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The Impact of the Mediterranean Diet on the Course of Rheumatoid Arthritis (RA)

Aim: To determine the role of diet therapy as a non-pharmacological adjuvant treatment.

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Abstract

Objective: To determine the role of the Mediterranean diet as a non-pharmacological adjuvant treatment in rheumatoid arthritis (RA).

Methods: A review of PubMed-indexed literature (2021–2026) was conducted, focusing on the diet's impact on disease activity (DAS28), inflammatory markers, oxidative stress, and cardiovascular risk.

Results: High adherence to the Mediterranean diet correlates with reduced clinical RA activity (lower DAS28) and improved metabolic parameters. This is driven by the intake of bioactive compounds—omega-3 fatty acids, dietary fiber, and polyphenols—which modulate inflammatory pathways and gut microbiota. The diet also provides essential cardioprotection, mitigating the high vascular risk in RA patients. However, the impact of diet on objective biochemical markers (CRP, ESR, anti-CCP) remains ambiguous. Notably, combining a personalized diet with targeted exercise therapy synergistically enhances quality of life and reduces pain.

Conclusions: The Mediterranean diet is an effective adjuvant treatment in RA, reducing clinical disease activity and improving cardiovascular prognosis. While its effect on specific immunological markers requires further study, the complexity of RA mandates a holistic, interdisciplinary approach to patient care.

Keywords: rheumatoid arthritis, Mediterranean diet, diet therapy, adjuvant treatment, inflammation, oxidative stress, DAS28 score, cardioprotection.

Introduction

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disease whose pathogenesis is centrally driven by persistent inflammation and intensified oxidative stress. The disruption of the pro-oxidant/antioxidant balance significantly accelerates the destruction of joint structures. Studies demonstrate that RA patients are characterized by a decreased serum total antioxidant status (TAS) alongside an elevated total oxidant status (TOS) (Bekar et al., 2025).

Although standard pharmacotherapy remains the cornerstone of clinical management, the growing awareness of the disease's complexity necessitates the search for effective non-pharmacological adjuvant therapies.

One of the most important modifiable environmental factors directly influencing the course of rheumatic diseases is nutrition. Appropriately balanced diet therapy, with particular emphasis on the Mediterranean diet, shows high potential in mitigating RA activity. This model provides the body with numerous bioactive compounds—including omega-3 polyunsaturated fatty acids, dietary fiber, and polyphenols—which actively modulate inflammatory pathways and promote the restoration of gut microbiota eubiosis (Kupczyk et al., 2025; Nikiphorou & Philippou, 2023). The data accumulated to date from numerous clinical and observational studies confirm that a high degree of adherence to this dietary pattern significantly correlates with a reduction in the disease activity score (DAS28) and the optimization of patients' metabolic and anthropometric parameters (Alawadhi et al., 2023; Charneca et al., 2023; Papandreou et al., 2023).

However, it must be noted that the impact of the Mediterranean diet on objective biochemical markers of inflammation (such as C-reactive protein [CRP], erythrocyte sedimentation rate [ESR], rheumatoid factor [RF], or anti-cyclic citrullinated peptide antibodies [anti-CCP]) is not always unequivocal. This suggests that while optimizing nutritional quality yields measurable clinical benefits, its independent impact on the modulation of systemic inflammation may depend on additional population factors and requires holistic support (Mostafaei et al., 2024).

The implementation of the Mediterranean diet in RA patients is also highly justified in the context of its potent cardioprotective effects. Chronic inflammation drastically amplifies the cardiovascular burden, exposing the RA patient population to a significantly higher risk of cardiovascular disease (CVD) events. In this regard, the adoption of an anti-inflammatory dietary pattern represents a crucial element in the prevention of vascular complications, improving the overall prognosis of patients (Chen et al., 2025; Zhan et al., 2023). Moreover, the highest therapeutic efficacy—manifested by an improved quality of life (RAQoL), better physical functioning, and pain reduction—is observed when personalized diet therapy is synergistically combined with regular, targeted exercise therapy (Abdel-Aal et al., 2025; Raad et al., 2024).

