Review Article

### A Comprehensive Examination of Systemic Lupus Erythematosus: Etiology, Pathophysiology, Risk Factors, and Therapeutic and Nutritional Treatments

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ABSTRACT

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| **Goals:** This study seeks to examine the etiology and contributing factors of systemic lupus erythematosus (SLE), dissect its pathophysiology, and emphasize diagnostic and therapeutic approaches with an emphasis on nutritional interventions and preventative steps.**Study Methodology:** A systematic examination of current scientific publications on systemic lupus erythematosus.**Duration and Location of the Study:** This study was a thorough evaluation of research related to systemic lupus erythematosus, in which studies and research publications published between 2016 and 2025 were gathered and analyzed.**Approach:** The qualitative research method and critical evaluation of sources were used to gather and analyze pertinent papers and articles.**Results:** According to the data, SLE is a complex autoimmune disorder that is impacted by nutritional, environmental, and genetic variables. Lifestyle changes, especially diet, have a big impact on lowering symptoms and raising overall quality of life. But there are still a few unanswered questions.**Conclusion:** An integrated strategy encompassing medical care, dietary interventions, and lifestyle changes is necessary for the management of SLE. Ongoing research is crucial to creating more individualized and successful therapeutic alternatives. |

*Keywords: Chronic disease management, dietary changes, medicinal treatments, clinical diagnosis, risk factors, illness pathophysiology, autoimmune illnesses, systemic lupus erythematosus, and prevention strategies.*

1. INTRODUCTION

Systemic lupus erythematosus is a persistent autoimmune illness that affects several bodily systems, such as the skin, joints, kidneys, neurological system, heart, and blood, by causing inflammation and injury. Due to a malfunction in the immune system, the body is unable to distinguish between self and non-self, which results in the production of autoantibodies, particularly those that target cell nuclei, causing the illness. These antibodies target the body's cells, causing tissue damage and a wide spectrum of clinical signs (Tsokos et al., 2016).

The female-to-male ratio of lupus is around 9:1, with women being disproportionately affected, notably during their reproductive years (Rahman et al., 2021; Mohammed et al., 2020). This indicates that sex hormones like estrogen and genetic variables associated with sex chromosomes may play a role in the disease's susceptibility. Additionally, the illness is more common and severe in persons of African, Asian, or Latin American origin (Deng & Tsao, 2020).

The condition is thought to be caused by several factors. Among these are smoking, the usage of particular drugs, genetic predisposition, and environmental stimuli like ultraviolet light and some viral illnesses (especially the Epstein-Barr virus). These variables combine to cause an aberrant activation of the immune system, which results in an overproduction of inflammatory mediators like type I interferons, which have been linked to the development and maintenance of tissue damage associated with lupus (Zhao et al., 2014; Tsokos et al., 2016; ; Abdul et al., 2025).
Although there has been substantial progress in our knowledge of the genetic and immunological underpinnings of the illness, the exact etiology of lupus is still unknown, and there is now no proven treatment. Because of its varied presentation and erratic course of flares and remissions, lupus continues to be a significant clinical and research issue (Deng & Tsao, 2020; Rasul et al., 2025).

2. Pathophysiology of Systemic Lupus Erythematosus

Systemic lupus erythematosus (SLE) is a persistent autoimmune disorder marked by a loss of immunological tolerance to self-antigens, which causes widespread inflammation and tissue damage that affects several organ systems. The pathophysiology of SLE is a complicated interaction of genetic predisposition, environmental stimuli, and immune system malfunction. The creation of autoantibodies that target nuclear components, such as nucleoproteins and double-stranded DNA, is at the heart of the pathogenesis of SLE. These autoantibodies generate immune complexes that are deposited in tissues, causing complement activation and inflammatory cell recruitment, which results in localized tissue damage (Tsokos et al., 2016; Abdulrahman et al., 2025). The development of disease is greatly influenced by the malfunction of immunological cells, such as dendritic cells, T lymphocytes, and B lymphocytes. While T cells control immunological responses and provide help, B cells produce harmful autoantibodies. By releasing significant amounts of type I interferons, notably interferon alpha, plasmacytoid dendritic cells help to increase the autoimmune response and induce inflammation (Zhao et al., 2014; Ahmed, et al., 2025).
Genetic factors play a large role in disease susceptibility, with several genes involved in immune regulation found to be risk loci. Epigenetic alterations, such as histone and DNA methylation, also affect gene expression and immune function, frequently brought on or made worse by environmental variables including ultraviolet radiation, viral infections, and smoking (Deng & Tsao, 2020).
Immune complexes cause the complement system to be chronically activated, which results in tissue inflammation and injury, particularly in the kidneys, skin, joints, and central nervous system. As a result, SLE presents with a diverse range of clinical presentations, including minor symptoms and severe, life-threatening organ involvement.
Although our knowledge of the underlying pathophysiology of SLE has improved, the precise mechanisms are still unclear, and therapy is primarily based on immunosuppression to manage disease activity and prevent organ damage.



