

Review

The Benefits of Mediterranean Diet in Systemic Lupus Erythematosus



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Article Info	Abstract
Article history: Received: 11 August 2024 Accepted: 28 October 2024	<p><i>Introduction:</i> Dietary patterns have been studied for their influence on the burden of disease in patients with SLE. The Mediterranean diet has been shown to be beneficial in lowering chronic inflammation, but no study has summarized its effect on SLE. This article aims to review the association between the Mediterranean diet and SLE.</p> <p><i>Methods:</i> A literature review was conducted following PRISMA guidelines. PubMed, ScienceDirect and Google Scholar databases were searched using the keywords Mediterranean diet and SLE. Articles published in English between 2013 and 2023 were included. The initial search yielded 526 records, which were narrowed down to five studies for final inclusion. A narrative synthesis approach was used to analyze the impact of the Mediterranean diet on SLE disease activity.</p> <p><i>Results:</i> Five cross-sectional studies were included, with a total of 1,165 participants. The studies used the SLE Disease Activity Index (SLEDAI) and the Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index (SDI) as outcome measurements. Three of the five studies found that higher adherence to the Mediterranean diet was associated with a lower burden of SLE, as measured by reduced SLEDAI and SDI scores. One study found no association between adherence to the Mediterranean diet and SLEDAI or SDI scores, while another study found no association between adherence and the risk of developing SLE.</p> <p><i>Conclusion:</i> High adherence to a Mediterranean diet may help reduce the damage caused by SLE. Further cohort studies or clinical trials are needed to investigate the impact of diet on SLE.</p>
Keywords: dietary patterns, inflammation, mediterranean-diet, systemic lupus- erythematosus.	

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INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by the presence of autoantibodies against autoantigens, the formation of immune complexes, and immune system dysregulation, causing damage to several body organs [1]. The global prevalence of SLE is estimated to be 43.17 per 100,000 people, with approximately 3.41 million people currently affected [2]. This disease occurs more frequently in women and creates severe physical and psychological impacts on those affected. As a result, both pharmacologic and nonpharmacologic interventions continue to be developed [3].

Dietary patterns have been studied for their influence on the disease burden in patients with SLE, though the appropriate diet for SLE patients remains unclear. Lupus sufferers often face dietary challenges due to the nature of their autoimmune condition. The inflammation associated with lupus can affect various organs, leading to digestive issues and nutrient deficiencies [4], [5]. Many lupus patients struggle with food sensitivities or allergies that can trigger flare-ups, making it difficult to maintain a balanced diet. Some medications used to treat lupus, such as corticosteroids, can cause weight gain and increase the risk of osteoporosis, necessitating careful nutritional management. Additionally, lupus sufferers may need to limit their intake of certain foods that can exacerbate inflammation or interfere with medication effectiveness [6], [7]. Fatigue and joint pain, common in lupus, can also make meal preparation challenging, potentially leading to reliance on less nutritious convenience foods. Furthermore, the

photosensitivity experienced by many lupus patients may limit their sun exposure, potentially resulting in vitamin D deficiency. Balancing these various dietary concerns while ensuring adequate nutrition is a complex and ongoing process for those living with lupus [8]–[10].

The Mediterranean diet is one of the popular modern diets that has been shown to be beneficial in lowering chronic inflammation in cancer and decreasing the risk of cardiovascular disease [11]–[13]. In autoimmune diseases, the Mediterranean diet has been extensively studied in patients with rheumatoid arthritis and osteoarthritis [14], [15]. However, there are limited studies regarding the Mediterranean diet in SLE patients.

The Mediterranean diet is based on the traditional eating patterns of people living in the Mediterranean region. It is characterized by high consumption of fiber and extra virgin olive oil, a key source of monounsaturated fatty acids (MUFAs). It also includes a high intake of fish and seafood, which provide polyunsaturated fatty acids (PUFAs). This diet emphasizes plant-based foods rich in vitamins, minerals, antioxidants, and complex carbohydrates. While it still allows consumption of protein and fat sources such as white meat, red meat, and eggs, these are consumed in smaller quantities, with a limit on sugar and artificial sweeteners. In this diet, large meals are typically eaten once a day, usually between midday and the evening. The recommended time for large meals is between 1 and 3 p.m. [12], [13], [16], [17].

