

# COMPENSATOR-ADAPTIVE REACTIONS OF PATIENTS' ORGANISM WITH GNATHIC FORM OF DENTAL OCCLUSION ANOMALIES

Makhmud Z. Dusmukhamedov<sup>1</sup>, Jasur A. Rizaev<sup>2</sup>, Dilshod M. Dusmukhamedov<sup>3\*</sup>,  
Abdug'affor A. Khadjimetov<sup>4</sup>, Abduazim A. Yuldashev<sup>5</sup>

*Declarations of interest: none*

*This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.*

**Abstract--Background.** According to the latest information about the flexibility of patients with congenital anomalies of the dentofacial system has increased. **The aim** of the research was to assess psycho-emotional state, the state of tissue hypoxia and the protective system in patients with gnathic forms of occlusion abnormalities dentition. **Methods and materials.** 67 patients with defects and deformations of jaws participated in this research to investigate psycho-emotional state of the patients. In order to estimate patients' psychological condition we used clinical questionnaire and technique of emotional states self-assessment. To evaluate tissue hypoxia, hypoxemia and protective system condition in patients with gnathic forms of occlusion abnormalities, depending on the type of occlusion anomaly, patients were divided into two groups: 1<sup>st</sup> group included 17 patients with distal occlusion (upper macro-prognathia, lower micro-retrognathia) and 2<sup>nd</sup> group consisted of 38 patients with mesial occlusion (lower macro-prognathia, upper micro-retrognathia). The control group amounted to 8 healthy individuals without occlusion anomalies. **Findings.** Evaluation of HbF levels in combination with clinical data provides much more information about the development of tissue hypoxia and hypoxemia in patients with gnathic forms of occlusion abnormalities. Determination of the level of HbF in patients with denticular gnathic forms of occlusion abnormalities can be used to diagnose chronic tissue hypoxia and supports to clarify the severity of the pathological process, which allows us to predict the progression of the disease and the development of their complications.

**Key words**--gnathic forms of occlusion abnormalities; psycho-emotional state; defects and deformations of jaws; hypoxia; rhinomanometry; orthognathic surgery; total volume flow.

## I. INTRODUCTION

According to the data of domestic and foreign authors, in our time, the reversibility of patients with congenital anomalies of the dentofacial system has increased [1]. An anomaly of occlusion, which is based on abnormal growth of the bones of the facial skeleton, is often accompanied by a violation of facial aesthetics, chewing, breathing and speech. In addition, dentoalveolar anomalies (DAA) cause a person very difficult emotional experiences. The patient suffers

<sup>1</sup>Professor, Department of Pediatric Maxillofacial Surgery, Tashkent State Dental institute, Tashkent, Uzbekistan.

<sup>2</sup>Professor, Rector of the Tashkent State Dental Institute, Tashkent, Uzbekistan

<sup>3</sup>Associate professor, Department of Surgical Dentistry and Dental Implantology, Tashkent State Dental institute, Tashkent, Uzbekistan.

<sup>4</sup>Professor, Department of Biochemistry, Tashkent State Dental institute, Tashkent, Uzbekistan.

<sup>5</sup>Researcher, associate professor, Tashkent State Dental Institute, Tashkent, Uzbekistan (author.uzb@mail.ru).

deformation of the face much harder than the loss of the peripheral part of the body. This causes functional and psychological problems in patients, which leads to social maladaptation [2].

When considering negative factors affecting a person in a modern environment, along with professional, environmental factors, psycho-emotional stresses leading to a violation of the functional state of the body are highlighted. The optimal ratio of homeostatic performance indicators of different functional systems characterizes the state of health; violation of this ratio leads to the development of pathology [3]. The functional state determines the quality of protective and adaptive reactions in case of any negative effects on the body, including during psychoemotional stresses [4].

Recently, the increasing demandingness of patients with AF to the condition not only of the dentofacial system, but also to the overall assessment of functional and aesthetic rehabilitation in the postoperative period, is noteworthy. The presence of a complex complex of pathological symptoms in patients with CFA, in particular, difficulty in the nasal type of breathing, leads to disturbances in the structure of the facial skeleton, and is considered as a cause of mental and physical development disorders. This fact requires predicting the outcome of operations not only taking into account the restoration of occlusion and changing the appearance of patients, but also taking into account the restoration of the function of nasal breathing and aesthetic parameters of the nose [5].

In recent years, scientific and technological progress has contributed to the emergence and development of new methods for studying the respiratory function of the nasal cavity. Their main advantages are non-invasiveness, non-invasiveness, and safety of use. Such methods include acoustic rhinometry and anterior active rhinomanometry [6]. An analysis of scientific research on a statistical assessment of the impact of orthognathic surgery on the size and function of the upper respiratory tract indicates both similar and conflicting data. It should be emphasized that racial features in the structure of the nasal cavity are important [7]. It is known that the normative parameters of the nasal cavity of Asians differ from the nasal cavity of black representatives or Europeans [8]. Therefore, the committee for the standardization of acoustic rhinometry and rhinomanometry [9] recommends that every researcher who deals with the problems of the geometry of the nasal cavity and breathing take into account the local characteristics of the population of the region in which he works. That is why it is important for the researcher to have regulatory data for his region.