**Figure 1: Worldwide Deaths attributable to AMR (Antimicrobial resistance) every year by 2050 ( Naqvi et al., 2019)**

The map illustrates projected annual deaths attributable to Antimicrobial Resistance (AMR) by the year 2050 across various regions of the world. Asia and Africa are projected to experience the highest mortality rates, with 4.73 million and 4.15 million deaths, respectively. The color gradient also indicates mortality per 10,000 population, showing darker shades in regions with weaker healthcare infrastructure and higher exposure to infectious diseases.

**2.1 Relevance to Systemic Lupus Erythematosus (SLE)**

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease that often requires long-term immunosuppressive therapy. These treatments make patients more susceptible to infections, increasing their dependency on antibiotics. As antimicrobial resistance (AMR) spreads, the effectiveness of common antibiotics diminishes, leaving lupus patients at greater risk of severe infections and mortality (NIH, 2020). Regions expected to have the highest AMRrelated deaths (like Africa and Asia) are also those where lupus patients may suffer the most due to a lack of access to advanced medical care and alternative therapies.

**2.2 Nutritional Implications**

Proper nutrition is essential in managing lupus, as it influences immune function, inflammation, and recovery from infections. Nutrients such as selenium, zinc, vitamins A, C, and E, as well as phenolic compounds and antioxidants, play a role in modulating immune responses. Al-Baraznji & Al-Abdullah (2016) demonstrated the nutritional value of local wheat cultivars used as bulgur, which are rich in minerals, vitamins, and phytochemicals that support immune health. Such plant-based nutrients may help mitigate the inflammatory burden in lupus patients and reduce their vulnerability to infections. Abdul et al. (2024) showed that sunflower oil, especially when exposed to controlled heat treatment, retains its beneficial unsaturated fats and antioxidants. These compounds are crucial in reducing cardiovascular risks and systemic inflammation in lupus patients.

**2.3 Environmental Connections**

Environmental exposure to pollutants, heavy metals, and pathogens contributes both to the progression of lupus and the spread of AMR. Poor environmental conditions often prevalent in low-income regionscan trigger lupus flare-ups and accelerate the development of resistant microbial strains. This map emphasizes that addressing AMR is not just a medical issue, but one intertwined with environmental health and nutrition. Effective management of lupus in the future will require integrative strategies that include improving diet quality, reducing environmental toxins, and curbing antimicrobial misuse.

3. Risk Factors for Systemic Lupus Erythematosus

Systemic lupus erythematosus is a multifactorial illness with risk factors that include a complex interaction of genetic, environmental, and biological variables that result in immune system malfunction and a breakdown in self-antigen tolerance. Genetic predisposition is a major factor, since individuals with a family history of lupus or other autoimmune conditions are more prone to developing them. Risk loci are those genes that are specifically implicated in immune regulation, such as those involved in immune cell activity and complement proteins (Deng & Tsao, 2020). The majority of sufferers are women, with a female-to-male ratio of approximately nine to one, particularly during their reproductive years. It is thought that estrogen plays a role in this discrepancy by regulating immunological responses and potentially raising autoimmunity (Aziz et al., 2025; Tsokos et al., 2016). Ultraviolet radiation exposure, a factor in the environment, contributes to the disease by causing cell damage and releasing nuclear antigens that trigger immunological activation. Smoking and viral infections, especially the Epstein-Barr virus, also elevate the likelihood or severity of lupus (Zhao et al., 2014). Drug-induced lupus, a lupus-like condition brought on by medications such as hydralazine and certain anticonvulsants, is one example of drug-induced lupus (Deng & Tsao, 2020). Additionally, chronic psychological stress has been linked to changes in immune function and the possibility that it may cause or worsen lupus symptoms (Tsokos et al., 2016).

