EXCELLENCIA
INTERNATIONAL MULTI-DISCIPLINARY JOURNAL OF EDUCATION
Volume 02, Issue 07, 2024 ISSN (E): 2994-9521

Systemic Lupus Erythematosus in Children: Clinical and Laboratory Aspects of Diagnosis and Course

Shermatova Z. A. [1], Ashurova D. T. [2], Fayzullaeva N. Ya. [3], Raufov A. A. [4]

[1, 2] Tashkent pediatric medical institute

[3, 4] Institute of Human Immunology and Genomics

Abstract:

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease of unknown etiology characterized by the hyperproduction of organ-nonspecific autoantibodies to various components of the cell nucleus, leading to immune-inflammatory damage to tissues and internal organs. Research aim: to study the role of immunological markers in the pathogenesis of SLE development in children. Materials and methods: data collection was conducted between 2022-2024 at the Tashkent Pediatric Medical Institute clinic. Preliminary studies show that the imbalance of immunological markers and the increase in autoantibodies are associated with the severity and recurrent nature of the disease.

Keywords: systemic lupus erythematosus, autoimmune disease, children, immunological markers, pathogenesis.

Relevance: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease of unknown etiology, characterized by overproduction of organ-nonspecific autoantibodies to various components of the cell nucleus with the development of immunoinflammatory damage to tissues and internal organs [1, 3].

The disease debuts in childhood only in 10-20% of cases, but according to the results of numerous studies, SLE that debuts in childhood tends to have a more severe course: in children, kidney and central nervous system damage is more common, and organ damage occurs more quickly [5, 10].

It has been proven that in SLE there is an interaction between the components of the adaptive immune system and the cells and tissues of the body, caused by the dysregulation of autoreactive B cells, which is based on a violation of immunological tolerance [6, 11].

Purpose of the study: To study the role of immunological markers in the pathogenesis of the development of systemic lupus erythematosus in children.

Materials and research methods: The material was collected during 2022-2024. on the basis of the clinic of the Tashkent Pediatric Medical Institute. A total of 75 children with SLE were examined. The control group consisted of 20 practically healthy children.

In our work, we used clinical-anamnestic, laboratory-instrumental immunological and statistical research methods.

Expression of CD receptors was carried out in a rosette reaction using monoclonal antibodies of the LT series produced by Sorbent LLC.

To determine the concentrations of IFNγ, CRP, lactoferrin, C3, C4 in the blood serum of the study groups, a three-stage "sandwich" method was used - this is a type of three-phase ELISA.

Statistical processing of the research results was carried out using the SPSS v16.0, R, PLINK and Haploview 4.2 software packages.

Research results: When analyzing the data obtained by age of children with SLE, we obtained the following results: children from 3 to 7 years old were 14.5%, from 8 to 14 years old – 50.9%, from 15 years old and over were 34.5% (fig.1).

