ЎЗБЕКИСТОН РЕСПУБЛИКАСИ СОҒЛИҚНИ САҚЛАШ ВАЗИРЛИГИ
ТОШКЕНТ ТИББИЁТ АКАДЕМИЯСИ

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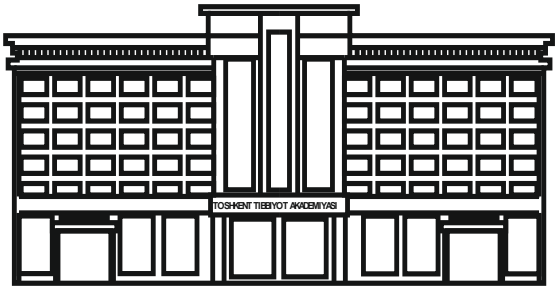
# TOSHKENT TIBBIYOT AKADEMIYASI AXBOROTNOMASI




# ВЕСТНИК ТАШКЕНТСКОЙ МЕДИЦИНСКОЙ АКАДЕМИИ

Тошкент

УДК:616.5-002.525.2:616.13/14-002:616-02

# ESTIMATION OF THE DEVELOPMENT OF THE CARDIOVASCULAR MANIFESTATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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# TIZIMLI QIZIL YUGURIKDA YURAK-QON TOMIR KASALLIKLARINI RIVOJLANISHINI BAHOLASH

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# ОЦЕНКА РАЗВИТИЯ СЕРДЕЧНО-СОСУДИСТЫХ ПРОЯВЛЕНИЙ ПРИ СИСТЕМНОЙ КРАСНОЙ ВОЛЧАНКЕ

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***Summary.*** *The aim of the study was to study the state of the cardiovascular system and assess the level of cardiovascular risk in patients with systemic lupus erythematosus (SLE) during the study, 70 patients with SLE were studied. In patients with SLE and identified changes in the cardiovascular system, there was a high and very high risk of developing CVD, associated with a high frequency*

*of traditional risk factors, subclinical damage to the heart and blood vessels, as well as a high prevalence of coronary artery disease, CHF.*

***Key words****: Systemic lupus erythematosus, atherosclerosis, cardiovascular risk factors*

***Hulosa:*** *Tadqiqotning maqsadi Tizimli qizil yuguruk (TQY) bilan kasallangan bemorlarda yurak-qon tomir tizimining holatini o'rganish va kardiovaskulyar xavf darajasini baholash edi. Tadqiqot davomida TQY bilan kasallangan 70 nafar bemor o'rganildi. TQY bilan kasallangan va yurak-qon tomir tizimida o'zgarishlar aniqlangan bemorlarda, yurak-qon tizimi tomonidan kelib chiqadigan asoratlarning rivojlanish xavfi yuqoriligi aniqlandi, bu esa an'anaviy xavf omillarining ko'p ucrashi, yurak va qon tomirlarining subklinik shikastlanishi, hamda gipertoniya kasalligi, yurak ishemik kasalligi va surunkali yurak yetishmovchiligining keng tarqalganligidadir.*

***Kalit so'zlar:*** *tizimli qizil yuguruk, ateroskleroz, yurak-qon tomir xavf omillari*



**Introduction.** Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by the production of a wide range of pathogenic autoantibodies, multivariable manifestations, course and prognosis, development of exacerbations and remissions [1, 11]. The prevalence of the disease varies from 1.4 to 11 cases per 100,000 population [4]. Along with a diverse clinical picture during the course of the disease, a characteristic "bimodality" can be distinguished. Thus, in the first three years after diagnosis, the predominant cause that determines the severity of the disease and the mortality of patients is kidney damage and infectious complications against the background of high disease activity. However, the second peak in mortality, 4–20 years after diagnosis, is predominantly caused by cardiovascular disease (CVD) [5, 6]. It should be noted that, while all-cause mortality in SLE has significantly decreased over the past decades due to the increase in the effectiveness of therapy, mortality from cardiovascular diseases remains at a high level and they remain the leading cause of death in patients [7, 8]. At the same time, it should be noted the high prevalence of CVD in patients with SLE, which significantly exceeds that in the general population [9]. An important link in the pathogenesis of SLE is microcirculation disorders with activation and proliferation of endothelium and smooth muscle cells, vasospasm, aggregation of formed elements, stasis, deformation and reduction of the capillary network [1, 2, 5].

