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# FEATURES OF INTERLEUKINS IN THE DEVELOPMENT OF HEART COMPLICATIONS IN CHILDREN WITH DIABETES AFTER COVID-19 INFECTION

**A. A. Sadirkhodjaeva, D. T. Ashurova**
Tashkent pediatric medical institute, Tashkent, Uzbekistan

**Key words:** diabetes mellitus, complications, interleukins, COVID-19, heart.
**Tayanch so‘zlar:** qandli diabet, asorat, interleyinlar, COVID -19, yurak.
**Ключевые слова:** сахарный диабет, осложнения, интерлейкины, COVID -19, сердце.

The article describes research on the study of interleukins indicators in the development of heart complications in children with diabetes after COVID-19 infection. Thus, in type 1 diabetics, there was an increase in interleukin 1, 10, and TNF alpha, but in the main group of children, the increase in the concentrations of these cytokines was more pronounced in the presence of COVID-19 infection.

## COVID-19 INFEKSIDAN SO‘NG 1-TUR QANDLI DIABET BILAN KASALLANGAN BOLALARDA YURAKDAGI ASORATLAR RIVOJLANISHIDA INTERLEYKINLARNING O‘ZIGA XOS XUSUSIYATLARI

**A. A. Sadirxodjaeva, D. T. Ashurova**
Toshkent pediatriya tibbiyot instituti, Toshkent, O‘zbekiston

Maqolada 1 tur qandli diabet bilan kasallangan COVID-19 infekyasi o‘tkazgan bolalarda yurak asoratlari rivojlanishida interleykinlar o‘rni o‘rganilgan. Shunday qilib 1- tur qandli diabet bilan kasallangan bolalarda inteley-kin 1,10 va TNFα ko‘rsatkichlarini ortishi kuzatilmoqda bunday xolat ayniqsa COVID-19 infeksiyasidan so‘ng asosiy gurux bolalarida yaqqol namoyon bo‘lgan.

## ОСОБЕННОСТИ ПОКАЗАТЕЛЕЙ ИНТЕРЛЕЙКИНОВ В РАЗВИТИИ СЕРДЕЧНЫХ ОСЛОЖНЕНИЙ У ДЕТЕЙ С САХАРНЫМ ДИАБЕТОМ ПОСЛЕ COVID-19 ИНФЕКЦИИ

**А. А. Садирходжаева, Д. Т. Ашурова**
Ташкентский педиатрический медицинский институт, Ташкент, Узбекистан

В статье описывается исследование, посвященное изучению показателей интерлейкинов в развитии сердечных осложнений у детей с сахарным диабетом после COVID-19 инфекции. Так, у пациентов с сахарным диабетом 1 типа было выявлено повышение интерлейкинов 1, 10 и TNFα, причем увеличение концентрации этих цитокинов было более выраженным при наличии инфекции COVID-19 в основной группе детей.

Cardiovascular complications in children with type 1 diabetes mellitus (T1DM) after COVID -19 have become the subject of close study by foreign scientists. These studies cover a wide range of topics, including mechanisms of vascular and myocardial damage, long-term consequences, and features of the disease course in children with DM11. This review summarizes the most significant studies of foreign authors [1].

Multisystem inflammatory syndrome in children (MIS-C) American researchers pay great attention to multisystem inflammatory syndrome (MIS-C), which is observed in children after COVID-19. Whittaker et al. (2020) conducted a study of 58 children with MIS-C and found that about 70% of patients had cardiovascular disorders. This included myocarditis, dilated coronary arteries, and decreased left ventricular ejection fraction. The average age of participants was 10 years. Myocarditis was accompanied by increased levels of troponin and BNP (natriuretic peptide), which indicated significant myocardial damage [6,7]. Clerkin et al. (2020) studied the effects of COVVI-19 on blood clotting systems in children suffering from chronic diseases, including T1DM. Research has shown that the risk of thrombosis in children with diabetes is 20 to 30% higher than in children without diabetes, due to the increased D-dimer levels and platelet activation. In patients with T1DM, hypercoagulability was increased due to chronic hyperglycemia, which created an additional burden on the vascular system [3,4,5]. Rubino et al. (2020) showed that COVID-19 interferes with glycemic control in children with T1DM. 25% of patients developed diabetic ketoacidosis, that further increased the risk of cardiovascular disease and vascular complications. Proinflammatory cytokines, such as interleukin-6, played a key role in exacerbating metabolic and vascular complications [2,8].

**Purpose of the study.** To study the role of interleukins in the development of cardiac complications in children with diabetes mellitus after COVID-19 infection.

**Object and methods of research.** We conducted a study of 254 children with type 1 diabetes who had a COVID-19 infection and who received treatment in the children's department of the

Republican Specialized Scientific and Practical Medical Center of Endocrinology named after Academician E. Kh. Turakulov. The main group No. 1 consisted of children with type 1 diabetes mellitus after a COVID-19 infection with DKAN and cardiovascular complications. The main group N2 was made up of children with type 1 diabetes after being infected with ecological infections of DKAN, the comparison group is made up of children with type 1 diabetes after infection-19 without DKAN and the control group including 30 healthy children of the same age actually suffered from covid-19 infections. We conducted biochemical and immunological studies of HbA1c, Hf CRP, Il-1, Il-17, Il-10, TNF-α, and VEGF parameters.

