AJPMHS GLOBAL RESEARCH NETWORK

**AMERICAN Journal of Pediatric Medicine and Health Sciences**
*Volume 01, Issue 09, 2023 ISSN (E): 2993-2149*

# SYSTEMIC LUPUS ERYTHEMATOSUS AND RENAL LESIONS: CLINICOPATHOGENETIC ASPECTS

**Hamrayev B.E.**
*Resident Master, Department of Internal Medicine No. 1, Samarkad State Medical University, Samarkand, Uzbekistan.*

**Islamova K. A.**
*Docent, PhD Department of Internal Medicine No. 1, Samarkad State Medical Universiteti, Samarkand, Uzbekistan.*

**Ziyadullayev Sh.X.**
*Professor, Doctor of Medical Sciences, Head of the Department of Internal Medicine No. 1 of Samarkand State Medical Universiteti*

**Annotation:** Systemic lupus erythematosus (SLE) is a multifactorial disease caused by a complex interaction of genetic and exogenous factors underlying multiple disorders of innate and acquired immunity, including hyperproduction of cytokines, pathological activation of B cells, disturbances in intracellular signaling of T cells, and clearance defects. cells undergoing apoptosis and necrosis. The purpose of this review is to analyze recent literature data regarding the prevalence and pathogenetic mechanisms of the development of kidney damage (lupus nephritis) in SLE. Among human autoimmune diseases, SLE is predominantly prevalent among females (female to male ratio is approximately 10:1). The dependence of kidney damage on the degree of activity and course of SLE was noted. Most often, lupus nephritis occurs in acute and subacute SLE. Lupus nephritis develops in 55% of adult patients with SLE and 75% of children. The clinical picture of lupus nephritis, in most cases, is due to histological changes. Prognostically unfavorable clinical manifestations of lupus nephritis are nephrotic proteinuria, arterial hypertension, and a decrease in glomerular filtration rate for three months. Detection of subendothelial deposits, damage to more than 50% of the glomeruli, class IV lupus nephritis, including foci of fibrinoid necrosis and crescents, are considered predictors of deterioration in renal function.

***Key words:*** *systemic lupus erythematosus, lupus nephritis, chronic kidney disease, exogenous factors, risk factors, chronic renal failure.*

In recent years, the cause of the earlier and more frequent development of chronic kidney disease (CKD) in systemic lupus erythematosus (SLE) has been actively discussed [1,2]. According to modern concepts, SLE is based on a complex interaction of genetic and exogenous factors, leading to complex disorders of the innate and acquired immune system; hyperproduction of pro-inflammatory cytokines; pathological activation of B cells; disruption of intracellular signaling of T cells; defect in the clearance of cells subjected to apoptosis and necrosis [3,4,8]. Among human autoimmune diseases, SLE is predominantly prevalent among females, with a female to male ratio of approximately 10:1 [22]. Moreover, in 88% of cases, the disease affects young women of childbearing age (20–40 years), although it can develop both in childhood and in old age in both

sexes. It is worth noting here that in older age groups, a relatively calm course of both lupus nephropathy and SLE is observed. Approximately 20% of patients develop SLE before the age of 17 years. As indicated in international clinical guidelines, the involvement of the kidneys in the pathological process in SLE is most often formed due to the deposition of immune complexes in the glomeruli, which leads to the development of an inflammatory reaction in the glomeruli and, with progression, to the involvement of the renal interstitium in the process [10,48]. In addition, renal damage may be maintained by other mechanisms such as thrombotic microangiopathy [43,48]. As the researchers note, SLE is a classic manifestation of type V cardiorenal syndrome, when damage to the heart and kidneys develops simultaneously [24,30]. It is now recognized that CKD continues to have a major impact on the life prognosis of patients with SLE.