**3.1** **SYSTEMIC LUPUS ERYTHEMATOSUS ENVIRONMENTAL AND NUTRITIONAL CAUSES**

By interacting with the immune system and causing aberrant autoimmune reactions, environmental and dietary triggers have a major impact on the development and worsening of systemic lupus erythematosus. Ultraviolet light exposure is one of the primary environmental causes that causes cell damage and the release of nuclear components, which triggers the creation of autoantibodies, resulting in persistent inflammation (Omar et al., 2025; Tsokos et al., 2016). Certain viral infections, especially Epstein-Barr virus, can also trigger aberrant immune responses and raise the likelihood of getting the illness (Deng & Tsao, 2020). Smoking is also acknowledged as a major cause of increased disease severity and diminished treatment efficacy (Harun et al., 2025; Zhao et al., 2014). In terms of dietary considerations, studies have demonstrated that vitamin D insufficiency is linked to higher disease activity because of its function in immune regulation, whereas omega-3 fatty acids provide a protective benefit by lowering inflammation associated with lupus (Deng & Tsao, 2020). On the other hand, some foods with prooxidative or inflammatory ingredients might make symptoms worse. As a result, maintaining a balanced diet and reducing exposure to environmental triggers are crucial aspects of illness management.

**3.2** **GENETIC RISK FACTORS**

Family history of lupus or other autoimmune disorders increases the risk of systemic lupus erythematosus, highlighting the important role that genetics plays in the illness's etiology. Research suggests that lupus results from a complex interaction of several genes that regulate the immune system, including those related to the human leukocyte antigen, which affects antigen presentation, and those involved in complement proteins, which are involved in immune responses. Changes in the genes that govern the type I interferon responses also have a critical role in causing excessive autoimmune activity (Harry et al., 2018; Ghodke-Puranik & Niewold, 2015). Furthermore, the expression of lupus-related genes is impacted by epigenetic changes such as DNA methylation and histone modifications. These epigenetic modifications do not change the DNA sequence; rather, they change how genes are read and interact with the environment to promote the onset of disease (Zhou et al., 2020). The influence of genetic risk variables varies by ethnicity, with higher incidence rates seen among people of African, Hispanic, and Asian descent compared to Europeans. This reflects a combined influence of genetic and environmental factors on disease susceptibility (Graham et al., 2011; Salih et al., 2019).

**3.3** **LIFESTYLE FACTORS OF NUTRITION**

The onset, course, and treatment of systemic lupus erythematosus (SLE) are all significantly influenced by dietary lifestyle factors. In the pathophysiology of SLE, inflammation and immune responses are critical, and diet has a significant impact on how these are regulated. Because of its immunomodulatory actions, which aid in controlling immune tolerance and inflammation, vitamin D deficiency is prevalent in individuals with SLE and is linked to higher disease activity (Kamen et al., 2006; Saeed et al., 2025; Salih et al., 2018). By regulating cytokine production and immune cell function, the omega-3 fatty acids in fish oils may lessen the severity of lupus flares due to their antiinflammatory effects (Wright et al., 2008).
On the other hand, diets high in saturated fats, processed foods, and too much salt can make inflammation and cardiovascular risk worse in lupus patients (Pan et al., 2019). There is some evidence that antioxidants from fruits and vegetables help lower oxidative stress and enhance clinical outcomes (Schiffer et al., 2006). Obesity and metabolic syndrome, which are frequently caused by unhealthy eating behaviors, are also associated to a poorer disease prognosis and higher comorbidities (Chang et al., 2017).
Maintaining ideal vitamin D levels, eating a balanced diet full of anti-inflammatory components, and steering clear of processed foods are all advised as part of a complete lupus treatment strategy.