Endothelial dysfunction and hemorheological disorders characteristic of SLE are considered as early predictors of atherosclerosis. The general pathogenetic mechanisms of these diseases suggest a high probability of atherosclerotic vascular lesions in patients with SLE [3, 6, 10].

It is known that along with a generalized lesion of small-caliber vessels, which is determined already at the early stages of the disease, changes in medium-sized vessels are also observed in SLE [2,10]. Peripheral arterial lesions according to angiography and ultrasound scanning of blood vessels in patients with SLE were found with a significantly higher frequency when compared with the control group and was associated with a severe clinical course of the disease [9]. A number of studies in the study of medium-sized vessels in patients with SLE demonstrated a predominant lesion of the ulnar arteries, which is a predictor of the development of digital necrosis [2, 3]. A biopsy of the ulnar arteries revealed a narrowing of the lumen of the arteries, while there were no atherosclerotic plaques [8]. Angiography revealed stiff peripheral arteries in patients with SLE [7]. Other researchers determined a decrease in the elasticity of the carotid arteries in patients with limited and, to a greater extent, diffuse form of SLE [6]. According to the Scottish group for the study of systemic sclerosis [6], stenosis of the carotid arteries was observed in 64% of patients with SLE at an average age of 57 (31-82) years and almost twice as often (35%) in control group. The frequency of atherosclerotic plaques and peripheral vascular disease was also higher among patients with SLE, despite the absence of significant differences in the frequency of cardiovascular risk factors between the two groups [7, 9].

Thickening of the aortic walls, which is an independent factor of cardiovascular risk, was diagnosed in patients with SLE, regardless of the severity of skin and kidney fibrosis, and also significantly differed from the control group [5].

Interest data is that the decrease in the reserve of coronary arteries according to the results of doppler echocardiography with contrast in patients with SLE was determined with a higher frequency when compared with the control group [6].

A recent study showed a significant decrease in endothelium-dependent vasodilation as an early marker of atherosclerosis with a trend towards an increase in the thickness of the intima-media complex in patients with SLE compared with the control group, while the groups did not differ in cardiovascular risk factors [7].

Along with the data of instrumental examination, confirming the diagnosis of atherosclerosis, clinical signs of atherosclerosis against the background of SLE are also described. According to the results of the Edinburgh epidemiological study, the diagnosis of intermittent claudication was established in 22%, coronary heart disease (CHD) in 15%, cerebrovascular disease in 6.5% of patients with SLE [9].

According to various studies, patients with SLE are characterized by a high risk of mortality from cardiovascular diseases [8]. In a cause-of-death analysis of 344 patients with SLE in Denmark, it was shown that the group of patients with death caused by other, non-SLE conditions was twice as high as the group of patients whose direct cause of death was SLE. At the same time, the main cause of death in the former was cardiovascular pathology [9].

Thus, the diagnosis of SLE suggests the early development of vascular atherosclerosis, which is one of the main causes of death in patients. Research on the prevalence of atherosclerosis in patients with SLE is currently scarce, especially compared to the large number of studies on atherosclerosis in systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and antiphospholipid syndrome (APS). The problem of the relationship between atherosclerosis and vascular damage in SLE remains not fully understood.

**The aim of this study** was to estimation the frequency of traditional cardiovascular risk factors and clinical manifestations of atherosclerosis in patients with SLE.

**Material and methods**

From 2021 to 2022, we examined 70 patients with a reliable diagnosis of SLE (66 women and 4 men) admitted to the rheumatology, cardiorheumatology and rheumatology departments of the 1st clinic of the Tashkent Medical Academy. The average age of patients was 46 ± 10.8 years (from 20 to 64 years). The duration of the disease ranged from 6 months to 38 years, with an average of 10 (4-15) years. The criteria for inclusion in the study were a reliable diagnosis of SLE (ARA criteria) [10] and the age of patients from 17 to 65 years.

Clinical characteristics of patients with SLE are presented in Table 1.

