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CLINICAL COURSE OF SYSTEMIC LUPUS ERYTHEMATOSUS IN CHILDREN IN THE CONTEXT OF IMMUNOLOGICAL DISORDERS: DIFFERENTIAL DIAGNOSTIC CRITERIA

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Abstract
The study is devoted to the clinical and immunological features of systemic lupus erythematosus (SLE) in children in order to clarify the differential diagnostic criteria. It was found that the disease often manifests itself at school age and is characterized by pronounced clinical polymorphism with the involvement of the skin, joints and internal organs. Reliable immunological shifts were revealed - an increase in the levels of acute phase proteins, a decrease in complement components, as well as an increase in the titers of antinuclear and anti-DNA antibodies. The data obtained emphasize the importance of a comprehensive assessment of clinical and immunological markers in the early diagnosis of SLE. This allows timely initiation of pathogenetic therapy and prevention of the development of severe complications.

Keywords: Systemic lupus erythematosus, children, autoimmunity, antinuclear antibodies, complement, immunodiagnostics.

Introduction

Diagnosis of systemic lupus erythematosus in children is one of the most challenging tasks in pediatric rheumatology. The disease is characterized by pronounced clinical polymorphism and a tendency to rapid progression with the involvement of vital organs. In childhood, clinical manifestations are often atypical, which complicates early recognition of the disease. Immunological disorders, including the production of antinuclear and anti-DNA antibodies, play an important role in diagnosis, but their presence does not always correlate with the clinical picture [1,4,7,9,15]. In addition, immunological parameters in children can change under the influence of age-related physiological fluctuations. Differential diagnosis is especially important for excluding other autoimmune and infectious diseases typical of childhood. Establishing relationships between clinical manifestations and immunological data can improve the accuracy of diagnosis and reduce the time it takes to make a diagnosis [2,6,10,11,13]. This will allow timely initiation of pathogenetic therapy and prevent severe complications. In this regard, the study of clinical and immunological relationships in children with SLE is an extremely relevant area. In-depth analysis of such data will allow the formation of more effective and safe treatment and diagnostic approaches in pediatric practice [3,5,8,12,14].

Objective of the study:

To analyze the clinical manifestations of systemic lupus erythematosus in children in combination with immunological parameters in order to clarify differential diagnostic criteria and improve the accuracy of diagnosis in the early stages of the disease.

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.

To determine the concentrations of IFNγ, 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.

Study results: Age-related analysis of children diagnosed with systemic lupus erythematosus (SLE) revealed distinct distribution patterns. The youngest age group, comprising children aged 3 to 7 years, accounted for 14.5% of the total cohort. The majority of patients (50.9%) were between 8 and 14 years of age. Adolescents aged 15 years and older represented 34.5% of the study population. (fig.1).

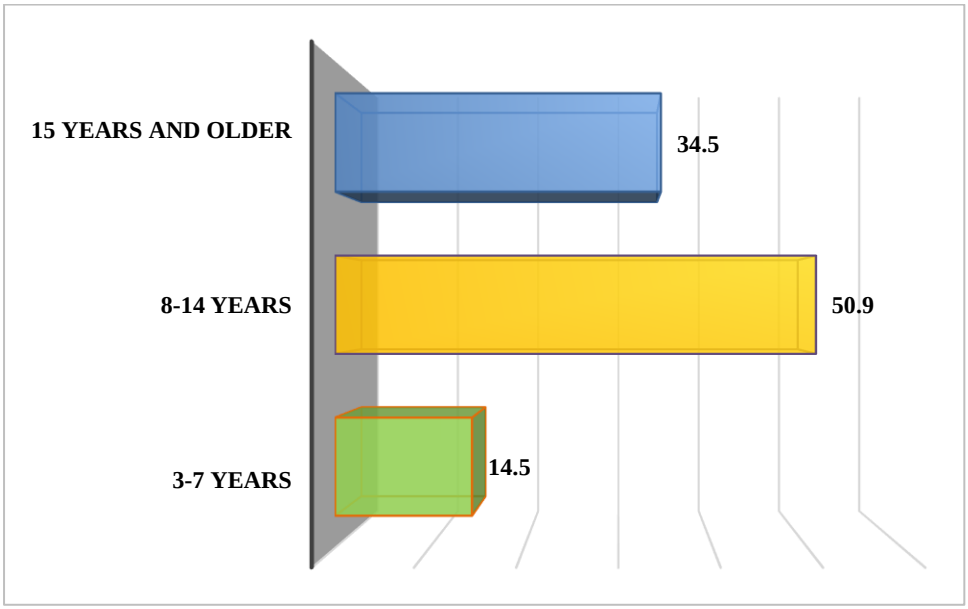

Fig.1. Data on the age of children with SLE, (%)

Gender distribution analysis demonstrated a minimal male predominance, with 50.9% of the study population being male. Female participants comprised 49.1%, indicating an overall balanced gender ratio. (fig.2).