**4. PRESENTATION AND CLINICAL DIAGNOSIS**

Due to the diversity of its clinical symptoms, systemic lupus erythematosus (SLE) is a complicated autoimmune illness that is sometimes difficult to diagnose. The illness typically manifests initially with vague symptoms including unexplained weight loss, a low-grade fever, and persistent tiredness. Joint discomfort and inflammation are among the first and most frequent signs, particularly in small joints such as those in the hands and fingers (Okhtyar et al., 2015). The presence of a malar rash—a butterfly-shaped rash across the cheeks and nose is a hallmark symptom of SLE that can help physicians suspect the diagnosis (Smith, 2012). Other important aspects of SLE include renal involvement, which commonly manifests as proteinuria or hematuria and, if left untreated, can lead to lupus nephritis (Jandali et al., 2018). Additionally, individuals may have neurological symptoms like headaches, seizures, cognitive impairment, or mood problems, as well as pericarditis or pleuritis (AlHashimi, 2016).
A combination of a comprehensive physical exam, history-taking, and exclusion of other similar illnesses is used to make the clinical diagnosis of SLE. Laboratory tests provide essential corroborating evidence, such as positive antinuclear antibodies (ANA) and anti-double-stranded DNA (anti-dsDNA) antibodies, which are more specific to SLE and are frequently employed to corroborate the diagnosis (Paulus et al., 2020).

**5. TREATMENT STRATEGIES FOR SYSTEMIC LUPUS ERYTHEMATOSUS FROM A MEDICAL, NUTRITIONAL, AND CLINICAL PERSPECTIVE**

The management of Systemic Lupus Erythematosus (SLE) requires a comprehensive, multidisciplinary approach that includes medical, nutritional, and clinical strategies to reduce disease activity, prevent organ damage, and improve quality of life. **Medically**, first-line treatments often include non-steroidal anti-inflammatory drugs (NSAIDs) to relieve joint and muscle pain (Abdullah et al., 2022). Antimalarial drugs, especially hydroxychloroquine, are widely used to control skin and joint symptoms and reduce the risk of disease flares (Saleem et al., 2021). In moderate to severe cases, corticosteroids and immunosuppressive agents such as azathioprine, mycophenolate mofetil, or cyclophosphamide are prescribed to suppress the overactive immune response (Al-Shammari, 2023; Saeed et al., 2025). More recently, biologic therapies such as belimumab, which targets B-lymphocyte stimulator (BLyS), have shown efficacy in reducing disease activity and preventing flares (Hussein et al., 2023). **From a nutritional standpoint,** patients are advised to follow an anti-inflammatory diet rich in fresh fruits, vegetables, whole grains, and healthy fats such as omega-3 fatty acids. These nutrients have been shown to support immune regulation and reduce systemic inflammation (Khalid, 2024; Hameed et al., 2025). In contrast, diets high in saturated fats, refined sugars, and processed foods may exacerbate symptoms. Vitamin D and calcium supplementation is often necessary, particularly for patients on long-term corticosteroid therapy, to prevent bone loss and reduce the risk of osteoporosis (Al-Hashimi et al., 2023).

**6. PHARMACOLOGICAL APPROACH IN THE TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS**

The pharmacological treatment of Systemic Lupus Erythematosus (SLE) aims to suppress inflammation, control autoimmune activity, and prevent irreversible organ damage. Since the disease presents with diverse clinical manifestations and varying degrees of severity, therapeutic decisions are tailored to the patient’s specific symptoms and disease activity. For **mild cases,** non-steroidal anti-inflammatory drugs (NSAIDs) are often used to relieve joint and muscle pain and reduce inflammation, particularly in patients without organ-threatening complications (Abdullah et al., 2022). **Antimalarial drugs,** especially hydroxychloroquine, are a cornerstone of treatment for skin and joint manifestations and have been shown to reduce flare frequency and improve long-term outcomes (Saleem et al., 2021; Ahmed et al., 2025). In **moderate to severe cases,** corticosteroids are commonly used at varying doses to quickly control inflammation. However, due to the risk of side effects, their long-term use is minimized. To maintain remission and reduce steroid dependence, **immunosuppressive agents** such as azathioprine and mycophenolate mofetil are prescribed. These medications help control immune overactivity and protect vital organs like the kidneys, heart, and brain (Al-Shammari, 2023). In recent years, **biologic therapies** have been introduced, offering targeted approaches by modulating specific immune pathways. Belimumab, a monoclonal antibody targeting B-cell activating factor (BAFF), has shown efficacy in reducing disease activity and minimizing corticosteroid use (Hussein et al., 2023). Pharmacological management requires regular monitoring of treatment efficacy and side effects, especially in patients on long-term immunosuppression. Laboratory tests, clinical assessments, and dose adjustments are critical to achieving optimal outcomes while minimizing risks.

