The Bioscan
AN INTERNATIONAL QUARTERLY JOURNAL OF LIFE SCIENCES
20(3): S.I(3). 1826-1842, 2025 www.thebioscan.com

# THERAPEUTIC POTENTIAL OF THE MEDITERRANEAN DIET IN PRIMARY SJÖGREN'S SYNDROME: A SYSTEMATIC REVIEW OF CLINICAL AND IMMUNOLOGICAL OUTCOMES

**MONISHA L[1], SINDHU R[2*], BANU JOTHI A[3], RAJMOHAN M [4], DINESH DHAMODHAR [5], LUBNA FATHIMA[6], PRABU D [7], HARIPRIYA R[8]**

[1]Undergraduate, SRM Dental college, Ramapuram, Bharathi salai, Chennai, TN, India.
[2,6]MDS, Senior lecturer, Department of Public health dentistry, SRM Dental college, Ramapuram, Bharathi salai, Chennai, TN, India.
[3,8]Postgraduate, Department of Public health dentistry, SRM Dental college, Ramapuram, Bharathi salai, Chennai, TN, India.
[4,5]MDS, Reader, Department of Public health dentistry, SRM Dental college, Ramapuram, Bharathi salai, Chennai, TN, India.
[7]PhD, Head of the Department, Department of Public health dentistry, SRM Dental college, Ramapuram, Bharathi salai, Chennai, TN, India.

**DOI: 10.63001/tbs.2025.v20.i03.S.I(3).pp1826-1842**

***Corresponding Author**: **Dr Sindhu R:** Email: researchphdsrm@gmail.com

**KEYWORDS:**
**Mediterranean diet, primary Sjögren's syndrome, dry eye syndrome, autoimmune disease, inflammation, polyunsaturated fatty acids**

**Received on:**

**16-09-2025**

**Accepted on:**

**12-10-2025**

**Published on:**

**24-11-2025**

**ABSTRACT**

The Mediterranean diet (MD) is increasingly recognized for its anti-inflammatory and immunomodulatory effects. Given the autoimmune nature of primary Sjögren's syndrome (pSS), dietary modification through MD may hold clinical promise. A thorough search of the literature was conducted using PubMed, Scopus, and Web of Science until March 2025. Research articles evaluating the association between MD adherence and clinical or immunological outcomes in primary pSS and DES were included. Six relevant studies met the inclusion criteria. Higher adherence to MD correlated with lower disease activity scores (ESSDAI, ClinESSDAI), better ocular surface parameters (OSDI, TBUT), and favorable changes in biomarkers (IgG, C3, anti-Ro/La). Consumption of fish and foods high in polyunsaturated fatty acids (PUFAs) appeared particularly advantageous. However, some studies failed to demonstrate statistically significant effects. This review emphasizes the MD's possible role in reducing symptoms and controlling immunological dysfunction in pSS. Although the results are encouraging, further longitudinal and interventional research is needed to assess its potential as a treatment.

## Introduction:

The MD emphasizes a diet that includes plant-based foods, such as fruits,

vegetables, whole grains, legumes, nuts, and seeds, is advised by MD. It consists of a moderate intake of fish, poultry, dairy, and olive oil, which is the main source of fat and is renowned for its abundance in omega-3 and monounsaturated fatty acids [1]. While moderate wine consumption with meals is customarily included in the dietary pattern, red meat, processed foods, refined sugars, and sweetened beverages are restricted [2]. Beyond its nutrient-rich composition, the MD is a sustainable, culturally rooted lifestyle. UNESCO has honored this as an Intangible Cultural Heritage, it emphasizes community, regular mealtimes, and mental well-being [1,14]. Following the usual eating patterns of the people living around the Mediterranean Sea, the MD has drawn interest from all over the world due to its sustainability, palatability, and several health advantages. Regular mealtimes and social eating are encouraged by its structured, culturally entrenched framework, which enhances psychological well-being [3]. Sjögren's syndrome is a lifelong autoimmune disease in which the body's defense system mistakenly attacks its own moisture-producing glands, leading mainly to dry mouth and dry eyes. It can also involve other glands and organs, so some people have symptoms affecting joints, skin, lungs, kidneys, nerves, and overall energy levels. Additionally, polyphenols commonly found in the MD—such as oleuropein and resveratrol—have been shown to suppress inflammatory pathways, including NF-κB and MAPK, which have important roles in the pathogenesis of autoimmune diseases like primary Sjögren's syndrome (pSS) [4]. This diet also supports a diverse gut microbiota. It promotes the synthesis of short-chain fatty acids, especially butyrate, which strengthens mucosal immunity and contributes to maintaining immune tolerance5) Additionally, the MD contains a lot of antioxidants that counteract reactive oxygen species (ROS), reducing oxidative stress and shielding the lacrimal and salivary glands from harm in SS [6]. Omega-3 fatty acids, specifically docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), derived from fatty fish, have been shown to lower the levels of key pro-inflammatory cytokines, including interleukin-6 (IL-6) and tumour necrosis factor-alpha (TNF-α), Potentially contributing to reduced disease activity in primary SS (pSS). Omega-3 fatty acids also regulate immune function by lowering pro-inflammatory cytokine levels, such as IL-6 and TNF-α, major contributors to disease progression in autoimmune disorders [7]. Specific elements of the MD promote the absorption and metabolism of vitamin D, which aids in the development of regulatory T cells and helps maintain immune system balance in pSS [8]. In addition to physical symptoms, people with pSS frequently have mood disruptions. Because of its capacity to promote neurochemical equilibrium, the MD has shown a protective effect against

