

INTEGRATIVE MEDICINE SECTION

Proinflammatory diet is associated with higher pain, disease severity and biochemical parameters associated with inflammation in fibromyalgia

Nursena Ersoy Söke , PhD^{1,*}, Hansa İnceöz, MD², İlker Solmaz, MD³, Hülya Yardımcı, PhD⁴

¹Institute of Health Sciences, Ankara University, Ankara 06110, Türkiye

²Ankara Etlik City Hospital, Neurology-Orthopedic Hospital, Ankara 06170, Türkiye

³Traditional and Complementary Medicine Practice Center, University of Health Sciences, Ankara 06010, Türkiye

⁴Faculty of Health Sciences, Ankara University, Ankara 06290, Türkiye

*Corresponding author: Ankara University, Diskapı Campus Şehit Ömer Halisdemir Boulevard, Ankara 06110, Turkey. Email: nersoy@ankara.edu.tr

Abstract

Objective: Fibromyalgia, which is becoming increasingly common today, affects the quality of life of those affected. The aim of this study was to investigate the relationship between diet and pain, disease severity, and biochemical parameters in fibromyalgia.

Design: Cross-sectional design using validated questionnaires.

Setting: Fibromyalgia patients with Traditional and Complementary Medicine clinics.

Subject: In total, 84 patients with fibromyalgia (FM), which was diagnosed by a rheumatologist.

Methods: The cross-sectional study was conducted with 84 fibromyalgia patients in Turkey. The Dietary Inflammatory Index (DII) was calculated by a 24-hour diet recall. Self-reported pain levels and disease severity were evaluated by the Visual Analog Scale (VAS) and a Revised Fibromyalgia Impact Questionnaire (FIQR), respectively. Anthropometric measures and biochemical parameters associated with inflammation were also evaluated.

Results: Linear regression analysis revealed that the VAS pain score [β (95% confidence interval [CI])=1.72 (0.90–2.55), $P < .001$], FIQR [β (95% CI)=5.62 (0.14–11.09), $P < .001$] and uric acid/creatinine ratio [β (95% CI)=0.21 (–0.10 to 0.52), $P < .001$] were positively associated with the DII after adjustments for body mass index (BMI), body fat, fat free mass, cholesterol, fiber, caroten, iron, magnesium, vitamin C reported by the patients with FM.

Conclusions: A pro-inflammatory diet was associated with higher pain, disease severity and uric acid/creatinine ratio in patients with FM.

Keywords: dietary inflammatory index; fibromyalgia; pain; life quality; nutrients.

Introduction

Fibromyalgia (FM) is a common condition characterized by chronic pain, sleeping problems, physical fatigue and cognitive symptoms.¹ The quality of life of FM patients is affected by all these symptoms. Therefore, the management of fibromyalgia is aimed at improving the quality of life.² Treatment strategies to improve quality of life in FM emphasize the importance of lifestyle changes, including dietary habits.³

The global prevalence of FM is 2.7%;⁴ approximately 2.3% of the European population (ranging from 0.4% in Greece to 8.8% in Türkiye),^{5,6} and 2–6% of the US population⁷ but the etiology of FM remains unknown. However, dysfunction of the nervous system, neurotransmitters, hormones, immune system, stressors draws attention to increased FM susceptibility.⁸ Moreover, pro-inflammatory cytokines can be role in the onset and maintenance of FM.^{9,10} In particular, interleukin (IL)-8, tumor necrosis factor (TNF)- α and IL-6, which have pro-inflammatory and algescic have been shown to have higher serum levels in FM patients compared to controls.¹¹ In addition, IL-4 and IL-10, which have anti-inflammatory and analgesic

activity, have been shown to be at low levels in FM patients compared to healthy controls.¹² These findings may support the hypothesis that FM patients with chronic pain may have an innate or acquired imbalance in cytokine production and secretion. However, the results of studies on the role of cytokines in the pathogenesis of FM are debated, so high-quality studies involving more patients are needed.⁹

Moreover, it has been shown in the literature that various ratios such as neutrophil/lymphocyte, uric acid/creatinine, uric acid/HDL, other than cytokines, are biochemical parameters associated with inflammatory processes in different disease groups.^{13–15} For example, fibromyalgia patients were found to have higher neutrophil/lymphocyte ratios and C-reactive protein (CRP) levels, which are associated with inflammatory conditions other than cytokines. Moreover, fibromyalgia patients were found to have higher neutrophil/lymphocyte ratios and CRP levels, which are associated with inflammatory status other than cytokines.^{16,17} In addition, these patients have been shown to have higher levels of hs-CRP, and higher levels of hs-CRP are associated with higher