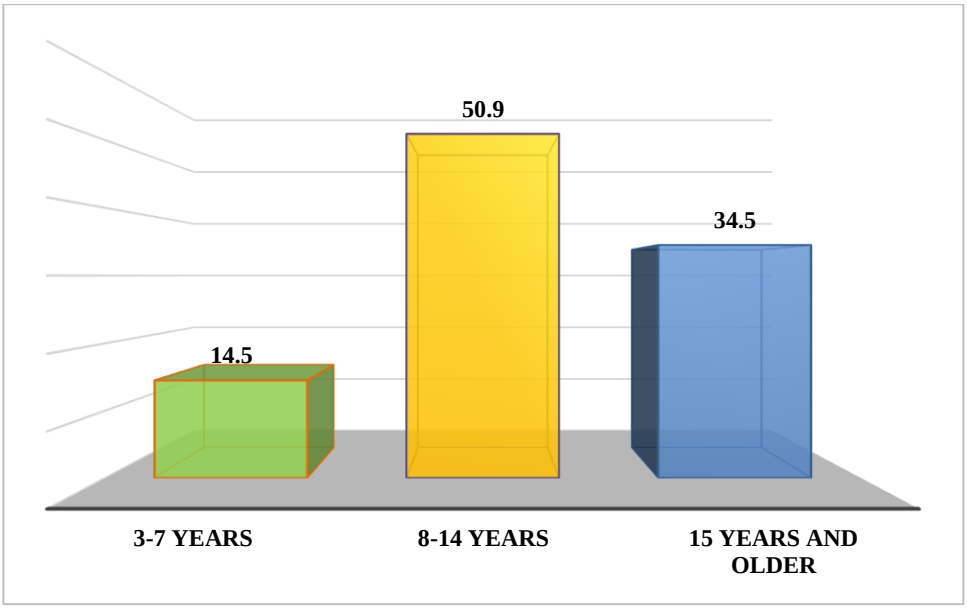

Fig.1. Data on the age of children with SLE, (%)

When analyzing gender, a slight predominance of males (50.9%) than females (49.1%) was revealed (fig.2).

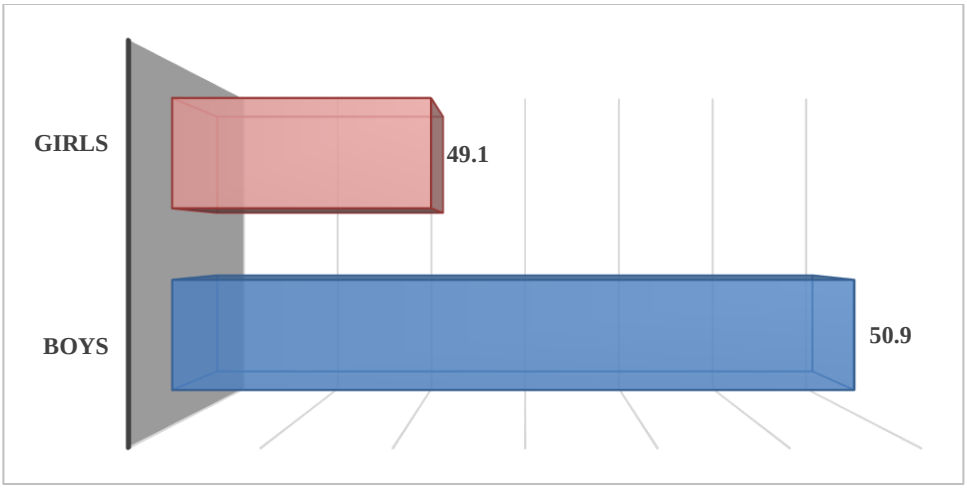

Fig.2. Gender distribution of children with SLE (%)

The main complaints of children with systemic lupus erythematosus were the following: butterfly symptoms were present in 70.9%, pain in the joints of the legs and arms was detected on average in 18.2%. Local articular signs of SLE (limited movement, swelling) occurred in 12.7% of children. Signs of intoxication (fever, general weakness, loss of appetite, tachycardia) were observed on average - 28.8%. Neurological disorders were present in an average of 1.82% of children with SLE; lupus nephritis occurred in 21.8% of children (fig.3).