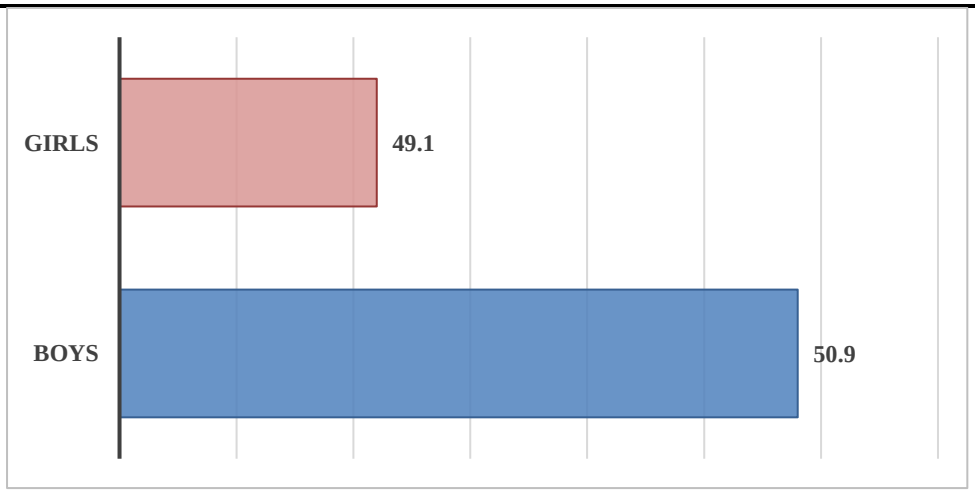

Fig.2. Gender distribution of children with SLE (%)

Among children diagnosed with systemic lupus erythematosus (SLE), a range of clinical complaints was identified. The most frequently reported manifestation was the characteristic 'butterfly' facial rash, observed in 70.9% of cases. Joint pain involving the upper and lower extremities was reported in 18.2% of the patients. Localized articular symptoms, such as restricted mobility and joint swelling, were noted in 12.7% of children. General signs of systemic intoxication—including fever, fatigue, decreased appetite, and tachycardia—were present in 28.8% of cases. Neurological involvement was relatively uncommon, occurring in 1.82% of patients. Lupus nephritis, as a manifestation of renal involvement, was detected in 21.8% of the pediatric cohort. These findings underscore the multisystem nature and clinical heterogeneity of SLE in the pediatric population (fig.3).

