Nutritional Modulation of the Gut-Kidney Axis in Lupus Nephritis

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Abstract:

Background: Nutrition and dietary therapy play an increasingly important role in regulating immune and metabolic pathways associated with chronic inflammatory diseases. Interactions between dietary factors, gut microbiota, and immune regulation in lupus nephritis (LN) mediate renal inflammation, oxidative stress, and disease progression. Growing evidence suggests that the gut–kidney-immune axis represents an important mechanism through which nutritional interventions may promote renal protection. **Methods:** This narrative review synthesises evidence from preclinical, experimental, and clinical studies investigating the role of nutrition, dietary patterns, gut microbiota, and food-derived bioactive compounds in LN. Keywords used to search major scientific databases included lupus nephritis, nutrition, diet therapy, gut microbiota, probiotics, immunometabolism, and related terms. **Results:** Nutritional approaches such as targeted micronutrient supplementation, optimization of macronutrients, and the use of anti-inflammatory dietary regimens, such as the Mediterranean diet, demonstrate potential renoprotective properties due to the regulation of the immune system and oxidative stress. Functional foods, particularly probiotics, prebiotics, and short-chain fatty acids, play a mechanistic role in restoring gut barrier integrity and enhancing immunological tolerance. Nevertheless, there is still a scarcity of clinical evidence, and microbiome-related responses show substantial inter-individual variability. **Conclusions**: Nutritional and microbial modulation is a prospective complementary approach to enhancing renal outcomes in lupus nephritis. Artificial intelligence-based tools may support the future development of personalized nutrition strategies in LN. However, standardized dietary guidelines supported by strong clinical evidence are still lacking.

Keywords: Lupus Nephritis, Diet Therapy, Gut Microbiota, Mediterranean Diet, Inflammation

Introduction:

Dietary behavior, nutritional status, and gut microbiota-immune interactions are increasingly recognized as key determinants in chronic inflammatory diseases. Nutrition acts as a major modifiable factor regulating immune activation, oxidative stress, and metabolic homeostasis. Food-derived bioactive compounds offer a potential means of controlling disease severity and renal disease progression in immune-mediated renal diseases like lupus nephritis.

Background and disease burden of lupus nephritis

Lupus nephritis (LN) has been known for more than a century. In the 19th century, it was first identified as a dermatological disorder. After the autopsy investigations in the early 20th century, it was revealed that it also affected the kidneys. Renal biopsy advancement in the mid-20th century enabled histological classification, leading to the ISN/RPS 2003 system used today (Gasparotto et al., 2020; Weening et al., 2004). Although such developments have been made, LN remains one of the most common causes of morbidity and mortality among pediatric patients. Moreover, 30% of patients who have systemic lupus erythematosus develop end-stage renal disease, and they can receive immunosuppressant treatment. About 40 to 60% of SLE patients develop LN (Almaani, 2017). The disease burden is the highest in women and other African, Asian, and Hispanic origins, the result of genetic susceptibility and disparities in socioeconomic conditions. The International Society of Nephrology and Renal Pathology Society has developed six different types of LN based on the severity and immune complex deposition patterns in the glomeruli (Markowitz and Agati, 2007).

Symptoms and Diagnosis of LN:

Common clinical symptoms include proteinuria, hematuria, hypertension, and reduced glomerular filtration rate. Urine analysis, renal biopsy, creatinine and complement assessment confirm diagnoses (Almaani, 2017).

Causes and risk factors:

In lupus nephritis, environmental, immunological, microbiological, and genetic factors all work together and contribute to kidney injury. Gut microbiome dysbiosis increases intestinal permeability and systemic autoimmunity (Hevia et al., 2014; Mu et al., 2017), leading to immune complex deposition and renal inflammation (Bao et al., 2015; Dai et al., 2025). Risk is also increased by genetic susceptibility, including variation in HLA (Anders et al., 2020). Lifestyle factors, including high-protein and high-sodium dietary patterns, smoking, and micronutrient deficiencies, can exacerbate disease activity. Collectively, these factors emphasize the importance of dietary patterns in modulating immune imbalance and renal outcomes in lupus nephritis.