It is well known that a developing violation of the biochemical status against the background of malocclusion against the background of a hypoxic state has a significant effect on the course of the pathological process, the development of purulent-inflammatory complications and the outcome of surgical treatment [10]. Numerous studies have shown that HbF has an extremely high ability to bind oxygen and the increased affinity of HbF for oxygen helps the body adapt in conditions of relative hypoxia and provide tissues with sufficient oxygen. An increase in the concentration of fetal hemoglobin (HbF) in red blood cells under various pathological conditions is a consequence of adaptive reactions of the erythron to a state of hypoxia [11]. It is believed that an increase in the HbF level is a biochemical mechanism of long-term adaptation of the body to hypoxia, which is based on the phenomenon of “adaptive stabilization of structures”, which is realized when the genetic apparatus of the cell is activated in response to a change in homeostasis [12]. Therefore, HbF is a marker of tissue hypoxia not only in newborns, but also in various pathologies in humans.

In accordance with modern scientific principles, cytokines are important participants and connecting links of the immune systems, homeostasis and nonspecific resistance in any pathology [13]. Since the production of cytokines is mainly induced in the pathological focus, it is advisable to determine their level in the corresponding tissues or media. In

the CLA clinic, the study of the dynamics of the cytokine status is of great importance. First of all, this concerns the diagnostic significance of the level of cytokines associated with the dynamics of the disease and treatment.

Thus, according to the results of literature analysis over the past 10 years, significant success has been achieved in the diagnosis, preoperative planning and treatment of patients with AF [14], in particular gnathic forms of occlusion abnormalities (GFOA) of the dentition. An analysis of clinical research data from domestic and foreign authors suggests that finding the best treatment algorithm for this category of patients does not lose its relevance to this day [15]. Despite the significant interest in the study of fetal hemoglobin and the content of cytokines in the blood serum and oral fluid in patients with AF, in particular from gnathic forms of occlusion anomalies (GFOA) of the dentition, it remains practically unstudied, which was one of the main reasons for this study.

**Purpose of the study.** To study the psycho-emotional state, the state of tissue hypoxia and the protective system in patients with GFOA dentition.

## II. MATERIALS AND METHODS

The study of the psycho-emotional state was attended by 67 patients with defects and deformations of jaws (DDJ) (Table 1) who were registered in the clinic of the surgical dentists of the Tashkent State Dental Institute from 2009 to 2017.

**Table 1.** The distribution of patients depending on the form of pathology and age

Form of pathology	Gender	Age groups (years)			Total	
		14-19	20-24	25-35		
Congenital DDJ	Male	7	5	1	13	30
	Female	6	9	2	17	
Acquired DDJ	Male	5	8	2	15	37
	Female	8	10	4	22	
TOTAL		26	32	9	67	

To achieve this goal, a survey was conducted using two types of questionnaires:

1) Clinical Questionnaire - to identify and evaluate neurotic conditions. It is used to identify and evaluate neurotic conditions. The test was developed by K.K. Yakhin and D.M. Mendelevich (1978). The test is intended for a qualitative analysis of neurotic manifestations and allows you to identify the main syndromes of neurotic conditions on the following six scales: anxiety, neurotic depression, asthenia, hysterical type of response, depressive - phobic disturbances (obsessions), autonomic disorders. The test subject is asked to evaluate his current condition using a five-point system: 5 points - never had, 4 points - rarely, 3 points - sometimes, 2 points - often, 1 point - constantly or always.

2) The technique of self-assessment of emotional states [16], is used for self-assessment of emotional states and the degree of wakefulness. Measurement in this technique is carried out in a ten-point system. If the total score is from 26 to 40, then the test subject highly assesses his emotional state, if from 15 to 25 points, then the average assessment of his emotional state is low - from 4 to 14 points.

To assess the state of tissue hypoxia, hypoxemia and the state of the protective system in patients with GFOA of the dentition, patients after diagnosis, depending on the type of occlusion anomaly, were divided into the following 2 groups: 1 - group II patients (n=17) [15] - distal occlusion (upper macro-prognathia, lower micro-retrognathia); 2<sup>nd</sup> group (n=38) - patients of class III - mesial occlusion (lower macro-prognathia, upper micro-retrognathia). The control was the results of studies of 8 apparently healthy individuals - without occlusion anomalies, aged 16-30 years.

For an objective assessment of nasal breathing, we used a computer rhinomanometer RINOLAN - an apparatus that allows examinations using the method of anterior active rhinomanometry (AARM). The main quantitative indicators determined during PARM are the total volume flow (TVF) and total resistance to airflow (TR) at a fixed pressure point of 150 Pa/cm<sup>3</sup>/s. These indicators are inversely proportional. To assess the results of AARM, nasal obstruction is divided into 3 degrees: I degree - (700-870 cm<sup>3</sup>/s; II degree - 500-700 cm<sup>3</sup>/s, III degree - less than 500 cm<sup>3</sup>/s [17]. The comparison group consisted of 17 students without pathology of the maxillofacial region and ENT organs.

For biochemical studies, venous blood sampling in patients was performed in the morning on an empty stomach. Blood cells were counted using a SysmexKX-21 hematology analyzer in capillary blood taken from EDTA. Alkaline denaturation of 1.2 M NaOH, salting out with ammonium sulfate, gel filtration on a Sephadex G-25 column (working buffer 0.05 M phosphate buffer solution, pH 7.4) and ion exchange chromatography on DEAE-Sephadex G-50 on 0.01 M Tris-chloride buffer pH 8.1. Quantitative determination of HbF was carried out by agar gel electrophoresis with sodium dodecyl sulfate.

As indicators of the protective system of saliva, we studied: lysozyme, lactoferrin, secretory immunoglobulin A (sIgA) in saliva. The amount of secretory immunoglobulin A, lactoferrin and lysozyme in saliva was determined by the enzyme immunoassay on a COBAS-411 analyzer using HUMAN kits.

