrity of the VDP mucosa is the best physiological barrier to infection. The protective factors of a tear are determined not only by its mechanical properties, but also depend on the biological substances dissolved in it that can cause the lysis of foreign agents.

Such substances include lysozyme, immunoglobulin A, and a large number of interleukins with bactericidal and antiviral effects. A powerful factor of local protection is the secretory IgA contained in saliva. [1,2,5,8,9]. Nonspecific immunity of the VDP mucosa is provided by cellular elements - neutrophils and macrophages, as well as secretory elements - various chemotaxis factors for inflammatory agents (interleukins, leukotrienes, etc.) Specific immunity is provided by lymphoid tissue contained in a significant amount around the oral cavity - in the form of diffuse infiltration or in the form of nodular clusters devoid of a closed connective tissue case. The cells providing specific

immunity are T-lymphocytes and plasmocytes [3,4].

In most cases, non-specific and specific immune protective factors neutralize bacteria and viruses. However, microorganisms often overcome these barriers, penetrate into the internal environment of the body and cause disease. This is facilitated by the weakening of local immunity, in particular against the background of COVID-19 [2,6,7,10].

In this regard, **the purpose** of this research work was to study the local immunity of the VDP mucosa in patients with different duration of the inflammatory process in the VDP.

## 2. Materials and Methods

The methodology of the work is based on a systematic and comprehensive data analysis.

In the period from 2020-2021, we examined COVID-19 infected 53 patients who applied to the infectious diseases department of the Bukhara Regional Infectious Diseases Medical Center. Of these, 32 people suffered from acute rhinosinusitis and 21 people-acute purulent tonsillitis.

All patients underwent a standard examination: clarification of complaints and anamnestic data. Examination of the upper respiratory tract organs was carried out according to the generally accepted scheme. We also studied the indicators of local immunity of the mucous membranes of the upper respiratory tract using immunohistochemical studies with antibodies to T-helper lymphocytes (CD4 +), suppressor T-lymphocytes (CD8 +) and B-lymphocytes

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(CD20) in patients of different groups.

Indicators of local immunity of the mucous membrane of the nasal cavity and pharynx in the first two weeks of the acute process correspond to an adequate response of local immunity to an infectious agent; the third week is characterized by an imbalance of local immune protection, which indicates a high activity of the inflammatory process, which is a milestone in the course of the disease. Among the examined patients there were 19 (35.8%) men and 34 (64.1%) women aged 25 to 45 years. The duration of the disease ranged from 2 days to 2 years or more.

Group 1 (5 patients 9.4%) – 1st week of the disease; group 2 (6 patients; 11.3%) - 2nd week of the disease; group 3 (6 patients; 11.3%) – 3rd week of the disease; group 4 (4 patients; 7.5%) – the 4th week of the disease; group 5 (32 children; 60.4%) - patients with a disease duration of 6 months or more. All patients underwent a standard examination: clarification of complaints and anamnestic data. The inspection of the organs of the VDP was carried out according to the generally accepted scheme. Statistical data analysis was performed using Microsoft Excel 2010 and STATISTICA 10.0.

We also studied the indicators of local immunity of the mucous membranes of the VDP using immunohistochemical studies with antibodies to helper T-lymphocytes (CD4+), suppressor T-lymphocytes (CD8+) and B-lymphocytes (CD20) in patients of different groups. Analyzing the data obtained, it can be stated that in the 1st group of patients (1st week of the disease), there was a tendency for a slight increase in CD8 + T-suppressor lymphocytes ( $17.0 \pm 4.9$ ) and B-lymphocytes (CD20) ( $2.6 \pm 1.9$ ), with simultaneously unchanged CD4 + T-lymphocytes-helper cells ( $32.4 \pm 12.9$ ), which is associated with an adequate response of local immunity to a foreign agent.