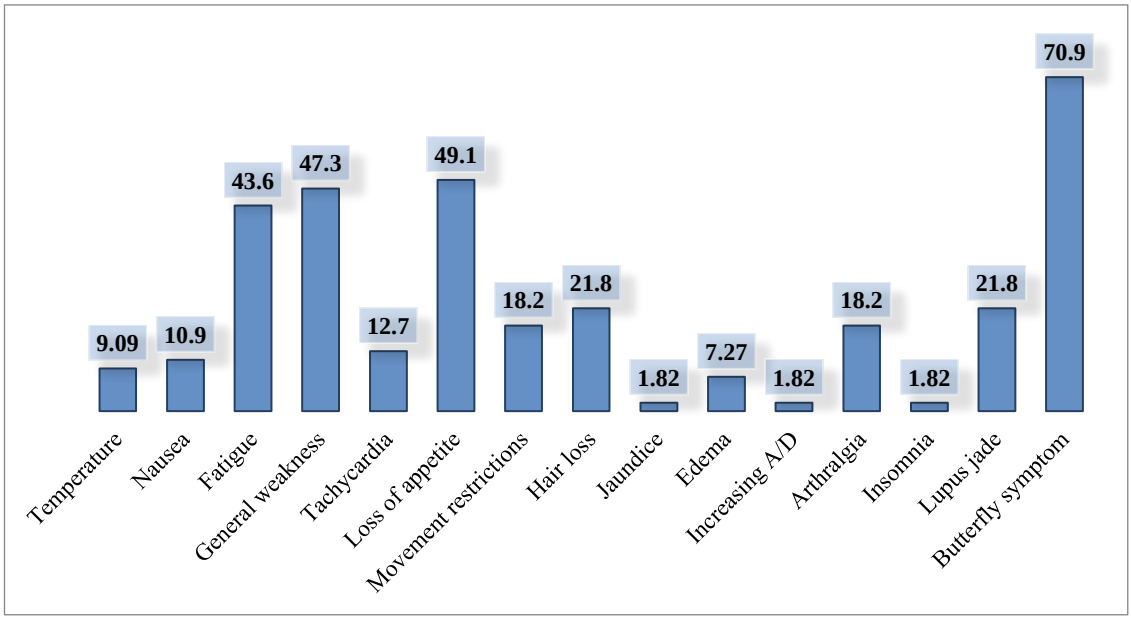

Fig.3.Main complaints of children with SLE (%)

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The assessment of comorbid somatic conditions in children with systemic lupus erythematosus (SLE) revealed a high prevalence of anemia, making it the most frequently observed associated disorder. Urinary system involvement was noted in 27.3% of cases, reflecting the impact of SLE on renal function. Diseases of the ear, nose, and throat (ENT) were identified in 23.6% of the patients. Neurological disorders were present in 14.5% of children diagnosed with SLE. Cardiovascular system pathologies were detected in 14.2% of the study population. Respiratory diseases were relatively uncommon, occurring in 5.45% of cases. Additionally, reactive hepatitis was observed among some patients. Ophthalmologic conditions were reported with similar frequency. Gastrointestinal tract disorders were also noted, each of these three conditions being found in approximately 3.45% of children. These data emphasize the wide spectrum of somatic comorbidities accompanying pediatric SLE and underline the need for multidisciplinary clinical management. (fig.4).