**Prevalence of chronic kidney disease in systemic lupus erythematosus**

Kidney lesions in SLE (lupus nephritis, lupus nephritis, lupus nephropathy) develop in acute and subacute SLE with high immunological activity, less often in its chronic course [10]. S.A. Tripolka, I.Yu. Golovach and E.A. Dyadyk indicate that most renal disorders usually appear within the first 6-36 months after the diagnosis of SLE [28]. There is evidence that the risk of developing lupus nephritis in patients with SLE 5 years or more after the onset of the disease is relatively small [10,14,39]. Many researchers argue that lupus nephritis is more common in children with SLE (clinically diagnosed in 70–75%) and is more severe than in adults [10,14]. A.V. Alexandrov, L.N. Shilova, N.V. Aleksandrova et al analyzed data from 60 patients with a definite diagnosis of SLE with various clinical manifestations. As the researchers note, kidney damage was extremely diverse and was detected in 24 (40%) patients with SLE. In the vast majority (15 people), lupus nephritis developed within the first 6 years from the onset of the disease; in 12% of patients, kidney damage was the first manifestation of SLE [1]. According to the literature, clinical and laboratory manifestations of kidney damage in SLE are observed in 30-80% of cases, and morphological changes in the renal tissue occur in almost every patient [26]. In a number of studies, the presence of CKD based on the K/DOQI classification, Kidney Disease Outcomes Quality Initiative, 2007, was established in 83% of patients with SLE [24]. Moreover, in 50% of SLE patients with CKD, grade C2 of the disease was detected [24]. In one study, among 64 patients with SLE, clinical and laboratory manifestations of kidney damage were noted in 48 people in 75% of cases [26].

**Lupus nephritis.**

It is important to emphasize that lupus nephritis occurs in 60% of adults and 80% of children. As already mentioned, lupus nephritis is less often recorded in chronic SLE. In patients with SLE, kidney damage can occur in the form of chronic glomerulonephritis, rapidly progressive glomerulonephritis, acute kidney injury, nephrotic syndrome, interstitial nephritis, or (less commonly) distal tubular acidosis, a progressive decrease in glomerular filtration rate, often with hyperkalemia [10]. It is believed that lupus nephritis is a model of immune complex inflammation, the mechanism of development of which reflects the pathogenesis of SLE [14]. Pronounced activation of B lymphocytes, which play an important role in providing humoral immunity, is accompanied by the production of autoantibodies, primarily to nuclear and cytoplasmic proteins, followed by the formation of circulating immune complexes (CIC). From a pathophysiological point of view, it must be remembered that when encountering an antigen or stimulation by T lymphocytes, some B lymphocytes are transformed into plasma cells capable of producing antibodies [10]. It is equally important to note that in SLE, activated B lymphocytes begin to intensively produce cytokines, which from cell to cell transmit an inflammatory signal at the level

of deoxyribonucleic acid (DNA) [12]. In patients with SLE, autoantibodies to double-stranded DNA are closely related to the activity of lupus nephritis and are detected as part of immune complexes in the glomeruli of the kidneys. Deposition of CEC on renal structures is accompanied by activation of monocytes and macrophages, resulting in increased damage to the glomerular vascular endothelium, apoptosis and blood flow disorders in the microvasculature [46,47]. It has been established that macrophages transmit to T lymphocytes simultaneously the processed antigen and interleukin-1, which prepares surface receptors on T helper cells to bind the transmitted antigen [40,44].

Here we would like to note that the rate of CEC clearance is greatly influenced by sex hormones, in particular estrogens, which slow down their elimination [22]. Perhaps this is one of the reasons for the more frequent detection of autoimmune diseases and SLE in women, among others. As noted in the works of V.A. Nasonova, among the important mechanisms of the development of SLE and, possibly, lupus nephritis, a special place is occupied by the slowdown in the elimination of CECs from the bloodstream with an increase in their circulation time, which is associated with the failure of macrophages and monocytes [22]. In addition, the elimination of CEC is also ensured by peripheral blood erythrocytes (through their binding to complement receptors C3). As a rule, when interacting with complement receptors, immune complexes lose the ability to be fixed in the tissues of target organs, in particular the kidneys. In SLE, a genetic defect is recorded that disrupts the receptor link for binding immune complexes, which leads to an increase in circulation time and deposition. It was previously shown that some patients with SLE have a genetic deficiency of complement C4, the marker of which is part of the HLA/Human Leukocyte Antigens and is often detected in carriers of HLA B8 [40]. Apparently, the frequent development of lupus nephritis at the onset and exacerbation of SLE (in acute and subacute course of the disease) are explained by a consistently increased level of immune complexes, the property of auto-antibodies (small size and easy solubility), which determine the damaging activity of the CEC. It must be said that small-sized and soluble immune complexes are poorly phagocytosed and circulate in the bloodstream longer [22]. The direct participation of the complement system in the development and progression of lupus nephritis is confirmed by the fact that complements are found in the focus of damage to kidney tissue (immunohistochemical studies reveal deposits of complement C3 and C1q in the glomeruli), their activity in the blood increases and the consumption of individual complement components (C1-C3) - C4-C5) [5]. In particular, in SLE, deficiency of early components of the complement system plays a role in the development of lupus nephritis. However, elevated anti-DNA antibody titers and low levels of complement C3 and C4 in the blood often indicate active lupus [28]. Along with the CEC, damage to the glomeruli is also promoted by damage to the endothelium by antiphospholipid antibodies, disruption of the production and biological action of nitric oxide, and the formation of microthrombosis. Taken together, disruption of the integrity of the glomerular basement membrane, changes in charge selectivity and fluctuations in intraglomerular pressure provoke proteinuria and often increased blood pressure.