depression, likely attributed to its ability to reduce inflammation and support neurochemical balance [9].

Recent studies also indicate that nutrients associated with the MD can affect gene expression via epigenetic processes, such as histone modifications and DNA methylation, potentially influencing the course of autoimmune diseases such as SS [10]. Considering the increased cardiovascular risk in patients with SS, the MD offers added cardioprotective benefits by enhancing HDL function and decreasing LDL oxidation [11]. Consumption of olive oil and nuts—core elements of the MD—boosts salivary antioxidant capacity, potentially shielding exocrine glands from the reactive oxygen species (ROS)-induced damage frequently observed in SS [12]. Collectively, the Mediterranean diet's (MD) anti-inflammatory, antioxidant, and metabolic properties hold strong potential for chronic disease prevention and may offer comprehensive benefits in managing autoimmune disorders like pSS [13]. Adherence to the MD was associated with better lifestyle habits (e.g., regular meals, family-based eating). It contributed to psychological well-being, possibly due to its structure, cultural ties, and nutrient quality [14].

Evidence from numerous randomized clinical trials has shown that greater adherence to the traditional MD has beneficial effects in secondary prevention of CVD, type 2 diabetes, atrial fibrillation, and breast cancer. While the precise mechanisms behind these positive outcomes remain unclear, growing research suggests that five key adaptations contribute to its health benefits: Characteristics that reduce cholesterol, protection against oxidative stress, inflammation, and platelet aggregation, hormonal regulation and growth factors linked to cancer development, inhibition of nutrient-sensing pathways through specific amino acid restriction, and production of health-promoting metabolites by the gut microbiota [15]. According to the World Health Organization (WHO), nutrition is a major factor in reducing non-communicable diseases. Chronic respiratory disorders, diabetes, cancer, and CVD are all significantly influenced by poor diet and other bad lifestyle choices.

Epidemiological research, including the Seven Countries Study from the 1960s, highlighted growing interest in the MD as a healthy way of eating. These studies found that people who closely followed the traditional MD had lower death rates and reduced risk of cardiovascular disease. Prospective studies have shown that adherence to the MD reduces overall mortality— particularly from cardiovascular causes—thereby promoting increased longevity. In Addition, it has been connected to a decreased incidence of age-related cognitive decline and a reduced incidence of neurodegenerative diseases, especially Alzheimer's disease [16]. Sjögren's syndrome (SS) is a long-term autoimmune condition marked by

lymphocytic inflammation of exocrine glands, especially the salivary and lacrimal glands, which causes dryness of the eyes and mouth [17,18]. It affects approximately 0.1–1% of the population, with a strong female predominance of up to 90% [18]. Patients may also develop systemic indications as fatigue, skeletal discomfort, cognitive dysfunction, and gastrointestinal problems in addition to the classic symptoms of xerophthalmia and xerostomia [19]. Because of its varied presentation, diagnosis is frequently difficult and includes salivary gland biopsies, serological tests, and clinical examination [20]. Individuals with SS are more susceptible to oral infections and dental cavities, particularly if they have decreased salivary flow [21]. The proposed mechanisms underlying the MD's benefits include modulation of immune responses, reduced systemic inflammation, and favorable changes in gut microbiota composition and function [22]. According to estimates, persons with SS have a 7–19 times higher risk of developing lymphoma than the expected incidence in a generally healthy population [23]. In SS, ocular dryness (OD) is a key symptom resulting from tear film instability, elevated tear production and ocular surface inflammation [24].