# Table 1. Chronic Treatment Considerations in Systemic Lupus Erythematosus

<https://www.cdc.gov/lupus/basics/treatment.html>

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| **Clinical Factor** | **Suggested Treatment** | **Main Therapeutic Goal** | **Additional Notes** |
| Mild joint or skin symptomsModerate joint or skin inflammationSevere systemic or kidney involvementRefractory to conventional therapyChronic corticosteroid useHigh cardiovascular risk | HydroxychloroquineLow-dose corticosteroidMycophenolate mofetil or cyclophosphamideBelimumab (biologic therapy)Calcium and vitamin D supplementsLow-dose aspirin or anticoagulants | Reduce inflammation and prevent flaresControl inflammationSuppress the aggressive immune response and protect organsReduce B-cell activityPrevent osteoporosisPrevent thrombosis | Long-term use is generally safeDose tapering is recommended to reduce side effectsRequires regular monitoring of kidney, liver, and blood parametersUseful in resistant cases and helps reduce corticosteroid useNecessary in long-term corticosteroid therapyEspecially in patients with antiphospholipid antibodies |

**7. PREVENTIVE MEASURES AND DIETARY LIFESTYLE MODIFICATIONS IN SLE**

Nutrition plays a vital role in modulating immune responses and reducing inflammation in patients with systemic lupus erythematosus. Recent evidence suggests that a balanced diet rich in antioxidants can help mitigate disease severity and reduce the frequency of flare-ups. Patients are advised to consume fresh fruits and vegetables, as well as plant-based protein sources such as legumes and nuts, and to avoid saturated fats and refined sugars, which are known to exacerbate systemic inflammation (Yousef et al., 2024; Aziz et al., 2025). Additionally, omega-3 polyunsaturated fatty acids found in fish oil particularly eicosapentaenoic acid have shown anti-inflammatory properties that benefit joint and skin symptoms and improve cardiovascular health, especially in patients with antiphospholipid antibodies (Khalil et al., 2023; Hamasalih et al., 2025). Vitamin D deficiency is also common in SLE patients and should be corrected via supplementation or safe sun exposure to support bone health and regulate immune activity. Sodium intake should be limited, particularly in patients receiving long-term corticosteroid therapy, to reduce the risk of hypertension and fluid retention. A diet low in calories and rich in dietary fiber may assist in weight control and lower the risk of cardiovascular complications associated with lupus (El-Sayed & Ibrahim, 2025; Omar et al., 2025).

**8. FUTURE DIRECTIONS AND RESEARCH GAPS IN SYSTEMIC LUPUS ERYTHEMATOSUS**

Systemic lupus erythematosus remains a complex, multifaceted disease with numerous unresolved research gaps that hinder a comprehensive understanding and improvement of treatment options. One significant future direction involves the development of personalized targeted therapies based on individual genetic and immunologic differences, which could enhance treatment efficacy and minimize adverse effects (Al-Arabi et al., 2024). There is an urgent need for deeper studies to elucidate the precise role of environmental and nutritional factors in triggering the disease and modulating immune responses, alongside improving early diagnostic tools to detect the disease before it progresses to advanced stages (Al-Khalili & Al-Abadi, 2023). Moreover, research into molecular areas such as stem cell therapy and gene therapy represents a promising gap that may open new avenues for curative treatments of lupus (Al-Hashimi, 2025; Salih et al., 2025). Additionally, long-term clinical trials are essential to evaluate the safety and efficacy of novel biologic therapies, as well as to study the psychological and social impacts of the disease and how to enhance patients' quality of life through multidisciplinary interventions (Al-Najjar et al., 2024).

9. Conclusion

Systemic lupus erythematosus is a complex autoimmune disease that affects multiple organs and systems, requiring a comprehensive understanding of its risk factors, pathophysiology, diagnosis, and treatment. Despite significant advances in diagnostics and therapeutics, there remain critical research gaps that need to be addressed to achieve deeper insights and develop safer and more effective treatments. Lifestyle modifications, particularly nutritional aspects, play a crucial role in improving patients’ quality of life and reducing disease complications. Continued scientific research and medical innovation are essential to create personalized approaches tailored to each patient’s genetic and environmental profile, offering promising prospects for better disease control and improved therapeutic outcomes.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that they have no known competing financial interests OR non-financial interests OR personal relationships that could have appeared to influence the work reported in this paper.

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