According to the literature, proteinuria >0.5 g/day (or more than 3 “+” when determined by a test strip) and/or the presence of cellular accumulations, including accumulations of red blood cells and casts, tip the scales regarding the diagnosis of kidney damage in SLE [45,46] . A urine albumin/creatinine ratio of >0.5 and the presence of more than 5 erythrocytes and/or more than 5 leukocytes per field of view on urine sediment microscopy to rule out infection are considered very valuable. The results of a histological study of nephrobiopsy specimens confirming the presence of immune complex kidney damage characteristic of lupus nephritis are also of

undoubted value [44]. Many researchers have noted that the technique of nephrobiopsy plays an important role in pathomorphological interpretation. To adequately assess the histopathological changes in lupus nephritis, the required biopsy sample should contain from 8 to 25 glomeruli [6,7,28]. It is important to remember that patients with SLE and proteinuria less than 0.5 g/day are not eligible for a kidney biopsy. Nephrobiopsy should be performed in most patients with SLE who have signs of kidney damage, not only to establish the diagnosis, but also the type of lupus nephritis [28]. As noted in clinical guidelines [10], the presence of all immunoreactants in the nephrobiopsy is called "full house" and makes the diagnosis of lupus nephritis highly probable even in the absence of other clinical and serological markers of SLE. Depending on the histopathological picture of the nephrobiopsy, the following morphological types of lupus nephritis are distinguished (classification ISN, International Society of Nephrology / RPS, Renal Pathology Society):

I. Minimal mesangial changes;

II. Mesangial proliferative changes with deposits in the mesangium;

III. Focal proliferative changes in the glomeruli;

IV. Diffuse (≥50% of glomeruli) proliferative changes;

- diffuse segmental proliferative (IV-S, > 50% of affected glomeruli) with segmental changes;

- diffuse global proliferative (IV-G, >50% of affected glomeruli) with global changes;

V. Membranous glomerulonephritis;

VI. Advanced glomerulosclerosis:

As the researchers point out, the involvement of >50% of the glomeruli in the pathological process is designated as diffuse changes, and <50% of the glomeruli as focal; Changes that cover more than half of the glomerular capillaries are considered global, and segmental changes are considered to be less than half [6,28]. Different types of lupus nephritis have different histological, clinical and prognostic characteristics, and they can often overlap [28]. With type I lupus nephritis, there are no clinical symptoms of kidney damage. In a number of patients with types I or II of lupus nephritis, nephrotic level proteinuria may appear as a result of lupus podocytopathy. In this category of patients, electron microscopic examination reveals spreading of the podocyte feet. Approximately 10–15% of patients with lupus nephritis experience a decrease in glomerular filtration rate, arterial hypertension and massive proteinuria within three months. As a rule, these changes are observed in type IV lupus nephritis, and in such patients, nephrobiopsy often reveals foci of fibrinoid necrosis and crescents. Although nephrotic proteinuria and arterial hypertension are also recorded in type III lupus nephritis. Consequently, types III and IV lupus nephritis will require active immunosuppressive therapy and monitoring of renal function [10]. In clinical practice, the classification of lupus nephritis proposed by is also used I.E. Tareeva. This classification is convenient in that, depending on the clinical features, nature of the course and prognosis of the disease, it identifies several variants of lupus nephritis [27,29].