The complexity of the described mechanisms and the constantly growing body of scientific evidence highlight the urgent need for close interdisciplinary collaboration between rheumatologists and clinical dietitians. Given these premises, the primary aim of this study is to determine and systematize the role of diet therapy—based on the principles of the Mediterranean diet—as an effective, non-pharmacological adjuvant treatment in the course of rheumatoid arthritis.

Methods

This review was conducted to analyze the role of diet therapy—specifically the Mediterranean diet—on the course of RA. A comprehensive literature search was performed using the PubMed database to identify relevant studies published between 2021 and 2026, with a particular focus on papers published after 2023. The keywords included: "Mediterranean diet", "rheumatoid arthritis", "disease activity", "DAS28 score", "inflammation", "oxidative stress", and "gut microbiota".

To ensure the selection of highly relevant and methodologically sound literature, rigorous inclusion and exclusion criteria were established. The inclusion criteria comprised: (1) peer-reviewed studies published between 2021 and 2026; (2) research involving adult patients (>18 years of age) with a confirmed diagnosis of rheumatoid arthritis (RA); (3) studies explicitly evaluating the implementation of or adherence to the Mediterranean diet as a dietary intervention or exposure; and (4) articles reporting measurable outcomes related to clinical disease activity (e.g., DAS28 score), biochemical inflammatory markers (e.g., CRP, ESR, anti-CCP), oxidative stress, or cardiovascular risk. Eligible study designs encompassed randomized controlled trials (RCTs), observational studies, and cross-sectional analyses. Conversely, the exclusion criteria were defined as follows: (1) animal model or *in vitro* studies; (2) research focusing on pediatric populations, such as juvenile idiopathic arthritis (JIA); (3) studies evaluating isolated nutritional supplements or other dietary patterns without a direct focus on the Mediterranean diet; (4) case reports, editorials, letters to the editor, conference abstracts, and non-peer-reviewed preprints; and (5) articles not available in full-text or published in languages other than English.

Data extraction focused on participant characteristics and reported parameters (e.g., DAS28, CRP, ESR, anti-CCP, RF, body weight, glucose levels, and pain intensity on the VAS scale). The analysis involved the synthesis of quantitative results and qualitative conclusions, identifying recurring themes and gaps in the existing literature.

The applied methodological approach ensured a reliable assessment of the Mediterranean diet's role in modifying the course of the disease in conjunction with pharmacotherapy and a holistic patient approach. This enabled the formulation of evidence-based recommendations and the identification of areas requiring further research.

Author & Year	Study Design	Population	Intervention / Exposure	Main Findings
Abdel-Aal et al. (2025)	Randomized Controlled Trial (RCT)	Females with RA	6-month Mediterranean diet + aerobic and strengthening exercise program.	Significant reduction in CRP levels and pain (VAS); improved muscle performance and optimized body weight compared to exercise alone.
Bekar et al. (2025)	Case-control study	Adult women with RA	Evaluation of Mediterranean diet adherence and oxidative stress markers.	RA patients exhibited lower total antioxidant status (TAS) and higher total oxidant status (TOS). Diet directly impacts the oxidative balance.
Mostafaei et al. (2024)	Cross-sectional study	184 Iranian female RA patients	Assessment of Mediterranean diet pattern and disease activity.	Higher adherence improved overall nutritional profile but showed no statistically significant correlation with DAS28, CRP, ESR, RF, or anti-CCP in adjusted models.
Raad et al. (2024)	Randomized Controlled Trial (RCT)	Adults with RA (MEDRA trial)	Telehealth-delivered	Measurable improvements in physical functioning

