SMJ- Sohag Medical Journal, Vol. 29 (1) 2025

Print ISSN1687-8353 Online ISSN2682-4159

Review Article

Prevention of Complications in Systemic Lupus Erythematosus

Mai Hassan Gad El Rab[1], Esam Mohamed Abu Al Fadl[1] , Essam Abda[2], Osama Sayed DaifAllah[1]

1- Rheumatology & rehabilitation department, faculty of medicine, Sohag University, Sohag
2- Rhumatology & rehabilitation department, Assuit faculty of medicine, Assuit university

Abstract:

Background: Systemic lupus erythematosus (SLE) is a complex autoimmune disease characterized by a chronic relapsing–remitting course and diverse clinical manifestations ranging from mild to life-threatening conditions. It primarily affects women of childbearing age due to genetic, hormonal, immunological, and environmental factors. The pathogenesis involves impaired apoptotic clearance, immune system hyperactivity, complement activation, and chronic tissue inflammation, leading to irreversible organ damage and increased mortality. Approximately half of SLE patients develop organ damage within a decade of diagnosis. Current treatments, including corticosteroids and immunosuppressants, control disease activity but can exacerbate long-term damage.

Aim: to identify preventive measures to avoid organ damage in SLE patients .

Conclusion: Early therapeutic intervention, reduced glucocorticoid use, and precision medicine approaches are crucial to improving patient outcomes. Biomarkers offer promise in refining risk stratification and treatment efficacy. Preventive strategies, such as vaccination, infection control, cardiovascular protection, and osteoporosis management, further reduce complications. Personalized medicine and early disease control remain essential to minimizing organ damage and enhancing long-term prognosis in patients with SLE.

Key words: systemic lupus, complications, prevention

DOI : 10.21608/SMJ.2025.357642.1532 **Received:** February 03, 2025 **Accepted:** February 14 , 2025

Published: march 24, 2025

Corresponding Author: Mai Hassan Gad El Rab **E.mail**: mai.gadelrab@gmail.com

Citation: Mai Hassan Gad El Rab . et al Prevention of Complications in Systemic Lupus Erythematosus
SMJ,2025 Vol. 29 No (1) 2025: 212- 217

Introduction:

Systemic lupus erythematosus (SLE) is a diverse autoimmune disorder characterized by a chronic pattern of relapsing and remitting symptoms, which can vary in severity from mild to potentially life-threatening. The onset of SLE results from a complex interplay between genetic factors and environmental, immunological, and hormonal influences, with a notable predisposition among women of reproductive age. Factors such as complement activation, immune complex formation, tissue inflammation, and impaired clearance of apoptotic cells play a significant role in sustaining the autoimmune response.[(1)]

Complement activation, immunological complexes, tissue inflammation, innate and adaptive immune system overexpression, and poor apoptotic clearance all combine intricately to cause SLE, a self-sustaining autoimmune disease. The clinical manifestations that we refer to as SLE are probably the result of many pathogenic pathways coming together. Although SLE can impact a wide range of organs and tissues, each patient's pattern of clinical symptoms and autoimmune phenomena is unique, and it may even vary over time .[(2)]

It is still one of the most difficult demanding illnesses in medicine, with widespread immune system failure and systemic and organ-specific clinical symptoms Every individual with systemic lupus erythematosus (SLE) will exhibit a distinct pattern of disease, which may affect various organ systems, including the skin, joints, kidneys, cardiovascular system, and central nervous system (CNS).[(3)]

Epidemiology of systemic lupus erythematosus in Egypt

The prevalence of adult systemic lupus erythematosus (SLE) in Egypt was estimated by Gheita et al. to be 6.1 per 100,000 population in 2021, with a breakdown of 1.2 per 100,000 in men and 11.3 per 100,000 in women.[(4)]

Chronic organ damage in SLE:

When autoimmune diseases like systemic lupus erythematosus target the immune system, the outcome is chronic organ damage, which is irreversible harm to the body's organs. Autoreactive B cells, which cause an excess of autoantibodies against a range of cytoplasmic and nuclear antigens, are a hallmark of SLE. According to **Arnaud and Tektonidou.[(5)],** this ultimately results in cumulative, permanent organ damage.