Received: 27 February 2024. Revised: 16 October 2024. Accepted: 30 October 2024

© The Author(s) 2024. Published by Oxford University Press on behalf of the American Academy of Pain Medicine. This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs licence (<https://creativecommons.org/licenses/by-nc-nd/4.0/>), which permits non-commercial reproduction and distribution of the work, in any medium, provided the original work is not altered or transformed in any way, and that the work is properly cited. For commercial re-use, please contact reprints@oup.com for reprints and translation rights for reprints. All other permissions can be obtained through our RightsLink service via the Permissions link on the article page on our site—for further information please contact journals.permissions@oup.com.

symptom burden. In addition, these elevated hs-CRP levels may be associated with higher body weight.^{18,19} Pro-inflammatory cytokine secretion is higher in obese individuals than in lean individuals, which may cause low chronic inflammation in obese individuals. In particular, visceral adiposity can cause systemic inflammation due to direct access and secretion of free fatty acids and inflammatory cytokines into the portal circulation.²⁰ Therefore, high adipose tissue in FM may cause an increase in disease severity by causing the release of pro-inflammatory cytokines that mediate inflammation and modulate pain. Therefore, body weight and composition may be critical in the management of FM.

European Alliance of Associations for Rheumatology (EULAR) stated that the treatment of fibromyalgia requires a multidisciplinary approach with a combination of non-pharmacological and pharmacological treatments tailored to the symptoms.²¹ In addition, the first-line therapy to treat FM should focus on non-pharmacological treatments, which currently draws attention to nutrition.² The practical and valid DII, which shows the inflammatory properties of diets, is widely used in the literature in various fields of study.^{22,23} Moreover, the Dietary Inflammatory Index (DII), an approved dietary index developed to predict patient inflammation levels of diet, has been shown to be associated with higher pressure pain hypersensitivity. The findings that a pro-inflammatory diet is associated with hypersensitivity to pain in people with FMS have generated excitement in the field.²⁴ In this context, more research is still required on dietary interventions in FM and the relationship between the diet inflammatory state and symptoms. Although the relationship between diet and pain, the main symptom of FM, has been investigated,²⁵⁻²⁷ the relationship between DII and pain and disease severity in FM have attracted attention recently. In addition, inflammatory cytokines have been studied, but the biochemical parameters associated with the inflammatory state such as neutrophil/lymphocyte ratio, uric acid/HDL-C, uric acid/creatinine have shown conflicted results.

In the light of previous information, our study outcome shows as follows;

- 1) Primary outcome is the relationship between DII and pain severity.
- 2) Secondary outcomes are the relationship between DII and disease severity and inflammatory markers in FM patients.

Methods

This study had a cross-sectional design and was conducted in Department of Traditional and Complementary Medicine clinics. The study was approved from the Gülhane Education and Research Hospital Traditional and Complementary Medicine Ethical Committee (2023/3).

Participants

A total of 84 patients with FM, which was diagnosed by a rheumatologist according to the 2016 American College of Rheumatology criteria, and invited to the study from the Gülhane Education and Research Hospital, Department of Traditional and Complementary Medicine clinics, Turkey. Patients were included in the study using the convenience sample method. Patients were informed about the risks and benefits of prolotherapy. Prolotherapy has been evaluated as a treatment option in patients who do not respond to medical

treatment, physical therapy, manual therapy or other conservative treatments. In addition, prolotherapy is not used in patients with a bleeding tendency, systemic inflammatory diseases, oncological diseases, systemic infections, a history of infection in the treatment area or any intervention in the same area within the last 12 weeks.

All patients were informed about the study before data collection and participants were informed of the purpose of the study the "Informed Voluntary Consent Form" was signed by those who agreed to participate in the study.

The criteria for inclusion of patients with FM in this study were (1) a diagnosis of FM according to 2016 American College of Rheumatology criteria, (2) >18 age, (3) followed and treated with prolotherapy at the University of Health Sciences, (4) the absence of any acute or terminal illnesses. From the patients who met the inclusion criteria, the ones who: (1) a history of drug or alcohol abuse (2) women who were pregnant or breastfeeding (3) participants with an active tumor were excluded (Figure 1). Since fibromyalgia patients who routinely receive prolotherapy are followed up, patients receiving prolotherapy were included in the study.

Measurements

Questionnaire form

Participants' sociodemographic information, dietary habits and anthropometric measurements were collected by questionnaire.