The cytokine status in patients with GFOA has been studied in non-stimulated oral fluid (OF) and blood. An admission of breast cancer in each subject was performed in the clinic on an empty stomach from 8 to 9 in the morning. Patients were asked not to carry out procedures that stimulate salivation; previously, patients of all examined groups underwent professional brushing. In the study of the elemental composition, 0.9 ml of breast cancer were taken directly from the oral cavity. Then the mixed saliva was centrifuged for 15 minutes at 8000 rpm. Over the sedimentary part of the NLF, they were poured into plastic tubes and stored at a temperature of 30°C. A study in the blood and oral fluid of pro and anti-inflammatory cytokines (IL-1, IL-2, IL-4, IL-6, IL-8, IL-10 and TNF- $\alpha$ ) was determined by enzyme-linked immunosorbent assay using production test systems CJSC Vector-Best (Novosibirsk, Russia).

Mathematical processing of the results was carried out by the method of parametric statistics on a personal computer using the Statistica 6.0 program and included descriptive statistics, an estimation of the significance of differences by Student and correlation analysis with an assessment of the reliability of correlation coefficients. When assessing the significance of differences, a value of  $p < 0.05$  was used.

Statistical processing of the results was performed using the methods of parametric and nonparametric statistics. Statistical processing of the material was carried out on a computer using the standard software package for applied statistical analysis (Statistica for Windows 6.0). The critical level of reliability of the null statistical hypothesis (the absence of significant differences or factor effects) was taken equal to 0.05.

### III. RESULTS AND DISCUSSION

To date, the importance of psychoemotional stress as a trigger link in a stress response in many diseases is beyond doubt. The presence of psychoemotional stress in young people undergoing prolonged stressful effects can cause many diseases, which are based on psychosomatic mechanisms. According to our results of the questionnaire survey of patients with GFOA according to the questionnaire, a high level of anxiety in 57% of respondents should be noted. Along with anxiety, 68% of patients had psychoemotional disorders manifested by neurotic conditions, in 41% of patients depressive reactions with a tendency to transition to pathological personality development, which affects the whole future life of a person. In 56% of the examined, complaints of nasal breathing disorders, nose deformity were recorded. At the same time, subjective sensations of a violation of nasal breathing were most common in 61% of patients with a mesial bite - group 2. It should be noted that 25% of patients in this group complained of a significant deterioration in nasal breathing, while in the first group, significant deterioration of nasal breathing was observed only in 14% of patients. In our opinion, this is due to narrowing of the bone cavity of the nose, which is most pronounced in patients with mesial occlusion - group 2. Values of the total volume flow of nasal breathing in patients of the control group were significantly higher than in the 1<sup>st</sup> and 2<sup>nd</sup> groups ( $P < 0.01$ ).

According to the results of AARM (Table 2), the average TVF in patients of the 1st group was  $610 \pm 47 \text{ cm}^3/\text{sec}$ , which is 29.9% lower than the control, and in patients with a mesial bite - 2 group, the average TVF was  $540 \pm 64 \text{ cm}^3/\text{sec}$ , which is 37.9% below the control (tab. 3).

**Table 2.**AARM results in patients with GFOA at Ra-150 (M±m)

Study group	TVF, $\text{cm}^3/\text{sec}$	TR, $\text{Pa}/\text{cm}^3/\text{sec}$
1 <sup>st</sup> Group	$610 \pm 47 *$	$0,31 \pm 0,11*$
2 <sup>nd</sup> Group	$540 \pm 64 *$	$0,27 \pm 0,12*$
Control	$874 \pm 21,4$	$0,21 \pm 0,01$

Control - data by O.V. Reshetnikova, 2013

( $p < 0.001$ ) \* - in comparison with the control group

The average value of the total resistance to airflow - SS in patients of the 1st group was  $0.31 \pm 0.11 \text{ Pa}/\text{cm}^3/\text{sec}$ , in the 2<sup>nd</sup> group -  $0.27 \pm 0.12 \text{ Pa}/\text{cm}^3/\text{sec}$ , which is higher than the control level by 12, 8 and 14.7%, respectively. The results of the study indicate that the majority of the examined showed symptoms of nasal breathing, and in patients of 2<sup>nd</sup> group they were more pronounced: nasal obstruction (NA) of 2 degrees was observed in  $45 \pm 6.5 \%$  and 3 degrees in  $25 \pm 4.3 \%$ .

According to the data obtained, despite a statistically significant correlation between the values of the total volume flow of nasal breathing in 27 ( $79.2 \pm 8.7 \%$ ) patients, the presence of nasal obstruction was noted to varying degrees compared with the control (Table 3), whereas according to the results of subjective sensations, violations were observed in ( $55.8 \pm 8.3 \%$ ) of the examined. Nasal obstruction was most common in the group of subjects with mesial occlusion of  $85 \pm 7.5 \%$ , which is 25% more than subjective indicators. The incidence rate of nasal obstruction of 2-3 degrees in this group was 70%, which is 10% more than the subjective sensations of patients. The values of nasal obstruction in patients of the 1<sup>st</sup> and 2<sup>nd</sup> groups were significantly higher than in the control group ( $P < 0.01$ ).

**Table 3.**Condition of nasal obstruction in patients with GFOA

Group	No obstruction		But 1 <sup>st</sup> degree		But 2 <sup>nd</sup> degree		But 3 <sup>rd</sup> degree		Total	
	n	%	n	%	n	%	n	%	N	%
1 <sup>st</sup> group	3	21,4±3,3	2	14,3±4,8	6	42,7±6,8%	3	21,4±3,2%	14	41,2 ±5,6
2 <sup>nd</sup> group	3	15±3,6	3	15±5,1%	9	45±6,5%	5	25±4,3%	20	58,8 ±8,3

From literary sources, it is known that when a person switches to breathing through his mouth, the whole mechanism of functioning of various organs and systems is disrupted. Respiratory rhythm, blood outflow and brain nutrition are impaired, and as a result - impaired memory, mental abilities, impaired blood composition, cardiovascular system functions. Based on the foregoing, the normalization of nasal breathing is a task of paramount importance.