***Table 1.***

**Clinical characteristics of patients with SLE**

| Signs | Patients with SLE | |
|---|---|---|
| Arthritis | 15 | 21 |
| Lupus rash | 49 | 70 |
| Discoid rash | 47 | 67 |
| Kidney fibrosis (USD) | 55 | 79 |
| S-m Reynaud | 70 | 100 |
| Restrictive violations (functional tests) | 21 | 30 |
| Arterial hypertension (ECHO-KG) | 14 | 20 |
| Diastolic dysfunction (ECHO-KG) | 28 | 40 |
| Violations of the rhythm of the heart (HM-ECG) | 31 | 44 |
| ANA (+)* | 58 | 83 |

**ANA (antinuclear antibody) was determined by indirect immunofluorescence*

The control group consisted of 50 "conditionally" healthy volunteers (employees of the department of the Tashkent Medical Academy) who do not have systemic rheumatic diseases, matched by sex (45 women and 5 men) and age (44.1 ± 7.4 years).

The study did not include patients and volunteers with clinical signs of infection, end-stage renal or hepatic insufficiency, uncontrolled diabetes mellitus.

To verify the diagnosis of SLE and characteristics of organ pathology, all patients underwent instrumental studies, including chest X-ray, ECG, Echo-KG, Holter ECG monitoring (HM-ECG), functional pulmonary tests (spirometry, study of the diffusion capacity of the lungs).

In all patients of the main and control groups, classical risk factors for atherosclerosis were analyzed: a family history of cardiovascular diseases (CVD) in the next of kin (myocardial infarction (MI) or sudden death in men under 55 years of age, in women under 65 years of age), an increase in body mass index (BMI) (weight, kg/height, m2 ≥ 25 kg/m2) [8], dyslipidemia (abnormal levels of one or more classes of lipoproteins [total cholesterol (CH) levels> 5.0 mmol/l, high-density lipoprotein cholesterol (HDL cholesterol) < 1.0 mmol/l, triglycerides (TG) > 1.7 mmol/l], arterial hypertension (systolic blood pressure (SBP) ≥140 mm Hg, diastolic (DBP) ≥90 mm Hg or taking antihypertensive drugs), smoking, menopause, diabetes mellitus. Total coronary risk (TCR%) (10-year risk of cardiovascular events) was assessed using the Framingham scale.

To identify clinical forms of atherosclerosis in patients with SLE (n=60) and in the control group (n=45),

an ultrasound scan of the carotid arteries was performed using a linear sensor with a radiation frequency of 7.5 MHz on a Voluson 730 Expert device (Austria) with measurement of the thickness of the intima complex - media (TIM) at three points (1 point - common carotid artery - 10 mm to the bulb; 2 point - 5-10 mm cranial from the beginning of the bulb; 3 point - internal carotid artery - 10 mm after bifurcation from two sides) and calculations average and maximum values of TIM. The presence of atherosclerosis was assessed by thickening of the intima-media complex (IMT from 0.9 to 1.2 mm) and the presence of atherosclerotic plaques (ATP) (local increase in IMT > 1.2 mm).

Statistical processing of the results was carried out using the Statistica 6.0 software package (StatSoft, USA). Quantitative values are given as M±SD with correct distribution and as Me(LQ-UQ)-median with an interquartile range ($25^{th}$ - $75^{th}$ percentile) with incorrect distribution of features. For the statistical evaluation of the results, nonparametric methods were used: the Mann-Whitney test, the calculation of Fisher's exact test, and Spearman's correlation analysis. Differences were considered statistically significant at $p<0.05$.

**Results**

Comparison of traditional cardiovascular risk factors in patients with SLE and in the control group did not reveal significant differences, except that the frequency of smoking was significantly higher in the control group (p=0.002), and menopause was more common among patients with SLE (p=0.005) (Table. 2).

TFR% in patients with SLE was 3 (1-27) %, which coincided with the average value of TFR% in the control group – 3 (1-15) %.

***Table 2.***

**Traditional cardiovascular risk factors in patients with SLE**

| Risk factors for atherosclerosis: | Patients with SLE n=70 n(%) | Control group n=50 n(%) |
|---|---|---|
| Heredity according to CVD | 22 (31%) | 18 (36%) |
| BMI≥25 kg/m2 | 28 (40%) | 22 (44%) |
| Dyslipidemia | 53 (76%) | 34 (72%) |
| Arterial hypertension | 25 (36%) | 12 (24%) |
| Smoking | 5 (7%) | 14 (28%) |
| Menopause | 38 (57%) | 11 (24%) |
| Diabetes | 3(4,3%) | - |

**p<0,05*

When analyzing the clinical manifestations of atherosclerosis, it turned out that coronary artery disease was determined more frequently among patients with SLE. IHD was diagnosed in 9 (13%) patients with SLE and only in 1 (2%) volunteer from the control group (p<0.05). MI (one case) was recorded only in the group of patients with SLE, stroke - in one patient with SLE and in 1 volunteer from the control group.