The intake of vegetables and fruit should be around 5 to 8 portions per day. One serving of fruit and vegetables is equivalent to half a

plate at each meal. In addition to fruits and vegetables, this diet also emphasizes whole grains. Foods made from whole grains include but are not limited to whole wheat bread, non-refined cereals, brown rice, and whole grain pasta. Unhealthy fats, such as trans fats and saturated fats, should be reduced. Cooking oil, margarine, butter, or palm oil is substituted with olive oil. Protein intake is recommended through consuming fish or seafood, rich in omega-3 fatty acids, at least twice a week. Fish should be grilled, steamed, or boiled instead of fried. Other recommended protein sources include poultry, eggs, and dairy products, which should be consumed no more than twice a week. Red meat and sweets should only be eaten monthly. Recommended snacks include dried or fresh fruit and unsalted nuts. Small amounts of milk, low-fat yogurt, and cheese are also advised. It is recommended to drink 6–8 glasses of water per day and reduce alcohol consumption [13], [16], [18], [19].

The existing literature on the Mediterranean diet and SLE is still scarce; therefore, this review article aims to summarize the evidence regarding the effect of the Mediterranean diet on SLE.

METHODS

Research Question

The research question for this study was: “What is the effect of the Mediterranean diet on the disease activity of SLE?” The SLE Disease Activity Index (SLEDAI) and Systemic Lupus International Collaborating Clinics/American College of Rheumatology

(SLICC/ACR) Damage Index (SDI) were used to measure SLE disease activity.

Study Design and Data Sources

The literature review was conducted in accordance with PRISMA guidelines. A literature search was performed in the PubMed, ScienceDirect, and Google Scholar databases using the following keywords: “Mediterranean Diet,” “MED diet,” “Systemic Lupus Erythematosus,” “SLE,” and “autoimmune.” Articles published between 2013 and 2023 were included, while those published in languages other than English were excluded.

Study Selection

Two reviewers conducted the database search, screening, and full-text assessment. Disagreements were resolved through discussion. The literature study selection process is illustrated in Fig. 1. The initial search yielded 526 results from the three databases: PubMed (17 records), ScienceDirect (337 records), and Google Scholar (172 records). Before screening, 148 records were removed due to duplication, leaving 337 records for screening. Of these, 323 were excluded for not being relevant to the topic under study. Fourteen reports were sought for retrieval, but four could not be retrieved. The remaining ten reports were assessed for eligibility, with five subsequently excluded as not relevant. Ultimately, five studies were included in the final literature review.

