

Diagnostic Value Of Salivator Cytokines In Dental Diseases In Children With Diabetes Mellitus Type 1

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Diabetes mellitus has the most significant effect on the state of the oral cavity. Therefore, pediatric dentists should be aware of the characteristics of the course of oral diseases in children with diabetes [Nirmala SVSG, Saikrishna D, 2016, Babu SR, Eisenbarth GS., 2012]. Diabetes mellitus is a multifactorial disease characterized by a chronic rise in blood glucose levels or hyperglycemia and is caused by impaired insulin secretion and / or insulin dysfunction. Diabetes is also called a silent epidemic and a major public health problem and accounts for 9% of all deaths worldwide [Nazir MA, Al Ghamdi L, Al Kadi M, Al Bejan N, Al Rashoudi L, Al Hussan M., 2018]. The accumulated scientific knowledge on the study of the biochemical and immunological composition of saliva in various chronic pathologies, including diseases of the gastrointestinal tract, stress, have shown the ability of the secretion of the oral cavity to reflect the processes occurring in the patient's body, and serve as an adequate substrate for monitoring homeostasis [Komarova L.G., Alekseeva O.P., 2016]. According to the Action Strategy for five priority areas of development of the Republic of Uzbekistan in 2017-2021, important tasks have been identified in order to ensure a full life for vulnerable segments of the population to improve the system of social protection of the population and health care, including, "increasing the availability and quality of medical and socio-medical services the population, the formation of a healthy lifestyle of the population.

1. GOAL:

To determine the diagnostic significance of cytokines in saliva in dental diseases in children with type 1 diabetes.

Material and methods:The study included 518 sick children with type 1 diabetes. Sick children were hospitalized at the Bukhara Regional Endocrinological Dispensary. To study the dental status, sick children were divided into 3 groups:1st group - 30 sick children with milk bite - at the age of 3-5 years;2nd group - 133 patients with changeable bite - at the age of 6-11 years;3rd group - 355 patients with permanent occlusion - at the age of 12-17 years.The control group consisted of 35 healthy children of the corresponding age. All patients were examined for general, biochemical blood tests, immunological research methods were carried out. The indicators of cytokines (IL-1 β , IL-4, IL-18, INF- γ) in saliva were studied.Statistical processing of the results was carried out on a Pentium-IV computer with the Microsoft Office Excel-2012 software package. The level of reliability at p <0.05 was taken as statistically significant.Based on the results of a scientific study, the prevalence of type 1 diabetes in girls was established, regardless of age. Revealed the ratio of boys and girls aged 3-5 years-1: 1.3; at 6-11 years old 1: 1.25; at 12-17 years old -1: 1.13, respectively. Analysis in terms of age

showed frequent hospitalization of children aged 12-17 years - 355 (68.5%). In the structure of the established causative factors for the formation of type 1 diabetes in children, viral infections prevail - 55.4%, stress factors - 14.28%, and diabetes in parents (in the family) - 13.21%.

The clinical manifestation of dental diseases was varied. Its structure is dominated by caries and chronic periodontitis (Table 1).

| № | Clinical manifestation | N | % |
|----|---------------------------------|-----|-----------|
| 1 | Chronic periodontitis | 393 | 75,8±3,3 |
| 2 | Catarrhal gingivitis | 148 | 28,6±1,3 |
| 3 | Hypertrophic gingivitis | 128 | 24,7±1,0 |
| 4 | Dystopia of teeth | 14 | 2,7±0,1 |
| 5 | Bite anomaly | 35 | 6,7±0,3 |
| 6 | Short frenulum of the upper lip | 27 | 5,2±0,2 |
| 7 | Short frenum of the tongue | 14 | 2,7±0,1 |
| 8 | Congenital amelogenesis | 11 | 2,2±0,09 |
| 9 | Tooth enamel hypoplasia | 11 | 2,2±0,09 |
| 10 | Congenital dentinogenesis | 7 | 1,4±0,06 |
| 11 | Congenital dentinogenesis | 2 | 0,38±0,01 |

A study of the health status of sick children with type 1 diabetes revealed comorbidity. Among all established concomitant pathologies, gastrointestinal tract diseases (gastritis, gastroduodenitis and hepatitis) prevail - 431 (83.2%) and urinary tract infections - 199 (38.4%). Cytokines, as a humoral factor of natural immunity, play a key role in the implementation of inflammatory reactions. As an inducible protein, interleukin -1 β is produced by monocytes, macrophages. Its synthesis is necessary for an acute phase response of the body. In our studies, a significant increase in its level was revealed in relation to the indicators of the control group - 34.5 \pm 1.8 p μ g / ml: - in the 1st group interleukin -1 β was increased by 1.97 times - 68.2 \pm 1.2 p μ g / ml, in the 2nd group - by 3.0 times - 106.5 \pm 2.3 p μ g / ml, in the 3rd group - by 2.5 times - 86.4 \pm 1.5 p μ g / ml, which indicates an acute phase of dental pathology against the background of diabetes in children.

