

1 **IMMUNE DISORDERS OF DENTOALVEOLAR ANOMALIES**
2 **IN SCHOOLCHILDREN**

3
4 **Abstract**

5 Increasing in IL-1, IL-6, IL-8 and TNF- α level in blood and oral fluid
6 indicates an increase in antigenic stimulation of monocyte-macrophage, lymphoid
7 cell elements, endothelial cells, fibroblasts of various organs and tissues, specifies
8 systemic inflammatory response syndrome development and protective-adaptive
9 reactions and maladaptation reactions formation at children with DAA.

10 **Key words:** antigens, inflammation, immunity, oral fluid

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12 **INTRODUCTION**

13 Using in clinical practice of immunologic analysis shows that frequency of
14 the main stomatology diseases, and in particular DAA (dental alveolar anomalies),
15 it is in direct or mediated condition dependence in both general, and local oral
16 cavity immunity factors [1, 2]. However, local immunity is not a simple reflection
17 in maintenance of the whole body immunity, and it caused by independent system,
18 in particular production of the sIgA (secretory immunoglobulin A), that has
19 expressed also on the systemic immunity formation. There are the components of
20 congenital, cellular and humoral immunity for maintenance of immune
21 homeostasis and control of microbial colonization in saliva [3, 4, 5].

22 The lysozyme is an important congenital antimicrobial factor, which takes
23 place from epithelial salivary ducts and due to its enzymes is able to destroy the
24 peptidoglycan bacteria paries [6, 7, 8]. Main immune component of the saliva is
25 secretory immunoglobulin A, which is characterized by antigen specificity for
26 local bacteria, fungi and viruses. Humoral immunity factors as well wide array of
27 inflammatory mediators, including IL-4 and IL-8 (interleukins) relates. These
28 cytokines are responsible for a local immune regulation, and they are informative
29 indicators of the oral cavity immune homeostasis [9, 10].

30 The goal of present research is studying in comparative aspect of local

31 immunologic ratings of the oral liquid and blood at schoolchildren with dental
32 alveolar anomalies.

33 MATERIAL AND METHODS

34 Immunologic status in unstimulated oral liquid (UOL) and blood has been
35 conducted at 18 healthy schoolchildren aged from 7 to 14 with intact teeth, as well
36 as 64 schoolchildren with DAA. Diagnosis was based on Angle's classification.
37 All patients with DAA were passed a clinical examination, including anamnesis
38 collection and medical screening. Anthropometric studies of face and head at all
39 children and teenagers, as well as jaws control-diagnostic models analysis of were
40 conducted. Teeth dimension ratio, tooth width ranges by Pont, sagittal variations
41 by Korkhaus's method was studied, dental arch segments ratio - by Gerlach, tooth
42 ranges shapes, its correlation, as well as location of individual teeth in sagittal,
43 transverse and vertical planes were evaluated. In addition, it was used X-ray
44 examination (orthopantomography, teleroentgenography, intraoral contact
45 radiography). A lateral teleroentgenograms analysis of the head has been
46 conducted by Schwartz's method.

47 UOL sampling at each surveyed person was conducted at clinic on an empty
48 stomach from 8 to 9 a.m. Patients were asked not to carry out stimulating
49 salivation procedures, previously professional teeth cleaning at all surveyed
50 patients groups was conducted. UOL sampling in 0,9 ml for element composition
51 study was made just from oral cavity. Then mixed saliva centrifuged during 15
52 minutes at 8000 rpm. The supernatant part of the UOL was poured into plastic test
53 tubes and stored at 30°C. The pro-inflammatory and anti-inflammatory cytokines
54 (IL-1, IL-2, IL-4, IL-6, IL-8, IL-10 and TNF- α) study in blood and oral fluid by
55 enzyme-linked immunosorbent assay method using test systems produced by JSC
56 «Vector-Best» (Novosibirsk, Russia) was determined. Mathematical processing of
57 the obtained results were carried out parametric statistics method on a personal
58 computer using by «Statistica 6.0» program, which was included descriptive
59 statistics, differences significance by Student's data assessment and correlation
60 analysis with correlation coefficients reliability assessment. It was used $P < 0,05$

61 value at reliability of differences assessing.

62 RESULTS AND DISCUSSION

63 Study results analysis presented in table 1 has allowed finding revealed
64 certain features of blood cytokine profile.