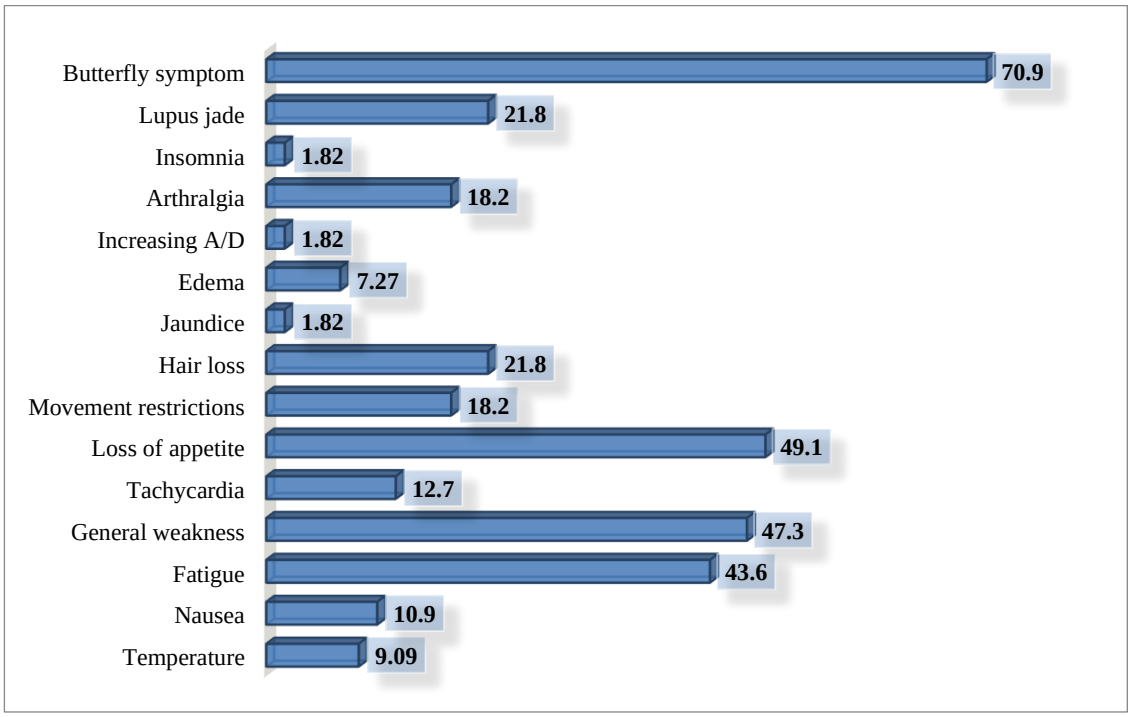

Fig.3. Main complaints of children with SLE (%)

Analysis of somatic diseases revealed that anemia was more common in children with SLE. Diseases of the urinary system were present in 27.3%. ENT diseases were detected in 23.6% of children with SLE. The incidence of nervous system diseases was 14.5%. Diseases of the cardiovascular system were also identified in 14.2%, diseases of the respiratory system in 5.45%, and children with SLE. Reactive hepatitis, ophthalmological diseases, and gastrointestinal diseases were detected on average in 3.45% of children with the pathology under study (fig.4).

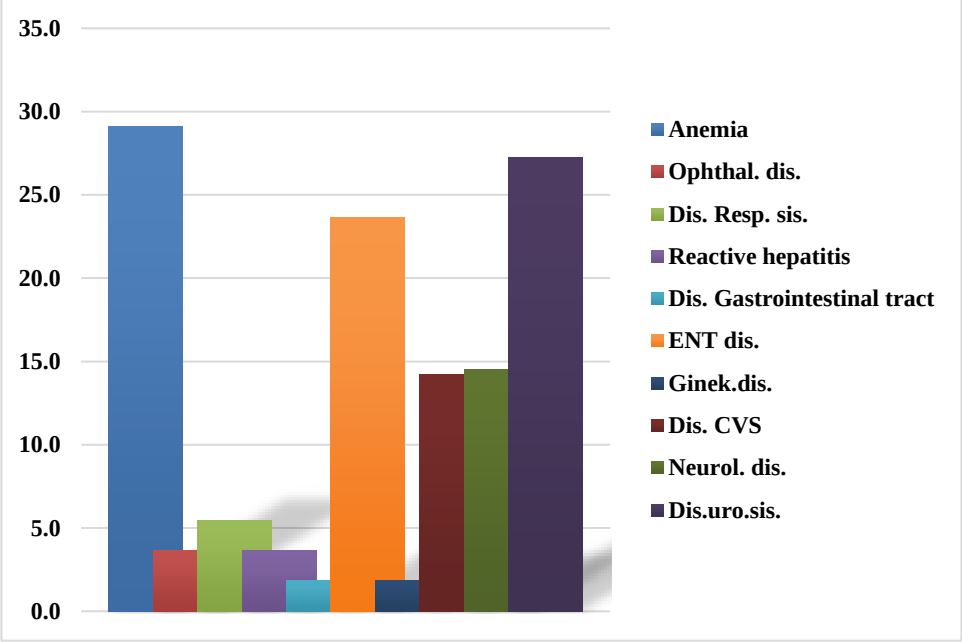

Fig.4. Concomitant pathology in children with SLE (%), (P<0.05)