Author & Year	Study Design	Population	Intervention / Exposure	Main Findings
			Mediterranean diet intervention.	(HAQ-DI) and disease-specific quality of life (RAQoL); increased daily physical activity.
Alawadhi et al. (2023)	Cross-sectional study	754 RA patients (KRRD cohort)	Evaluation of adherence to the Mediterranean diet and DAS28 score.	Inverse correlation observed: higher adherence to the diet significantly correlated with lower disease activity (reduced DAS28).
Charneka et al. (2023)	Observational study	RA patients	Evaluation of the Mediterranean diet vs. Dietary Inflammatory Index (DII).	High adherence to the Mediterranean diet reduced the probability of high RA activity (DAS28) by 70%, independent of age, BMI, or medication.
Papandreou et al. (2023)	Randomized Controlled Trial (RCT)	Women with RA (MADEIRA trial)	12-week isocaloric Mediterranean diet + physical activity nudges vs. usual care.	Significant reduction in DAS28; optimization of anthropometric and metabolic parameters (weight loss, lower glucose,

Author & Year	Study Design	Population	Intervention / Exposure	Main Findings
				increased vitamin D).
Zhan et al. (2023)	Cross-sectional analysis	Middle-aged and elderly (NHANES data)	Assessment of RA, Mediterranean diet adherence, and cardiovascular disease (CVD) risk.	Strong synergistic interaction (Synergy Index = 8.21) between RA and low diet adherence, drastically increasing the cardiovascular burden.

Results

Pathomechanism and the Role of Nutritional Interventions in RA

The scientific evidence gathered to date points to the significant role of nutritional interventions as an effective adjuvant treatment to standard pharmacotherapy for rheumatoid arthritis (RA). Diet constitutes a modifiable environmental factor that directly mitigates chronic inflammation and oxidative stress, both of which play a pivotal role in the pathogenesis of rheumatic diseases (Kupczyk et al., 2025). Disruptions in the pro-oxidant/antioxidant balance accelerate the destruction of joint structures; RA patients exhibit a lowered serum total antioxidant status (TAS) and an elevated total oxidant status (TOS) (Bekar et al., 2025). An appropriately balanced dietary therapy, highlighting the Mediterranean diet, demonstrates the capacity to lower disease activity through the provision of bioactive compounds (such as omega-3 polyunsaturated fatty acids, dietary fiber, and polyphenols), the modulation of inflammatory pathways, and the restoration of gut microbiota eubiosis (Kupczyk et al., 2025; Nikiphorou & Philippou, 2023). As researchers note, the volume of data confirming the efficacy of this dietary model is continually growing, creating an urgent need for closer collaboration between rheumatologists and clinical dietitians.

The Impact of the Mediterranean Diet on Clinical Disease Activity Indices

The efficacy of the Mediterranean diet in lowering RA activity is confirmed by numerous clinical and observational studies. A cross-sectional study involving 754 patients demonstrated an inverse correlation between the degree of adherence to this dietary model and the disease activity score, DAS28 (Alawadhi et al., 2023). Higher consumption of foods with anti-inflammatory potential positively correlated with remission or low disease activity. Similar conclusions emerge from an analysis conducted by Charneca et al. (2023), which showed that high adherence to Mediterranean diet principles reduces the likelihood of high RA activity (DAS28) by 70%, independent of age, body mass index (BMI), or the pharmacotherapy utilized. Conversely, Papandreou et al. (2023), in the randomized MADEIRA trial, observed that a 12-week, personalized, and isocaloric Mediterranean diet not only significantly lowered the DAS28 score but also optimized the anthropometric and metabolic parameters of the female patients (e.g., reducing body weight and glucose levels while increasing serum vitamin D).

Ambiguity of Evidence Regarding Inflammatory Markers

Despite many promising reports, some literature data regarding the direct impact of the Mediterranean diet on reducing RA activity provides ambiguous evidence concerning objective biochemical markers. In an observational study by Mostafaei et al. (2024), involving 184 female patients, it was shown that higher adherence to the Mediterranean diet was associated with a significantly more favorable nutritional profile (higher intake of vegetables, fruit, and fish, and lower intake of processed meat). Nevertheless, multivariable logistic regression models did not confirm a statistically significant correlation between the diet quality index and a reduction in DAS28 values or the concentrations of serum immunological and inflammatory markers (including C-reactive protein [CRP], erythrocyte sedimentation rate [ESR], rheumatoid factor [RF], and anti-CCP antibodies) (Mostafaei et al., 2024). These results suggest that although the diet improves overall nutritional quality, its independent effect on modulating systemic inflammation may be modified by population factors and requires verification in further prospective studies.