Materials and Methods:

This narrative review was based on a literature search of PubMed, Scopus, ScienceDirect, and Google Scholar using keywords related to lupus nephritis, nutrition, gut microbiota, dietary interventions, and artificial intelligence. Relevant experimental, clinical, and review articles published in English were included based on their relevance to the topic. Studies were screened based on relevance, study design, and their contribution to understanding lupus nephritis, nutritional modulation, and gut microbiome–immune interactions.

Pathophysiology of the Gut–Kidney–Immune Axis in Lupus Nephritis:

Gut Dysbiosis:

Current research indicates that one of the main causes of the rapid progression of lupus nephritis is dysbiosis or alterations in the gut microbiota. Patients with SLE and LN may develop increased intestinal permeability due to alterations in microbial composition and function, which weakens the intestinal epithelial barrier. This disruption facilitates the translocation of microbial products into systemic circulation, such as lipopolysaccharides and other pathogen-associated molecular patterns. These microbial products potently activate the

immune system by stimulating dendritic cells, increasing production of autoantibodies, and promoting pro-inflammatory Th17 T-helper cells, which cause the immune-complex deposition and systemic inflammation in renal tissue. Under physiological conditions, the fermentation of fibers by commensal bacteria generates short-chain fatty acids, which are reduced in dysbiosis, resulting in impaired immune tolerance and dysfunctional regulatory T-cell responses. All these microbiota-based mechanisms contribute to the gut-immune kidney inflammatory feedback loop, which later promotes the development and progression of LN (Hevia et al., 2014; Mu et al., 2017).

Immune Activation:

Lupus nephritis involves a complex immunological dysfunction, which leads to kidney inflammation and injury. The creation of autoantibodies, particularly anti-double-stranded DNA (dsDNA) antibodies, plays an important role in this illness. These antibodies combine to form immune complexes that deposit in the glomeruli and trigger inflammatory reactions. These immune complexes induce tissue damage by activating the complement system through the classical pathway, resulting in the generation of the membrane attack complex and pro-inflammatory mediators. T and B cell dysfunction plays an important role in apoptotic cell clearance, and regulatory T cell function is compromised, leading to excessive lymphocyte activation, persistent autoimmune responses, and renal injury. In LN, a self-amplifying cycle of inflammation and tissue damage is driven by three key factors, autoantibody synthesis, complement activation, and immune cell dysregulation (Bao et al., 2015; Dai et al., 2025).

Kidney involvement:

The primary mechanism of renal impairment in lupus nephritis is the deposition of circulating immune complexes containing autoantibodies, such as anti-dsDNA, within the glomeruli. These deposits recruit inflammatory cells and activate the complement system, leading to glomerular injury. Long-term immune-mediated damage leads to endothelial dysfunction and

mesangial proliferation, all of which collectively impair glomerular filtration. Ongoing inflammation gradually leads to glomerulosclerosis and tubulointerstitial fibrosis, which impairs nephron function and accelerates the progression of chronic kidney disease. Renal involvement is essential for assessing disease activity and guiding treatment because the extent and chronicity of renal involvement strongly influence long-term outcomes in SLE patients (Anders et al., 2020; Valiente et al., 2022). The gut–kidney–immune axis involved in lupus nephritis is illustrated in **Figure 1**.

Mechanistic Role of Nutrition in Modulating the Axis:

Macronutrients significantly influence the gut–kidney–immune axis in lupus nephritis by modulating inflammatory pathways and renal function.

Protein intake: High intake of protein promotes glomerular hyperfiltration. A moderate level of protein restriction may reduce fibrosis and lower glomerular pressure. Experimental models of nephritis show that low-protein diets reduce proteinuria and activate the reno-protective pathway (Neugarten et al., 1991).

Dietary fats: Omega-3 fatty acids (EPA and DHA) have been associated with anti-inflammatory effects by inhibition of NF-kB signalling and reduction of inflammatory cytokine synthesis. In contrast, omega-6-rich diets have been associated with increased renal inflammation (Calder, 2017).

Carbohydrates: High glycemic diets promote oxidative stress and kidney inflammation. A low glycemic index diet helps to improve gut health and metabolic control, and may contribute to disease modulation (Juraschek et al., 2016).