1. Active nephritis.

- Rapidly progressive lupus nephritis;

- Slowly progressive lupus nephritis;

A. with nephrotic syndrome;

B. with severe urinary syndrome;

2. Inactive nephritis with minimal urinary syndrome or subclinical proteinuria.

**Conclusion.** Summarizing the literature data, it should be noted that in SLE, kidney damage is one of the most common, severe and prognostically unfavorable forms of the disease. It is the involvement of the kidneys in the pathological process that determines the future prognosis of these patients in relation to the disease, and complications associated with lupus nephritis are the main cause of mortality in this category of patients.

**References**


1. Александров АВ, Шилова ЛН, Александрова НВ, и др. Роль антител к ксантиноксидазе в развитии нефрита у больных системной красной волчанкой // Актуальные вопросы и перспективы развития медицины. 2017.С.52-53.

2. Алексеева ЕИ, Дворяковская ТМ, Никишина ИП, и др. Системная красная волчанка: клинические рекомендации. Часть 1. // Вопросы современной педиатрии. 2018; 17(1): 19–37.doi:10.15690/vsp.v17i1.1853

3. Борисов ЕН, Иваницкий ЛВ, Самоходская ЛМ, и др. Взаимосвязь аллельных вариантов генов системы гемостаза на развитие и течение волчаночного нефрита // Нефрология. 2019;23:2:77-81. doi:10.24884/1561-6274-2019-23-2-77-81

4. Головач ИЮ. Люпус-нефрит: современная парадигма лечения // Почки.2018;7:2:122-131.

5. Длин ВВ, Игнатова МС. Нефропатии, связанные с патологией системы комплемента // Российский вестник перинатологии и педиатрии.2016;61:6:21-31.

6. Дядык ЕА. Интерпретация почечных биоптатов у больных системной красной волчанкой с клиническими проявлениями волчаночного гломерулонефрита // Укр. журн. нефрології та діалізу.2004;2:10-13.

7. Shamsiev E.A., Islamova K. A., & Ziyadullayev Sh.X. (2023). ARTERIAL HYPERTENSION IN PATIENTS WITH COVID-19. *Scholastic: Journal of Natural and Medical Education*, *2*(11), 13–18.

8. Akramovna, I. K., & Rustamovna, A. K. (2023, November). ULTRATOVUSH TEKHIRUV USULINING ERTA RIVOZHLANGAN OSTEOARTHROSIS KASALLIGIDAGI DIAGNOSTIC AHAMIYATI. In *International Conference on Medicine and Life Sciences* (pp. 72-75).

9. Amrillaevich, A. I., Akramovna, I. K., Sherzod, A. U., & Botirov, F. K. (2023, November). EFFECTIVENESS OF LASER PHYSIOTHERAPY METHOD IN TREATMENT OF PRIMARY KNEE JOINT OSTEOARTHRITIS. In *International Conference on Medicine and Life Sciences* (pp. 76-86).

10. Козловская НЛ, Захарова ЕВ, Коротчаева ЮВ. Национальные рекомендации «Диагностика и лечение нефрита при системной красной волчанке». Москва. 2014.С.31.

11. Alisherovna, K. M., Akramovna, I. K., Bakhtiyorovich, U. J., Nizamitdinovich, K. S., Jasurovna, J. S., Kairatovna, R. A., & Abdukholikovna, E. S. (2023). EXACERBATIONS OF

CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND CORONARY ATHEROSCLEROSIS. *Journal of new century innovations*, *39*(1), 176-178.

12. Акрамовна, И. К. (2023). Факторы Риска Раннего Развития Остеоартроза. *Journal of Science in Medicine and Life*, *1*(3), 1–7.

13. Краснова ТН, Соколова ИА, Георгинова ОА, и др. Особенности реологических свойств крови у больных волчаночным нефритом // Клиническая нефрология.2009;4:45-49.