Analysis of laboratory data revealed changes in the level of leukocytes in peripheral blood. The erythrocyte sedimentation rate was increased (18.2), which indicates an inflammatory response in the body. Signs of anemia were also detected. There were no statistically significant changes in the level of other parameters. A biochemical analysis of the blood of children with SLE revealed an increase in ALT and total protein.

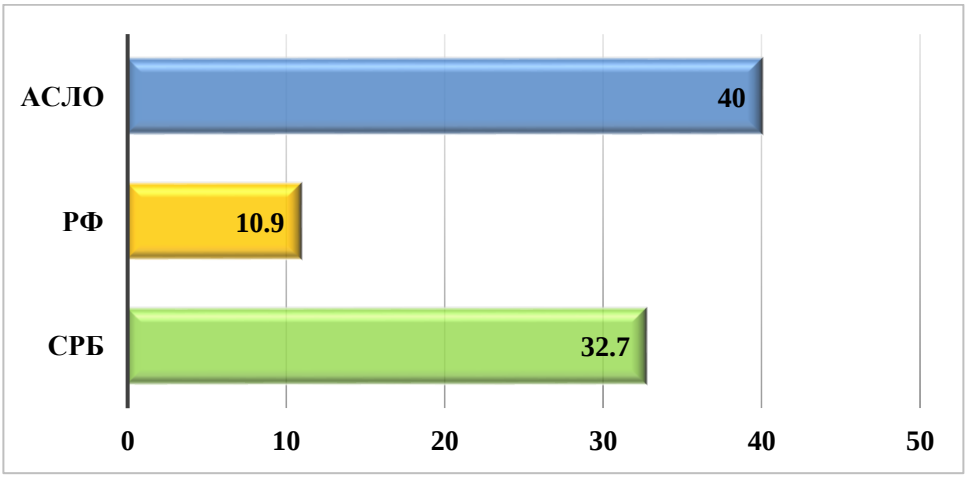

Fig.5. Concentration of CRP, ASLO and RF in subjects, (%)

To study the role of innate immune parameters in the development of SLE, we studied acute phase proteins.

The main function of the acute phase protein system is the removal (elimination) of foreign cells and regulation of the immune response. One of them is C-reactive protein (CRP), an acute phase protein related to nonspecific protective factors produced by liver cells [2, 8]. When analyzing the results of C reactive protein in children with SLE, an increase in its level was revealed in 32.7%.

Antistreptolysin O (ASLO) is an antibody produced by the body directed against streptolysin O, a toxic enzyme secreted by certain groups of hemolytic streptococci. An increase in this indicator indicates sensitization of the body to streptococcal antigens. During the period of convalescence, the indicator decreases compared to the acute period, therefore it can be used to monitor the dynamics

of the course and assess the degree of activity of the systemic process [4, 9]. In our study, this indicator was elevated in 40.0% of children with SLE.

Rheumatoid factor (RF) is a protein that is synthesized by the body's immune system. RF refers to autoimmune (attacking one's own body) immunoglobulins of class M (IgM), which act as autoantigens to antibodies of the IgG class, which have changed their properties under the influence of an infectious agent. RF production is carried out by the synovial (articular) membrane (the inner layer of the joint capsule or osteofibrous canal), from where it enters the bloodstream. In the blood, RF forms immune complexes IgG + rheumatoid factor, which cannot be destroyed by cells of the immune system (phagocytosis). As a result, complexes accumulate in the synovium and blood vessels, which causes their damage and the development of inflammation [10]. Analysis of the results of RF concentration revealed an increase in its level in 10.9% of children with SLE (fig.5).