**Research results and discussion.** When studying cytokine in children with type 1 diabetes with covid-19 infections, there have been multi-directional changes. Therefore, the level of IL-17 in patients with diabetes with COVID-19 infections decreases compared to the comparative group. The concentration of some cytokine causes higher inflammation in patients with diabetes with meals, especially meaningful when there is a previous infection of Covid-19. When comparing the two group of patients, we found that the level of TFN-α was beyond the group with children with diabetes with meals with covid-19 infections. It should be noted that the concentration of TFN-α in patients with diabetes without being contaminated with Covvi-19 is no different from the control group, on this basis we think that it is possible to consider the concentration of this cytokine as a specific sign of diabetic patients with myocardial damage. It tends to increase the IL-17 content in the patient's serum, but there is no statistical difference between groups. In patients with diabetes, IL-10 anti-inflammatory concentration has increased according to the presence of Covid-19 infection. Therefore, in this group, its content has exceeded the indicators of the control and comparison groups.

**Table 1.**

**Immunological characteristics of patients in the study groups.**

| Indicator | Main group (n=28) | Main group (n=74) | Comparison group (n=152) | Control group (n=30) |
|---|---|---|---|---|
| Il-1 pg/ ml | 9,8±0,6* | 4,5±0,3* | 4,15±0,33* | 3,8±0.3* |
| Il-17 pg/ ml | 6,7±0,48* | 7,7±1,1* | 6,7±0,5,7 | 6,7±0,5 |
| Il-10 pg/ ml | 7,2±0,75* | 2,1±03* | 1,47±0,2* | 0.84±0.1* |
| TNF-α mg / ml | 7,4±0,54* | 3,4±0,6* | 3,05±0,3* | 2,7±0,2* |
| VEGF pg/ ml | 305,3 ±132,59* | 266,1± 28,4* | 237,35±26,5* | 208,6±24,7* |
| Hf CRP mg / L | 4.62±0.1* | 3.2± 0.8* | 0.9±0.1* | 0.9±0.13* |
| HbA1c (%) | 10,9±0,35* | 10,6±1,89* | 6,8±0,5* | 5,4 ±0,3* |

*Note: * significance of the difference p<0.001.*

Currently, the role of immune activation in the progression of heart damage and the development of heart failure in type 1 diabetes mellitus has been proven.

The highest level of Il-1 was observed in the main group No. 1 (9.8 ± 0.6 pg/ml), which significantly exceeds the values in the main group No. 2 (4.5 ± 0.3; p<0.001), the comparison group (4.15 ± 0.3; p<0.001) and the control group (3.8 ± 0.3; p<0.001).

The Il-17 value in the main group No. 1 (6.7 ± 0.48) is significantly lower than in the second main group (7.7 ± 1.1; p<0.001), but does not differ from the comparison group (6.7 ± 0.5) and the control group (6.7 ± 0.5). An increase in the level in the DKAN group confirms a specific increase in Th17-mediated inflammation.

Il-10 levels of anti-inflammatory cytokine (7.2 ± 0.75 pg/ml) were significantly higher in main group No. 1 than in the second main group (2.1 ± 0.3; p<0.001), the comparison group (1.47 ± 0.1; p<0.001), and the control group (0.84 ± 0.1; p<0.001). It indicates a compensatory activation of the anti-inflammatory response in combined complications, also it indicates the maximum level of systemic inflammation in a combination of cardiovascular complications and DKAN.

The level of TNF-α was maximal in the main group No. 1 (7.4 ± 0.54 mg / ml) and significantly exceeded the values in all other groups: the main group No. 2 (3.4 ± 0.6; p<0.001), the comparison group (3.05 ± 0.2; p<0.001) and the control group (2.7 ± 0.2; p<0.001). This indicates an increased inflammatory response in cardiovascular complications.

The maximum level of VEGF was observed in the main group No. 1 (305.3 ± 132.59 pg/ml), which significantly exceeds the indicators of the main group No. 2 (266.1 ± 28.4; p<0.001), the comparison group (237.35 ± 24.7; p<0.001) and the control group (208.6 ± 24.7; p<0.001).

These data indicate significant vascular changes in combined complications.

The HbA1c level was significantly higher in main group 1 (10.9 ± 1.35%) and main group 2 (10.6 ± 1.89%) compared to the comparison group (6.8 ± 0.5; p<0.001) and the control group (5.4 ± 0.3; p<0.001). This reflects poor glycemic control in the presence of complications.

The highest levels of Hf CRP were registered in the main group No. 1, which is associated with a severe inflammatory response in a combination of cardiovascular complications and DKAN. The level of Hf CRP was maximal (4.62 ± 0.1 mg / L) and significantly exceeded the indicators of the main group No. 2 (3.2 ± 0.8 mg/L; p<0.001), the comparison group (0.9 ± 0.13 mg / L; p<0.001) and the control group (0.9 ± 0.13 mg / l; p<0.001). This data indicates severe inflammation in a combination of cardiovascular complications and DKAN.

**Conclusion.** Thus, in patients with type 1 diabetes mellitus, an increase in interleukins 1, 10, and TNFa was found, while the increase in the concentration of these cytokines was more pronounced in the presence of a previous COVID-19 infection in children of the main group. The formation of microangiopathies in adolescents with different levels of HbA1c is associated with changes in the serum concentration of almost all studied mediators involved in neoangiogenesis and remodeling vascular wall remodeling processes in various cardiovascular pathologies. TNFa, a universal inflammatory mediator, triggers a sequence of biological events that leads to apoptosis of vascular endothelial cells, which later leads to cardiovascular complications.

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