Visual analog scale for pain

Patients' general level of pain was assessed using the visual analogue scale (VAS). The VAS is scored from 0 to 10, with higher scores indicating more severe pain. The VAS is an important tool for assessing pain levels. It has been reported to be sensitive and specific in assessing pain in fibromyalgia patients.²⁸

Revised-fibromyalgia impact questionnaire

The Revised Fibromyalgia Impact Questionnaire (FIQR) is a shortened form of the Fibromyalgia Impact Questionnaire. FIQR is a reliable and valid measure of fibromyalgia in the Turkish population (Cronbach- α = 0.835). This questionnaire contains 21 questions and each question is scored between 0 and 10. FIQR consists of three subscales: (a) the "function" dimension includes 9 questions, (b) the "global impact" dimension includes 2 questions measuring symptom severity and the impact of global impact on function, and (c) "symptoms" includes 10 questions. The total score for "function" (0–90 points) is divided by 3, the total score for "overall impact" (0–20 points) remains same, and the total score for "symptoms" (0–100 points) is divided by 2. The FIQR score is determined by summing the scores of the three sub-dimensions, and a high score indicates increased disease severity.²⁹

Antropometric measures

Measurements were taken of height, waist circumference, and neck circumference taken by specialist. The height of the individuals was measured with a portable Seca769 stadiometer in the Frankfort plane without shoes.³⁰ In addition, body composition was assessed using the TANITA BCA601 device to determine body weight (kg), body fat percentage (%), muscle percentage (kg), water percentage (%), bone mineral content (kg), and internal fat status.

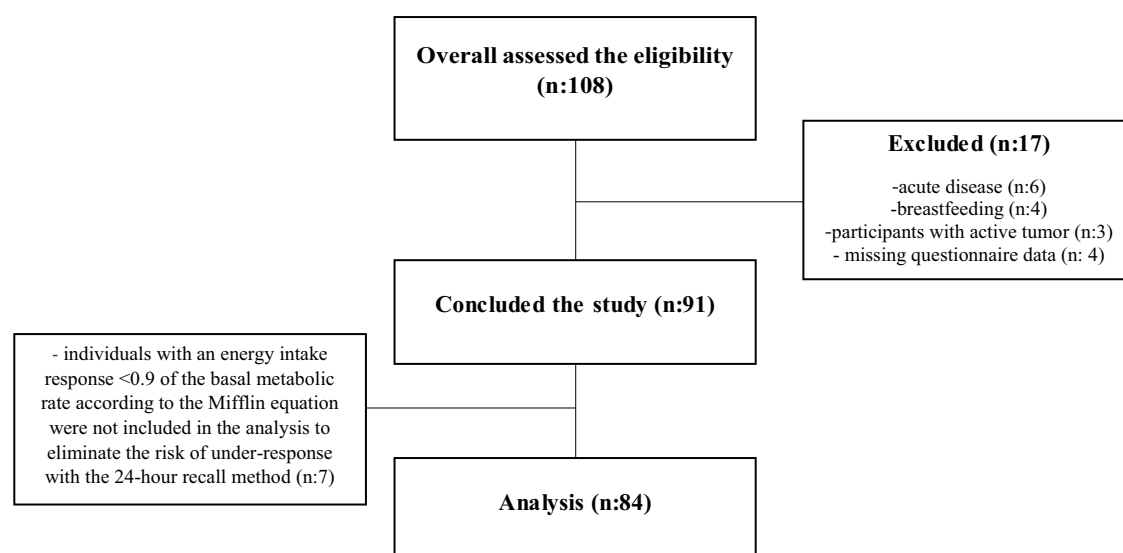


Figure 1. Flowchart.

Body mass index

Body mass index was calculated by dividing body weight by the square of height in meters for all the individuals, who were then classified as “underweight” for $<18.5 \text{ kg/m}^2$, “normal” for $18.5\text{--}24.9 \text{ kg/m}^2$, “overweight” for $25.0\text{--}29.9 \text{ kg/m}^2$, and obese if $\geq 30.0 \text{ kg/m}^2$.³¹

Waist circumference

The waist circumference was measured using an inflexible tape measure that passed through the midpoint between the lowest point of the costal bone and the crystalloid bone taken by specialist. Waist circumference was classified as $\geq 80 \text{ cm}$ risk and $\geq 88 \text{ cm}$ high-risk in women and $\geq 94 \text{ cm}$ risk and $\geq 102 \text{ cm}$ high-risk in men.³⁰

Dietary assessment

A 24-hour recall method was used to record participants' one day food consumption. Food consumption records were recorded once, using the face-to-face method, once the patients had completed their examination. The 24-hour dietary recall method consists of accurately recalling, identifying, and quantifying the foods and beverages consumed throughout the day in the 24-hour period before the interview, from the first intake in the morning to the last food or beverage. The information must describe the type and characteristics of the food (fresh, canned, etc), net amount consumed, method of preparation, trademarks, sauces.³² Energy and nutrients were calculated using the Nutrition Information System which is a food software program in compliance with Turkish food according to the food consumption record. In addition, the average nutrient and nutrient consumption calculated from the food record was used to calculate the Dietary Inflammatory Index (DII).