The MD is rich in bioactive compounds—such as polyphenols, omega-3 fatty acids, and antioxidants—that can modulate inflammatory pathways and immune responses, which are often dysregulated in autoimmune diseases like SS [25]. Furthermore, oxidative stress—a central mechanism in the pathogenesis of SS—is reduced by the MD's high content of antioxidants, particularly vitamins C and E, which help to protect exocrine tissues from damage and support overall immune regulation [26].

A comprehensive meta-analysis by Schwing Hackl et al. (2015) highlighted those individuals with higher adherence to the MD experienced up to a 25% reduction in the risk of developing type 2 diabetes. This finding confirms the diet's anti-inflammatory and metabolic benefits and highlights the importance of eating whole foods in a consistent dietary pattern to prevent chronic disease. Such Systemic effects have promising significance for the treatment of auto immune diseases like pSS [27]. With a focus on clinical results and immune-related alterations, this systematic review attempts to evaluate the available data to assess the MD's therapeutic potential in SS. The present review aims to systematically assess existing evidence on how adherence to the Mediterranean diet influences clinical manifestations, ocular outcomes, and immune-related biomarkers in individuals with primary Sjögren's syndrome.

**Materials And Methods:**

This review followed a systematic methodology, including database searches, article screening, data extraction, and evidence synthesis.

**Search Strategy**

A comprehensive literature search was carried out utilizing databases such as Web of Science, PubMed, and Scopus until MARCH 2025. The search combined terms such as:

"Sjögren's syndrome" OR "primary Sjögren's syndrome"
AND "Mediterranean diet"

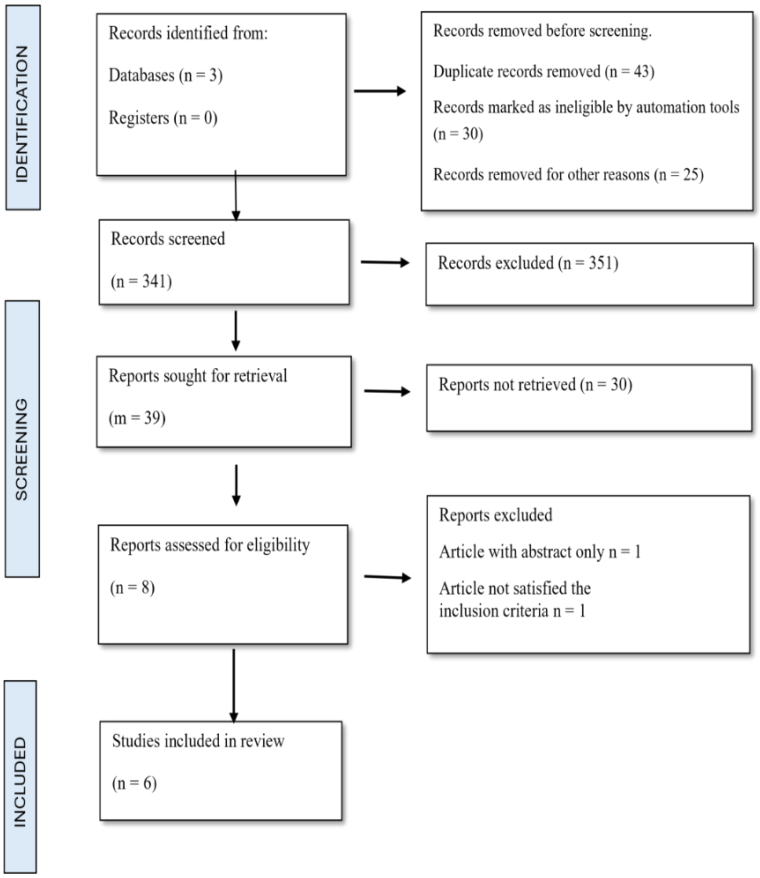
**Inclusion Criteria**

- Population included are the Individuals diagnosed with primary pSS and Dry Eye.
- Syndrome (DES) using established criteria (e.g., AECG 2002 or ACR/EULAR 2016).
- Assessment of MD adherence or intake of Mediterranean dietary components (e.g., olive oil, fish, PUFA, Moderate consumption of Alcohol).
- The Outcomes Reported on clinical outcomes (ESSDAI, ESSPRI, focus score, DEQ5 Score, TBUT, OSDI) and/or immunological markers (e.g., IgG, C3, anti-Ro).
- Observational studies (cross-sectional, cohort, case-control, Randomized controlled Trial).
- The study specifically explored the impact of MD on pSS, full-length articles compiled in a single language (English).

**Exclusion Criteria**

- Studies consisting of full-length articles curated in other languages other than English.
- Studies with insufficient data, inaccessible full texts, or unclear outcome reporting.