Micronutrients:

Vitamin D: Vitamin D increases immunological tolerance by supporting regulatory T-cell development and inhibition of pro-inflammatory cytokines, while maintaining podocyte function in LN models (Kramer et al., 2022).

Selenium: Selenium and its antioxidant enzymes reduce oxidative stress and inhibit B-cell hyperactivity, and are associated with reduced autoantibody activity in experimental models (Soni et al., 2019).

Zinc and Calcium: Zinc affects T-cell development and cytokine balance. Calcium is closely related to Vitamin D levels, maintaining podocytes healthy and glomeruli intact. Deficiencies in these micronutrients can exacerbate LN activity and kidney damage (Yu et al., 2019).

Functional foods & Nutraceuticals:

Curcumin: Curcumin decreases glomerular inflammation, proteinuria, and immune complex deposition, these benefits are partially ascribed to inhibition of NF-kB signalling and enhanced regulatory T-cell activity (Lee et al., 2013).

Resveratrol: Resveratrol has been shown to suppress CD4+ T-cell and B-cell activation and lower immune complex-mediated kidney damage through SIRT1-mediated immune control (Wang et al., 2014).

Polyphenols: Dietary polyphenols found in berries, green tea, and olive oil have been shown to reduce the production of pro-inflammatory cytokines and oxidative stress, thereby improving immune balance (Aparicio-Soto et al., 2017). The mechanistic Roles of Nutrients are summarized in Table 1

Nutrition and the Gut Microbiome in LN:

Microbiota composition:

Diet influences the gut microbial ecosystem, with nutritional factors either maintaining microbial balance or contributing to dysbiosis in LN. Plant-based fibre-rich, polyphenol and omega-3 fatty acid diets reduce the abundance of pro-inflammatory bacteria and increase beneficial taxa such as Lactobacillus and Bifidobacterium. These alterations further amplify systemic immune activation through microbial metabolites, contributing to renal inflammation. (Hevia et al., 2014).

Prebiotics, probiotics, and synbiotics:

Probiotics provide live microorganisms with immunoregulatory effects, and prebiotics provide fermentable substrates that promote the growth of beneficial organisms. Synbiotics formulations have been shown in experimental lupus models to improve gut barrier integrity, increase IL-10 secretion, and reduce autoantibody levels in the lupus disease model. Such approaches may support gut-derived immune tolerance and improve intestinal microbial diversity as adjunctive strategies in LN (Hevia et al., 2014).

SCFAs (Butyrate, Propionate):

The short-chain fatty acids (SCFAs), such as butyrate and propionate, are important metabolites produced through the microbial fermentation of dietary fiber. They inhibit histone deacetylase (HDAC) and enhance regulatory T cell responses. At the same time, SCFAs suppress pro-inflammatory cytokines, such as TNF-α and IL-6, via inhibition of NF-κB signaling. SCFAs also enhance tight junctions, lowering gut leakiness and systemic immune activation. This SCFA-mediated regulation of immune balance and barrier function contributes to kidney protection in LN (Habiballah et al., 2025).

Evidence from Animal Models and Early Clinical Insights:

In lupus-prone MRL/lpr mice, butyrate supplementation has been associated with rebalancing of the gut microbiota, reduced proteinuria, and improved renal histopathology (He et al., 2020). Probiotic strains (L. fermentum, L. reuteri, L. plantarum, L. casei) have been shown to reduce the pro-inflammatory cytokines, enhance regulatory T-cell function, and improve intestinal barrier function in the lupus animal model (Guo et al., 2021). Clinical trials using synbiotics have reported reduced IL-6 levels, improved microbial composition, and lower SLEDAI-2K scores in SLE patients (Widhani et al., 2022). Together, these insights suggest that microbiome-targeted therapy may be a promising adjunct strategy for modifying disease progression and improving outcomes in LN.

Nutritional Management and Reno-protective Strategies:

Salt restriction:

High dietary salt intake has been associated with hypertension, proteinuria and glomerular hyperfiltration, which are recognized contributors to renal injury. Meta-analyses in patients with chronic kidney disease have demonstrated that reducing dietary salt intake is associated with lower systolic blood pressure and reduced albuminuria, suggesting potential renoprotective benefits in early renal disease (McMahon et al., 2021).