The study of the cytokine status in patients with type 1 diabetes showed an insignificant decrease in the level of interleukin -4 in saliva in type 1 diabetes in children, regardless of age, with comorbidity with dental inflammatory diseases (Table 2).

Table 2. Concentration of cytokines in saliva in type 1 diabetes mellitus in children with dental diseases (M \pm m)

| Saliva indicators | Control group(n=30) | 1-group of patients(n=30) | 2-group of patients(n = 32) | 3-group of patients(n = 35) |
|----------------------------|---------------------|---------------------------|-----------------------------|-----------------------------|
| IL-1 β п μ г/мл | 34,5±1,8 | 68,2 \pm 1,2** | 106,5 \pm 2,3*** | 86,4 \pm 1,5*** |
| IL-4 п μ г/мл | 8,1±0,34 | 6,8±0,92 | 6,8±1,03 | 6,9±0,7 |
| IL-18 п μ г/мл | 35,27±4,7 | 55,5±14,99 | 83,9±11,79* | 101,1±15,06* |
| INF- γ п μ г/мл | 21,8±1,2 | 9,8±1,5** | 16,3±1,0* | 19,2 \pm 1,8 |

Note: * - differences relative to the data of the control group are significant (* - P < 0.05)

A decrease in the level of interleukin -4 in saliva was found: - up to 6.8 \pm 0.92 p μ g / ml in children with milk bite, - up to 6.8 \pm 1.03 p μ g / ml in children with variable bite - up to 6.9 \pm 0.7

pg / ml in children with permanent occlusion in relation to the indicators of the control group - 8.1 ± 0.34 pg / ml interleukin -4 is known as an anti-inflammatory cytokine and is produced by T-lymphocytes. The anti-inflammatory effect of interleukin -4 is manifested in the suppression of the pro-inflammatory activity of macrophages and their secretion of interleukin -1, tumor necrosis factor and Interleukin -6 [1]. Consequently, the established decrease in the concentration of interleukin -4 against the background of an increase in interleukin -1 β in saliva in children with type 1 diabetes indicates a decrease in the local anti-inflammatory response of the body. The study found an increase in Interleukin -18: - 1.57 times (55.5 ± 14.99 pg / ml) in sick children with type 1 diabetes with milk bite, - in the group of sick children with a changeable bite, there is a significant increase in Interleukin -18 by 2.37 times (83.9 ± 11.79 pg / ml, $P < 0.05$), - in sick children with permanent occlusion by 2.86 times (101.1 ± 15.06 pg / ml, $P < 0.05$) in relation to the indicators of the control group - 35.27 ± 4.7 pg / ml. At the same time, a characteristic clinical and immunological picture is noted: with age, depending on the formation of occlusion in type 1 diabetes in sick children, the rate of increase in the diabetogenic cytokine increases. The study noted an increase in the concentration of interleukin -18 in pediatric patients with type 1 diabetes with a changeable and permanent bite. It is known that Interleukin -18 is a type 1 proinflammatory cytokine that inhibits insulin production by pancreatic beta cells, while others, mainly anti-inflammatory type 2 (IL-4) cytokines, have a protective antidiabetic effect. [6]. Interleukin - γ plays an important role in coordinating the functional conjugation of the multicomponent immune system. Interferons are a group of biologically active proteins or glycoproteins synthesized by a cell in the process of a protective reaction to foreign antigens. Analysis of the results of a study to study the level of Interleukin - γ in saliva in patients with type 1 diabetes showed a significant decrease in group 1 by 2.2 times (9.8 ± 1.5 p μ g / ml) and 1.3 times in the 2nd group (16.3 ± 1.0 p μ g / ml) in relation to the control - 21.8 ± 1.2 p μ g / ml. In the group of children with permanent occlusion (group 3), there is an insignificant tendency towards a decrease in the level of Interleukin - γ in saliva in the presence of dental pathology against the background of type 1 diabetes. Therefore, salivating Interleukin -1 β and Interleukin 18 are markers of inflammatory diseases of the oral cavity in children with type 1 diabetes at the age of 6-17 years. Interleukin γ of saliva is an informative indicator of the protective reaction of the body of sick children with type 1 diabetes at the age of 3-11 years. The established data prove the need for an individual approach to the diagnosis and management of patients in this category. In order to study the significance and role of biochemical mechanisms in the pathogenesis of concomitant dental diseases in patients with type 1 diabetes of the 2nd group (aged 6-11 years), a comparative assessment of the clinical and biochemical parameters of blood was carried out.