**FIGURE 1: PRISMA 2020 flow diagram for newly conducted systematic reviews that solely involved database and registration searches[28]**




**RESULTS:**

This research resulted in 160 articles, from which 15 were full-text articles having accessibility and were assessed for eligibility. Ultimately, 6 articles were chosen for inclusion in this systematic review.

Table 1 Shows the Characteristics of the study included in the systematic review with Author name, samples recruited, sample characteristics, duration of the study and diet assessment tool.

Table 2 Shows the Clinical outcomes, immunological outcomes and major findings of the study

Table 3 shows the risk of bias in all the included studies based on the Office of Health Assessment and Translation assessment tool.

**Table 1: Features Of the Study Intervention**

| S. NO | AUTHOR (COUNTRY) | YEAR | STUDY DESIGN | SAMPLE SIZE | DURATION /FOLLOW UPS | DIET ASSESSMENT TOOL |
|---|---|---|---|---|---|---|

| | | | | | | |
|---|---|---|---|---|---|---|
| 1 | Carubbi et al. ITALY [29] | 2021 | Cross sectional | 93 PSS patients | 12 MONTHS (Dietary adherence) | PREDIMED (Prevention with Mediterranean diet), MEDLIFE (Medicine Delivery) |
| 2 | Machowicz et al. UK [30] | 2020 | Case control | 82 PSS, 51 controls | 4 YEARS (2014-2018) | MD Score (MDS) |
| 3 | Izzo et al. Italy [31] | 2021 | Cross-sectional | 40 female PSS 2020 patients | 5 YEARS (2015-) | MD Score (0-55) |
| 4 | Galor et al. USA [32] | 2014 | Cross-sectional | 247 older male's veterans (Mean Age:69 Years) | 12 MONTHS (Dietary recall via FFQ) No follow ups conducted | MD Score (MD) Serum 25-hydroxy vitamin D levels |
| 5 | Ignacio Molina Leyva et al. [33] | 2020 | Randomized controlled, multicenter field trial within the PREDIMED PLUS framework | 34 subjects (67 eyes), aged 55–75 with metabolic syndrome | 6 MONTHS | Food Frequency Questionnaire (FFQ)<br><br>PREDIMED 14-item Questionnaire<br><br>Biomarker Assessment |
| 6 | Chaaya et al.[34] | 2025 | Cross-sectional observational Study | 114 SS patients | Sept 2018 – Nov 2023 (5 years) | MD Adherence Score |

**TABLE 2: Features of the finding from the research that were part of the systematic review.**

| S. NO | AUTHOR (COUNTRY) | CLINICAL OUTCOMES | IMMUNOLOGICAL OUTCOMES | MAJOR FINDINGS |
|---|---|---|---|---|

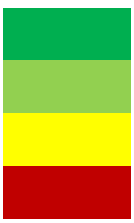
| | | | | |
|---|---|---|---|---|
| 1 | Carubbi et al. ITALY (2021) [29] | Higher adherence correlated with lower ESSDAI and ClinESSDAI scores. - Lower prevalence of hypertension with higher fish intake. | No strong direct correlation between MD adherence and autoantibody profiles (anti-Ro/La). - Suggestive reduction in systemic inflammation with higher adherence, possibly due to PUFA-rich foods (fish, olive oil). | Higher MDS associated with lower likelihood of pSS (OR = 0.81; p = 0.038). Fish intake showed strong protective effect (OR = 0.44; p = 0.011). No significant link with salivary function. |
| 2 | Machowicz et al. UK (2020) [30] | A higher Mediterranean Diet Score (MDS) was linked to a reduced risk of developing pSS, with each unit increase in MDS lowering the odds (adjusted OR = 0.81; p = 0.038). Among individual dietary components, fish intake showed the strongest protective effect (OR = 0.44; p = 0.011). | pSS patients had elevated IgG, IgA, and autoantibodies (anti-Ro/SSA, antiLa/SSB, RF). Fish intake was inversely linked to IgG (p = 0.024), but no overall association between MDS and immunoglobulin levels | Each unit increase in MDS reduced odds of pSS (adjusted OR = 0.81; p = 0.038). Strongest effect from fish intake. No link between MDS and symptom severity. |