65 The cytokines of the «first generation» are included IL-1 α , IL-6. Our studies
66 showed an increase in blood concentration of IL-1 α at children with DAA by an
67 average of 2,6 times at comparison with healthy children. It known, that IL-1 α is
68 inducible protein, which synthesizes in response to infection or tissue damage at
69 interaction of antigens with a group of «Toll-like» receptors. At the same time it is
70 a multifunctional cytokine, activates neutrophils, T- and B-lymphocytes, proteins
71 synthesis stimulates at “acute phase”, phagocytosis, and hematopoiesis, renders
72 pyrogenic effect, and induces production of such cytokines as IL-2, IL-4, IL-6,
73 IL-10 et al.

74 **Table 1**

75 **Comparative assessment of cytokine content rates in blood** 76 **at children with DAA**

77

Ratings	Health children (n=18)	Children with DAA (n=64)
TNF- α pkg/ml	12,67 \pm 0,78	33,41 \pm 3,24*
IL-1 α pkg/ml	10,23 \pm 1,34	26,45 \pm 1,33*
IL-2 pkg/ml	1,19 \pm 0,09	7,87 \pm 0,67*
IL-4 pkg/ml	1,18 \pm 0,12	2,13 \pm 0,02*
IL-6 pkg/ml	22,45 \pm 1,87	41,56 \pm 3,23*
IL-8 pkg/ml	1,67 \pm 0,13	4,09 \pm 0,32*
IL-10 pkg/ml	13,18 \pm 1,12	6,14 \pm 0,51*

78 **Note: *** - significance of differences (P<0,05)

79

80 Therefore, the fact of IL-1 α content increasing in blood at schoolchildren with
81 DAA, revealed by us, testified with high probability of infectious-allergic nature
82 development inflammatory process. Thus, respectively monitoring of these ratings
83 will allow using as an objective criterion of the risk to development of

84 inflammatory processes in oral mucosa as dynamic changes that content in
85 **schoolers'** blood with DAA.

86 In common with IL-1 as pro-inflammatory cytokines of the “first generation”
87 and IL-6 is integral to determining feasibility its level in the blood of
88 schoolchildren with DAA [10]. The obtained data testified to an increase in the
89 blood content of the IL-6 pro-inflammatory cytokine by 1.9 times, in comparing
90 with a group of healthy children. **As we know that** IL-6 synthesizes by various
91 cellular elements of monocyte-macrophage and lymphoid systems, fibroblasts,
92 endothelial cells, mesenchymal cells [11, 12]. **As we have been** indicated above the
93 TNF- α and IL-1 α level in the blood significantly increased in children with DAA
94 as inducers of IL-6 production [13]. Concerning importance of increase of the
95 content IL-6 that **has been revealed** by us in blood at **schoolers** with DAA, it is to
96 be noted that specified cytokine has system an effect to organism as activation of
97 B-lymphocytes and humoral immune reactions, stimulation of synthesis of acute-
98 phase proteins by hepatocytes, strengthens hematopoiesis [9, 12]. Thus, IL-6 level
99 increasing in children blood with DAA, on the one hand, demonstrates in
100 development of inflammatory process of infectious-allergic nature, and on the
101 other hand - causes development of the complex of protective-adaptive reactions at
102 the expense of activation of specific and nonspecific resistance mechanisms [3, 5].

103 Tumor necrosis factor (TNF) is a cytokine that takes a special place among
104 pro-inflammatory cytokines, which has an ability to stimulate other IL-1, IL-6 pro-
105 inflammatory cytokines production, activates B-dependent and T-dependent
106 immune responses [8, 11]. Significant increase in blood level of TNF- α at DAA in
107 **schoolchildren** by 2.6 times against the control children group was showed in our
108 **studies (table 1)**. According to the literature [4], the TNF- α prominent vasodilation
109 effect development in infectious diseases is a prognostic unfavorable sign, and in
110 some cases in combination with TNF with an increase in IL-1 α in blood indicates a
111 possible development of progressive hypotension until bacteria toxic shock
112 development.