Thus, the use of computer rhinomanometry in patients with GFOA helps to more reliably determine the presence and degree of nasal obstruction and to control it in the dynamics of the treatment process.

According to the results of our studies, the biochemical parameters of blood in patients with GFOA of the dentition have a certain imbalance (Table 4). As can be seen from the presented research results, blood hemoglobin in patients of group 2 was significantly reduced by 41% compared with healthy patients. In patients of group 1, the studied indicator decreased by 26% compared with the control group.

**Table 4.**Biochemical blood indices in patients with dentofacial ovarian prophylaxis (M±m)

N	Indicators	Controlgroup n =8	1 <sup>st</sup> group n =17	2 <sup>nd</sup> group n =38
1	The hemoglobin content g/l	148,51±8,02	110,48 ± 9,24	88,01 ± 8,14
2	The content of fetal hemoglobin (HbF) (g/l)	2,26±0,12	2,56 ± 0,21	3,92 ± 0,29*

Note: \* - significance of differences P <0.05

Another dynamics was noted relative to HbF in the blood of the examined patients with GFOA of the dentition. An analysis of the results showed a significant increase in the level of fetal hemoglobin in the blood of patients of group 1 by an average of 13%, while in patients of group 2 it increased by 1.7 times. At the same time, the observed state of hypoxia in patients can be both local and systemic.

It is well known that all negative effects on the body (including psycho-emotional stress) lead to a change in the rate of generation of reactive oxygen species, including disruption of the oxygen-dependent metabolism of phagocytic cells, and a decrease in their functional activity. In turn, one of the manifestations of the violation of the quality of the protective and adaptive reactions of the body under adverse environmental influences (violation of hemostasis, salivary enzyme systems, etc.) can be inflammatory diseases of the oral organs. It is believed that an increase in the level of fetal hemoglobin (HbF) is a biochemical mechanism of long-term adaptation of the body to hypoxia, which is based on the phenomenon of “adaptive stabilization of structures”. HbF is a marker of tissue hypoxia in various pathologies in humans.

Thus, an assessment of HbF levels in combination with clinical data provides much more information about the development of tissue hypoxia and hypoxemia in patients with GFOA. Determination of the level of HbF in patients with denticular GFOA can be used to diagnose chronic tissue hypoxia and helps to clarify the severity of the pathological process, which allows us to predict the progression of the disease and the development of their complications.

In accordance with modern scientific provisions, the state of the dentofacial system is considered as an indicator of somatic health, and changes in dental status with various health deviations are a reflection of metabolic, hemodynamic, immunological and neuroregulatory disorders occurring in the macroorganism. Therefore, one of the pressing problems of medical science and practical health care at the present stage is the improvement of diagnostic and therapeutic measures aimed at improving dental health, as well as the prevention of functional disorders of the dentition [2, 3, 8]. Despite the experience gained, there is insufficient coverage of issues of the state of local immunity in patients with GFOA of the dentition.

The results of the study of blood biochemical parameters: tissue hypoxia and hypoxemia in patients with GFOA (Table 5) showed a peculiar dynamic of all studied parameters in patients with GFOA. According to the research results, the saliva protective system parameters in patients with GFOA are characterized mainly by a decrease in all studied parameters.

**Table 5.**Indices of local immunity in patients with GFOA (M±m)

Immunity indicators	1 <sup>st</sup> group n =17	2 <sup>nd</sup> group n =38	Control group n =8
Lysozyme, mcg/L in saliva	1,14±0,09*	0,68±0,005*	2,28±0,17
Lactoferrin, ng/ml in saliva	1121,81±13,42*	838,51±11,06*	1628,93±33,24
sIgA, mg/l in saliva	146,54±9,13*	101,57±10,16*	249,23±11,67
IgE, mg/dl in blood	174,51±11,07*	208,24±14,33*	61,32±5,28

Note: \* - significance of differences P <0.05

The content of lysozyme in the saliva of patients of group 1 was reduced by 2 times in relation to the indicators of the comparison group. In group 2, the studied indicator was 0.68±0.005 µg/L, which is 3.4 times lower than the initial values. The level of lactoferrin had a significantly reduced value in relation to the indices of the control group in groups 1 and 2 on average 1.5 and 1.9 times, respectively. Significant is the decrease in sIgA content in the saliva of patients with GFOA by an average of 41% in the 1st group of examined individuals and by 60% in the 2<sup>nd</sup> group of patients relative to the comparison group. As can be seen from the research results, the concentration of IgE in the blood of the examined patients exceeded the values of the comparison group on average 2.8 times in the 1<sup>st</sup> group and 3.4 times in the 2<sup>nd</sup> group. The revealed fact of changes in IgE indices indicates that in patients with GFOA pathological changes are observed not only from the side of the dentofacial system, but also a decrease in the activity of the detoxification system.

An analysis of recent literature indicates that genes of the super family of glutathione-S-transferases encode xenobiotic detoxification enzymes. Changes in the functions of the enzymes of the xenobiotic detoxification system increase the susceptibility of the body to harmful effects and, as a result, to increase the risk of certain diseases. In this situation, an increase in IgE levels is observed under the influence of xenobiotics and allergens. The loss of the glutathione-S-

transferase gene region and high IgE values, in our opinion, is one of the predisposing factors for aggravation of dentoalveolar anomalies. Therefore, the observed dynamics relative to IgE in serum in patients with GFOA of the dentition is one of the indicators of the hypersensitivity of the body of the examined patients.