The ratio of CD4+ T helper lymphocytes to CD8+ T suppressor lymphocytes in patients of this group reflects the normal state of local immune protection. In the 2nd group of children (2nd week of the disease) in comparison with the 1st group, the indicators of CD4+ T-helper lymphocytes ( $32.4 \pm 12.9$  and  $31.7 \pm 8.1$ ) remain at the same level as a week ago, while a significant increase in the indicators of CD8 + T-suppressor lymphocytes ( $17.0 \pm 4.9$  and  $31.4 \pm 9.2$ ,  $p < 0.05$ ). B-lymphocytes (CD20) ( $2.6 \pm 1.9$  and  $12.4 \pm 7.3$ ,  $p < 0.05$ ) tend to moderate growth compared to the previous period of the disease. During this period, the ratio of CD4 + T-helper lymphocytes to CD8 + T-suppressor lymphocytes tends to 1, which indicates a severe course of the inflammatory process and a high activity of the immune system aimed at combating a foreign agent.

Changes in the local immunity of the mucous membrane of the middle ear in the third group of children (3rd week of the disease) in comparison with the 2nd group are characterized by the fact that the indicators responsible for the development of acute inflammation, namely the indicators of CD4 + T-helper lymphocytes ( $31.7 \pm 8.1$  and  $18.9 \pm 9.2$ ;  $p < 0.05$ ) and CD8+ T-suppressor lymphocytes ( $31.4 \pm 9.2$  and  $10.3 \pm 6.5$ ;  $p < 0.05$ ) decrease, and the index of

B-lymphocytes (CD20) ( $12.4 \pm 7.3$  and  $11.7 \pm 14.6$ ) remains approximately at the same level as a week ago. When analyzing the ratio of CD4+ T-helper lymphocytes to CD8+T-suppressor lymphocytes, a sharp increase was revealed, almost corresponding to the level of this indicator at the 1st week of the disease, i.e. the normal state of local immune protection.

Thus, at this time there is a clear imbalance in the local immune defense, indicating, most likely, a great activity of the inflammatory process and being a turning point throughout the disease, leading in the future, in the absence of adequate, timely treatment, in the conditions of bacterial superinfection, to the transformation of the acute inflammatory process into a persistent, irreversible chronic, the inflammatory process.

In the 4th group of children (4th week of the disease), in comparison with the 3rd group, an interesting trend of changes in all indicators responsible for local immunity is revealed. Indicators of both T-lymphocytes (CD4+ T-helper lymphocytes ( $18.9 \pm 9.2$  and  $151.3 \pm 14.9$ ,  $p < 0.05$ ), CD8+ T-suppressor lymphocytes ( $10.3 \pm 6.5$  and  $107.1 \pm 27.1$ ,  $p < 0.05$ ), and B-lymphocytes (CD20) ( $11.7 \pm 14.6$  and  $126.1 \pm 42.3$ ;  $p < 0.05$ ) increase sharply at this time.

At the same time, the ratio of CD4+ T-helper lymphocytes to CD8+ T-suppressor lymphocytes is again lower than the values indicating the normal state of local immune protection, which indicates a severe course of the inflammatory process on the one hand, and on the other hand, the available reserve in local immune protection. In children of the 5th group with a disease duration of 6 months or more in comparison with the 4th group, signs of suppression of the immune response were revealed, as indicated by an increase in B-lymphocytes (CD20) ( $126.0 \pm 42.3$  and  $214.4 \pm 114.4$ ,  $p < 0.05$ ).

The existing excess of T-lymphocytes (CD4+ T-helper lymphocytes, CD8+ T-suppressor lymphocytes) and B-lymphocytes (CD20) compared with the onset of the disease indicates that, despite the prescription of the process and the presence of subjective signs of remission, the inflammatory process is not completed and, apparently, the disease acquires the features of an autoimmune pathology.

Confirmation of the above is the approximation of the ratio of CD4+ T-helper lymphocytes to CD8+ T-suppressor lymphocytes to an indicator corresponding to hyperactivity.

Thus, the indicators of local immunity of the mucous membrane of the upper respiratory tract in the first two weeks of ORS and OT correspond to an adequate response of local immunity to an infectious agent; the third week is characterized by an imbalance in local immune protection (indicators of CD4 T-lymphocytes-helper and CD8 T-lymphocytes -suppressors decrease by 40.4% and 67.2%, respectively, and the indicator of B-lymphocytes (CD20) remains approximately at the same level), which indicates a large activity of the inflammatory process, which is a milestone stage during the disease.

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## Conflicts of Interest

The authors have no conflicts of interest.

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