



## CYTOKINE PROFILE OF BLOOD PLASMA AND ORAL FLUID IN PREGNANT WOMEN WITH ODONTOGENIC INFLAMMATORY DISEASES

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**ABSTRACT:** *This article is devoted to the study of the cytokine profile of blood serum and oral fluid, as well as the level of mucosal immunity in pregnant women with odontogenic inflammatory diseases of the maxillofacial region.*

*It was revealed that a comprehensive assessment of the condition of pregnant women indicates a combined effect of adverse factors on the oral cavity tissues, namely: a low level of oral hygiene, a decrease in the functional activity of the salivary glands, accompanied by a change in the properties of the secretion, in particular, the surface tension of saliva; suppression of local mucosal immunity of the mouth; increased degree of microbial contamination.*

**Keywords:** *odontogenic inflammatory diseases, cytokine profile, pregnant women, blood plasma*

### I. Introduction

Most of the odontogenic diseases of pregnant women, leading to intrauterine infection of the fetus, are subclinical, which makes diagnosis of this pathology in the antenatal period very difficult. Published statistics show that 27 to 36% of births, including more than 2/3 of premature babies, are intrauterine infected. In the neonatal mortality structure, infectious pathology is the leading cause, accounting for 11-45% of stillbirths[3, 5]. The incidence of spontaneous miscarriage and premature birth increases in pregnant women as a result of odontogenic infection. Specific therapy to eliminate the pathogen from the body is often ineffective or of temporary effect, resulting in 30-50% recurrence of the disease. [1, 5, 7]. The inflammatory genesis of non-pregnancy is due to the nature of the penetration of micro-organisms through the placenta to the foetus from the mother's blood. The presence of micro-organisms in the mother may be asymptomatic or accompanied by characteristic signs of inflammatory disease. Often the pathogen, passing through the placenta, causes the placenta to develop with certain histopathological changes. [8].

Any disruption of the body's internal environment, irrespective of the nature, timing and strength of the damaging agent, is an extreme situation for the immune system. When the constancy of the internal environment is disturbed, the scenario of immunological events will be roughly the same, whether it is a small cut on the skin or a massive trauma. The same types of immune system cells will be involved in the healing process, the same mediators synthesized by these cells will be approximately the same stages of the unfolding of protective reactions. The intensity of the defence reactions and the rate of their unfolding will be determined by the strength and duration of the damaging agent. An exception to this pattern is damage to the body that results in shock reactions.

**Objective of the study.** To investigate the cytokine profile of blood plasma and oral fluid in pregnant women with odontogenic inflammatory diseases of the oral cavity.

## II. Material and methods of investigation.

Sixty-five pregnant women with purulent inflammatory diseases of the craniofacial cavity were examined in the VHS department of the TSSI clinic. The mean age of the patients was 22-45 years.

Concentration of interleukin 1, interleukin 2 (IL-2), interleukin 6 (IL-6), and interleukin 8 (IL-8) in oral fluid was determined by enzyme immunoassay using test system "Interleukin-2 "Vector-Best" (Russia). The quantitative content of defensins in saliva was determined by "sandwich" method by enzyme immunoassay using commercial test-system of Nu Cult biotechnology b.v. in accordance with the manufacturer's instructions.

Statistical data processing was performed on a personal computer using the programs developed in the EXCEL package with the use of the library of statistical functions. Significance of differences in parameter values was determined by Student's t-test.