| | | | | |
|---|---|---|---|---|
| 3 | Izzo et al. Italy (2021) [31] | MD adherence showed no association with ESSDAI (p = 0.85) or sarcopenia (p = 0.610). Patients with more dryness had lower PUFA intake (p = 0.057) | Greater adherence to the MD was significantly associated with lower serum C3 levels (p = 0.004, r = –0.08), suggesting a possible anti-inflammatory effect. However, there was no obvious connection between MD score and systemic disease activity (ESSDAI) | Patients with higher lymphocytic infiltration in salivary glands (focus score) showed lower MD adherence (p = 0.058), suggesting a possible anti-inflammatory effect. Lower PUFA intake was also linked to increased dryness symptoms |
| 4 | Galor et al. (2014) USA [32] | "Higher adherence to the MD was unexpectedly associated with increased risk and severity of Dry Eye Syndrome (OR = 1.25; p = 0.007), particularly linked to meibomian gland dysfunction, reduced TBUT, and corneal staining. However, Schirmer's test scores improved (p = 0.02), with no significant link to subjective symptoms (DEQ5) | The study did not assess direct immunological markers, such as cytokine levels or immune cell profiles. Instead, it focuses on clinical parameters of Dry Eye Syndrome (DES). | Adherence to the MD was associated with a higher risk and greater severity of Dry Eye Syndrome (DES), primarily due to impaired meibomian gland function and corneal changes, rather than patient-reported symptoms |

| | | | | |
|---|---|---|---|---|
| 5 | Ignacio Molina Leyva et al. (2020) [33] | Significant reductions in DESS (−0.35; p = 0.02) and OSDI (−1.75; p = 0.03) scores. Objective improvements included increased TBUT (+0.67 s), Schirmer's test (+0.51 mm), and reduced Oxford staining (−0.10; all p = 0.01), with better results in the intensive group. | Though no direct immunological markers were assessed, findings suggest a systemic anti-inflammatory effect via higher PUFA/omega-3 intake and reduced BMI | The MD, especially when combined with lifestyle changes (e.g., exercise, calorie control), improved both symptoms and clinical signs in individuals with metabolic syndrome. It enhanced tear film stability, reduced ocular surface damage, and increased tear secretion—supporting its role as a non-pharmacological approach |
| 6 | Chaaya et al (2025) [34] | The Ocular Surface Disease Index (OSDI) ranged from 0 to 100, with a median score of 23, indicating moderate ocular discomfort. Subjective dryness was reported by 80.7% of participants | "Diagnosis of SS was based on either a Chisholm and Mason score ≥3 from salivary gland biopsy or the presence of anti-SSA/SSB antibodies. These criteria were used for patient inclusion and not assessed in relation to diet adherence | A significant inverse correlation was found between MD adherence and ocular dryness severity ($\rho = -0.73$, $p < 0.01$). Participants with high adherence (MEDAS ≥10) had notably lower OSDI scores compared to those with low to moderate adherence (mean score: 33). Polyunsaturated fat–rich foods like olive oil, nuts, and seeds were especially associated with reduced symptoms. This association held across all diagnostic subgroups and treatment statuses |

**TABLE 3: QUALITY ASSESSMENT OF ALL THE INCLUDED STUDIES [35,36]**

| Author (Year) | Selection | Comparability | Outcome/Exposure | Randomization | Blinding | Incomplete Data | Selective Reporting | Overall Risk |
|---|---|---|---|---|---|---|---|---|
| Carubbi et al. (2021) | | | | — | | | | |
| Machowicz et al. (2020) | | | | — | | | | |
| Izzo et al. (2021) | | | | — | | | | |
| Galor et al. (2014) | | | | — | | | | |
| Molina-Leyva et al. (2020) | | | | | | | | |
| Chaaya et al. (2025) | | | | — | | | | |



Very low risk of bias

Low risk of bias

High risk of bias

Very high risk of bias

The risk of bias in the included studies was evaluated using a standardized tool based on established systematic review guidelines. Most studies were found to have a low to moderate risk of bias, as shown in Table 3[35,36].

**Discussion:**

This systematic review examined whether the MD could help manage clinical symptoms and immune markers in people with pSS. In most of the included studies, higher adherence to the diet was linked to improvements in eye-related symptoms, lower levels of inflammation, and better systemic disease scores. However, the strength and consistency of these links varied depending on study design and population. Overall, the findings suggest that dietary changes might support the management of autoimmune diseases, though more research is needed to draw firm conclusions. The following discussion highlights the major findings and limitations of the reviewed literature.

**Carubbi et al.** [29] conducted a cross-sectional study involving 91 Italian pSS patients using validated adherence tools (PREDIMED and MEDLIFE). Their findings indicated that higher adherence to the MD was significantly associated with lower systemic disease activity as measured by ESSDAI and ClinESSDAI, though not with subjective symptom severity (ESSPRI). Fish intake was negatively correlated with activity indices and hypertension, indicating a dietary effect that is both anti-inflammatory and cardioprotective.

