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The impact of diet on systemic lupus erythematosus - a review article

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Abstract

Introduction. Systemic lupus erythematosus (SLE) is a chronic autoimmune disease affecting multiple organs and systems, with a complex pathogenesis involving genetic, hormonal, and environmental factors. The disease manifests with variable clinical features and can lead to significant morbidity and increased cardiovascular risk.

Aim of Study. The aim of the study was to evaluate the role of diet and supplementation with specific nutrients in the management of SLE, focusing on omega-3 and omega-6 fatty acids, vitamin D, gut microbiota, and dietary patterns like low glycemic index and Mediterranean diets.

Materials and methods. More than 30 articles addressing these issues were analyzed. They were found using the PubMed search engine, and the time frame of these publications covered the last 10 years.

Results. Studies suggest that omega-3 supplementation, vitamin D, and synbiotics can reduce disease activity, inflammation, and fatigue in SLE patients. A balanced omega-6/omega-3 ratio, along with specific dietary patterns, improved cardiovascular function and reduced inflammation. The Mediterranean and low-GI diets also contributed to better disease control and quality of life.

Conclusions. Dietary interventions discussed in the paper can be beneficial adjuncts to pharmacological treatments in SLE management. These changes may improve disease activity and overall well-being. Further long-term studies are needed to confirm these findings.

Key words: systemic lupus erythematosus, diet, omega-3 fatty acids, vitamin D, gut microbiome

Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease. The development of the disease is associated with genetic, hormonal, and environmental factors. The disease can negatively affect the functioning of multiple organs and systems, such as joints, muscles, skin, kidneys, cardiovascular system, central nervous system, hematopoietic system, and coagulation system. The clinical presentation varies widely, ranging from mild to severe. One of the early symptoms is often a facial rash shaped like a butterfly.

SLE is characterized by autoimmune intolerance to autoantigens, leading to the production of numerous antibodies and activation of T lymphocytes, which produce cytokines promoting inflammation [1]. The presence of genetic factors and their interaction with environmental triggers (UV radiation exposure, viral infections including EBV and CMV, and emotional stress) and hormonal influences can result in disturbances in the humoral and cellular immune responses [2]. This is considered to be the core mechanism of the disease, although the exact pathomechanism remains unclear. High levels of cytokines such as TNF, IL-4, IFN-γ, IL-6, IL-12, IL-10, IL-18, and IL-17 have been observed in patients with active SLE. The increased pro-inflammatory response, particularly in active disease, may result from an imbalance between regulatory T cells (Treg) and subgroups of helper T cells (Th17/Th1/Th2), immune complexes (IC), and autoantibodies, leading to tissue damage [3]. Moreover, in SLE patients, the increased response of Th17 cells is associated with disease activity. IL-17 induces local inflammation by activating the innate immune system and immune response, which correlates with the activation of B cells.

The global incidence of SLE is 5.14 per 100,000 person-years [3]. The disease predominantly affects women of reproductive age, with a peak incidence around the age of 45, posing a significant challenge to public health.

The diagnosis is based on clinical and laboratory criteria; however, it remains a challenge in clinical practice. The diagnostic criteria for SLE are presented in Table 1. The diagnosis of SLE can be made after fulfilling the entry criterion and obtaining 10 or more points from additive

criteria. The treatment of SLE primarily focuses on reducing inflammation and improving patients' quality of life for patients. Treatment regimens are based on immunosuppressive and cytotoxic drugs.

SLE is associated with an increased risk of cardiovascular diseases due to atherosclerosis, significantly increasing the risk of death.

Increasingly, lifestyle interventions, including diets based on appropriate nutrients, are highlighted as potential therapies for autoimmune diseases. This paper will discuss the impact of diet and supplementation with specific nutrients on the course of SLE.