## III. Results of the study:

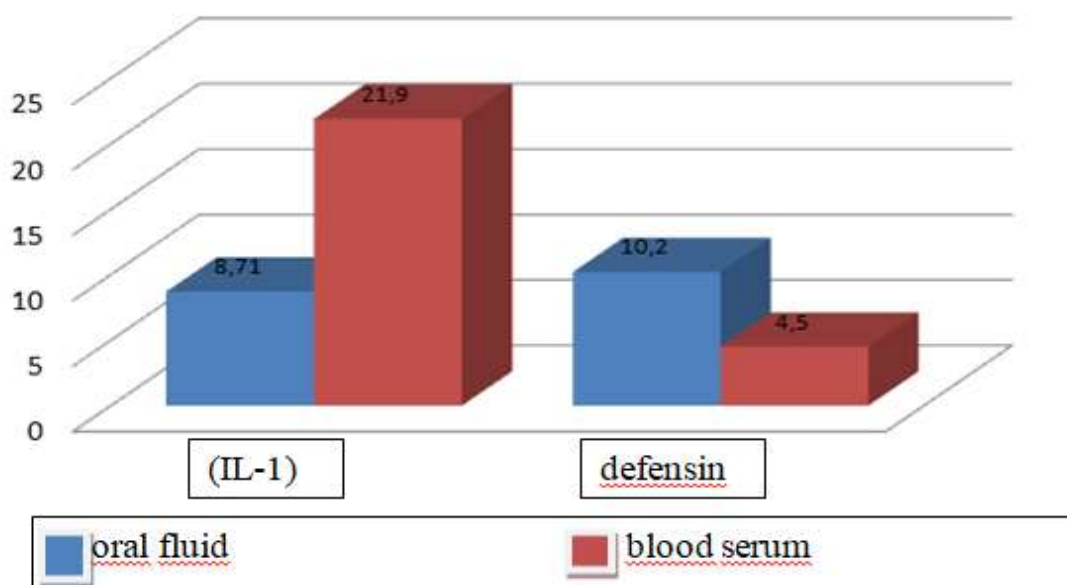
It is known that determination of alarmins as endogenous activators of innate immunity is more appropriate, as it will combine all substances stimulating various parts of the immune system.

In this connection, a complex of techniques has been developed to determine the content of the following alarmins in human biological fluids: interleukin-1B and defensins to assess the state of the mucosal barrier in inflammatory diseases in the oral cavity [4].a-Defensins form a large family of low molecular weight (4-kd), cysteine-rich, cationic antimicrobial peptides that are capable of killing a wide range of pathogens, including a variety of bacteria, fungi and also enveloped viruses. The main source of a-defensins in humans is neutrophils. They have also been found in lymphocytes, neutrophils and monocytes. Some free amounts of diphenzine can also be found in the circulating blood. In addition, diphenzines are found in saliva, milk, nasal mucus, tears, semen, urine, sweat and other body fluids, but in varying concentrations. Reduced or absent production, as well as changes in the activity of antimicrobial peptides, leads to increased susceptibility of the macroorganism to microorganisms and the development of disease[2, 6].

In the women examined, the state of the oral defence system was accompanied by significant disturbances in the immune defence mechanisms manifested by local changes in the cytokine profile.

One of the key links in the dysfunction of the oral immune system is the inflammatory mediator interleukin-1 (IL-1). IL-1 stimulates the production of adhesive molecules by endothelial cells, which contributes to the attachment of polymorphonuclear granulocytes and monocytes and the mobilisation of these cells to the site of inflammation. Proinflammatory cytokines (IL-1) stimulate matrix

metalloproteinase production, decrease tissue metalloproteinase inhibitor production, induce the activity of the bone remodelling cytokine system RANKL (Receptor activator of nuclear factor kappa-B ligand) and thus potentiate alveolar bone resorption, and directly activate osteoclasts.



**Fig.1. Cytokine profile of blood plasma and oral fluid in the patients examined**

An imbalance of cytokines in the oral fluid may serve as an additional diagnostic and prognostic marker of the severity of the course of inflammatory periodontal disease.