Thus, a comprehensive study of blood and saliva parameters in patients with GFOA allows recommending the concentration of IgE in peripheral blood as diagnostic markers. Elevated concentrations of the identified marker can be used to develop appropriate preparation of patients with GFOA of the dentition for orthognathic surgery.

It is known that the content of circulating cytokines in blood serum in healthy people is usually low, but when they meet with pathogens of the infectious process, cytokines of both pro-inflammatory (IL-1, IL-6, IL-8, etc.) and anti-inflammatory (IL- 4, IL-10, etc.) nature, and their content varies depending on the period of the disease and the severity of the process. For this reason, in our opinion, the determination of the concentration of cytokines in patients with GFOA of the dentition can be one of the objective criteria for assessing the severity of the condition.

Our studies of the state of the cytokine system of blood and saliva in patients with GFOA (Tab. 6) revealed certain features of the blood cytokine profile. According to the results of our studies, an increase in blood concentrations of IL-1a in patients of the 1<sup>st</sup> and 2<sup>nd</sup> main groups was observed to be 1.8 times on average, and IL-6 was 1.4 times higher than in healthy individuals. If we take into account that IL-1a and IL-6 are synthesized in response to infection or tissue damage during the interaction of antigens with the Toll-like group (TLR) of receptors, considered as a key component of innate and acquired immunity, then the fact that we found to increase their blood levels in patients with GFOA, it is highly likely that a chronic inflammatory process develops.

**Table 6.**Comparative assessment of blood cytokines in patients with GFOA (M±m)

Indicators	Control group (n =8)	Patients 1 <sup>st</sup> group (n =17)	Patients 2 <sup>nd</sup> group (n =38)
TNF- $\alpha$ pkg/ml	12,67 $\pm$ 0,78	19,41 $\pm$ 1,13*	26,58 $\pm$ 3,11*
IL -1 $\alpha$ pkg/ml	10,23 $\pm$ 1,34	16,33 $\pm$ 1,18*	21,67 $\pm$ 2,39*
IL -2 pkg/ml	1,19 $\pm$ 0,09	4,13 $\pm$ 0,37*	6,07 $\pm$ 0,42*
IL -4 pkg/ml	1,18 $\pm$ 0,12	1,04 $\pm$ 0,11	0,94 $\pm$ 0,01
IL -6 pkg/ml	22,45 $\pm$ 1,87	30,54 $\pm$ 4,27*	34,06 $\pm$ 3,12*
IL -8 pkg/ml	1,67 $\pm$ 0,13	3,01 $\pm$ 0,27*	3,24 $\pm$ 0,22*

IL -10 p <sub>g</sub> /ml	13,18 ±1,12	7,58±0,63*	5,89±0,57*
---------------------------	-------------	------------	------------

Note: \* - significance of differences (P <0.05)

In addition, IL-1 $\alpha$  and IL-6 in terms of functional activity are pro-inflammatory cytokines that are synthesized, secreted, and act through their receptors on target cells in the early stages of inflammation, participating in triggering a specific immune response. An increase in blood IL-6 in patients with GFOA has a systemic effect on the body in the form of activation of B-lymphocytes and humoral immune responses, stimulation of the synthesis of acute phase proteins by hepatocytes, and enhances hematopoiesis. Many pro-inflammatory effects of IL-1 are carried out in combination with IL-6 and TNF- $\alpha$  (Tumor Necrosis Factor). In turn, IL-1 $\alpha$  and TNF- $\alpha$  (tumor necrosis factor) are the inducers of IL-6 production, the level of which in the blood according to the results of our studies significantly increases in patients of the 2<sup>nd</sup> group - 2.1 times.

A special place among pro-inflammatory cytokines is occupied by the cytokine – TNF- $\alpha$ , which has the ability to stimulate the production of other anti-inflammatory cytokines, activate B-dependent and T-dependent immune reactions. The results of our studies indicate a significant increase in the level of TNF- $\alpha$  in the blood in patients with GFOA of the dentition - by 1.9 times, especially in patients of the 2<sup>nd</sup> group by 2.2 times compared to healthy individuals. According to the literature, the development of the vasodilation effect of TNF- $\alpha$  in combination with an increase in IL-1 $\alpha$  in the blood indicates a possible development of endogenous intoxication.

An analysis of the results of our studies also indicates an increase in blood concentrations of IL-8: in patients of the 1<sup>st</sup> and 2<sup>nd</sup> main groups, they were almost at the same high level and averaged 1.8 times in comparison with healthy individuals. A similar dynamics was noted with respect to the cytokine IL-2, where its concentration in the blood of the examined patients with GFOA exceeded the initial level by 4.6 times. Anti-inflammatory cytokines also include IL-4 and IL-10; according to the results of our studies, the indicators of anti-inflammatory interleukins IL-4 and IL-10 were of the same type, i.e. tended to decrease, which indicated the prevalence of the inflammatory nature of the changes and, consequently, intoxication.

It is known that IL-8 belongs to the category of “second generation” cytokines and is a glycoprotein that forms the following types of cells: macrophages, lymphocytes, fibroblasts, skin cells, tumor cells, hepatocytes. Its production is stimulated by bacterial toxins, cytokines (mainly IL-1 and TNF- $\alpha$ ). In addition, IL-8 creates a gradient for chemotaxis in phagocytosis. This chemokine stimulates the formation of receptors in vascular endothelial cells, which attract neutrophils and monocytes to the site of inflammation and leave these cells in the capillaries and induce the launch of an antigen-specific immune response. According to the literature, an increase in the level of IL-8 in the blood is usually associated with the development of an acute or chronic inflammatory process.