Protein Modulation:

A high-protein diet has been associated with increased nitrogenous waste, leading to glomerular hyperfiltration and potentially increasing renal injury. Excessive restrictive protein intake risks malnutrition. Evidence from CKD populations suggests that moderate protein intake may support both nutritional status and renal preservation (Ko et al., 2017; Mafra et al., 2025).

Mediterranean Diet:

The intake of anti-inflammatory dietary patterns, such as the Mediterranean diet, has been associated with reduced oxidative stress and improved immunological regulation in LN. The Mediterranean dietary pattern is characterized by high consumption of extra-virgin olive oil, whole grains, legumes, fruits, vegetables, and nuts. Its high fiber and polyphenol content promotes short-chain fatty acid production through gut microbial fermentation and reduces pro-inflammatory cytokine signaling, thereby supporting renal protection in LN. Studies suggest that lupus patients adhering to this dietary pattern demonstrate lower disease activity, supporting its potential reno-protective role (Islam et al., 2020).

Micronutrient Supplementation:

Immunological homeostasis and kidney protection are influenced by micronutrient balance. Vitamin D deficiency is commonly observed in LN, which has been associated with T-cell

function and immune checkpoint modulation. Supplementation may support immune balance. Evidence regarding other micronutrients, including omega-3 fatty acids, selenium, and zinc, has demonstrated antioxidant and immunomodulatory benefits largely derived from experimental and autoimmune disease models (Youssry et al., 2021).

Clinical Nutrition Guidelines & Patient Centred Interventions:

Diet alone is not curative for systemic lupus erythematosus or LN, but remains important for symptom management and the overall patient well-being. Clinical nutrition strategies in LN commonly focus on anti-inflammatory dietary practices, nutritional management of drug side effects, and preservation of bone health through adequate calcium and vitamin D intake (Sciascia et al., 2024). All nutritional strategies are summarized in **Table 2.**

Artificial Intelligence and Personalized Nutrition in Lupus Nephritis

Artificial intelligence (AI) has emerged as a supportive tool in lupus nephritis (LN) for outcome prediction and renal flare risk stratification. Machine learning models integrating clinical parameters with biomarker data have demonstrated promising performance in predicting treatment response and short-term outcomes (Stojanowski et al., 2022; Yang Panyu et al., 2024). Computational approaches incorporating serological and urinary biomarkers have also been explored to predict renal relapse and long-term prognosis (Chen et al., 2021; Chen Ayoub et al., 2022). However, most predictive systems remain in early validation stages and require external confirmation before routine clinical implementation. AI-based image analysis has also shown potential in assisting renal biopsy interpretation in LN (Zheng et al., 2021; Tianqi et al., 2025). These systems are designed to complement expert pathological assessment rather than replace clinical judgment. Future integration of predictive algorithms with dietary intake, metabolic biomarkers, and gut microbiome profiles may support personalized nutritional strategies aimed at reducing inflammation and preserving renal function. Nevertheless,

standardized validation and structured clinical integration frameworks are necessary before widespread adoption.

Complications:

Renal Complications: Lupus nephritis frequently progresses to chronic kidney damage characterized by fibrosis and declining renal function. Approximately 10-30% of patients develop end-stage renal disease (ESRD) that requires dialysis or transplantation. Even partial remission does not eliminate risk, and renal preservation remains a major therapeutic goal (Bao et al., 2015; Dai et al., 2025).

Systemic complications:

In addition to kidney damage, LN is associated with systemic inflammation, cardiovascular diseases, hypertension, and treatment-related adverse effects. Long-term corticosteroid and cytotoxic treatment is associated with increased risks of infection, diabetes, osteoporosis, and malignancy (McMahon et al., 2021; Ko et al., 2017; Mafra et al., 2025). Nutritional and microbiome-targeted therapies that reduce the effects of inflammation and metabolic stress can be used in conjunction with pharmacologic approaches to decrease disease burden (Calder, 2017).

Challenges and Research Gaps:

Limited Clinical Trials in Lupus Nephritis:

Clinical trials investigating nutritional therapy in lupus nephritis (LN) are scarce and often limited in scope, and involve fish oil supplementation as an adjunct to standard immunosuppressive therapy. In combination with low-dose cyclophosphamide, fish oil modestly improved lipid profiles and remission rates, but did not significantly impact key renal outcomes, such as GFR or proteinuria (Zhang et al., 2021). Likewise, previous crossover studies on omega-3 supplementation did not show significant differences between it and

placebo on renal function markers (Pestka, 2010). These results highlight the need for properly designed, diet-oriented RCTs in LN to establish evidence-based nutritional recommendations.