113 It is known that IL-8 belongs to the category of second-generation cytokines,

114 has chemokine properties, and is an activation factor for neutrophils and
115 monocytes [9]. Our research results were indicated an increase IL-8 level in blood
116 of schoolchildren with DAA up to 2.5 times. According to literature, an increase
117 IL-8 level in blood, as a rule, is associated with the development of an acute or
118 chronic inflammatory process [3, 7]. Similar dynamics noted with respect to IL-2
119 cytokine, where its concentration in blood exceeded an initial level at 6.6 times.

120 IL-4 and IL-10 are anti-inflammatory cytokines [2]. The anti-inflammatory
121 interleukins indicators were as a same type, i.e. tended to decrease as can see from
122 presented research findings [1]. At the same time, the average IL-4 indicators
123 among schoolchildren with DAA were $2,13 \pm 0.02$ pkg/ml, which is 18% higher
124 than initial values. The other dynamics noted relative to IL-10, where IL-10 level
125 was $6,14 \pm 0.51$ pkg/ml, which is 53,5% lower than initial values.

126 Cytokines level study in oral fluid in schoolchildren with DAA was next task
127 of our research. Analysis results presented in table 2 allowed us to identify certain
128 features of the cytokine blood profile. As can be seen from the presented study
129 results, children with DAA are lead to an increase IL-1 level in oral fluid about 2
130 times in comparing with a healthy children group. It is known that IL-1 α is an
131 inducible protein, synthesized in response to infection or tissue damage during
132 antigens interaction with Toll-like receptor group, at the same time induces such
133 cytokines as IL-2, IL-4, IL -6, IL-10 and others production.

134 Referring to presented research results, an increase in IL-2 concentration by
135 4,0 times, IL-4 - by 4,7 times and IL-6 - by 2,3 times were observed. Other
136 dynamics noted relatively to IL-10 concentration, which in oral fluid decreased at
137 2,3 times. An increase in IL-6 level in oral fluid of children with DAA, on the one
138 hand, manifests in inflammatory process development of an infectious-allergic
139 nature, and on the other hand, causes the development of protective-adaptive
140 reactions complex due to specific and non-specific mechanisms of resistance [4,
141 10, 13].

142

Table 2

143

Comparative assessment of cytokines content in oral fluid of

schoolchildren with DAA

Ratings	Health children (n=18)	Children with DAA (n=64)
TNF- α pkg/ml	4,63 \pm 0,31	22,56 \pm 2,13*
IL-1 α pkg/ml	6,21 \pm 0,45	12,34 \pm 0,87*
IL-2 pkg/ml	0,29 \pm 0,01	1,22 \pm 0,14*
IL-4 pkg/ml	1,03 \pm 0,01	4,81 \pm 0,2*1
IL-6 pkg/ml	11,08 \pm 1,04	25,34 \pm 2,45*
IL-8 pkg/ml	2,87 \pm 0,25	7,01 \pm 0,61*
IL-10 pkg/ml	5,17 \pm 0,43	2,25 \pm 0,17*

145

146 According to literature, an increase in TNF and IL-1 α might indicate a
 147 progressive hypotension development up to a bacterial-toxic shock development.
 148 TNF concentration in oral fluid has been showed an increase the level in it by an
 149 average 4,9 times comparing with healthy children in our studies [2, 3].

150 According to literature, an increase in IL-8 level, as a rule, is associated with
 151 an acute or chronic inflammatory process development [5-8]. As research results
 152 noted, the IL-8 concentration in oral fluid of children with DAA increased by an
 153 average of 2,4 times in comparing with healthy schoolchildren group. Analysis
 154 research results of anti-inflammatory cytokines (IL-4, IL-10) showed that its
 155 concentration in oral fluid in children with DAA were of the same type changes.

CONCLUSION

- 157 1. Concurrent increase in blood and oral fluid of the IL-1 α , IL-6, IL-8 and
 158 TNF- α level are a manifesting symptom of DAA at schoolchildren.
- 159 2. Increasing of the IL-1 in IL-6, IL-8, TNF- α level in blood and oral fluid
 160 indicates an increase in antigenic stimulation of monocyte-macrophage, lymphoid
 161 cell elements, endothelial cells, fibroblasts of various organs and tissues, indicates
 162 systemic inflammatory response syndrome development and protective-adaptive
 163 reactions and maladaptation reactions formation at children with DAA.

CONSENT

164 It is not applicable.

166 **ETHICAL APPROVAL**

167 It is not applicable.

168 **COMPETING INTERESTS**

169 Authors have declared that no competing interests exist.

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