Based on the results obtained, a shift in the biochemical parameters of blood was established in type 1 diabetes. Table 3.2.1.

Blood biochemical parameters of the examined patients with type 1 diabetes and concomitant dental diseases, ($M \pm m$)

| Indicators | Control group n = 30 | caries with diabetes n = 43 | Chronic periodontitis with diabetes n = 38 | Catarrhal gingivitis with diabetes mellitus n = 45 |
|--------------------|-------------------------|-----------------------------------|---|---|
| Glucose g / l | $5,2 \pm 1,0$ | $14,7 \pm 1,5^{**}$ | $18,5 \pm 1,5^{***}$ | $16,9 \pm 1,3^{***}$ |
| Urea μ mol / l | $7,8 \pm 0,7$ | $11,8 \pm 1,0^*$ | $13,8 \pm 1,2^*$ | $9,5 \pm 1,3$ |
| ALT mmol / l | $32,4 \pm 0,5$ | $21,0 \pm 1,2^{***}$ | $54,6 \pm 1,3^{***}$ | $44,7 \pm 1,9^*$ |

| | | | | |
|------------|------------|-------------|---------------|--------------|
| ASTmmol /l | 31,0 ± 2,1 | 44,8 ± 1,4* | 57,0 ± 1,6*** | 47,8 ± 1,2* |
| CRB units | 2,1 ± 0,8 | 6,6 ± 0,9* | 9,5 ± 1,8* | 11,4 ± 1,5** |
| ASLO unit | 3,72 ± 1,3 | 7,7 ± 1,4* | 13,3 ± 0,8** | 8,8 ± 1,5* |

Note: * Values are reliable in relation to the control group (P <0.05 - 0.001)

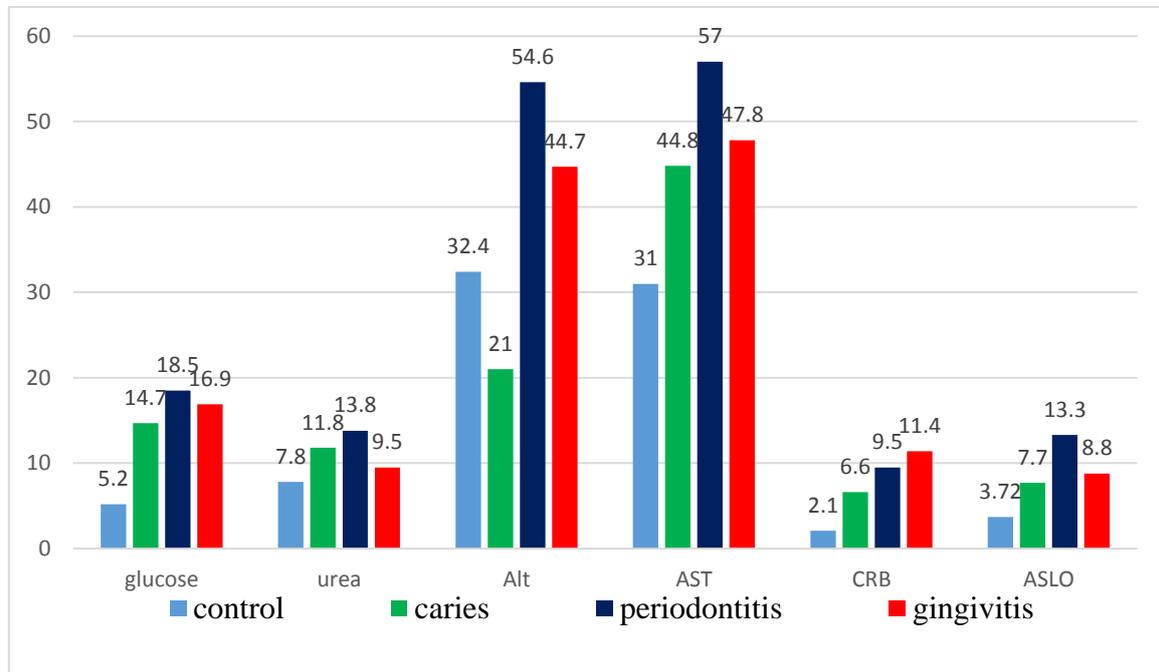


Figure 3.2.1. Biochemical parameters of blood in dental diseases in children with type 1 diabetes