Within ten years of being diagnosed with SLE, around half of all patients will experience some organ impairment. Additionally, compared to the general population, SLE patients die earlier and at a greater rate .[(6)]

Systemic lupus erythematosus (SLE) causes permanent organ damage, just as other illnesses. Organ damage is categorized as such by the Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index (SDI) if it has continued for six months or longer. The SDI shows that despite improvements in illness management worldwide, the present quality of care is still linked to serious organ damage. However, new research indicates that by stopping additional harm, prompt diagnosis and efficient treatment can improve results and prognosis. [(7)]

Review Methodology

We comprehensively analysed on strategies to prevent chronic organ damage in individuals with systemic lupus erythematosus (SLE). Treatment options for SLE include low-dose corticosteroids (CS) and antimalarial drugs for mild cases, while moderate-to-severe cases often require high-dose CS and immunosuppressive therapies. While these treatments have significantly improved long-term survival in SLE patients, they carry the risk of causing irreversible organ damage, particularly due to high disease activity (HDA) and prolonged use of corticosteroids and immunosuppressants. Therefore, preventing long-term organ damage remains a critical unmet need in SLE management. [(8)]

To prevent the accumulation of organ damage, early therapeutic intervention, prompt and persistent disease activity control, and GC limitation have become crucial treatment methods for SLE. We could be discussing a "window of opportunity" given that the rate of damage accrual is higher in the initial years and the burden of damage-derived illness appears to be high throughout that crucial time. [(7)]

Utilizing biomarkers to track damage and assess individual treatments is another tactic to stop treatment-induced early organ damage. It has been

difficult for physicians to differentiate symptoms that result from ongoing illness from those that follow irreversible organ damage. Future precision medicine techniques and novel biomarkers may offer new instruments to support risk stratification, enable tailored medication, and enable a more effective treat-to-target strategy because SLE is a diverse illness.[9]

Early control of the disease activity:

The main objective of the treat-to-target method for SLE is remission, or the lowest level of disease activity, early treatment has an impact on the patient's quality of life and the costs associated with the illness. Preventive measures are also strongly recommended since flares, particularly the severe ones, lead to the buildup of organ damage and produce worse outcomes. Out of all the available treatments. [10]

Tapering of glucocorticoid therapy:

Although GCs are known to be effective in quickly reducing symptoms, prolonged use of them can have several negative consequences, including organ damage. The 2019 EULAR recommendations state that because of the dangers involved, glucocorticoid (GC) usage should be avoided wherever feasible. Intravenous GC pulses can be used in place of oral prednisone to lessen or even completely eliminate the need for GC dosages in the treatment of systemic lupus erythematosus (SLE). This could be done in conjunction with the early initiation of other efficacious therapies like immunosuppressive or biologic treatments.[11]

Early effective therapeutic intervention:

Early illness therapy is crucial for averting any potential chronic organ damage and for improving prognosis. Therefore, it is hypothesized that early and widespread usage of HCQ will stop harm from accruing. It's interesting to note that retrospective research assessing the impact of HCQ administration in 130 US military personnel concluded that patients with incomplete SLE who received HCQ treatment early on experienced a delayed development of fully developed "complete" SLE. A nested case-control research examined 481 SLE patients to see if HCQ may prevent early damage. Three years after diagnosis, the authors demonstrated that HCQ was substantially linked to decreased organ damage. [12]

When combined with Target synthetic DMARDs, novel pharmacological and targeted therapies—particularly belimumab—have been shown in many randomized controlled studies to be successful in reducing disease activity and symptoms. Additionally, they seem to be able to lessen the need for GCs. Furthermore, independent of baseline damage accrual, individuals receiving long-term belimumab had a low rate of organ damage accrual. Additionally, utilizing other drugs that were previously discussed assesses the results. [13]

Moreover, additional studies have suggested that HCQ may exert a protective effect not only on the prevention of organ damage but also on improving long-term survival rates in SLE patients. The drug's ability to modulate immune responses and decrease flare frequency has been linked to better clinical outcomes.[14]

A cohort study involving 580 patients with early-stage SLE found that those treated with HCQ had a lower incidence of disease-related complications, such as renal and cardiovascular issues, compared to those who did not receive the treatment[15]. These findings reinforce the hypothesis that early intervention with HCQ can significantly alter the progression of the disease, supporting its continued role as a first-line treatment in managing SLE.