Thus, a biochemical study revealed an increase in the concentration of pro-inflammatory and anti-inflammatory cytokines in the blood serum of patients with GFOA of the dentition. The data obtained indicate inhibition of the protective factors of the immune system. In our opinion, monitoring the dynamics of changes in their blood levels in patients with GFOA of the dentition can be used as one of the objective criteria for the risk of inflammatory processes.

The pathogenetic community of many general somatic processes and inflammatory diseases of the oral cavity is due to the development of common mechanisms of cell damage and tissue modification for the whole organism with the

acquisition of autoantigenic properties. Failures and dysfunctions of the cytokine regulation of immunobiological processes play a leading role in the occurrence of these changes.

Based on the foregoing, the next objective of our study was to study the level of cytokines in the oral fluid in patients with GFOA of the dentition. Table 5 presents the content of cytokines in the oral fluid in patients with GFOA of the dentition and in healthy donors.

**Table 5.** Comparative assessment of the content of cytokines in the oral fluid in patients with GFOA (M ± m)

Indication	Control group (n =8)	Patients 1 <sup>st</sup> group (n =17)	Patients 2 <sup>nd</sup> group (n =38)
TNF-α pkg/ml	4,63±0,31	12,78±1,53*	18,56±2,15*
IL -1α pkg/ml	6,21±0,45	13,34±0,92*	16,28±1,34*
IL -2 pkg/ml	0,29±0,01	0,68±0,05*	0,72±0,07*
IL -4 pkg/ml	1,03±0,12	1,01±0,11	0,94±0,08
IL -6 pkg/ml	11,08±1,04	21,56±2,05*	23,78±3,01*
IL -8 pkg/ml	2,87±0,25	7,24±0,63*	8,01±0,72*
IL -10 pkg/ml	5,17±0,43	4,01±0,52	3,34±0,41

Note: \* - significance of differences P <0.05

As can be seen from the presented results of studies of GFOA lead to an imbalance in the level of IL -1 in the oral fluid, for example, in patients of the 1st group, it is approximately 13.34±0.92 pg/ml, which is 2.1 times higher, and patients in the 2<sup>nd</sup> group - 16.28±1.34 pg/ml, which is 2.7 times higher compared to healthy individuals.

According to the results of our studies, an increase in the content of IL -2 was also noted: in patients of group 1 by 2.3 times and averaged 0.68±0.05 pg/ml, and in patients of group 2 by 2.5 times and averaged 0.72±0.07 pg/ml. The results of the study of the concentration of IL-6 in the oral fluid of patients with GPAO of the dentition showed a similar picture: in patients of the 1<sup>st</sup> group it averaged 11.08±1.04 pkg/ml, and in patients of the 2nd group 21.56±2.05 pkg/ml which is 1.9 and 2.2 times higher than the control level. An increase in the level of IL-6 in the oral fluid in patients with denticular HPAI, on the one hand, contributes to the development of the inflammatory process of an infectious-allergic nature, and on the other hand, determines the development of a complex of protective and adaptive reactions due to the activation of specific and non-specific resistance mechanisms.

Our results of biochemical studies show that the concentration of IL-8 in the oral fluid in GFOA patients is also increased by an average of 2.8 times in comparison with a group of healthy patients. A different dynamics was noted with respect to IL-10, the concentration of which in the oral fluid was 36% lower. This circumstance testified to the low activity of the immune and antiviral defense in the oral cavity in pregnant women of group 2, which contributed to the protracted nature of the existing clinical manifestations of inflammatory diseases of the oral cavity.

Recent studies have shown that the content of cytokines in saliva does not correct with their level in the blood, which indicates a certain autonomy of local immunity of the oral cavity, while at the same time reflects the general trends of the cytokine cascade in the patient's body. The secretion of the oral cavity may be used to identify markers of systemic

immune activation. This is consistent with the notion that salivary criteria reflect not only local, but also general disorders of homeostasis [19].

Thus, an assessment of HbF levels in combination with clinical data provides much more information about the development of tissue hypoxia and hypoxemia in patients with GFOA. Determination of the level of HbF in patients with denticular GFOA can be used to diagnose chronic tissue hypoxia and helps to clarify the severity of the pathological process, which allows us to predict the progression of the disease and the development of their complications. As a result of a biochemical study, an increase in the concentration of pro-inflammatory and anti-inflammatory cytokines in the blood serum of patients with GFOA of the dentition was revealed. A comprehensive study of blood and saliva parameters in patients with GFOA allows recommending the concentration of IgE in peripheral blood as diagnostic markers. Elevated concentrations of the identified marker can be used to develop appropriate preparation of patients with GFOA of the dentition for orthognathic surgery.

#### **IV. DISCUSSION**

Treatment of patients with maxillofacial anomalies (MFA) remains relevant to date throughout the world. A special place in the medical rehabilitation of patients with jaw deformities is given to orthognathic surgery, which eliminates anatomical, functional and aesthetic disorders. Studies conducted over the past years have made it possible to determine the most effective methods of surgical treatment of patients with jaw deformities, to modernize existing methods in order to achieve high functional and aesthetic results of treatment.

At the same time, publications periodically report complications arising at various stages of medical rehabilitation of patients with jaw deformities. In these works, data are presented on the analysis of complications encountered in the near and long term after surgical treatment.