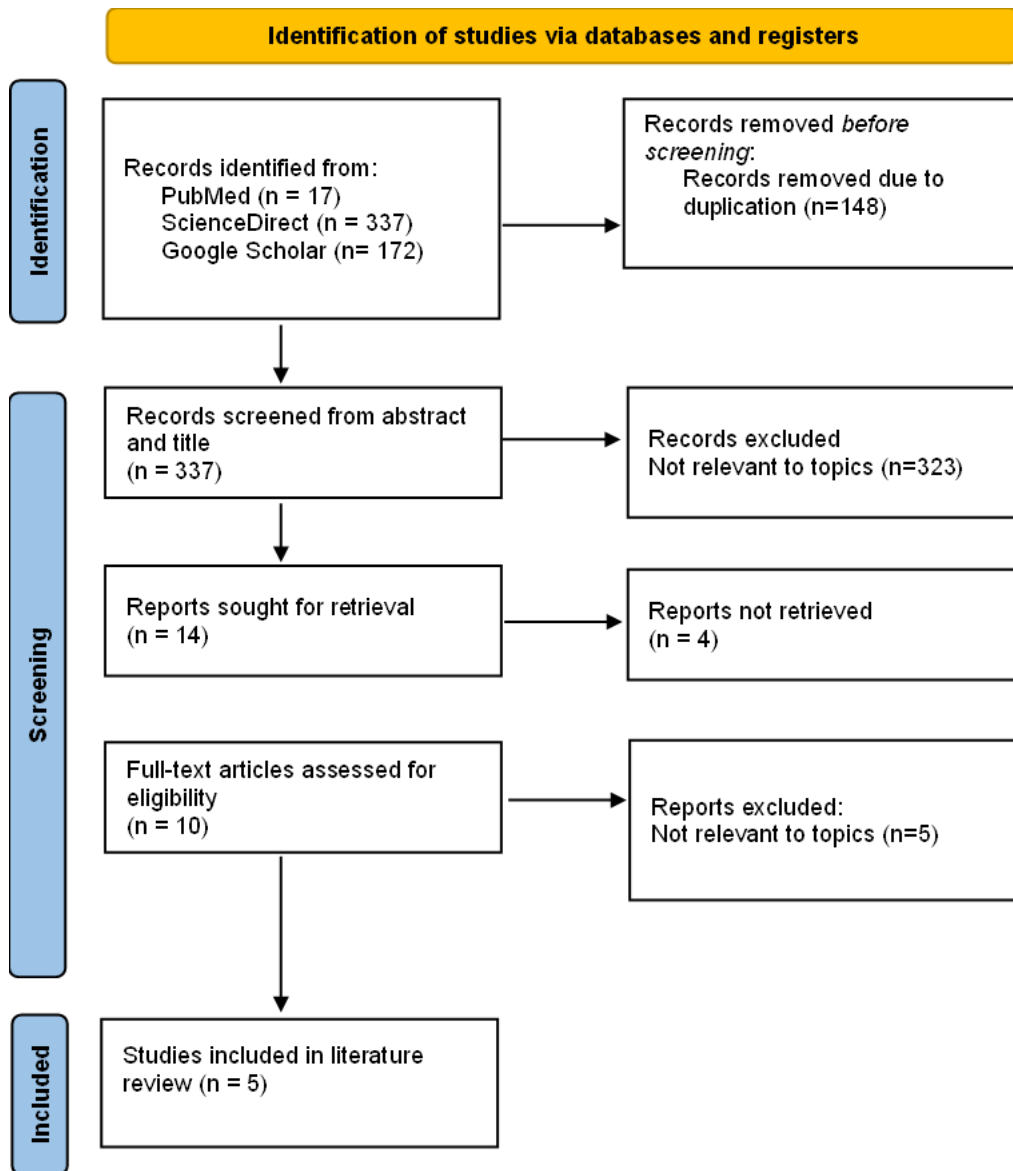


Fig. 1. Study Selection Flow Diagram

Data Extraction

The extracted data included study characteristics (author, year, country of origin, study design), population characteristics (number of subjects, gender, age), outcome measurements, and study results. Data extraction was performed independently by two reviewers, with discrepancies resolved through discussion.

Data Synthesis and Analysis

A narrative synthesis approach was adopted to summarize and interpret the collected data, focusing on the impact of the Mediterranean diet on SLE disease activity. The data in the literature review were presented in a table.

RESULT

Study Characteristics

We included five studies regarding the Mediterranean diet in SLE (Table 1). All the studies were cross-sectional in design, with a total of 1,165 participants. Two studies were conducted in Spain, one in England, one in Germany, and one in the United States.