Absence of Standardised Dietary Guidelines:

Dietary guidelines for lupus nephritis (LN) are neither well-defined nor evidence-based, although it is known that nutrition influences the outcome of systemic lupus erythematosus (SLE). Various diets have been proposed, targeting inflammation reduction or macronutrient balance, but none of them is currently officially recommended in clinical practice. A thorough patient-initiated survey highlighted that there is insufficient evidence to recommend any specific diet to control SLE activity, and dietary recommendations relied, as a rule, on general rather than LN-specific clinical evidence (Sciascia et al., 2024).

Variability in Microbiome Research:

Although microbiome research in LN reveals encouraging mechanistic connections, reproducibility remains a major challenge. Identifying reliable LN-specific microbial signatures is made more difficult by inter-individual variations in microbiota and due to variability in sample collection, sequencing platforms, and bioinformatic pipelines (Mangalam et al., 2021).

Barriers to AI Integration in Nephrology Care:

Artificial intelligence has potential applications in microbiome characterization, predictive modelling, and customized nutrition, although practical clinical implementation remains limited. Key obstacles include data fragmentation, algorithmic bias, ethical concerns, and limited clinician acceptance (Hueso and Vellido, 2024; Jayaraman et al., 2025). These gaps underscore the need for interdisciplinary approaches in the field of nutrition, microbiome science, and AI to advance LN care.

Future Directions:

The combination of nutrition, microbiome control, and AI may substantially advance the management of LN. Personalized, reno-protective dietary strategies, based on AI-driven models of immune, genetic, and microbial data, have the potential to guide the individualized management of inflammation and disease progression (D'Urso and Broccolo, 2024; Gabriela et al., 2021). Emerging AI-enabled biosensors and wearable products may enable real-time monitoring and inform adaptive dietary strategies (Sara et al., 2024).

Conclusion:

Lupus nephritis represents a complex interaction between immune dysregulation and progressive renal injury. Emerging evidence highlights the contributory role of the gut–kidney–immune axis, linking intestinal microbiota and dietary factors to renal inflammation and disease progression. Targeted dietary modulation and microbiome-based interventions may serve as adjunctive approaches to existing immunosuppressive therapies. In parallel, AI-based tools for outcome prediction, pathology evaluation, and disease phenotyping may enhance clinical decision-making, but their applications remain investigational. Further well-designed clinical trials integrating dietary patterns, microbiome-targeted interventions, and AI-assisted predictive tools are essential to advance personalized and evidence-based nutritional management in lupus nephritis.

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Conflict of Interest

The authors declare that there is no conflict of interest.

Authors' Contributions

Yogesh R, Senthilrajan D, Sobana S, Srividhya R, Rajeswari D and Tamizharasu M contributed to the conception and design of study, literature review, drafting of manuscript, and critical revision for important intellectual content. All authors approved the final version of the manuscript.

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Reference:

Almaani S, Meara A, Rovin BH. 2017. Update on lupus nephritis. *Clin J Am Soc Nephrol.* 12(5):825–835.

Anders HJ, Saxena R, Zhao MH, Parodis I, Salmon JE, Mohan C. 2020. Lupus nephritis. *Nat Rev Dis Primers.* 6(1):7.

Aparicio-Soto M, Sánchez-Hidalgo M, Cardeno A, et al. 2017. The phenolic fraction of extra virgin olive oil modulates the activation and the inflammatory response of T cells from patients with systemic lupus erythematosus and healthy donors. *Mol Nutr Food Res.* 61(9):1601080.

Bao L, Cunningham PN, Quigg RJ. 2015. Complement in lupus nephritis: new perspectives. *Semin Nephrol.* 35(5):500–509.

Calder PC. 2017. Omega-3 fatty acids and inflammatory processes: from molecules to man. *Biochem Soc Trans.* 45(5):1105–1115.