Healthcare professionals must take patient-specific considerations into account when determining whether to use primary preventive therapy in asymptomatic patients with serological abnormalities, as a large portion of the data supporting their efficacy is dependent on expert opinion. Furthermore, it is still uncertain if screening is necessary for asymptomatic people who are at risk for systemic lupus erythematosus (SLE). Addressing modifiable risk factors, such as smoking, excessive sun exposure, and medication usage that might aggravate SLE, is one way to prevent SLE. On whether pharmaceutical therapies are suitable for prophylaxis, there is disagreement. For asymptomatic people, vitamin D supplementation may be helpful since it has the potential to have immunomodulatory benefits without causing serious adverse medication responses.[16]

Stratifying asymptomatic autoantibody-positive people according to other risk factors, including hypergammaglobulinemia, low levels of C3 and/or C4, or a family history of systemic lupus

erythematosus (SLE), may be helpful in determining the chance of disease development. Patients with a higher risk of developing SLE, such as pregnant women, should be regularly watched for the existence of specific autoantibodies (such as those against dsDNA, U1RNP, ribosomal P, or Sm) and/or a consistently high antinuclear antibody (ANA) titre (>1:80). However, a single instance of a low ANA titre might not call for more research.[17]

Patients with low complement levels and/or positive serology for anti-dsDNA or specific anti-extractable nuclear antigen (ENA) antibodies may benefit from hydroxychloroquine treatment, however those with ANA positivity alone may not require it. This is because they are more likely to experience the development of their condition than individuals who only have an ANA-positive result. [18]

Primary prevention should take into account the risk of thromboembolic events in individuals with systemic lupus erythematosus (SLE) who test positive for antiphospholipid antibodies (aPLs) but do not have a history of thrombosis. Notably, compared to the general population, SLE patients are more susceptible to thrombosis due to pro-thrombotic risk factors such smoking, hereditary hypercoagulability, renal illness, or glucocorticoid usage. According to **Al-Homood et al.[19],** these variables must to be evaluated at the time of diagnosis and, if feasible, removed.

Second, low-dose aspirin may help asymptomatic people who test positive for numerous antiphospholipid antibodies (aPLs) (double or triple positive) in serological testing since they are at higher risk of thrombosis. Expert opinion and a meta-analysis back up this suggestion. But according to a prior randomized controlled study (RCT), this therapy did not offer asymptomatic aPL-positive people any further protection. [20]

In contrast, other studies have highlighted the complexity of managing asymptomatic aPL-positive individuals. While low-dose aspirin is commonly recommended to reduce the risk of thrombotic events, there remains debate about its efficacy in preventing clinical manifestations in those without symptoms. A longitudinal study involving 250 asymptomatic aPL-positive patients found that aspirin therapy did not significantly alter the incidence of thrombotic events over a 5-year follow-up period, suggesting that additional therapies or more targeted interventions may be necessary. Further research is needed to establish clearer guidelines on the role of aspirin in this population, particularly focusing on the duration and intensity of treatment required to achieve clinical benefits.

Specifically for preventing chronic organ damage, many agents are used such as for infection prevention: [18]

- Human papillomavirus vaccination in young women to prevent cervical cancer; vaccination against influenza, Haemophilus influenzae type B, and pneumococcus; and delivery of additional vaccinations than live attenuated vaccines (per national recommendations).
- Antimicrobials should be administered as soon as an infection appears.
- Co-trimoxazole is used as primary prophylaxis for patients with low CD4 cell counts (less than 200 cells per microliter), while traditional antibiotic and antifungal prophylaxis is used for individuals with severe neutropenia (less than 400–500 cells per microliter).
- In situations of severe hypogammaglobulinemia (IgG <4 g/L), intravenous immunoglobulin may be used for the prevention of cardiovascular disease.[21]

To avoid cardiovascular disease [21]:

- Arterial: smoking cessation; statin and antimalarial medication administration; treatment of conventional risk factors (e.g., hyperlipidemia, arterial hypertension [prescription of angiotensin II receptor blockers and angiotensin-converting enzyme inhibitors], hyperuricaemia, immobility).
- Venous: thromboprophylaxis using medical (e.g., heparin) and non-medical (e.g., stockings) methods when exposed to additional risk factors (e.g., immobilization, fracture, hospitalization, and procedures).
- Primary prophylactic treatment with low-molecular-weight heparin and low-dose aspirin throughout pregnancy is recommended for people who have a history of miscarriages.
- decrease high-dose glucocorticoids as early as possible, which increase the risk of venous and arterial problems.
- Vitamin K antagonists are used as a supplementary prophylactic measure for vascular occlusions in individuals with coexisting antiphospholipid syndrome (avoid direct oral anticoagulants).

To prevent osteoporosis and fractures. [22]

Non-pharmacological interventions include:

1. Physical therapy and exercise, which includes coordination training.
2. Quitting smoking, consuming less alcohol and coffee, and consuming more protein.

Medical interventions.[23]

1. Supplementing with vitamin D.
2. For people who are at risk, denosumab or bisphosphonates.
3. Bisphosphonates and teriparatide in fracture patients.
4. Justify use of high doses of glucocorticoids (>7–5 mg daily) for the shortest needed period.
5. Vitamin D or bisphosphonates for high-risk individuals to prevent osteoporosis.

For Skin flare prevention [24];

Skin cancer prevention by the use of sunscreen and other UV protection measures; primary and secondary prevention through shielding the skin from ultraviolet (UV) radiation. [24]

To avoid renal complications:

Treatment of severe proliferative lupus nephritis involves induction and maintenance therapy to preserve kidney function. Cyclophosphamide or mycophenolate mofetil with corticosteroids help achieve remission. Long-term outcomes depend on early diagnosis, effective management, and relapse prevention.[25]

To avoid neuropsychiatric complications:

Managing Neuropsychiatric systemic lupus is challenging due to its complex pathogenesis and diagnostic difficulties. Treatment focuses on symptom management with appropriate medications and addressing the underlying SLE process whether the pathogenesis is primarily related to an inflammatory or ischemic disease pathway. Drug-induced psychosis and Progressive multifocal leukoencephalopathy are potential complications requiring careful monitoring.[26]

References:

1. Grammatikos AP, Tsokos GC. Immunodeficiency and autoimmunity: lessons from systemic lupus erythematosus. Trends Mol Med. 2012;18(2):101-108.
2. Fava A, Petri M. Systemic lupus erythematosus: diagnosis and clinical management. J Autoimmun. 2019;96:1-13.
3. Crow MK. Pathogenesis of systemic lupus erythematosus: risks, mechanisms and therapeutic targets. Ann Rheum Dis. 2023;82(8):999-1014.
4. Gheita TA, Noor RA, Abualfadl E, Abousehly OS, El-Gazzar II, El Shereef RR, Raafat HA. Adult systemic lupus erythematosus in Egypt: the nation-wide spectrum of 3661 patients and world-wide standpoint. Lupus. 2021;30(9):1526-1535.
5. Arnaud L, Tektonidou MG. Long-term outcomes in systemic lupus erythematosus: trends over time and major contributors. Rheumatology. 2020;59(Suppl 5):v29-v38.
6. Urowitz MB, Gladman DD, Ibañez D, Su J, Mursleen S, Sayani A, Iczkovitz S. Effect of disease activity on organ damage progression in systemic lupus erythematosus: University of Toronto Lupus Clinic Cohort. J Rheumatol. 2021;48(1):67-73.
7. Taraborelli M, Cavazzana I, Martinazzi N, Lazzaroni MG, Fredi M, Andreoli L, Tincani A. Organ damage accrual and distribution in systemic lupus erythematosus patients followed-up for more than 10 years. Lupus. 2017;26(11):1197-1204.
8. Arnaud L, Mathian A, Devilliers H, Ruffatti A, Tektonidou M, Forastiero R, Amoura Z. Patient-level analysis of five international cohorts further confirms the efficacy of aspirin for the primary prevention of thrombosis in patients with antiphospholipid antibodies. Autoimmun Rev. 2015;14(3):192-200.
9. Dörner T, Furie R. Novel paradigms in systemic lupus erythematosus. Lancet. 2019;393(10188):2344-2358.
10. Ritprajak P, Kaewraemruaen C, Hirankarn N. Current paradigms of tolerogenic dendritic cells and clinical implications for systemic lupus erythematosus. Cells. 2019;8(10):1291.
11. Fanouriakis A, Bertsias G. Changing paradigms in the treatment of systemic lupus erythematosus. Lupus Sci Med. 2019;6(1):1-11.
12. Rua-Figueroa Fernández de Larrinoa Í, Lozano MJC, Fernández-Cid CM, Cobo Ibáñez T, Salman Monte TC, Freire Gonzalez M, Cortés-Hernández J. Preventing organ damage in systemic lupus erythematosus: the impact of early biological