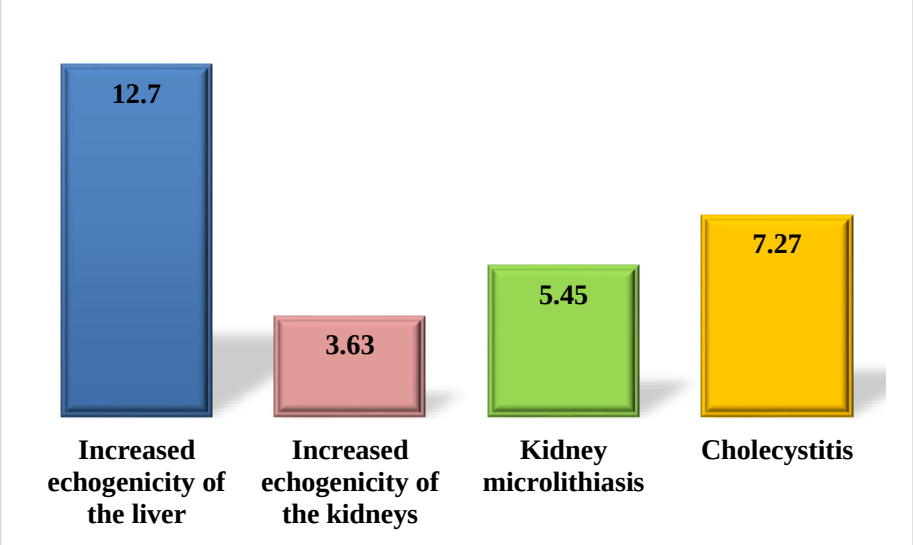

Fig.6. Ultrasound diagnostics of abdominal organs in children with SLE, (%), P≥0.05

Analysis of data on ultrasound examination of the abdominal organs in children with SLE revealed inflammatory changes in the liver in 12.7%, in the gall bladder in 7.27%, as well as inflammatory changes in the kidneys in 3.63% and disorders of water-salt metabolism in the kidneys at 5.45% (fig.6).

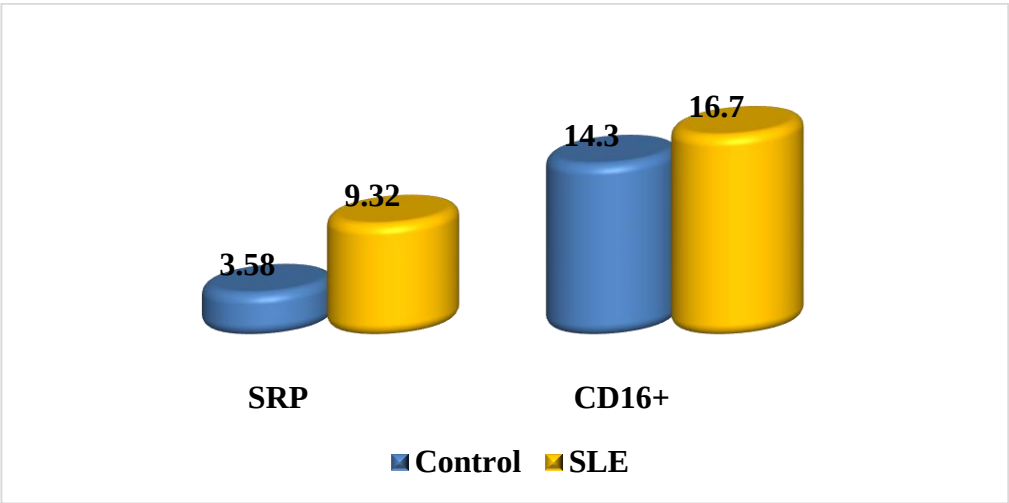

Fig.7. Concentration of CRP and NK cells in subjects (mg/l, %), (P<0.05)

The progression of inflammatory processes in systemic diseases occurs due to the activation of autoimmune mechanisms that initiate a violation of tolerance to self-antigens, resulting in an

immune response directed against normal tissues. This process is caused by a complex interaction of genetic, immunological, infectious and environmental factors, as well as defects in hormonal and neuroendocrine regulation. The development of inflammation is based on a whole cascade of biochemical and immunological processes regulated by various humoral mediators [7, 9].