Mediterranean Diet in SLE Patients

The Mediterranean diet protocol for SLE patients is largely similar to the general Mediterranean diet recommendations, with tailored considerations to address the specific needs of individuals with SLE. This diet emphasizes a high intake of plant-based foods, including 3–4 servings of vegetables and 2–3 servings of fruits daily, along with whole grains, legumes, nuts, and seeds. Extra virgin olive oil serves as the primary source of added fat, with a recommended intake of 2–4 tablespoons daily. The protocol includes moderate consumption of fish and seafood (2–3 servings per week), particularly fatty fish rich in omega-3 fatty acids, while limiting poultry, eggs, and dairy. Red meat consumption is restricted to no more than 1–2 servings per week, and processed foods and added sugars are minimized. For SLE patients, the diet places additional emphasis on foods rich in antioxidants to combat oxidative stress, omega-3 fatty acids to manage inflammation, and probiotic-rich foods to support gut health. Special attention is given to vitamin D sources due to common deficiencies in SLE patients. The protocol also considers individual food sensitivities and

encourages adequate hydration. Implementation typically involves the gradual adoption of these dietary habits under the guidance of healthcare professionals, with personalization based on the patient's specific needs, disease activity, medications, and comorbidities [20]–[24].

Outcome Measurement

Most of the studies (four out of five) used the SLEDAI-2K and SDI damage index as outcome measures. Only one study investigated the effect of the Mediterranean diet on the risk of developing SLE.

Benefits of the Mediterranean Diet in SLE Patients

Three out of five studies reported that higher adherence to the Mediterranean diet was associated with lower SLEDAI scores and lower SDI damage index. One study found no association between Mediterranean diet adherence and SLEDAI or SDI damage index, while another study found no association between Mediterranean diet adherence and the risk of developing SLE.

Three out of five studies reported that higher adherence to the Mediterranean diet was associated with lower SLEDAI scores and lower SDI damage index. One study found no association between Mediterranean diet adherence and SLEDAI or SDI damage index, while another study found no association between Mediterranean diet adherence and the risk of developing SLE.

Table 1. Summarizes studies regarding the Mediterranean Diet and SLE

Authors (Year)	Title	Design	Number of Subjects	Outcome Measurement	Results
Pocovi-Gerardino (2021), England	The beneficial effect of Mediterranean diet on disease activity and cardiovascular risk in systemic lupus erythematosus patients: a cross-sectional study	Cross-sectional	280 SLE patients	CRP, homocysteine, SLEDAI-2K, SLICC/ACR, and SDI Damage Index	Higher adherence to the Mediterranean Diet was associated with lower SLEDAI and damage accrual scores, fewer cardiovascular disease risk factors, and improved anthropometric profiles.
Vordenbaumen et al (2023), Germany	Beneficial effects associated with a healthy lifestyle in systemic lupus erythematosus: A cross-sectional study	Cross-sectional	49 SLE patients (high adherence, MEDAS \geq 4), 96 SLE patients (low adherence)	SLEDAI, CES-D, FSS, FFbH, PCS, MCS	Higher adherence to the Mediterranean Diet was associated with higher physical quality of life, lower depression, and lower fatigue.
DelOlmo-Romero et al (2023), Spain	Metabolic syndrome in systemic lupus erythematosus patients under the Mediterranean diet	Cross-sectional	293 SLE patients	SLEDAI, SDI Damage index	No association between Mediterranean diet adherence and SLEDAI or SDI damage index
Barbhaiya et al. (2021), United States	Association of Dietary Quality with Risk of Incident Systemic Lupus Erythematosus in the Nurses' Health Study and Nurses' Health Study II.	Cross-sectional	173,122 samples 194 SLE patients	Risk of SLE	No association between Mediterranean diet adherence and the risk of developing SLE
Rodriguez, et. al. (2021), Spain	Adherence To The Mediterranean Diet And Its Association With Disease Activity And Damage Accrual In Women With Systemic	Cross-sectional	253 SLE women	SLEDAI, SDI Damage index	Higher adherence to the Mediterranean diet was associated with lower SLEDAI and SDI.