14. Макарова ТП, Сукало АВ, Козыро ИА, и др. Характеристика системной красной волчанки и люпус-нефрита у детей в Республике Беларусь и Республике Татарстан // Рос вестн перинатол и педиатр.2019;64:(5):199–203. doi:10.21508/1027– 4065–2019–64–5–199–203

15. Akramovna I. K., Zaynobiddin o'g'li F. J. RISK FACTORS OF EARLY DEVELOPED OSTEOARTHRITIS //IMRAS. – 2023. – Т. 2. – №. 1. – С. 28-35.
16. Исламова К. А. Факторы Риска Раннего Развития Остеоартроза //Journal of Science in Medicine and Life. – 2023. – Т. 1. – №. 3. – С. 1-7.
17. Исламова К. А., Хамраева Н. А. Факторы Риска И Качество Жизни Больных Остеартрозом //Central Asian Journal of Medical and Natural Science. – 2023. – Т. 4. – №. 6. – С. 268-273.
18. Мамасаидов АТ, Мамасаидова ГМ. Встречаемость поражения печени при ревматоидном артрите и системной красной волчанке // Научно-практическая ревматология. 2004;42:2:С.160.

19. Мамасаидов АТ, Юсупов ФА. Взаимосвязь показателей В-клеточной активации и клинических проявлений неврологических осложнений при ревматоидном артрите // Наука и новые технологии. 2001;3.С.21.

20. Abdurasulovna, H. N., Akramovna, I. K., Rustamovna, A. K., & Egamkulovich, X. B. (2023). INFLAMMATORY ACTIVITY AND RENAL PATHOLOGY IN LUPUS NEPHRITIS. *Spectrum Journal of Innovation, Reforms and Development*, *13*, 89-94.
21. Мамасаидов ФА, Ташболотов КЖ, Мамасаидов АТ. Оценка эффективности при ревматоидном артрите анти-В-клеточной терапии в зависимости от уровня В-клеточной активации in vitro // В книге: The scientific heritage No 58 (2021) 43 Дни ревматологии в Санкт-Петербурге – 2017.Сборник тезисов конгресса с международным участием. Под редакцией В.И. Мазурова. 2017. С.154-155.

22. Насонова ВА, Астапенко МГ. Клиническая ревматология: Руководства для врачей. АМН СССР. М. Медицина, 1989.С.592.

23. Носков СМ, Василевская ОА, Носкова ТС, и др. Значение С-реактивного белка при системной красной волчанке // Клиницист.2012;1:10-15.

24. Ребров АП, Оксеньчук АН, Карпова ОГ. Встречаемость хронической болезни почек и ее структура у больных системной красной волчанкой // Современные проблемы науки и образования.2013;3.URL: http://www.scienceeducation.ru/ru/article/view?id=9239

25. Серикова СЮ, Козловская НЛ, Бобкова ИН. Преждевременное развитие атеросклероза при системной красной волчанке: факторы риска // Клиническая нефрология.2013;3:11-16.

26. Абдушукурова, К., & Исламова, К. (2023). ВЗАИМОСВЯЗЬ НЕРВНО-ЭНДОКРИННЫХ НАРУШЕНИЙ У БОЛЬНЫХ РЕВМАТОИДНЫМ АРТРИТОМ. *International Bulletin of Medical Sciences and Clinical Research*, *3*(11), 16-20.

27. Тареева ИЕ. Варианты течения волчаночного нефрита // Клиническая нефрология.2011;2:5- 8.

28. Триполка СА, Головач ИЮ, Дядык ЕА. Волчаночный гломерулонефрит: на пересечении клинического и гистологического диагнозов // Практикуючий лікар.2018;7(4):22-29.

29. Шилов ЕМ, Козловская НЛ. Волчаночный нефрит: современная терапия // Клиническая нефрология.2010;1:36-40.

30. Шолохова ВР, Петрачкова АИ. Клиникоиммунологическая характеристика системной красной волчанки у детей, получающих противоспалительную терапию // 73-я Итоговая научная конференция студентов Ростовского государственного медицинского университета.2019.С.172-172.

31. Исламова, К., & Карабаева, Г. (2020). ОСОБЕННОСТИ КЛИНИЧЕСКОГО ТЕЧЕНИЯ ЗАБОЛЕВАНИЙ СЕРДЕЧНО-СОСУДИСТОЙ СИСТЕМЫ НА ФОНЕ САХАРНОГО ДИАБЕТА. *Журнал кардиореспираторных исследований*, *1*(3), 59-62.