Of the immunological markers, the level of C-reactive protein was significantly increased in the main group by 2.6 times compared to the control group. Killer activity (CD16+ lymphocytes) in the main group of children with systemic lupus erythematosus was increased, but this indicator was not significant (fig.7).

Table 1. Lactoferin concentration in those examined children with SLE pg/ml

Indicators	SLE, n=55	Control group, n=20
Lactoferrin, ng/ml	332±9.75	414.1 ± 10.9

In addition to CRP, BF also includes lactoferrin, the level of which is reduced in systemic lupus erythematosus. The results obtained suggest that the reduced level of serum lactoferrin is due to the fact that it retains neutrophils at the site of inflammation, probably due to this its content in the blood is reduced (table 1).

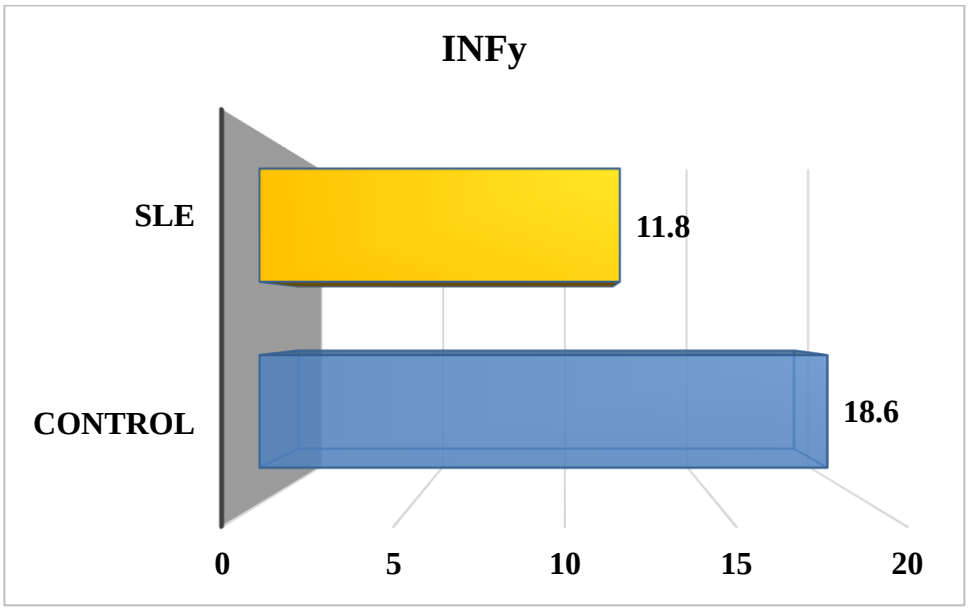

Fig. 8. INFy level in children with SLE, pg/ml

Of particular importance in this context are acute phase proteins and cytokines - protein molecules responsible for intercellular interactions. Currently, changes in the cytokine profile are considered as one of the possible trigger mechanisms contributing to the development of systemic lupus erythematosus (SLE) [2, 11].

The next stage of our research was to determine the level of the cytokine INFy. The synthesis of interferon-γ in children with SLE was significantly reduced compared to the control group (fig.8).