* Systemic Lupus Erythematosus (SLE), Systemic Lupus Disease Activity Score (SLEDAI), Depression Scale (CES-D), Fatigue Severity (FSS), functional status (FFbH), physical and mental quality of life (PCS, MCS), (Mediterranean Diet Adherence Score (MEDAS)

DISCUSSION

This review suggests that high adherence to a Mediterranean diet may help reduce disease activity and organ damage in SLE. The most commonly used outcome assessments in SLE studies are the SLEDAI-2K and the SDI. The Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) is an instrument with 24 clinical and laboratory variables to measure disease activity in SLE. SLEDAI-2K is a modification of the original SLEDAI score. It assesses disease activity over the past 30 days, while the original SLEDAI focused on the previous 10 days. SLEDAI-2K also includes persistent and active illness, in addition to new or recurring events. Moreover, SLEDAI-2K adds scoring for alopecia, rash, mucous membrane ulcers, and proteinuria. This system has been validated as a measure of SLE disease activity and can be used as a predictor of mortality [25], [26].

The Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index (SDI) measures permanent organ damage resulting from SLE disease activity and its treatment. First developed in 1996, the SDI has undergone repeated validation [27]. While the SLEDAI-2K focuses on disease activity, the SDI assesses cumulative organ damage. Utilizing standardized outcome measurements like SLEDAI-2K or SDI in clinical trials is crucial to understanding the

association between the Mediterranean diet and the burden of SLE.

The studies included in this review provide varied perspectives on the Mediterranean diet's impact on SLE. Several studies, such as those by Pocovi-Gerardino et al. (2021) and Rodriguez et al. (2021), demonstrated a positive association between adherence to the Mediterranean diet and improvements in disease activity, as measured by SLEDAI and SDI. These findings suggest that dietary intervention could be an important strategy in controlling SLE disease progression, which is especially relevant given the chronic inflammatory nature of SLE and the risk of ongoing organ damage [21], [24].

The anti-inflammatory and antioxidant properties of the Mediterranean diet may explain its benefits. This diet, rich in fruits, vegetables, whole grains, olive oil, and omega-3 fatty acids, is well-established for promoting cardiovascular health and reducing inflammation, both critical concerns for SLE patients. Cardiovascular disease is a leading cause of morbidity and mortality in SLE, and the reduction in cardiovascular risk factors reported by Pocovi-Gerardino et al. underscores the value of addressing dietary habits as part of a comprehensive care plan for SLE patients [21].

However, not all studies found positive outcomes. DelOlmo-Romero et al. (2023) reported no significant association between

Mediterranean diet adherence and disease activity or organ damage, and Barbhuiya et al. (2021) found no association between the Mediterranean diet and the risk of developing SLE [20], [23]. These differences may be due to variations in population characteristics, methods of measuring adherence, or differences in dietary patterns. It is also possible that other factors, such as genetics, environmental triggers, or comorbidities, play a more significant role in influencing disease outcomes, making the impact of diet less pronounced in certain populations [28].

Beyond disease activity, the Mediterranean diet's effects on mental health and quality of life in SLE patients are noteworthy. Vordenbaumen et al. (2023) found that higher adherence to the Mediterranean diet was associated with improvements in physical quality of life, depression, and fatigue. Given that SLE is often accompanied by chronic fatigue and depression, this suggests dietary changes may serve as a complementary therapy to alleviate some of the disease's non-physical burdens [22].

Mechanisms of Action

The mechanism by which the Mediterranean diet affects SLE disease activity and damage is not entirely clear, but several theories have been proposed. One involves the modulation of gut microbiota, which is believed to play a role in SLE pathophysiology. SLE patients have been found to have distinct gut microbiota profiles, including a lower Firmicutes-to-Bacteroidetes ratio and increased levels of *Enterococcus gallinarum* and *Lactobacillus reuteri* [29]. An imbalance

in gut microbiota has been linked to inflammatory conditions, and in SLE, this imbalance may contribute to autoimmunity through the formation of antinuclear antibodies and disruption of immune regulation [30]. This gut microbiota imbalance has been linked to several inflammatory conditions. The alteration of gut microbiota may contribute to the pathophysiology of SLE through the formation of antinuclear antibodies and an imbalance in the ratios of T helper 17 (Th17) and Treg cells. Another mechanism of how gut microbiota could induce autoimmunity is molecular mimicry, as some gut commensals share the same protein epitope with autoantigen. Last, some proteins may attach to B and T cells and induce immune response. The Mediterranean diet, rich in fiber and plant-based foods, may help restore gut microbiota balance and thereby reduce inflammation and autoimmunity in SLE [21], [31].