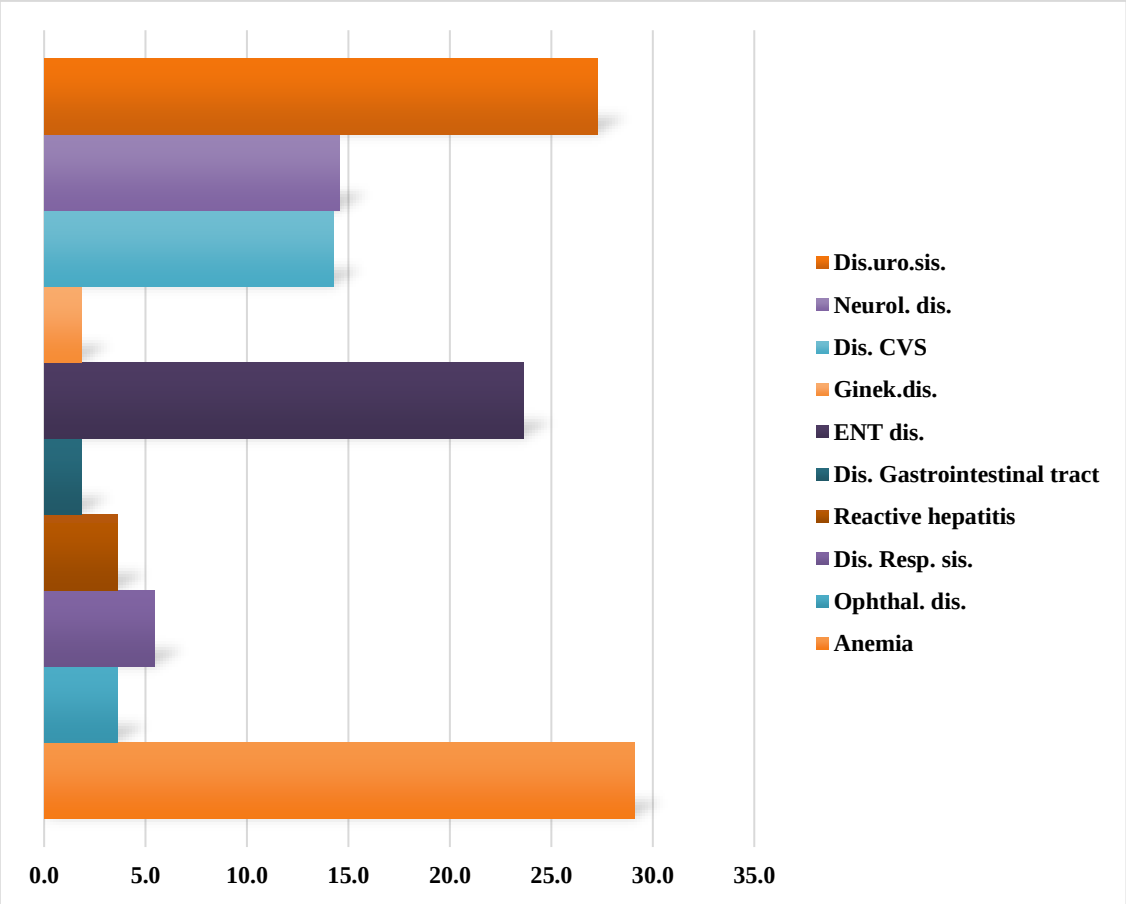

Fig.4. Concomitant pathology in children with SLE (%), (P<0.05)

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.

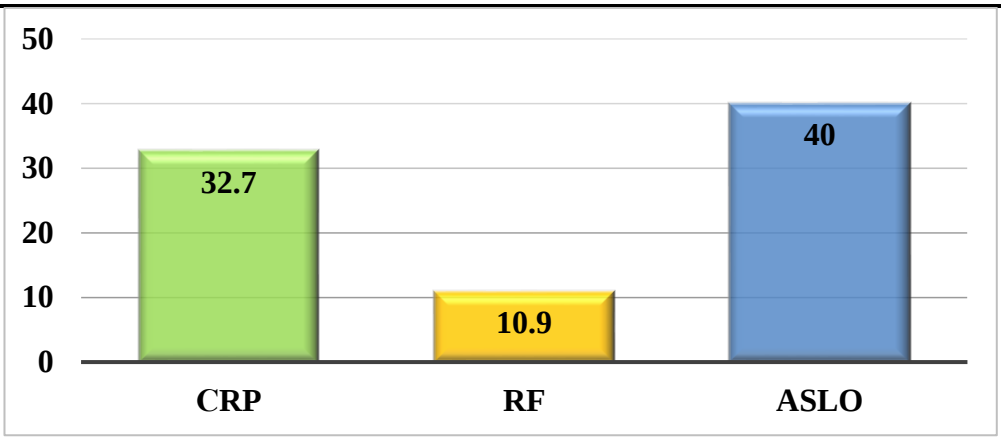

Fig.5. Concentration of CRP, ASLO and RF in subjects, (%)

To better understand the contribution of innate immunity to the pathogenesis of systemic lupus erythematosus (SLE), we conducted an analysis of acute phase reactants. These proteins, which are rapidly synthesized in response to inflammatory stimuli, play a key role in the clearance of pathogens and modulation of immune responses. One of the most studied markers is C-reactive protein (CRP), synthesized by hepatocytes and functioning as a nonspecific defense factor. Elevated CRP levels were detected in 32.7% of pediatric patients with SLE, indicating ongoing systemic inflammation.

Another significant biomarker is antistreptolysin O (ASLO), an antibody formed in response to the presence of streptolysin O—atoxic cytotoxic enzyme produced by β-hemolytic streptococci. Increased ASLO titers reflect sensitization to streptococcal antigens and are often observed in post-infectious immune responses. The level of ASLO typically declines during convalescence, making it a useful indicator for monitoring disease progression and immune activity. In our cohort, elevated ASLO values were found in 40.0% of children diagnosed with SLE, suggesting frequent post-streptococcal immunologic reactivity.

Rheumatoid factor (RF), an autoantibody of the IgM class, is another innate immune marker relevant to autoimmune pathology. RF targets altered IgG molecules, forming immune circulating complexes that evade normal phagocytic clearance. These immune complexes tend to accumulate in synovial tissue and vascular endothelium, triggering chronic inflammation and tissue damage. RF is predominantly synthesized in the synovial membrane and then enters systemic circulation. Its presence is associated with immune complex-mediated mechanisms, which are central to the pathophysiology of autoimmune diseases such as SLE. In our study, elevated RF levels were identified in 10.9% of pediatric SLE cases.