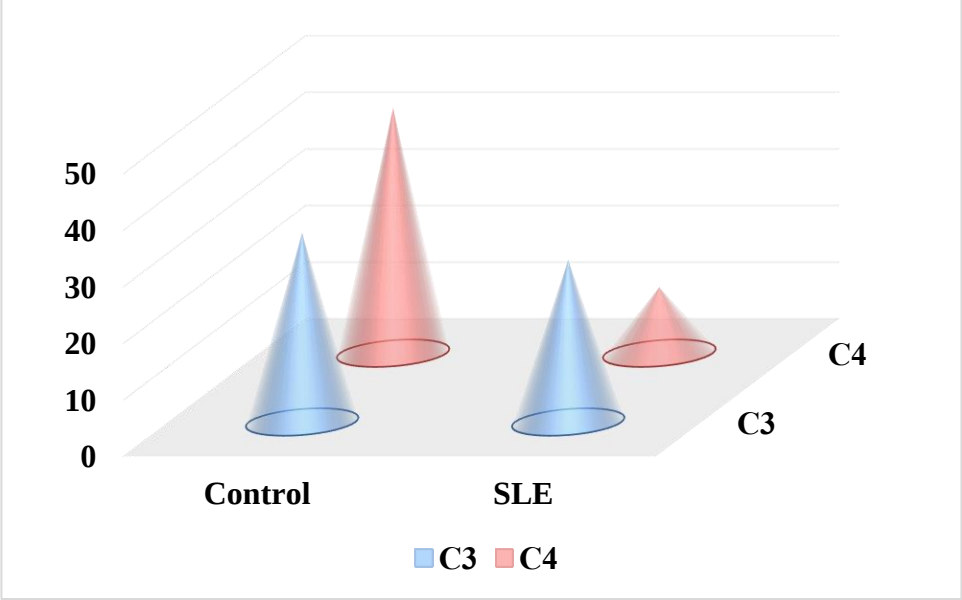

Fig.9. C3 and C4 compliment components in children with SLE (P≤0.05)

A decrease in the overall hemolytic activity of complement components (C3 and C4) is observed in patients with lupus nephritis and in some cases is associated with exacerbation of the disease. There are also reports that complement levels may be predictive of SLE activation.

Our study revealed a tendency towards a decrease in its concentration in the main group, and the level of C4 was significantly reduced by 3.7 times compared to the control group (fig.9).

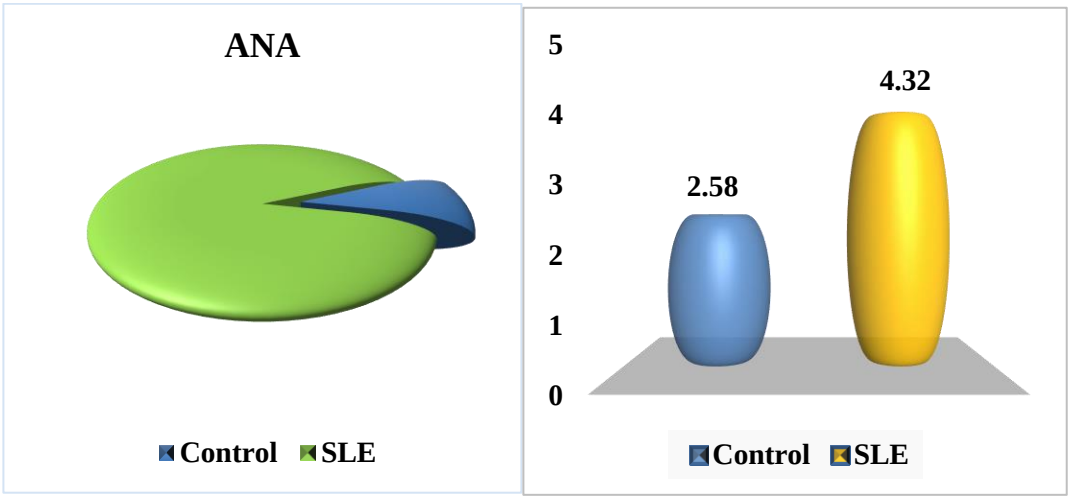

Fig. 10. Concentration of autoantibodies in children with SLE (%, U/ml)