The Mediterranean diet's anti-inflammatory effects are well-documented. Its phytonutrients and natural antioxidants, such as polyphenols, lycopene, vitamins, minerals, and omega-3 fatty acids, may alleviate oxidative stress and suppress inflammation [32]. In addition, the Mediterranean diet is rich in vitamins, minerals, and omega-3 fatty acids that also have anti-inflammatory properties. The anti-inflammation effect of the Mediterranean diet can be achieved by improving cell adhesion, complement activity, autophagy regulation, oxidative stress and preventing the production of pro-inflammatory cytokines [33]. In the study by Han et al., lycopene was found to have a protective effect on SLE

mortality [34]. Studies have shown that adherence to this diet can reduce levels of inflammatory biomarkers, such as C-reactive protein (CRP) and homocysteine [21]. In a systematic review, 82 of 133 studies showed a positive association between good adherence to a Mediterranean diet with lower inflammatory markers [35].

Another mechanism of how the Mediterranean diet may lessen the damage of SLE is by reducing cardiovascular and metabolic syndrome risk, therefore preventing permanent organ damage [36], [37]. The Mediterranean diet may modify the pattern of inflammation, glucose metabolism, and leukocyte telomere length (LTL)[38], [39]. Genetic variations in the Telomerase RNA Component (TERC) have been linked to LTL and aging-related disorders. Monounsaturated fatty acids interact with the Telomerase RNA Component (TERC) and suppress the telomere elongation and inflammation linked to cardiovascular disease [33]. Patients with higher adherence to the Mediterranean diet have been shown to have better lipid profiles and fat mass percentage, as well as a lower prevalence of obesity, which is a component of metabolic syndrome [21]. In an RCT and a systematic review, the Mediterranean diet is revealed as a protective factor for cardiovascular disease and may improve HDL [40], [41].

Epigenetic Influence

Recent research highlights the role of dietary patterns, particularly the Mediterranean diet, in modifying disease processes through epigenetics. Epigenetics refers to how environmental factors and behaviors

influence gene expression. The Mediterranean diet has been associated with beneficial epigenetic changes, including the promotion of immune regulation and the rejuvenation of energy metabolism [42].

IMPLICATIONS

The findings of this review suggest that the Mediterranean diet could be a valuable non-pharmacological strategy in the management of SLE, offering potential benefits beyond traditional treatments. Given the chronic nature of SLE and its complex, multi-system involvement, incorporating dietary interventions may provide an accessible and sustainable way to improve patient outcomes. The Mediterranean diet's potential to reduce inflammation, improve cardiovascular health, and enhance overall quality of life makes it particularly relevant for SLE patients, who are at heightened risk of cardiovascular complications and experience significant disease-related burdens. Additionally, addressing gut microbiota imbalances and leveraging the diet's epigenetic effects could lead to novel approaches in disease management. Healthcare providers, including dietitians and rheumatologists, should consider integrating personalized nutritional counseling into SLE treatment plans, and future clinical trials are warranted to explore the long-term impact of diet on disease progression and patient well-being. This approach could open the door to broader preventive measures and individualized care strategies that go beyond medication alone.

LIMITATIONS

This review has several limitations. First, the review includes only a limited number of studies due to the scarcity of literature on this topic. Second, all the included studies are cross-sectional, making it impossible to establish a causal relationship between the Mediterranean diet and SLE outcomes. Future longitudinal studies or clinical trials are necessary to clarify the diet's effects on SLE. Additionally, many confounding variables—such as physical activity, smoking, and medication doses—were not analyzed in the included studies, which may have influenced the results.

CONCLUSION

High adherence to the Mediterranean diet may help lessen the burden of SLE, but the evidence primarily comes from cross-sectional studies. Further cohort studies or clinical trials are needed to investigate the diet's impact on SLE in greater depth.

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