Collectively, these findings highlight the relevance of acute phase proteins and autoantibodies in the diagnostic evaluation of SLE in children. The data support the notion that both infectious triggers and dysregulated innate immune responses contribute to disease activity and clinical manifestations. (fig.5).

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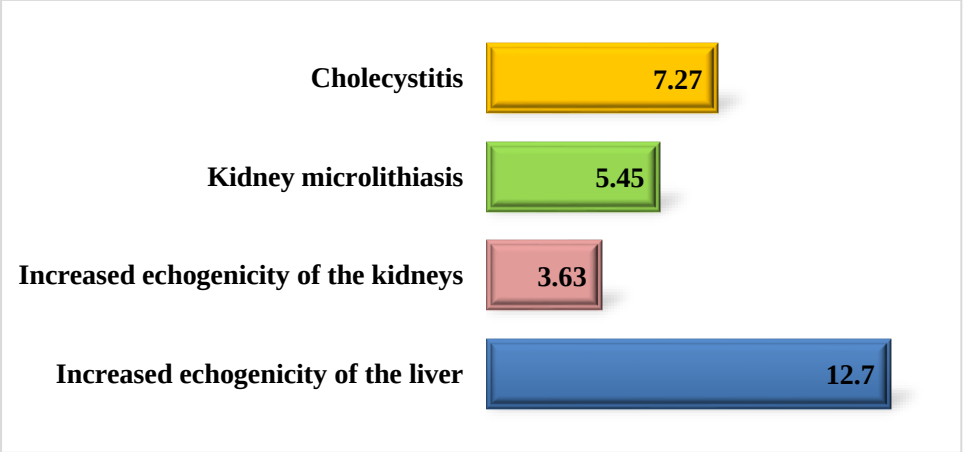

Fig.6.Ultrasound diagnostics of abdominal organs in children with SLE, (%), P≥0.05

Ultrasound evaluation revealed a range of structural abnormalities in internal organs among children with systemic lupus erythematosus (SLE). Increased hepatic echogenicity, indicative of possible fatty infiltration or chronic inflammation, was observed in 12.7% of the cases. Renal ultrasonography showed increased parenchymal echogenicity in 3.63% of patients, suggesting early nephropathic changes. Evidence of microlithiasis in the kidneys, reflecting possible metabolic disturbances or early lithogenic processes, was found in 5.45% of children. In addition, sonographic signs of cholecystitis, including gallbladder wall thickening and altered motility, were present in 7.27% of the examined cohort. These findings underscore the importance of routine ultrasonographic monitoring in pediatric SLE to detect subclinical organ involvement. (fig.6).

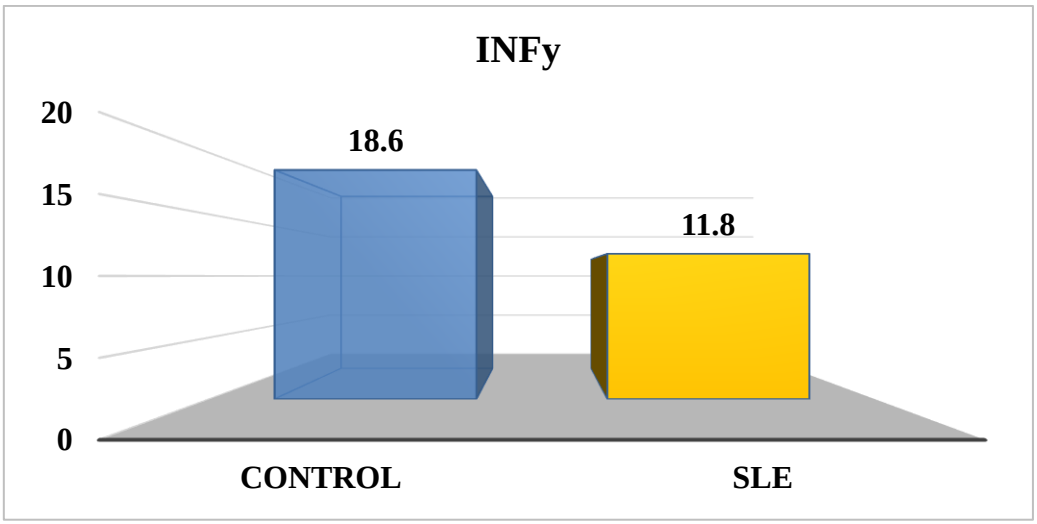

Fig. 8. INFy level in children with SLE, pg/ml

Acute phase proteins and cytokines play a critical role in immune regulation, acting as essential mediators of intercellular communication. These protein molecules are pivotal in coordinating inflammatory responses and immune activation. In the context of systemic lupus erythematosus