Entry criterion **Antynuclear antibodies (ANA) at a titer of ≥ 1:80**	
Additive criteria	
Clinical domains and criteria	**Weight**
Constitutional	
Fever	2
Hematologic	
Leukopenia	3
Thrombocytopenia	4
Autoimmune hemolysis	4
Neuropsychiatric	
Delirium	2
Psychosis	3
Seizure	5
Mucocutaneous	
Non-scarring alopecia	2
Oral ulcers	2
Subacute cutaneous OR discoid lupus	4
Acute cutaneous lupus	6
Serosal	
Pleura lor pericardial effusion	5
Acute pericarditis	6
Musculoskeletal	
Joint involvement	6
Renal	
Proteinuria >0,5g/24h	4
Renal biopsy Class II or V lupus nephritis	8
Renal biopsy Class III or IV lupus nephritis	10
Immunology domains and criteria	**Weight**
Antiphospholipid antibodies	
Anti-cardiolipin antibodies OR Anti-β2GP1 antibodies OR Lupus anticoagulant	2
Complement proteins	
Low C3 OR low C4	3
Low C3 AND low C4	4
SLE-specific antibodies	
Anti-dsDNA antibody OR Anti-Smith antibody	6

Table 1 2019 EULAR/ACR Criteria. From Aringer et al. Arthritis Rheumatol. 2019. PMID: 31385462

Omega-3 and omega-6 fatty acids

Polyunsaturated fatty acids (PUFAs), including omega-3 and omega-6, are essential nutrients responsible for suppressing inflammatory processes, regulating cellular signaling, and maintaining cellular membrane fluidity. Omega-3 fatty acids are primarily anti-inflammatory, whereas excessive omega-6 can elicit pro-inflammatory effects. Maintaining an appropriate omega-6 to omega-3 ratio is crucial. Both omega-3 and omega-6 are essential for proper immune system functioning [5,6].

PUFAs have been documented to benefit lipid profiles, particularly by lowering blood triglyceride levels [7]. However, debates persist regarding omega-3's role in preventing cardiovascular disease (CVD) events. Some studies suggest moderate benefits, while others demonstrate significant reductions in heart attack risks and mortality [8]. For instance, the 2018 REDUCE-IT study reported a 25% reduction in cardiovascular events with high-dose EPA supplementation [9].

Since humans cannot synthesize PUFAs, they must be obtained through diet. Key omega-3 forms include eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and alpha-linolenic acid (ALA), while linoleic acid (LA) and arachidonic acid (ARA) are primary omega-6 representatives. EPA and DHA are found in fatty fish like salmon, mackerel, and sardines, whereas ALA originates from plant sources such as walnuts and flaxseeds.

Omega-3 fatty acids reduce inflammation by inhibiting the nuclear factor-kappa B (NF-κB) pathway and decreasing the expression of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) [10]. They also suppress T-cell activation, thus modulating immune responses.

In a randomized placebo-controlled clinical trial by Arriens et al., supplementation with EPA- and DHA-rich fish oil improved the quality of life in SLE patients. Improvements were particularly noted in fatigue and psychological well-being, assessed through the RAND SF-36 questionnaire. Additionally, the omega-3 group showed reduced erythrocyte sedimentation rates and serum IL-12 levels compared to placebo [11].

Similarly, Wright et al., in a randomised interventional trial evaluated the effects of omega-3 supplementation on endothelial function and disease activity. 60 patients with active SLE participated in the study. Endothelial function was assessed via flow-mediated dilation (FMD) of the brachial artery. At the same time, disease activity was measured using the Systemic Lupus Activity Measure (SLAM-R) and British Isles Lupus Assessment Group (BILAG) indices. In addition, levels of IL-6, CRP, and other inflammatory exponents were measured. Patients taking omega-3 fatty acids showed a significant improvement in endothelial function

compared to the placebo group. Significant reductions in IL-6 and CRP levels were observed, indicating a reduction in chronic inflammation. Significant improvements in the BILAG disease activity index and Systemic Lupus Activity Measure (SLAM-R) were observed in patients who followed a fish oil-based diet. Patients also reported improved well-being and a reduction in symptoms such as fatigue and joint pains [12].

Both studies highlighted limitations such as small sample sizes, short trial durations, and the absence of dose-response analyses for omega-3 supplementation.

Bozhou Wang et al. conducted a meta-analysis and literature review in which they considered Randomized Controlled Trials (RCTs) and observational analyses related to the effects of fatty acids on SLE. In total, they analyzed data from 17 studies, 10 of which focused on omega-3. Results included assessments of disease activity using indices such as SLAM-R, SLEDAI, and levels of inflammatory biomarkers such as IL-6 and TNF-α. The analysis concluded that omega-3 supplementation could be a safe and effective adjunct to standard SLE therapies, particularly for patients with high inflammation and fatigue risks. However, it was pointed out that larger clinical trials with more diverse demographics and taking into account the long-term effects of omega-3 supplementation are needed [13].