Chen Ayoub I, Wolf BJ, Song H, Khatiwada, Aastha, et al. 2022. Prediction models of treatment response in lupus nephritis. *Kidney Int.* 101(2):379–389.

Chen Y, Huang S, Chen T, Liang D, Yang J, Zeng C, et al. 2021. Machine learning for prediction and risk stratification of lupus nephritis renal flare. *Am J Nephrol.* 52(2):152–160.

D'Urso F, Broccolo F. 2024. Applications of artificial intelligence in microbiome analysis and probiotic interventions. An overview and perspective based on the current state of the art. *Appl Sci.* 14(19):8627.

Dai X., Fan Y, Zhao X, Sullivan KE. 2025. Systemic lupus erythematosus: updated insights on the pathogenesis. *Signal Transduct Target Ther.* 10:123.

Gasparotto M, Gatto M, Binda V, Doria A, Moroni G. 2020. Lupus nephritis: clinical presentations and outcomes in the 21st century. *Rheumatology (Oxford).* 59(Suppl 5):v39–v51.

Guo X, Yang X, Li Q, Shen X, Zhong H, Yang Y. 2021. Microbiota in systemic lupus erythematosus: an update on the potential function of probiotics. *Front Pharmacol.* 12:759095.

Habiballah DN, Li F, Jiang L. 2025. Immune metabolic restoration in systemic lupus erythematosus: the impact of gut microbiota, probiotics, and nutritional synergy. *Front Immunol.* 16:1602235.

He X, Xu X, Zhao Y, Lin H, Zhou L, Nie L et al. 2020. Sodium butyrate ameliorates gut microbiota dysbiosis in lupus-like mice. *Front Nutr.* 7:604283.

Hevia A, Milani C, López P, Cuervo A, Arboleya S, Duranti S et al. 2014. Intestinal dysbiosis associated with systemic lupus erythematosus. *mBio.* 5(5):e01548-14.

Hueso M, Vellido A. 2024. How artificial intelligence is transforming nephrology. *BMC Nephrol.* 25:276.

Islam MA, Khandker SS, Kotyla PJ, Hassan R. 2020. Immunomodulatory effects of diet and nutrients in systemic lupus erythematosus: a systematic review. *Front Immunol.* 11:1477.

Jayaraman P, Vasudev I, Bhardwaj A, Nadkarni G, Sakhuja A, Meena P. 2025. Artificial intelligence in nephrology: pioneering precision with multimodal intelligence. Indian J Nephrol. 35:470–479.

Juraschek, SP, Chang A.R, Appel LJ, et al. 2016. Effect of glycemic index and carbohydrate intake on kidney function in healthy adults. *BMC Nephrol.* 17:88.

Ko, Gang Jee, Obi, Yoshitsugu, Tortorici, Amanda R, et al. 2017. Dietary protein intake and chronic kidney disease. *Curr Opin Clin Nutr Metab Care.* 20(1):77–85.

Krämer AN, Schäfer A-L, Sprenger DTL, Sehnert B, Williams JP, Luo A, et al. 2022. Impact of dietary vitamin D on immunoregulation and disease pathology in lupus-prone NZB/W F1 mice. *Front Immunol.* 13:933191.

Lee H, Kim H, Lee G, Chung HS, Bae H. 2013. Curcumin attenuates lupus nephritis upon interaction with regulatory T cells in New Zealand Black/White mice. *Br J Nutr.* 110(1):69–76.

Mafra D, Brum I, Borges NA, Leal VO, Fouque D. 2025 Low-protein diet for chronic kidney disease: evidence, controversies, and practical guidelines. J Intern Med. 298:319–335.

Mangalam AK, Yadav M, Yadav R. 2021. The emerging world of microbiome in autoimmune disorders: opportunities and challenges. *Indian J Rheumatol.* 16(1):57–72.

Markowitz GS, D'Agati VD. 2007. The ISN/RPS 2003 classification of lupus nephritis: an assessment at 3 years. *Kidney Int.* 71(6):491–495.

McMahon EJ, Campbell KL, Bauer JD, Mudge DW, Kelly JT. 2021. Altered dietary salt intake for people with chronic kidney disease. *Cochrane Database Syst Rev.* (6):77–78.