There is a significant increase in all studied biochemical parameters of blood in patients with caries, chronic periodontitis and catarrhal gingivitis against the background of type 1 diabetes. Only the level of urea in catarrhal gingivitis has an insignificant tendency to increase - up to $9.5 \pm 1.3 \mu\text{mol} / \text{L}$ versus control - $7.8 \pm 0.7 \mu\text{mol} / \text{L}$. With comorbidity of type 1 diabetes, a significant change in liver enzymes was noted in all cases. Thus, when diabetes is combined with caries, there is a significant decrease in the ALT level to $21.0 \pm 1.2 \text{ mmol} / \text{l}$ and a significant increase to $54.6 \pm 1.3 \text{ mmol} / \text{l}$ with comorbidity with chronic periodontitis and up to $44.7 \pm 1.9 \text{ mmol} / \text{l}$ with a combination of diabetes mellitus with catarrhal gingivitis versus control - $32.4 \pm 0.5 \text{ mmol} / \text{l}$. The same significant upward trend is observed in relation to AST in the blood in all groups of examined patients with diabetes. In this case, it should be noted that the presence of acute viral hepatitis C and B was excluded in all examined patients. And the noted characteristic change in liver enzymes in diabetes indicates a peculiar reaction of the liver tissue in response to extrahepatic disease. C-reactive protein-glukleprotein produced by the liver belongs to the proteins of the acute phase of inflammation. In our studies, there is a significant increase in its level by 3.2 times in patients with a combination of diabetes with dental caries and 4.5 times with comorbidity of diabetes and chronic periodontitis, as well as 5.5 times with a combination of diabetes with catarrhal gingivitis, versus control - $2.1 \pm 0.8 \text{ units}$ (P <0.05). Consequently, an increase in the level of CRP in the blood indicates the activity of the inflammatory process and the degree of damage to dental tissues. In clinical practice, its increase was combined with unexpressed pain syndrome and the addition of a bacterial infection. The study of the concentration of Antistreptolysin About in the examined patients showed an increase in its level in all groups of the examined, which indicates the presence of infection of the oral cavity. Therefore, our results indicate a violation of metabolic processes and pronounced biochemical changes in the blood in patients with type 1 diabetes mellitus indicate a high probability of early tooth

loss as a result of the formation of multiple dentition defects as a result of secondary early adentia. With age, patients in this category have an increased risk of developing such orthodontic diseases as dental dystopia, malocclusion and various dental-jaw deformities. All of the above affects the quality of life of sick children with type 1 diabetes. The introduction of modern methods and methods of early prevention of dental diseases in children with endocrine diseases is relevant for many countries and its medical and social significance is currently increasing. The study of salivary cytokines during early diagnosis and preventive work in the dentist's office on the basis of regional endocrinological centers for the prevention of dental diseases in type 1 diabetes in children improves the quality of medical service and allows early detection and reduction of dental morbidity. The dentist, already at the stage of the initial examination of patients, determines the method and type of diagnosis to determine the tactics of management and targeted treatment. This approach to the comprehensive examination and prevention of dental diseases in patients with type 1 diabetes mellitus improves the quality of dental and endocrinological services while maintaining the quality of life of patients and reducing morbidity and disability. Currently, the treatment of children with type I diabetes is being improved, at the moment it is the introduction of insulin pumps. An insulin pump is an electronic device for the subcutaneous administration of insulin in small doses, which replaces injection with a syringe pen. The pump delivers insulin according to the pre-programmed values. It is an alternative for people with diabetes who use intensive insulin therapy and have their blood sugar measured regularly. This scheme of insulin administration is most consistent with the rhythm of a healthy pancreas. To determine the effectiveness of treatment, an assessment of the quality of life is used. The PedsQL™ Generic Core Scales for Children was developed by J. Varney in the USA and includes separate forms for children and parents to fill out. This questionnaire is a general tool for researching the quality of life and includes 23 questions combined into 4 scales. Scales of children's and parental forms of the questionnaire: • physical functioning (FF) - 8 questions; • emotional functioning (EF) - 5 questions; • social functioning (SF) - 5 questions; • life at school (FS) - 5 questions. Children's and parental forms of the questionnaire differ only in the grammatical structures of the questions while maintaining their basic meaning and the way of filling out the questionnaire. The assessment is made on a 100-point scale after the scaling procedure. The higher the score, the better the child's quality of life.

Conclusions: caries (75.8%), chronic periodontitis (28.6%) and catarrhal gingivitis (24.7%) prevail in children with type 1 diabetes. Type 1 diabetes is characterized by comorbidity. Of all established concomitant pathologies, gastrointestinal diseases (gastritis, gastroduodenitis and hepatitis) prevail - 83.2% and urinary tract infections - 38.4%. Against the background of comorbid pathology in type 1 diabetes, a decrease in the concentration of Interleukin γ and an increase in Interleukin -1β and Interleukin -18 in saliva were found. All the established evidence proves that salivating Interleukin -1β and Interleukin -18 are markers of inflammatory diseases of the oral cavity in children with type 1 diabetes at the age of 6-17 years. Interleukin γ of saliva is an informative indicator of the protective reaction of the body of sick children with type 1 diabetes at the age of 3-11 years.

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