(SLE), growing evidence suggests that alterations in the cytokine network may serve as one of the initiating factors in disease pathogenesis. Recent studies have highlighted the significance of cytokine imbalances in driving autoimmune processes and sustaining chronic inflammation. In our investigation, we focused on assessing the concentration of interferon-gamma (IFN-γ), a key pro-inflammatory cytokine involved in Th1-mediated immune responses. Measurement of IFN-γ levels revealed a marked decrease in its production among children diagnosed with SLE when compared to healthy controls. This downregulation may reflect a state of impaired cellular immunity or a compensatory mechanism in response to ongoing immune dysregulation. These findings further support the hypothesis that cytokine dysfunction is a central feature in the immunopathology of pediatric SLE (Fig. 8).

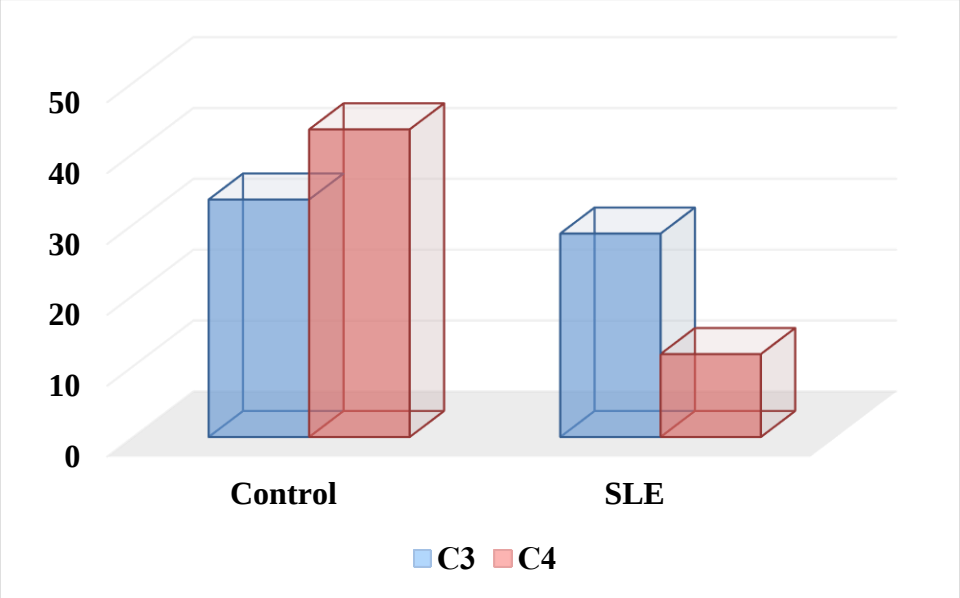

Fig.9.C3 and C4 compliment components in children with SLE (P≤0.05)

The complement system, particularly components C3 and C4, plays a fundamental role in immune complex clearance and the regulation of inflammatory responses. In patients with lupus nephritis, a reduction in total hemolytic complement activity is frequently observed and is often linked to disease exacerbation. Fluctuations in complement levels are increasingly recognized as potential biomarkers for monitoring disease activity in systemic lupus erythematosus (SLE). In the present study, we identified a clear trend toward decreased complement levels in children with SLE. Notably, the concentration of C4 was significantly diminished, showing a 3.7-fold reduction compared to healthy controls. This pronounced decrease may reflect ongoing immune complex deposition and complement consumption during active disease phases. These findings underscore the diagnostic value of complement profiling in assessing immune dysregulation in pediatric SLE (fig.9).