Cardioprotective Significance of the Mediterranean Diet in RA Patients

Regardless of the ongoing debate over the direct impact of dietary interventions on the activity of the disease itself, the implementation of the Mediterranean diet is highly justified due to its strong cardioprotective effects. The RA patient population is characterized by a significantly elevated risk of cardiovascular disease (CVD) events resulting from chronic inflammation

(Chen et al., 2025). Data analyses from the NHANES cohort prove a significant synergistic interaction between the co-occurrence of RA and low adherence to the Mediterranean diet, which drastically amplifies the patients' cardiovascular burden (synergy index, SI = 8.21) (Zhan et al., 2023). Thus, the implementation of this anti-inflammatory dietary pattern represents not only support for basic therapy but, above all, a key element of the non-pharmacological prevention of vascular complications, improving the overall prognosis of the patients (Chen et al., 2025; Zhan et al., 2023).

Synergistic Effect of Diet Therapy and Exercise Therapy and Their Impact on Quality of Life

Comprehensive non-pharmacological management in RA should be based on the targeted integration of diet therapy with physical activity. A randomized controlled trial conducted by Raad et al. (2024) demonstrated that adherence to the Mediterranean diet yielded measurable benefits in improving physical functioning (assessed by the HAQ-DI questionnaire) and quality of life (measured by the RAQoL scale), and stimulated patients to increase their daily physical activity. The significance of this synergism was corroborated by Abdel-Aal et al. (2025), who proved in a 6-month intervention that combining the Mediterranean diet with aerobic and resistance training resulted in lowered CRP levels and a significant reduction in pain (on the VAS scale) compared to isolated exercise therapy. Furthermore, an optimization of body weight and an improvement in muscle endurance were observed. These results clearly indicate the necessity for a holistic patient approach, where an individualized Mediterranean diet paired with programmed physical activity forms an integral element of clinical care.

Discussion

The primary aim of this study was to systematize the knowledge regarding the role of the Mediterranean diet as a non-pharmacological adjuvant treatment in patients with rheumatoid arthritis (RA). The accumulated scientific evidence unequivocally indicates that an appropriately balanced diet therapy serves as a crucial, modifiable environmental factor capable of mitigating the course of this chronic autoimmune disease (Kupczyk et al., 2025; Nikiphorou & Philippou, 2023).

An analysis of the available literature confirms that a high degree of adherence to the Mediterranean diet significantly correlates with a reduction in clinical disease activity. Both cross-sectional studies and randomized clinical trials, such as the MADEIRA trial, demonstrate that implementing this dietary model facilitates the reduction of the DAS28 score and the

optimization of metabolic and anthropometric parameters, including patient weight loss (Alawadhi et al., 2023; Charneca et al., 2023; Papandreou et al., 2023). The clinical improvement of patients most likely stems from a high intake of bioactive compounds with documented anti-inflammatory and antioxidant potential. These primarily include omega-3 polyunsaturated fatty acids, polyphenols, and dietary fiber, which collectively modulate inflammatory pathways and support the restoration of gut microbiota eubiosis. Additionally, as demonstrated by Bekar et al. (2025), nutritional interventions can counteract the pro-oxidant/antioxidant imbalance by elevating the total antioxidant status (TAS) and lowering the total oxidant status (TOS), the intensity of which directly correlates with the destruction of joint structures in the pathogenesis of RA.