Mu Q, Zhang H, Liao X, Lin K, Liu H, Edwards MR, et al. 2017. Control of lupus nephritis by changes in gut microbiota. *Microbiome.* 5(1):73.

Neugarten J, Kozin A, Gayner R, Schacht RG, Baldwin DS. 1991. Dietary protein restriction and glomerular permselectivity in nephrotoxic serum nephritis. *Kidney Int.* 40(1):57-61.

Pestka JJ. 2010. N-3 polyunsaturated fatty acids and autoimmune-mediated glomerulonephritis. *Prostaglandins Leukot Essent Fatty Acids.* 82(4–6):251–258.

Pocovi-Gerardino G, Correa-Rodríguez M, Callejas-Rubio JL, Ríos-Fernández R, Martín-Amada M, Cruz-Caparros MG, et al. 2021. Beneficial effects of Mediterranean diet adherence on disease activity in systemic lupus erythematosus. *Rheumatology (Oxford).* 60(1):160–169.

Sara DelOlmo-Romero, Irene Medina-Martínez, Rocio Gil-Gutierrez, Gabriela Pocovi-Gerardino, María Correa-Rodríguez, Norberto Ortego-Centeno, et al. 2024. Mediterranean diet adherence and metabolic health in SLE: findings from a clinical cohort. *Med Clin (Engl Ed).* 162(6):259–264.

Sciascia S, Ferrara G, Roccatello L, Rubini E, Foddai SG, Radin M, et al. 2024. The interconnection between systemic lupus erythematosus and diet: unmet needs, available evidence, and guidance—a patient-driven, multistep-approach study. *Nutrients.* 16(23):4132.

Soni C, Sinha I, Fasnacht MJ, Olsen NJ, Rahman ZS, Sinha R. 2019. Selenium supplementation suppresses immunological and serological features of lupus in B6Sle1b mice. *Autoimmunity.* 52(1):57–68.

Stojanowski J, Konieczny A, Rydzyńska K, Kasenberg I, Mikołajczak A, Gołębiowski T, et al. 2022. Artificial neural network—an effective tool for predicting the lupus nephritis outcome. *BMC Nephrol.* 23:381.

TU T, WANG H, Pei J, Yu X, Men A, Wang S, et al. 2025. Deep learning-based quantitative assessment of renal chronicity indices in lupus nephritis. *Ann Diagn Pathol.* 1–20.

Valiente GR, Munir A, Hart ML, Blough P, Wada TT, Dalan EE, et al. 2022. Gut dysbiosis is associated with acceleration of lupus nephritis. *Sci Rep.* 12:152.

Wang ZL, Luo XF, Li MT, Xu D, Zhou S, Chen HZ, et al. 2014. Resveratrol possesses protective effects in a pristane-induced lupus mouse model. *PLoS One.* 9(12):e114792.

Weening JJ, D'Agati VD, Schwartz MM, Seshan SV, Alpers CE, Appel GB, et al. 2004. The classification of glomerulonephritis in systemic lupus erythematosus revisited. *Kidney Int.* 65(2):521–530.

Widhani A, Djauzi S, Suyatna FD, Dewi BE. 2022. Changes in gut microbiota and systemic inflammation after synbiotic supplementation in patients with systemic lupus erythematosus: a randomized, double-blind, placebo-controlled trial. *Cells*. 11(21):3419.

Yang P, Liu Z, Lu F, Sha Y, Li P, Zheng Q, et al. 2024. Machine learning models predict risk of proliferative lupus nephritis. *Front Immunol.* 1–13.

Youssry S, Hussein A, Moaaz M. 2021. The immunoregulatory axis (programmed death-1/programmed death ligand-1) on CD4+ T cells in lupus nephritis: association with vitamin D and chemokine C-X-C motif ligand 12. *Microbiol Immunol.* 65:392–399.