It should be noted that in more than 20% of patients with SLE, the results of the ANA (antinuclear antibodies) test may be negative, especially at the onset of the disease. On the contrary, cases have been described in which positive results of ANA determination were several years ahead of the appearance of a full-blown clinical picture of SLE. Among ANAs, the most specific diagnostic and prognostic markers are anti-sDNA (single-stranded DNA) antibodies. Their detection is considered the "gold standard" for diagnosing SLE, but the search for new, more specific and sensitive markers of disease activity and prognosis continues. An increase in anti-sDNA titer correlates with SLE activity and the development of lupus nephritis. Determination of this immunological indicator is useful in monitoring SLE activity. A number of studies have demonstrated an association between anti-sDNA titers and the degree of irreversible organ damage [6, 8].

The next stage of our research was to determine autoantibodies in children with SLE. Among the examined children, antinuclear antibodies were detected in 16.4% of children. And the level of single-stranded DNA concentration was significantly increased by 1.67 times in children with SLE compared to the control group (fig.10).

Conclusions: Thus, the identified imbalance of immunological markers, such as primary disruption of the complement system, increased killer activity, concentrations of acute phase proteins and autoantibodies in some patients with SLE explains the early onset, severity of clinical manifestations and recurrent course of the lupus process. We continue our research to identify immunogenetic markers such as INFy and IL-4.

List of used literature

1. Kostik M.M. , Snegireva L.S. , Dubko M.F. , etc. How to recognize a patient with autoinflammatory syndrome: Clinical and diagnostic algorithms // Modern rheumatology. – 2013. – No. 3. – P. 14–20.
2. Kostik M.M. , Kuchinskaya E.M. , Abduragimova F.N. and others. Experience with the use of rituximab in children with systemic lupus erythematosus: a retrospective study of a series of cases // Issues of modern pediatrics. – 2016. – T. 15. – No. 3. – P. 295–300.
3. Kuchinskaya E.M. , Kostik M.M. , Chasnyk V.G. Modern foundations of a formalized description of the course of systemic lupus erythematosus in children // Pediatrician. – 2017. – T. 8. – No. 2. – P. 68–80.
4. Arici ZS, Batu ED, Ozen S. Reviewing the Recommendations for Lupus in Children. Curr Rheumatol Rep.2015;17:17-30. doi:10.1007/s11926-014-0489-5.
5. Bertsias GK, Tektonidou M, Amoura Z, et al. Joint European League Against Rheumatism and European Renal Association-European Dialysis and Transplant Association (EULAR/ERA-EDTA) recommendations for the management of adult and pediatric lupus nephritis. Ann Rheum Dis. 2012;71(11):1771-1782. doi: 10.1136/annrheumdis-2012-201940.
6. Brunner HI, Gladman DD, Ibañez D, et al. Difference in disease features between childhood-onset and adultonset systemic lupus erythematosus. Arthritis Rheum. 2008;58(2):556-562. doi: 10.1002/art.23204.
7. Group KDIGOKGW. KDIGO clinical practice guideline for glomerulonephritis. Kidney Int. 2012;2:139-274.
8. Mok CC. Treat-to-target in systemic lupus erythematosus: are we there yet? Expert Rev Clin Pharmacol. 2016;9(5):675-680. doi: 10.1586/ 17512433.2016.1146589.
9. Mosca M, Bombardieri S. Assessing remission in systemic lupus erythematosus. Clin Exp Rheumatol. 2006;24(6):99-104.
10. Van Vollenhoven RF, Mosca M, Bertsias G, et al. Treat-to-target in systemic lupus erythematosus: recommendations from an international task force. Ann Rheum Dis. 2014;73(6):958-967. doi: 10.1136/annrheumdis-2013-205139.
11. Van Vollenhoven RF, Voskuyl A, Morand E. Remission in SLE: closing in on the target. Ann Rheum Dis. 2015;74:2103-2106. doi: 10.1136/annrheum-dis-2015-208231.