Omega-6 fatty acids, often regarded as pro-inflammatory, exhibit dual effects. ARA, a key omega-6 component, serves as a precursor for both pro-inflammatory eicosanoids like prostaglandin E2 and anti-inflammatory lipoxins. The dietary balance between omega-3 and omega-6 is critical for inflammation regulation.

The role of omega-6 in SLE remains controversial. Duffy et al. found that ARA supplementation combined with fish oil did not significantly affect disease activity but improved certain quality-of-life indicators. This suggests that an appropriate omega-6 to omega-3 ratio is vital in managing SLE [14].

The modern population's omega-6 to omega-3 ratio averages 15:1 to 20:1, favoring pro-inflammatory mechanisms. For SLE, increasing omega-3 intake is recommended to restore the pro- and anti-inflammatory balance. Simopoulos emphasized an optimal dietary ratio of 4:1 to 2:1, supporting anti-inflammatory and regenerative processes [15].

Vitamin D

Vitamin D is a fat-soluble compound available in two forms: D2 (ergocalciferol) and D3 (cholecalciferol). Key sources include UVB-induced skin synthesis and dietary intake (e.g., fatty fish, fortified foods, supplements). The main function of vitamin D is to regulate calcium-phosphorus metabolism, thereby determining bone health [16]. Currently, a number of works

indicate that vitamin D may have an important role in modulating the immune system. Receptors for vitamin D - VDR are expressed in many cells of the immune system. Vitamin D in in vitro studies inhibits the differentiation and production of antibodies by B lymphocytes [17], modulates the activity of T lymphocytes, reducing their ability to induce an autoimmune response [18,19]. It also decreases the production of pro-inflammatory cytokines (e.g. IL-17, IL-21) [20] and increases the production of anti-inflammatory cytokines (e.g. IL-10).

Promising results from in vitro studies on the immunomodulatory role of vitamin D have led to an increasing number of studies examining whether a similar effect can be produced in the human body and thus whether vitamin D can affect autoimmune diseases including SLE.

SLE patients often exhibit lower vitamin D levels than the general population for several reasons. First, patients often avoid exposure to sunlight. This is due to the photosensitivity characteristic of SLE. Secondly, the very essence of SLE, i.e. the body's inflammatory processes, reduces vitamin D levels. It should also be mentioned that medications used in SLE, such as corticosteroids, can reduce serum vitamin D levels. [21,22,23].

In a randomized, double-blind, placebo-controlled, multicenter trial by Schoindre et al., the correlation between vitamin D levels and SLE activity, as well as the impact of vitamin D deficiency on disease flares, was investigated [22].] The study was conducted in a group of 170 patients with SLE. Participants had monitored levels of 25-hydroxyvitamin D (25(OH)D) and disease activity as assessed by the SLEDAI index. Patients with deficient vitamin D had significantly higher SLEDAI scores, indicating greater disease activity, along with elevated pro-inflammatory cytokines like IL-6, linking deficiency to increased inflammation. The study, in turn, did not confirm that low vitamin D levels were a clear predictor of future disease exacerbations. Exacerbations were more related to the presence of factors such as infections or changes in treatment than to vitamin D levels. These results indicate that vitamin D deficiency is common among SLE patients and associated with higher disease activity. Nevertheless, vitamin D does not appear to be an independent indicator of risk for disease exacerbations. A limitation of the study was the small number of patients and the short follow-up time, making it difficult to fully understand the long-term effects of vitamin D on the course of SLE.

Fiblia et al. conducted a study on 100 patients (ages 18–60) with stabilized SLE. All participants had confirmed vitamin D deficiency (<20 ng/ml). The study group received 50,000 IU of cholecalciferol once a week for 12 weeks, while the control group received placebo. The following parameters were assessed: disease activity (SLEDAI-2K index), quality of life (SF-36 questionnaire) and inflammatory markers (IL-6 and TNF-α). After supplementation, 25-hydroxyvitamin D (25(OH)D) levels in the intervention group increased on average from 14

ng/ml to 38 ng/ml. In the intervention group, the SLEDAI-2K index decreased by an average of 4 points, indicating a statistically significant reduction in disease activity. IL-6 and TNF-α levels decreased in the cholecalciferol-supplemented group, indicating a reduction in inflammation. In the intervention group, improvements were observed in the physical and mental domains of the SF-36 questionnaire, particularly in physical functioning, energy and overall health. No similar results were observed in the control group [24].