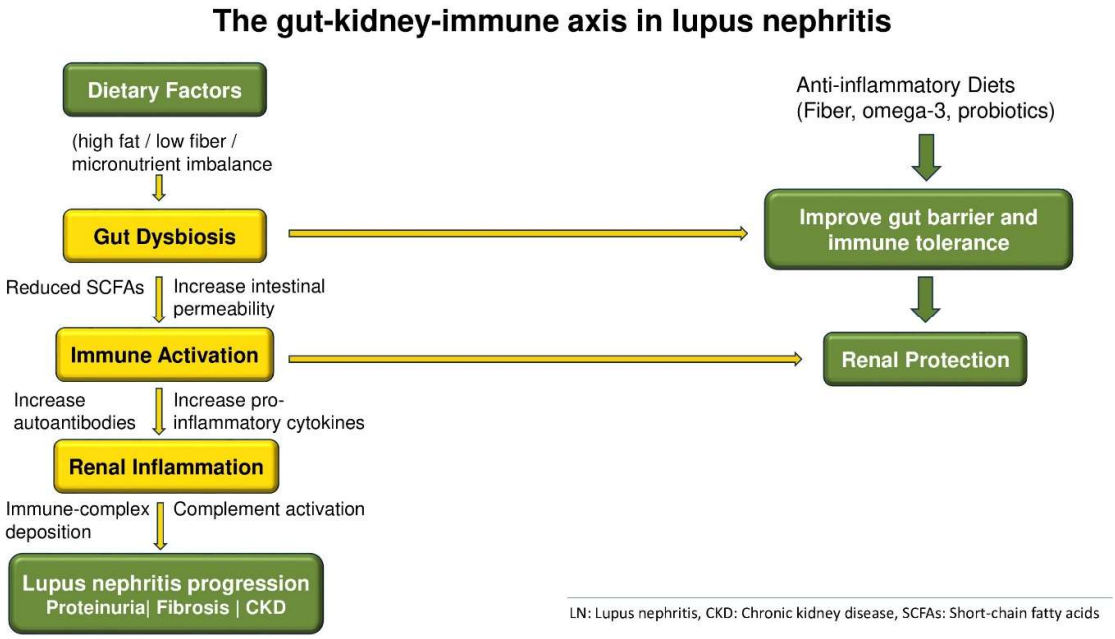
Yu Q, Qiao Y, Liu D, Liu F, Gao C, Duan J et al. 2019. Vitamin D protects podocytes from autoantibodies-induced injury in lupus nephritis by reducing aberrant autophagy. *Arthritis Res Ther.* 21:19.

Zhang C, Ge C, Wang J, Sun D. 2021. Fish oil enhanced the efficacy of low-dose cyclophosphamide regimen for proliferative lupus nephritis: a randomized controlled double-blind trial. *Food Nutr Res.* 65:7842.

Zheng Z, Zhang X, Ding J, Zhang D, Cui J, Fu X, et al. 2021. Deep learning-based artificial intelligence system for automatic assessment of glomerular pathological findings in lupus nephritis. *Diagnostics.* 11:1–12.

Figure

Figure 1. The gut–kidney–immune axis in lupus nephritis.



Tables

Table 1: Nutrients & Mechanisms.

Nutrient	Mechanism	Evidence	Reference
Protein [moderate level]	Decrease glomerular hyperfiltration and fibrosis	Experimental nephritis model	Neugarten et al., 1991.
Omega-3 PUFAs	Decrease NF-kB and cytokines, support regulatory immune responses	Animal and clinical studies	Calder, 2017.
Vitamin D	Increases regulatory T cells, reduces inflammatory cytokines, and protects podocytes	Lupus nephritis mouse model	Krämer et al., 2022.
Selenium	Decrease oxidative stress and modulation of autoimmune activity	Autoimmune model	Soni et al., 2019.

Curcumin	Inhibits NF-kB signaling, reduces proteinuria, and enhances regulatory T cell activity	Lupus nephritis mouse model	Lee et al., 2013.

Table 2: Nutritional management strategies.

Strategy	Recommendation	Effect on LN/CKD	Reference
Salt restriction	<4 g/day salt and 1.6–1.7 g sodium	reduce blood pressure and albuminuria	McMahon et al., 2021.
Protein intake	0.6–0.8 g/kg/day	reduce hyperfiltration and maintain nutrition	Mafra et al., 2025.
Probiotics/Synbiotics	Lactobacillus strains, synbiotics	decrease IL-6, increase microbial diversity	Widhani et al., 2022.
Micronutrients (Vitamin D, Zinc, Selenium)	Supplement if deficient	immune regulation, potential modulation of autoimmune responses	Youssry et al., 2021.