treatment. Expert Opin Biol Ther. 2022;22(7):821-829.

13. Bruce IN, Urowitz M, Van Vollenhoven R, Aranow C, Fettiplace J, Oldham M, Gordon D. Long-term organ damage accrual and safety in patients with SLE treated with belimumab plus standard of care. Lupus. 2016;25(7):699-709.

14. Dima A, Jurcut C, Chasset F, Felten R, Arnaud L. Hydroxychloroquine in systemic lupus erythematosus: overview of current knowledge. Ther Adv Musculoskelet Dis. 2022 Feb 14;14:1759720X211073001. doi:10.1177/1759720X211073001.

15. Pons-Estel GJ, Alarcón GS, González LA, Zhang J, Vilá LM, Reveille JD, McGwin G Jr; Lumina Study Group. Possible protective effect of hydroxychloroquine on delaying the occurrence of integument damage in lupus: LXXI, data from a multiethnic cohort. Arthritis Care Res. 2010;62(3):393-400.

16. van Vollenhoven RF, Navarra SV, Levy RA, Thomas M, Heath A, Lustine T, Roth D. Long-term safety and limited organ damage in patients with systemic lupus erythematosus treated with belimumab: a phase III study extension. Rheumatology. 2020;59(2):281-291.

17. Rana RS, Naik B, Yadav M, Singh U, Singh A, Singh S. Serum complements and immunoglobulin profiles in systemic lupus erythematosus patients: an observational study at a teaching hospital. J Family Med Prim Care. 2022;11(2):608-613.

18. Alghabban NA, Shakoor Z. Pattern of antinuclear antibody and antiextractable nuclear antigen antibody test requisitions in Riyadh. J Family Med Prim Care. 2019;8(11):59-64.

19. Al-Homood IA. Thrombosis in systemic lupus erythematosus: a review article. Int Sch Res Notices. 2012;2012:1-6.

20. Bustamante JG, Goyal A, Rout P, Singhal M. Antiphospholipid syndrome. In: StatPearls [Internet]. StatPearls Publishing; 2024.

21. Borghi C, Levy BI. Synergistic actions between angiotensin-converting enzyme inhibitors and statins in atherosclerosis. Nutr Metab Cardiovasc Dis. 2022;32(4):815-826.

22. Body JJ, Bergmann P, Boonen S, Boutsen Y, Bruyere O, Devogelaer JP, Reginster JY. Non-pharmacological management of osteoporosis: a consensus of the Belgian Bone Club. Osteoporos Int. 2011;22:2769-2788.

23. Zaheer S, LeBoff MS. Osteoporosis: prevention and treatment. In: Endotext [Internet]. 2022.

24. Sander M, Sander M, Burbidge T, Beecker J. The efficacy and safety of sunscreen use for the prevention of skin cancer. CMAJ. 2020;192(50):E1802-E1808.

25. Chan T. Preventing renal failure in patients with severe lupus nephritis. Kidney Int. 2005;(67):S116-S119.

26. Justiz-Vaillant AA, Gopaul D, Soodeen S, Arozarena-Fundora R, Barbosa OA, Unakal C, Thompson R, Pandit B, Umakanthan S, Akpaka PE. Neuropsychiatric systemic lupus erythematosus: molecules involved in its imunopathogenesis, clinical features, and treatment. Molecules. 2024;29(4):747.