SLE patients face increased osteoporosis and fracture risks due to vitamin D deficiency and corticosteroids side effects. Vitamin D supports calcium-phosphorus absorption, bone mineralization, and inhibits osteoclastogenic cytokines, reducing bone resorption. Supplementation may thus benefit bone health in SLE patients.

Vitamin D3 supplementation in SLE patients with deficiencies can lower disease activity and improve quality of life. Although the results of the study are promising, long-term analyses involving larger populations are needed to confirm the efficacy and safety of vitamin D supplementation in different groups of patients with SLE.

Gut microbiota

Intestinal homeostasis is a state of balance between gut microorganisms and the host. Disruption of this balance, called dysbiosis, leads to increased permeability of the intestinal barrier and stimulation of abnormal immune responses. Functions of the gut microbiota include, among others: the metabolism of nutrients – the microbiota converts fiber into short-chain fatty acids, such as butyrate, propionate, and acetate, which support the integrity of the intestinal barrier; and regulation of the immune system – the microbiota influences the activation of regulatory T lymphocytes, preventing excessive inflammatory reactions. [25]

Thus, the hypothesis was proposed as to whether the state of the gut microbiota could influence the course of autoimmune diseases.

In a randomized, double-blind, placebo-controlled trial by A. Widhani et al., the potential of synbiotics to modulate microbiota and their effect on disease activity and inflammatory markers was assessed. [26] The study involved 60 SLE patients who were randomly assigned to the synbiotic or placebo groups. For 12 weeks, a synbiotic containing various probiotic strains (e.g., Lactobacillus and Bifidobacterium) and a prebiotic supporting their activity were administered. After 12 weeks of synbiotic supplementation, a significant increase in gut microbiota diversity was observed. The number of probiotic bacteria, such as Lactobacillus and Bifidobacterium, increased, while the number of pro-inflammatory bacteria, such as Escherichia coli, decreased. Levels of pro-inflammatory cytokines, such as IL-6 and TNF-α, were significantly lower in the

synbiotic group compared to the placebo group. Levels of IL-10, an anti-inflammatory cytokine, increased, indicating an improvement in immune balance. In the synbiotic group, a decrease in the SLEDAI index was observed, indicating a reduction in disease activity. Symptoms such as fatigue, joint pain, and skin lesions decreased. Patients supplementing with synbiotics reported improvements in physical and mental well-being compared to the placebo group.

Synbiotics support the development of beneficial bacterial strains that produce short-chain fatty acids (SCFAs), such as butyrate, which support the integrity of the intestinal barrier. Reducing dysbiosis leads to a reduction in inflammation in the intestines and throughout the body, which is crucial in autoimmune diseases such as SLE. The results suggest that synbiotics may be an effective support for immunosuppressive therapies, reducing the severity of inflammation and supporting the gut microbiota. Supplementation with synbiotics may be particularly beneficial for patients with active forms of SLE and accompanying intestinal disorders.

Low Glycemic Index Diet

The glycemic index is a measure of the impact of consumed foods on blood glucose levels. Low-GI foods release glucose gradually, resulting in smaller fluctuations in blood sugar and insulin levels. A low-GI diet, rich in vegetables, fruits, whole grains, nuts, and seeds, while low in simple carbohydrates and processed foods, is considered beneficial in managing chronic inflammatory diseases, including systemic lupus erythematosus (SLE).

A review of studies published by Aline Mizusaki Imoto suggests that a low-calorie, low-glycemic diet can have a beneficial effect on disease activity in SLE patients [27]. Lowering glucose and insulin levels through a low-GI diet may influence the reduction of inflammation and improve patients' overall health. In vitro and in vivo studies have shown that a low-glycemic diet alters immune balance, reducing the activity of the immune system, which plays a key role in the pathogenesis of SLE.

A low-GI diet can also reduce fatigue symptoms, which are commonly observed in SLE patients. One of the mechanisms through which a low-GI diet reduces fatigue is by improving the body's energy metabolism. Low-GI foods support stable energy levels throughout the day.

The low-GI diet may influence inflammation, which is a key mechanism in SLE's pathogenesis. One of the main inflammatory factors are cytokines, which play a crucial role in the immune response. A low-glycemic diet can reduce pro-inflammatory cytokines such as TNF-α, IL-6, and interleukin 1 beta (IL-1β), while increasing anti-inflammatory cytokines like IL-10. These

changes in the cytokine profile may contribute to reducing the severity of inflammatory processes, which is beneficial in the context of SLE treatment.