The greatest attention is paid to identifying the frequency of relapse, determining the causes and mechanisms of their occurrence. It should be noted that these studies were episodic in nature, based on a small amount of clinical material, and boiled down to only stating the most common complications without identifying ways and methods of preventing them. In the domestic literature, such studies were practically not carried out, which indicates the importance and relevance of this direction.

The successful medical rehabilitation of patients with MFA in general, and gnathic forms of occlusion anomalies (GFOA) of dentitions in particular, in our opinion, should be based on careful preoperative preparation and planning of surgical treatment, taking into account the quality of protective and adaptive reactions of the body under adverse environmental influences. Each environmental factor acting on the body, due to its own nature, causes a specific response, adequate to the quality and strength of irritation. External influence and adverse factors in turn violate the constancy of the internal environment and individual indicators.

Despite the obvious successes in the field of orthognathic surgery, inflammatory complications are one of the most common. A number of studies have established that the severity of the pathological process and its progression depend on the level and balance of cytokines. Cytokines have both stimulating and inhibitory effects on lymphocytes. The nature and magnitude of the resulting immune response is determined by the relative concentrations of various cytokines at the site of activation of the immune response, which determines the relevance of studying the cytokine status.

The results of the study indicate that the majority of the examined showed symptoms of nasal breathing, and in patients of 2<sup>nd</sup> group they were more pronounced: nasal obstruction (NO) of 2 degrees was observed in  $45 \pm 6.5\%$  and 3 degrees in  $25 \pm 4.3\%$ .

AARM results indicate that nasal obstruction was most common in the group of subjects with mesial occlusion of  $85 \pm 7.5\%$ , which is 25% more than subjective indicators. The incidence rate of nasal obstruction of 2-3 degrees in this group was 70%, which is 10% more than the subjective sensations of patients. From literary sources, it is known that when a person switches to breathing through his mouth, the whole mechanism of functioning of various organs and systems is disrupted.

An analysis of the results of biochemical studies indicates that in patients with GFOA there is an increase in the production of pro-inflammatory cytokines, along with a decrease in the production of anti-inflammatory cytokines, which ultimately leads to the development of inflammatory diseases, which can lead to disruption of regenerative processes. Regarding anti-inflammatory cytokines, the results show the same type of changes in their concentration in the oral fluid in patients with GFOA and their tendency to increase. The data obtained indicate inhibition of the protective factors of the immune system. In our opinion, monitoring the dynamics of changes in their blood levels in patients with GFOA of the dentition can be used as one of the objective criteria for the risk of inflammatory processes.

The data obtained in the work indicate that the manifesting symptom in patients with GFOA is a combined increase in the level of IL-1P, IL-6, IL-8, and TNF- $\alpha$  in the blood and oral fluid. An increase in the level of IL-1 in, IL-6, IL-8, TNF- $\alpha$  in the blood and oral fluid indicates an increase in antigenic stimulation of monocytic macrophage, lymphoid cell elements, endotheliocytes, fibroblasts of various organs and tissues, indicates the development of a systemic inflammatory syndrome response and the formation of adaptive protective and adaptive reactions and maladaptation reactions from the cytokine system in patients with GFOA.

Our results of biochemical studies show that the concentration of IL-8 in the oral fluid in GFOA patients is also increased by an average of 2.8 times in comparison with a group of healthy patients. A different dynamics was noted with respect to IL-10, the concentration of which in the oral fluid was 36% lower. This circumstance testified to the low activity of the immune and antiviral defense in the oral cavity in pregnant women of group 2, which contributed to the protracted nature of the existing clinical manifestations of inflammatory diseases of the oral cavity.

Thus, the use of computer rhinomanometry in patients with GFOA helps to determine more reliably results the presence and degree of nasal obstruction and to control it in the dynamics of the treatment process. assessment of HbF levels in combination with clinical data provides much more information about the development of tissue hypoxia and hypoxemia in patients with GFOA. Determination of the level of HbF in patients with denticular GFOA can be used to diagnose chronic tissue hypoxia and helps to clarify the severity of the pathological process, which allows us to predict the progression of the disease and the development of their complications. A comprehensive study of blood and saliva parameters in patients with GFOA allows recommending the concentration of IgE in peripheral blood as diagnostic markers. Elevated concentrations of the identified marker can be used to develop appropriate preparation of patients with GFOA of the dentition for orthognathic surgery.

The data obtained indicate inhibition of the protective factors of the immune system. In our opinion, monitoring the dynamics of changes in their blood levels in patients with GFOA of the dentition can be used as one of the objective criteria for the risk of inflammatory processes.

A comprehensive study of blood and saliva parameters in patients with GFOA allows recommending the concentration of IgE in peripheral blood as diagnostic markers. Elevated concentrations of the identified marker can be used to develop appropriate preparation of patients with GFOA of the dentition for orthognathic surgery.