Comparison of blood lipid concentrations showed that the level of triglycerides in patients with SLE was significantly higher than in the control group (p<0.001) (Table 3).

***Table 3.***

**Mean lipid values in SLE patients and in the control group**

| Lipids: (mmol/l) | Patients with SLE D, n=70 | Control group, n=50 |
|---|---|---|
| Cholesterol | 5,5 (4,8-6,4) | 5,6 (5,0-7,3) |
| Triglycerides | 0,87 (0,63-1,76)* | 0,55 (0,30-0,93)* |
| HDL | 1,24 (0,99-1,68) | 1,4 (1,21-1,62) |

*Me(LQ-UQ); * p<0,001*

The mean and maximum IMT values of the carotid arteries, obtained by ultrasound scanning of these vessels, did not differ significantly in the groups of SLE patients and controls. There was only a slight tendency to increase TIM max. (1.0 ± 0.36 and 0.88 ± 0.14) and the frequency of IMT thickening (42% and 38%, respectively) in patients with SLE compared with the control group. Atherosclerotic plaques (IMT>1.2 mm) were determined in 10% of patients with SLE and were absent in the control group (p<0.05) (Table 4).

***Table 4.***

**The thickness of the intima-media complex of the carotid arteries in patients with SLE and in the control group**

| TIM, mm | Patients with SLE n=60 | Control group, n=45 |
|---|---|---|
| TIM average | 0,78 ±0,18 | 0,74 ± 0,08 |
| TIM middle right | 0,77 ± 0,18 | 0,74 ± 0,09 |
| TI M middle left | 0,8 ± 0,2 | 0,75 ± 0,09 |

| | | |
|---|---|---|
| TIM maximum | 1,0 ± 0,36 | 0,88 ± 0,14 |
| TIM 0.9-1.2 (n,%) | 25 (42%) | 17 (38%) |
| TIM>1.2 (n,%) | 6 (10% )* | 0* |

*M±SD, n (%), *p<0.05*

A high positive correlation was established between IMT average and IMT max. with the age of patients with SLE (respectively, r=0.64, t=6.28, p<0.001 and r=0.44, t=3.74, p<0.001). Mean IMT also correlated with disease duration (r=0.28, t=2.23, p<0.05).

In the group of patients with SLE, positive correlations were found between TFR% and IMT, both mean (r=0.51, t=4.5, p=0.00003) and max. (r=0.41, t=3.4, p=0.001). In addition, they revealed a correlation between mean IMT and cholesterol levels (r=0.31, t=2.44, p<0.05).

**Conclusion**

A high prevalence of cardiovascular pathology and atherosclerotic vascular lesions in patients with SLE in the absence of significant differences in the frequency of major cardiovascular risk factors was also observed in other studies [6, 8, 9]. It can be assumed that the factors involved in the pathogenesis of this disease are of paramount importance in the development of early atherosclerosis in patients with SLE. This assumption is confirmed by a series of studies that show that anti-endothelial antibodies, dysfunction of the coagulation and fibrinolytic systems, an increase in the level of homocysteine, CRP, and intercellular adhesion molecules significantly increase the risk of atherosclerosis in SLE. Thus, in patients with SLE, along with scleroderma angiopathy, there are clinical and subclinical signs of atherosclerosis. These data indicate the advisability of prescribing drugs that have a protective effect on the vascular wall - statins and antioxidants - to patients with SLE.

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## ОЦЕНКА РАЗВИТИЯ СЕРДЕЧНО-СОСУДИСТЫХ ПРОЯВЛЕНИЙ ПРИ СИСТЕМНОЙ КРАСНОЙ ВОЛЧАНКЕ

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***Резюме.*** *Целью исследования было изучение состояниясердечно-сосудистой системы и оценка уровня кардиоваскулярного риска у больных системной красной волчанкой (СКВ). В ходе исследования было изучено 70 больных СКВ. У пациентов с СКВ и выявленными изменениями сердечно-сосудистой системы, отмечался высокий и очень высокий риск развития ССО, связанный с высокой частотой традиционных ФР, субклиническим поражением сердца и сосудов, а также высокой распространенностью ГБ, ИБС, ХСН.*

***Ключевые слова:*** *системная красная волчанка, атеросклероз, сердечно-сосудистые факторы риска.*