According to studies by Hanxiao Jiao, a low-glycemic diet may reduce the risk of disease flare-ups and improve overall well-being in patients [28]. Reducing the intake of high-GI foods leads to the stabilization of glucose and insulin levels, which decreases oxidative stress, a factor contributing to increased inflammation. Furthermore, such a diet helps maintain a healthy body weight, which is important because overweight and obesity are associated with a higher risk of complications in SLE, including atherosclerosis, hypertension, and heart disease.

Mediterranean Diet

The Mediterranean diet, based on the consumption of vegetables, fruits, whole grains, fish, olive oil, and the restriction of red meat and processed foods, is considered one of the healthiest diets in the world. It is particularly valued for its protective effects on heart health, the vascular system, and the prevention of chronic inflammatory diseases.

In recent years, research has indicated the potential benefits of the Mediterranean diet in the treatment of SLE, both in terms of controlling disease activity and reducing the risk of complications such as heart disease and insulin resistance.

In a study by Gabriela Pocovi-Gerardino conducted on a group of SLE patients, it was shown that the Mediterranean diet can reduce disease activity and improve overall health [29]. Researchers noted that patients following this diet had lower levels of inflammatory markers in the blood, such as C-reactive protein (CRP) and interleukin 6 (IL-6). Additionally, this diet had an impact on reducing fatigue symptoms, one of the most common manifestations of SLE. Regular consumption of fish, olive oil, and foods rich in fiber and antioxidants contributed to reduced inflammation, which directly impacted the improvement in patients' quality of life.

In studies by Sara DelOlmo-Romero, the positive effect of the Mediterranean diet on reducing metabolic risk in SLE patients was documented [30]. This diet, rich in omega-3 fatty acids, fiber, and antioxidants, improved lipid profiles, lowered triglyceride levels, and increased HDL (good cholesterol) levels. Furthermore, the Mediterranean diet had a favorable impact on reducing insulin resistance, which is particularly important in the context of the risk of developing metabolic syndrome, which is common among patients with systemic lupus erythematosus.

Blanca Gavilán-Carrera, in her study, analyzed the relationship between the Mediterranean diet and inflammation among women with SLE [31]. The results showed that individuals following this diet had lower levels of TNF-α and IL-6, which are key in the pathogenesis of autoimmune

diseases. Additionally, the Mediterranean diet impacted the reduction of arterial stiffness, indicating its beneficial effect on the cardiovascular system.
The Mediterranean diet seems to be beneficial for patients with systemic lupus erythematosus. With its anti-inflammatory properties, its effect on cardiovascular health, and its improvement of metabolism, this diet can be effective supplement to drug therapy in treating SLE.
It is recommended that patients with SLE consider following a Mediterranean diet to reduce inflammation, improve cardiovascular function and improve overall health. Before making dietary changes, patients should consult a doctor or nutritionist to tailor the diet to their individual health needs.

Conclusions

SLE is a disease that can significantly reduce quality of life and risks serious complications. In addition to drug treatment, which is by far the mainstay of SLE therapy, patients should maintain an appropriate lifestyle. The above review shows that an appropriate diet, rich in omega-3 and omega-6 fatty acids with the proper ratio between them, can reduce disease activity and fatigue among patients. Vitamin D and synbiotics supplementation may also have a beneficial effect in patients with active SLE. Dietary models such as the low glycemic index diet and the Mediterranean diet have positive effects on SLE activity. Due to the safety and low cost of introducing these changes in diet and supplementation, they may be recommended to SLE patients.

Disclosure

Author's contribution

Natalia Dąbrowska: Conceptualization, check, writing - review and editing, supervision, project administration
Zuzanna Kudas: methodology, investigation, resources, data curation
Paweł Nowocin: software,
Martyna Koszyk writing – investigation, rough preparation,
Aleksandra Litwin writing - investigation , rough preparation,
Karolina Krzywicka writing - investigation , rough preparation,
Dawid Wiktor Kulczyński vizualization,
Paulina Kumięga, methodology, investigation, resources, data curation
Nikola Perchel, methodology, investigation, resources, data curation
Piotr Wasiński - investigation , rough preparation,

All authors have read and agreed with the published version of the manuscript.

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The authors deny any conflict of interest

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