Despite evident clinical benefits reported by patients, the direct impact of the Mediterranean diet on objective biochemical and immunological markers of inflammation remains a subject of debate. As noted by Mostafaei et al. (2024), despite the observation of a significant improvement in the quality of the nutritional profile, a statistically significant reduction in the concentrations of parameters such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), rheumatoid factor (RF), or anti-CCP antibodies is not always observed. The ambiguity of these results suggests that the independent impact of diet therapy on the suppression of generalized inflammation may be a complex phenomenon, modified by an array of population factors, the stage of disease advancement, and the potential influence of concurrently utilized pharmacotherapy (Disease-Modifying Antirheumatic Drugs – DMARDs).

Irrespective of the controversies surrounding biochemical parameters, the unquestionable added value of the Mediterranean diet in RA patients is its potent cardioprotective action. Chronic inflammation drastically increases the risk of cardiovascular disease (CVD) events in this patient group. Studies on the NHANES cohort have proven a high synergy index between the co-occurrence of RA and low adherence to the described diet in the context of cardiovascular burden (Zhan et al., 2023). Therefore, implementing this dietary model should be treated not only as a joint-targeted therapy but, predominantly, as an essential component of non-pharmacological vascular complication prophylaxis that conditions the improvement of overall prognosis (Chen et al., 2025).

It is also worth emphasizing that non-pharmacological interventions exhibit the highest efficacy when implemented holistically. Interventional studies unequivocally demonstrate the

synergistic effect of combining personalized diet therapy with targeted exercise therapy (e.g., aerobic and resistance training). Such a combination not only stimulates patients towards greater daily activity but also results in a significant improvement in the quality of life (RAQoL), better physical functioning (HAQ-DI), and a noticeable reduction in pain as measured by the VAS scale (Abdel-Aal et al., 2025; Raad et al., 2024).

In summary, the complexity of the pathomechanisms of rheumatoid arthritis and the expanding base of scientific evidence underscore the urgent need for close interdisciplinary collaboration among rheumatologists, clinical dietitians, and physiotherapists. While the Mediterranean diet does not replace standard pharmacotherapy, it constitutes a highly effective complement to it, significantly improving the prognosis and quality of life of patients. Future prospective studies of high methodological quality should focus on the standardization of dietary protocols and the long-term evaluation of their impact on immunological markers in patients with varying degrees of RA activity.

Conclusions

The accumulated scientific knowledge and the conducted literature analysis allow for the formulation of the following conclusions:

- **Adjuvant Efficacy:** The Mediterranean diet represents a highly effective, non-pharmacological adjuvant treatment to standard therapy for rheumatoid arthritis (RA). A high degree of adherence to this dietary pattern significantly correlates with a reduction in clinical disease activity, expressed by the DAS28 score.
- **Multidirectional Metabolic Action:** This model, rich in bioactive compounds such as omega-3 polyunsaturated fatty acids, polyphenols, and dietary fiber, promotes the normalization of pro-oxidant/antioxidant imbalances, supports the restoration of gut microbiota eubiosis, and optimizes the anthropometric and metabolic parameters of patients.
- **Cardioprotection as a Preventive Priority:** Given the drastically elevated risk of cardiovascular events in this patient group, the implementation of the Mediterranean diet plays a critical role in the prevention of vascular complications, significantly improving overall prognosis.
- **Ambiguity of Biochemical Markers:** The independent, direct influence of diet therapy on lowering the concentrations of objective inflammatory and immunological markers (including CRP, ESR, RF, and anti-CCP antibodies) remains a complex phenomenon

and requires further investigation in prospective studies utilizing standardized protocols.

- **Synergism of Non-Pharmacological Interventions:** The highest therapeutic efficacy, manifested by an improved quality of life (RAQoL), better physical functioning, and pain reduction, is achieved through a holistic combination of a personalized anti-inflammatory diet with regular, targeted exercise therapy.
- **Necessity for Interdisciplinary Care:** The complexity of RA pathomechanisms necessitates close collaboration among rheumatologists, clinical dietitians, and physiotherapists to ensure comprehensive and optimal patient care.

Disclosure

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The authors declares no conflict of interest.

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