Future interventional research are required to show clinical efficiency, and the cross-sectional methodology restricts causation despite the positive findings. Despite the positive correlations, the cross-sectional design limits causality, and future interventional studies are needed to establish clinical efficacy. [28]

In a complementary case-control study, **Machowicz et al.** [30] evaluated the dietary habits of 133 suspected pSS patients (82 diagnosed with pSS) prior to disease onset using a semiquantitative MD Score (MDS). A higher MDS was associated with significantly reduced odds of having pSS, with each one-point increase correlating with a 19% lower likelihood of disease. Among individual dietary components, fish and vegetable intake demonstrated the strongest inverse associations. Interestingly, the study also found higher vitamin A (retinol equivalents), vitamin C, and galactose intakes to be protective. This Design limits the support and idea that MD may reduce inflammation and immunological function to prevent disease, but memory bias may be introduced by the retrospective nature of dietary assessment.

**Izzo et al.** [31] in a smaller Italian study, focused on 40 women with isolated SS and examined both nutritional state and MD adherence using a 55-point scoring system. Although not statistically significant, higher MD scores showed a trend toward reduced lymphocytic infiltration in salivary glands (focus score) and lower serum C3 levels, suggesting immunomodulatory Potential. Interestingly, these patients consumed a diet high in fats— possibly to

counteract oral dryness—which skewed macronutrient balance. PUFA intake appeared lower in patients with greater subjective dryness, indicating a possible link between lipid quality and symptom expression. The study highlights the need for tailored nutritional counseling and draws attention to the intricacy of food behavior in SS patients. The small, all-female sample restricts generalizability and statistical power, and dietary behaviors associated with xerostomia might have affected nutritional intake.

**Galor et al.** [32] conducted a cross-sectional analysis among 247 older male veterans to explore these associations. This cross-sectional study examined the association between adherence to MD, serum vitamin D levels, and omega-3 intake with dry eye syndrome (DES) in older male veterans. Contrary to expectations, the study found that higher adherence to the MD was associated with an increased risk and severity of DES, particularly affecting meibomian gland function and corneal staining. One of the findings was that moderate alcohol consumption—typically considered a component of the MD— was significantly associated with worsened DES outcomes. This suggests that while the MD may reduce systemic inflammation, it may not confer ocular surface benefits, or may even exacerbate certain DES features. The study's cross-sectional methodology restricts drawing conclusions about causality, its assessment of solely clinical outcomes without immunological markers, and its limitation to older male veterans limit generalizability.

**Molina-Leyva et al.** [33] evaluated the effect of an MD on dry eye symptoms in 34 individuals with metabolic syndrome in a randomized trial located inside the PREDIMED-PLUS project. They discovered that both conventional and intensive dietary interventions improved dry eye metrics using meal frequency questionnaires and ophthalmologic evaluations, with the intensive group benefiting more. Significant advancements were made in ocular surface staining, Schirmer's test, and TBUT. These findings support the anti-inflammatory Potential of the MD in ocular health, although the small sample size and lack of explicit diet adherence scoring tools (e.g., PREDIMED or MEDLIFE index) limit generalizability.

**Chaaya et al.** (2025) [34] investigated the possible association between adherence to the MD and the degree of ocular dryness (OD) in a cross-sectional research with 114 people who had been diagnosed with SS. The study found a strong inverse relationship between MD adherence and OD symptoms using validated instruments, the MD Adherence Screener (MEDAS) to evaluate dietary habits and the Ocular Surface Disease Index (OSDI) to measure symptom severity. It is noteworthy that those who closely followed the MD had milder ocular problems, since higher MEDAS scores were reliably linked to lower OSDI levels ($\rho = -0.73$, $p < 0.01$).

Among the several elements of the diet, those high in polyunsaturated fatty acids seemed to be more important in promoting ocular surface health. Patients with strong adherence to the MD (MEDAS ≥10) demonstrated significantly reduced symptom burden compared to those with lower adherence.

These results demonstrate the MD's potential as a nonpharmacological, supportive treatment for ocular symptoms of autoimmune diseases such as SS, providing a viable path toward enhancing quality of life by comprehensive lifestyle modifications. The cross-sectional design limits causal conclusions, with self-reported data prone to bias and no longitudinal or biomarker evaluation.

**Conclusion**:

This systematic review indicates that the MD may be associated with improvements in both clinical symptoms and immunological markers among patients with pSS. Given its content of anti-inflammatory and antioxidant nutrients—such as polyunsaturated fatty acids and vitamins—the MD shows Potential as a supportive, non-pharmacological approach. However, current evidence remains limited, and well-designed randomized controlled trials are needed to clarify its effectiveness and define its role in clinical practice.