As can be seen from the results shown in Figure 1, the IL-1 content in blood serum was 2.51 times higher on average than in oral fluid. Similar dynamics was noted in relation to defensin content in the samples studied. So level of defensin in an oral liquid at women raises on 44,1. In general, we see an increase in the content of the studied alarmins in the blood serum and oral liquid of the examined subjects, which indicates the mobilization of pro-inflammatory cytokine and antimicrobial peptide against the background of the stress situation. The role of the mucous membranes in the realisation of immune function is explained by the fact that most of the antigens enter the body by crossing this physiological barrier. This fact seems to explain the importance of the mucous membranes as part of the intraepithelial immune system. As a gateway for antigens, the mucous membranes are defined as a crucial part of the immune system of the body as a whole. From this point of view, oral cavity occupies unique place: on one hand, it is ideal for reproduction of microorganisms, having optimal temperature, pH, humidity and availability of nutrients, which are absent in respiratory, excretory systems, and on the other hand, mucous epithelium of GIT differs from others in acid and alkaline pH, which is detrimental to most microorganisms. It is in these that the microbiocenosis is known to be represented by the greatest number of species. Various immunological indices of oral fluid have been found to be of great importance in the prevention of diseases of the tissues surrounding the tooth. Among them the determination of sIgA occupies a special place. The determination of these indicators allows to judge the state of local defence mechanisms of the oral cavity, and indirectly characterise the state of the immune system as a whole. It has been shown that sIgA levels correlate with the severity of dysbacteriosis. In degree I and II dysbacteriosis, sIgA and IgA levels in the oral fluid are increased

compared to controls. In degree III dysbacteriosis a decrease in sIgA and IgA was observed. IgG concentration increased as the degree of dysbiosis worsened. oralsIgA, a major component of the mucosal barrier, apparently ceases to effectively perform its biological function [4, 8,9]. A decrease in mucosal immunity has been shown to be accompanied by a disruption of the mucosal barrier, a decrease in the concentration of total salivary IgA and the occurrence of sIgA and lactoferrin deficiency in parotid ductal saliva. Although some authors have noted a short-term increase in sIgA, apparently of a compensatory nature. Thus, the state of mucosal immunity is an important indicator characterising oral tissues. Since changes in sIgA levels during inflammation in periodontal tissues, according to many literature data, are similar: sIgA concentration decreases in oral fluid and increases when the inflammatory potential decreases, it seems possible to use this indicator to assess the effectiveness of the therapy. The analysis of the data presented in Table 1 shows that in the women examined the level of mucosal immunity - sIgA decreased by 30%; the level of IL-2 decreased by 12%. The proinflammatory cytokines IL-6, 8 showed a different dynamics: the level of IL-6 was 4.8 times higher and also IL-8 was 15 times higher.

Table 1

**Dynamics of sIgA and oral cytokine levels in pregnant women with odontogenic inflammatory diseases of the humerus**

Indicators	Control n=20	Pregnant women with odontogenic inflammatory diseases of the womb n=65
sIgA (mg/mg-protein)	252,27±14,53	175,58±12,43
IL-2 (pg/ml-protein)	113,86±9,34	100,25±8,67
IL-6 (pg/ml/protein)	310,76±13,78	1498,22±17,23
IL-8 (pg/mg/protein)	368,48±13,62	5609,3±18,72

\*- differences before and after loading  $p < 0.05$

Assessment of oral mucosal immunity shows a marked decrease in sIgA. Decreased levels of IL-2 in oral fluid along with sIgA deficiency can be considered as an unfavourable factor contributing to the formation of chronic inflammatory periodontal diseases with subsequent development of destructive processes in bone tissue. Assessment of the dynamics of values of proinflammatory cytokine IL-6 indicates high activation of macrophage system, which leads to increased synthesis of acute phase reactants, which include C-reactive protein, transferrin, ceruloplasmin.

### Conclusion

Thus, the results of the comprehensive assessment of pregnant women indicate a combined effect of adverse factors on oral tissues, namely: low level of oral hygiene, reduced functional activity of salivary glands, accompanied by changes in secretion properties, particularly saliva surface tension; inhibition of local oral mucosal immunity; increased degree of microbial contamination. A multidisciplinary programme including not only the immunocorrection methods proposed in this paper, but also the optimisation of specialist care in the relevant specialists is needed to address the

rehabilitation of pregnant women with odontogenic inflammatory diseases of the oral cavity with foci of infection in the tissues of the oral cavity.

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