32. Islamova, K. A., Sh, K. F., & Toirov, E. S. (2020). Efficiency Of Intra-Articular Administration In Early Osteoarthrosis. *The American Journal of Medical Sciences and Pharmaceutical Research*, *2*(11), 22-27.

33. Юсупов ФА. Спонтанная иммуноглобулин синтезирующая активность В-клеток у больных системной красной волчанкой с поражением нервной системы // Неврологический вестник. 2006;38:1- 2:39-42.

34. Akramovna I. K., Sanatovich T. E. Functional evaluation of the effectiveness of intraarticular chondro hyaluronic injection in early knee osteoarthritis //Journal of Critical Reviews. – 2020. – Т. 7. – №. 7. – С. 410-413.

35. Хусинов А.А., Исламова К.А., & Зиядуллаев Ш.Х. (2023). Поражение Желудочно-Кишечного Тракта У Больных Коронавирусной Инфекцией. Central Asian Journal of Medical and Natural Science, 4(6), 580-585.

36. Юсупов ФА, Мамасаидов АТ, Мурзалиев АМ, и др. Клинико-иммунологическое значение показателя спонтанной пролиферативной активности В-лимфоцитов у больных системной красной волчанкой с поражением нервной системы // Медицинская иммунология. 2004;6:6:567-562.

37. Юсупов ФА, Грошев СА, Каримов УА. Легкие черепно-мозговые травмы и аутоиммунное поражение нервной системы: динамика показателей в-клеточной активности у больных в реабилитационном периоде // Бюллетень сибирской медицины. 2008;7:5-2:486-489.

38. Anders HJ, Saxena R, Zhao MH, et al. Lupus nephritis //Nature reviews Disease primers. 2020;6:1:1- 25. doi:10.1038/s41572-019-0141-9

39. Cervera R, Khamashta MA, Hughes GRV. The Euro-lupus project: epidemiology of systemic lupus erythematosus in Europe // Lupus.2009;18:869–874. doi:10.1177/0961203309106831

40. Christiansen FT, Dawkins RL, Uko G, et al. Complement allotyping in SLE: association with C4A null //Australian and New Zealand journal of medicine.1983;13:5:483-488. doi:10.1111/j.1445- 5994.1983.tb02699.x

41. Hadidi KT, Medhat BM, Abdel Baki NM. Characteristics of systemic lupus erythematosus in a sample of the Egyptian population: a retrospective cohort of 1109 patients from a single center // Lupus. 2018;27(6):1030–1038. doi:10.1177/0961203317751856 42. Hanly JG, O'Keeffe AG, Su L, et al. The frequency and outcome of lupus nephritis: results from an international inception cohort study // Rheumatology (Oxford). 2016;55(2):252-262. doi:10.1093/rheumatology/kev311

43. Lombel RM, Gipson DS, Hodson EM. Treatment of steroid-sensitive nephrotic syndrome: new guidelines from KDIGO // Pediatric nephrology. 2013;28:3:415-426.

44. Malattia C, Martini A. Paediatric-onset systemic lupus erythematosus // Best Pract Res Clin Rheumatol. 2013;27:351–362. doi:10.1016/j.berh.2013.07.007

45. Mejia-Vilet JM, Rovin BH. Epidemiology and Management of Lupus Nephritis //Dubois' Lupus Erythematosus and Related Syndromes. // Content Repository Only!, 2019.C.727-744. doi:10.1016/B978-0- 323-47927-1.00059-1

46. Scobell R, Pradhan M. Management of Lupus Nephritis in Children // Indian Pediatrics.2020;57:401- 406.

47. Umeda R, Ogata S, Hara S, et al. Comparison of the 2018 and 2003 International Society of Nephrology/Renal Pathology Society classification in terms of renal prognosis in patients of lupus nephritis: a retrospective cohort study // Arthritis Research & Therapy.2020;22:1:1-12. doi:10.1186/s13075-020-02358-x

48. Wilhelmus S, Bajema IM, Bertsias GK, et al. Lupus nephritis management guidelines compared // Nephrology Dialysis Transplantation.2016;31:6:904- 913