**Financial support and sponsorship**: Nil.

**Conflicts of interest**: There are no conflicts of interest.

**References**:

1. Kiani, A. K., Medori, M. C., Bonetti, G., Aquilanti, B., Velluti, V., Matera, G., Iaconelli, A., Stuppia, L., Connelly, S.T., Herbst, K.L., &Bertelli, M. (2022). Modern Vision of the Mediterranean Diet. *Journal of Preventive Medicine and Hygiene*, *63*, E36–E43.
2. Khavandegar, A., Heidarzadeh, A., Angoorani, P., Hasani-Ranjbar, S., Ejtahed, H.-S., Larijani, B., & Qorbani, M. (2024). Adherence to the Mediterranean diet can beneficially affect the gut microbiota composition: a systematic review: BMC Medical Genomics. *BMC Medical Genomics*, *17*(1), 1–25.
3. M.T, I.L. (2019). Culture and Mediterranean Diet. *International Journal of Nutrition*,*3*(2),13–21.
4. Vezza T, Rodríguez-Nogales A, Algieri F, Utrilla MP, Rodríguez-Cabezas ME, Galvez J. (2016) Polyphenols: Potential mechanisms of action on inflammation. Oxid Med Cell Longev.;2016:5274128
5. De Filippis, F., Pellegrini, N., Vannini, L., Jeffery, I. B et.al (2015). High-level adherence to a Mediterranean diet beneficially impacts the gut microbiota and

associated metabolome. *Gut*, *65*(11), 1812–1821.

6. Pisoschi, A. M., & Pop, A. (2015). The role of antioxidants in the chemistry of oxidative stress: A review. *European Journal of Medicinal Chemistry*, *97*, 55–74.

7. Calder, P. C. (2017). Omega-3 fatty acids and inflammatory processes: from molecules to man. *Biochemical Society Transactions*, *45*(5), 1105–1115.

8. Prietl, B., Treiber, G., Pieber, T., & Amrein, K. (2013). Vitamin D and Immune Function. *Nutrients*, *5*(7), 2502–2521.

9. Lassale, C., Batty, G. D., & Akbaraly, T. (2019). Reply to Veronese and Smith: Healthy dietary indices and risk of depressive outcomes: a systematic review and meta-analysis of observational studies. *Molecular Psychiatry*.

10. Milagro, F. I., Mansego, M. L., De Miguel, C., & Martínez, J. A. (2013). Dietary factors, epigenetic modifications and obesity outcomes: Progresses and perspectives. *Molecular Aspects of Medicine*, *34*(4), 782–812. https://doi.org/10.1016/j.mam.2012.06.010

11. Ros, E. (2010). Health Benefits of Nut Consumption. *Nutrients*, *2*(7), 652–682.

12. COVAS, M. (2007). Olive oil and the cardiovascular system. *Pharmacological Research*, *55*(3), 175–186.

13. Davis, C., Bryan, J., Hodgson, J., & Murphy, K. (2015). Definition of the Mediterranean Diet; A Literature Review. *Nutrients*, *7*(11), 9139–9153. https://doi.org/10.3390/nu7115459

14. Gualtieri, P., Marchetti, M., Frank, G., Cianci, R., Bigioni, G., Colica, C., Soldati, L., Moia, A., De Lorenzo, A., & Di Renzo, L. (2022). Exploring the Sustainable Benefits of Adherence to the Mediterranean Diet during the COVID-19 Pandemic in Italy. *Nutrients*, *15*(1), 110.

15. Tosti, V., Bertozzi, B., & Fontana, L. (2018). Health Benefits of the Mediterranean Diet: Metabolic and Molecular Mechanisms. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, *73*(3), 318–326.

16. Guasch-Ferré, M., & Willett, W. C. (2021). The Mediterranean diet and health: a comprehensive overview. *Journal of Internal Medicine*, *290*(3), 549–566.

17. Negrini, S., Emmi, G., Greco, M., Borro, M., Sardanelli, F., Murdaca, G., Indiveri, F., & Puppo, F. (2022). Sjögren's

syndrome: a systemic autoimmune disease. *Clinical and Experimental Medicine*, *22*(1), 9–25.

18. Denko, C. W. (1965). Antibodies in the sicca syndrome (Sjogren's syndrome). *Arthritis and Rheumatism*, *8*(5), 970–975.

19. Brito-Zerón, P., Baldini, C., Bootsma, H., Bowman, S. J., Jonsson, R., Mariette, X., Sivils, K., Theander, E., Tzioufas, A., & Ramos-Casals, M. (2016). Sjögren syndrome. *Nature Reviews Disease Primers*, *2*(1), 1–20. https://doi.org/10.1038/nrdp.2016.47

20. Wang, B., Chen, S., Zheng, Q., Li, Y., Zhang, X., Xuan, J., Liu, Y., & Shi, G. (2021). Early diagnosis and treatment for Sjögren's syndrome: current challenges, redefined disease stages and future prospects. *Journal of Autoimmunity*, *117*, 102590.