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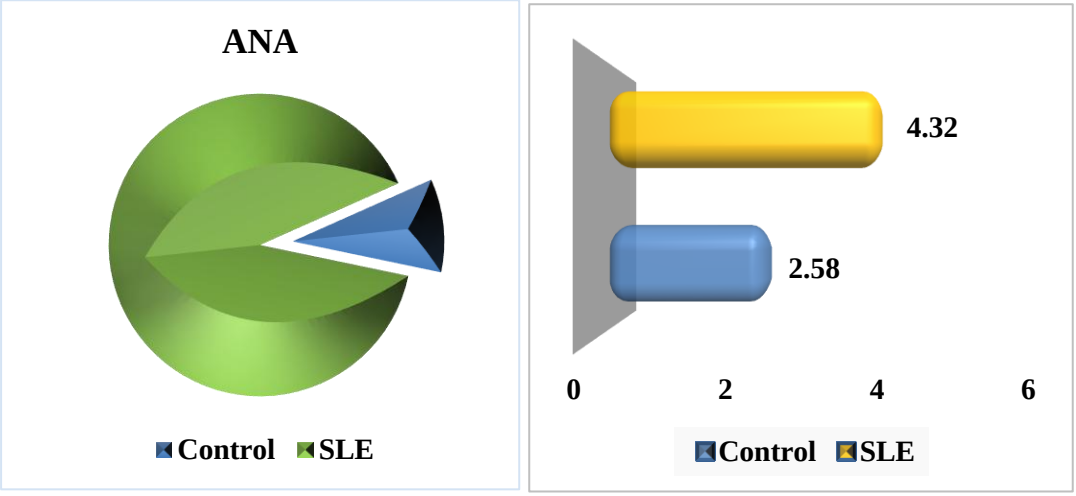

Fig. 10. Concentration of autoantibodies in children with SLE (%, U/ml)

It is important to emphasize that antinuclear antibodies (ANA), although widely used in the diagnosis of systemic lupus erythematosus (SLE), are not always present at the early stages of the disease. In fact, over 20% of patients may initially test negative for ANA despite harboring underlying immunological abnormalities. Conversely, some individuals exhibit positive ANA results years before clinical symptoms of SLE manifest, indicating their potential role in early detection. Among the spectrum of antinuclear antibodies, anti-single-stranded DNA (anti-ssDNA) antibodies are considered among the most specific markers for SLE diagnosis. Their presence not only supports the diagnosis but also serves as a reliable indicator of disease activity, particularly in relation to lupus nephritis. The diagnostic utility of anti-ssDNA has been widely accepted, yet the ongoing search for novel, more sensitive and specific biomarkers continues, especially those with prognostic significance. Several studies have demonstrated a strong association between rising anti-ssDNA titers and increased disease severity, organ involvement, and long-term tissue damage. Monitoring these autoantibodies has proven beneficial in clinical practice, aiding in early intervention and therapeutic adjustments. In our study, we focused on the evaluation of autoantibodies in children diagnosed with SLE. The results showed that 16.4% of the pediatric patients tested positive for ANA. Despite the relatively low detection rate, the presence of ANA remains diagnostically relevant in pediatric populations due to fluctuating immune responses. More importantly, our analysis revealed a statistically significant elevation in the concentration of single-stranded DNA antibodies in the main group. Compared to the healthy control group, children with SLE exhibited a 1.67-fold increase in ssDNA antibody levels. This marked increase underscores the heightened autoimmune activity in these patients. The correlation between elevated ssDNA titers and active SLE further supports their use in routine diagnostics and disease monitoring. Our data suggest that even in pediatric cases, anti-ssDNA quantification may serve as a reliable biomarker for assessing immune dysregulation. Moreover, the consistent rise in these antibodies could potentially predict disease flares. Taken together, these findings reinforce the clinical significance of both ANA and anti-ssDNA in the immunodiagnostic panel for SLE.

They also highlight the need for continued research into new autoantibodies that may offer greater sensitivity and specificity for pediatric lupus (fig.10).

Conclusion:

Based on the conducted study, it was established that systemic lupus erythematosus in children is characterized by a predominant lesion at the age of primary and middle school age with an almost equal gender distribution. The disease manifests itself with pronounced clinical and immunological heterogeneity with a predominant lesion of the skin, joints and internal organs against the background of systemic inflammation and activation of autoimmune mechanisms. The immunological profile includes an increase in acute phase indices, a decrease in complement components and an increase in autoantibody titers, which emphasizes the need for an integrated approach to the diagnosis and monitoring of the disease.

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