## REFERENCES

- [1] Abdukayumov A.A. Features of rhinomanometry in patients with chronic rhinosinusitis // *Pediatrics*. - Tashkent, 2014. - No. 3-4P14014-4 - P. 13-14.
- [2] Domenyuk D.A. Estimation of correlation between electrolyte composition and indices of local immunity of mixed saliva in patients with anomalies of the dentofacial system (Part I) // *Institute of Dentistry*. - 2014. - No. 2 (63). - S. 66–68.
- [3] Evdokimova N.A. Features of the structure of the upper respiratory tract in children with distal occlusion of the dentition / N.A. Evdokimova, S.A. Popov, E.A. Satygo // *Orthodontics*. - 2009. - No. 4 (48). - S. 25-27.
- [4] Ignatov M.Yu. The content of certain cytokines and autoantibodies to them in blood serum, oral and gingival fluid with odontogenic abscesses of the maxillofacial region / M.Yu. Ignatov, N.N. Tsybikov, E.T. Domanova [et al.] // *Dentistry*, 2010. - No. 5. - S.15 - 16.
- [5] Kasyanova, T.R. The content of fetal hemoglobin in patients with viral and alcoholic cirrhosis of the liver / T.R.Kasyanova, Yu.B. Titarenko, Yu.A. Kriventsev, B.N. Levitan // *Materials VII Nat. Congress of Physicians*. - M., 2012. -- S.93-94.
- [6] Kovalenko, A. V. Assessment of the perception of facial aesthetics by patients with gnathic forms of occlusion anomalies before and after combined treatment: author. dis. . K.M. / Moscow, 2011. 25 s
- [7] Kramar V.S., Dmitrienko S.V., Klimova T.N. Microecology of the oral cavity and its role in the development of dental diseases. - Volgograd, 2010. -- 250 p.
- [8] Markelova E.V. The role of local cytokine imbalance in the pathogenesis of caries in children / E.V. Markelova, S.A. Milekhina, L.S. Shushanyan // *Basic Research*, 2011. - No. 5. - S. 104 - 108.
- [9] Myagkova N. V. Gnathic forms of mesial occlusion: improving diagnostic methods and treatment of patients of different ages: abstract. thesis M.D., Moscow-2017, 38s.
- [10] Reshetnikova OV, Evseeva VV, Reshetnikov SV. Front active rhinomanometry in the diagnosis of chronic rhinitis // *Russian rhinology*. - M., 2013, No. 21 (4) .- S. 9-13.
- [11] Satygo E.A. The concept of interdisciplinary interaction in the restoration of nasal breathing in children / E.A. Satygo, S.A. Popov, N.A. Evdokimova // *Pediatric Dentistry*. - 2009. - No. 4 (31). -FROM. 39-41.
- [12] Spitsyna O. B. Quality assessment of orthodontic treatment in patients with various forms of dentoalveolar anomalies / abstract. Ph.D. / Veliky Novgorod 2018, 24s
- [13] Trezubov VV, Mikhailov S. M. The system for assessing the quality of orthopedic dental care / *Dentistry* 2012; 6: 69-71
- [14] Chapala V. M. Myofunctional correction of dentofacial anomalies and speech disorders using vestibular plates. - M., 2008.
- [15] Autoantibodies to inner ear and endothelial antigens in Cogan. s syndrome / C. Lunardi [et al.] // *Lancet* - 2002 - №360 - p. 915-921.
- [16] Chronic rhinitis. Clinical guidelines 2010 / A. Reshef [et al.] // *Harefuah*. - 2011. - Vol. 150. - Pp. 275-278.
- [17] Dmitrienko S.V., Domenyuk D.A., Vedeshina E.G. Shape individualization in lower dental arches drawn on basic morphometric features // *Archiveuromedica*. – 2015. – Vol. 5, № 1. – P. 11–15.
- [18] Haddad J.J., Harb H.L. Cytokines and the regulation of hypoxia-inducible factor (HIF)-1alpha / / *Int. Immunopharmacol*. - 2005. - Vol. 5, №3. - P. 461-483.
- [19] Howcroft T.K., Campisi J., Louis G.B., Smith M.T., Wise B., Wyss-Coray T., Augustine A.D., McElhaney J.E., Kohanski R., Sierra F. The role of inflammation in age-related disease // *Aging (Albany NY)*. – 2013. – Vol. 5, N 1. – P. 84-93.
- [20] Miller C.S., King C.P. Jr, Langub M.C., Kryscio R.J., Thomas M.V. Salivary biomarkers of existing periodontal disease: a cross-sectional study // *J Am Dent Assoc*. – 2006. – Vol. 137. – P. 322-329.
- [21] Nell A., Turner N.A., Das A. et al. Interleukin-1a stimulates proinflammatory cytokine expression in human cardiac myofibroblasts // *AJP*. — 2009. — Vol. 297, №3. — P. H1117—H1127.
- [22] Taba M. Jr, Kinney J., Kim A.S., Giannobile W.V. Diagnostic biomarkers for oral and periodontal diseases // *Dent Clin North Am*. – 2005. – Vol. 49. – P. 551-571.
- [23] Ye J., Keller J.N. Regulation of energy metabolism by inflammation: A feedback response in obesity and calorierestriction // *Cytokine*. — 2010. — Vol. . — P. 56—60.

- [24] Chauhan SP, Sheth NR, Jivani NP, Rathod IS, Shah PI. "Biological Actions of Opuntia Species." *Systematic Reviews in Pharmacy* 1.2 (2010), 146-151. Print. doi:10.4103/0975-8453.75064
- [25] Rajkumar,G., Shalini,A., Sujatha,A., Vinothini,G.,& Yuvarani,E. (2017). Tracking of Soldiers Location in anyEnvironment using Intelligent Trackingand Health Indication System by usingRSSI. *The SIJ Transactions on Computer Science Engineering & its Applications*, 5(3), 6-10.
- [26] Mohammed,S., Dr. Ramkumar,L.,& Rajasekar,V.R. (2017). A Novel Method using ConvolutionalNeural Network for Segmenting BrainTumor in MRI Images. *The SIJ Transactions on Computer Science Engineering & its Applications*, 5(3), 11-16.
- [27] Song, D. Efficiency in simulating information networks (2019) *NeuroQuantology*, 17 (1), pp. 112-116.
- [28] Fenwick, P., Di Bernardi Luft, C., Ioannides, A.A., Bhattacharya, J. Neural correlates of induced light experience during meditation: A pilot hyperscanning study (2019) *NeuroQuantology*, 17 (1), pp. 31-41.