21. Berman, N., Vivino, F., Baker, J., Dunham, J., & Pinto, A. (2019). Risk factors for caries development in primary Sjogren syndrome. *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*, *128*(2), 117–122.

22. Barber, T. M., Kabisch, S., Pfeiffer, A. F. H., & Weickert, M. O. (2023). The Effects of the Mediterranean Diet on Health and Gut Microbiota. *Nutrients*, *15*(9), 2150.

23. Baik, J., Hye Jin Baek, Ryu, K.-H., An, H.-J., Song, S., Lee, H.-J., & Kang, Y.-C. (2021). MALT Lymphoma of the Tongue in a Patient with Sjögren's Syndrome: A Case Report and Literature Review. *Diagnostics*, *11*(9), 1715–1715.

24. Vehof, J., Utheim, T. P., Bootsma, H., & Hammond, C. J. (2020). Advances, limitations and future perspectives in the diagnosis and management of dry eye in Sjögren's syndrome. *Clinical and experimental rheumatology*, *38 Suppl 126*(4), 301–309.

25. Castrejón-Morales CY, Granados-Portillo O, Cruz-Bautista I, Ruiz-Quintero N, Manjarrez I, Lima G, et al. (2020) Omega-3 and omega-6 fatty acids in primary Sjögren's syndrome: clinical meaning and association with inflammation. *Clin Exp Rheumatol*. 2020;38 Suppl 126(4):34–9.

26. Casas, R., Sacanella, E., & Estruch, R. (2014). The Immune Protective Effect of the Mediterranean Diet against Chronic Low-grade Inflammatory Diseases. *Endocrine, Metabolic & Immune Disorders-Drug Targets*, *14*(4), 245–254.

27. Schwingshackl, L., Missbach, B., König, J., & Hoffmann, G. (2014). Adherence to a Mediterranean Diet and

Risk of diabetes: a Systematic Review and meta-analysis. *Public Health Nutrition, 18*(07), 1292–1299.

28. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ 2021;372:n71.

29. Carubbi, F., Alunno, A., Mai, F., Mercuri, A., Centorame, D., Cipollone, J., Mariani, F. M., Rossi, M., Bartoloni, E., Grassi, D., & Ferri, C. (2021). Adherence to the Mediterranean diet and the impact on clinical features in primary Sjögren's syndrome. *Clinical and Experimental Rheumatology*, *39*(6), 190–196.

30. Machowicz, A., Hall, I., de Pablo, P., Rauz, S., Richards, A., Higham, J., Poveda-Gallego, A., Imamura, F., Bowman, S. J., Barone, F., & Fisher, B. A. (2020). Mediterranean diet and risk of Sjögren's syndrome. *Clinical and experimental rheumatology, 38 Suppl 126*(4), 216–221.

31. Izzo, R., Colafrancesco, S., Pinto, A., Gattamelata, A., Giardina, F., Freitas Cláudia, Donini, L. M., & Priori, R. (2021). AB0317 adherence to mediterranean diet and nutritional state in Italian women with isolated Sjogren's syndrome. *Annals of the Rheumatic Diseases*, *80*(1), 1183.2-1184.

32. Galor, A., Gardener, H., Pouyeh, B., Feuer, W., & Florez, H. (2014). Effect of a Mediterranean Dietary Pattern and Vitamin D Levels on Dry Eye Syndrome. *Cornea*, *33*(5), 437–441.

33. Molina-Leyva, I., Molina-Leyva, A., Riquelme-Gallego, B., Cano-Ibáñez, N., García-Molina, L., & Bueno-Cavanillas, A. (2020). Effectiveness of Mediterranean Diet Implementation in Dry Eye Parameters: A Study of PREDIMED-PLUS Trial. *Nutrients*, *12*(5), 1289.

34. Chaaya, C., Raad, E., Kahale, F., Chelala, E., Ziade, N., & Georges Maalouly. (2025). Adherence to Mediterranean Diet and Ocular Dryness Severity in Sjögren's Syndrome: A Cross-Sectional Study. *Medical Sciences*, *13*(2), 64–64.

35. Puljak L. Adequate and complete reporting of Cochrane risk of bias tool. Pain 2019;160:984.

36. Handbook for Conducting a Literature-Based Health Assessment Using OHAT Approach for Systematic Review and Evidence Integration (2nd d.) (2019). National Institute of Environmental Health Sciences. (Original work published 2015).