Dietary inflammatory index

The Dietary Inflammatory Index (DII) is a measure of the inflammatory potential of the diet, validated according to the effect of diet on inflammatory markers.³³ Overall, 26 food parameters including energy, carbohydrates, protein, total fat, monounsaturated fatty acid, polyunsaturated fatty acid, saturated fatty acid, omega-3, omega-6, niacin, cholesterol,

fiber, caffeine, folate, iron, magnesium, riboflavin, beta carotene, thiamine, vitamin A, vitamin B₁₂, vitamin B₆, vitamin B₉, vitamin C, vitamin E, zinc were used to calculate the global DII scores. To calculate the DII, z-scores ([individual average intake -global standard intake]/standard deviation) are calculated from the intakes of these foods/nutrients. These are then converted into percentile scores. As a result of the summing of the scores obtained by multiplying the percentile value obtained for each nutrient parameter by the 'parameter-specific overall inflammatory effect scores' calculated for that nutrient parameter, the DII score is obtained, which is an indicator of the inflammatory status of the individual's daily diet. Higher scores have more pro-inflammatory status. In the study, individuals will be divided into quartile groups according to their DII scores. As in similar studies, the DII is divided into quartiles because it does not have a cut-off point.^{34,35} The lowest DII score will be selected as the first quartile control group and the values of the other groups will be compared with this group.

Biochemical parameters

Biochemical parameters including C-reactive protein (CRP), neutrophil count, lymphocyte count, High Density Lipoprotein-Cholesterol (HDL-C), urea, uric acid, and creatinine were measured from the individuals. To assess these routine laboratory parameters, peripheral venous blood samples were taken from patients after a 12-hour fast. If there was no 12-hour fast after the examination, the patient donated blood the next day after a 12-hour fast. If there was a 12-hour fast after the examination, the patient donated blood on the same day. The blood was processed in the laboratory of Gülhane Education and Research Hospital immediately after donation. Using an enzymatic method (Olympus AU 2700, USA), the following parameters were measured: Triglyceride, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), uric acid, urea, and creatine. Uric acid applying its own kits with an Olympus AU2700 autoanalyzer (Olympus Diagnostics, Hamburg, Germany). The amounts of neutrophils and lymphocytes were measured with a Coulter Counter Model S (Coulter Electronic Limited, Luton, UK). CRP was examined nephelometrically with an automated

Immagine (Beckman Coulter, USA) analyzer. Additionally, ratios known to be associated with inflammation in the literature were calculated: Neutrophil/lymphocyte ratio, uric acid/HDL-C ratio, and uric acid/creatinine ratio. The neutrophil/lymphocyte ratio is calculated by dividing neutrophil count by lymphocyte count. The uric acid/HDL-C ratio is calculated by dividing serum uric acid level by serum HDL-C level. The uric acid/creatinine ratio is calculated by dividing serum uric acid level by serum creatinine level.

C-reactive protein (CRP), neutrophil, lymphocyte, High Density Lipoprotein- Cholesterol (HDL-C), urea, uric acid, and creatinine biochemical parameters were taken from the individuals. In addition, neutrophil/lymphocyte ratio, uric acid/HDL-C, uric acid/creatinine parameters, which have been shown to be related to inflammation in the literature, were calculated. Neutrophil/lymphocyte ratio is calculated with division of neutrophil by lymphocyte.³⁶ Uric acid/HDL-C is calculated with division serum uric acid by serum HDL-C.¹⁴ Uric acid/creatinine ratio is calculated with division of serum uric acid by serum HDL cholesterol.³⁷

Statistics

The data were analyzed using the SPSS package program. The distribution of all dependent and independent variables was evaluated with the Kolmogorov Smirnov test. Energy, cholesterol, fibre, caffeine, folate, cobalamin, vitamin C, vitamin A, beta-carotene, iron, and zinc from energy and nutrients; fat-free mass and body fluid from body composition; CRP, neutrophils, lymphocytes, HDL, urea, uric acid, creatinine, uric acid/HDL, uric acid/creatinine from biochemical parameters are not normally distributed, that is, they are non-parametric variables. All other dependent and independent variables are normally distributed. Descriptive statistics were presented as mean±standard deviation for normally distributed variables, median and minimum-maximum value for non-normally distributed variables, and number and percentage (%) for nominal variables. The Independent Samples *t* test was used to compare the means of 2 parametric independent groups, and the Mann-Whitney *U* test was used in nonparametric conditions. One-way ANOVA was applied for the comparison of the means of more than two independent parametric groups and Kruskal-Wallis test was applied for the comparison of the means of more than 2 nonparametric groups. “Bonferroni Test,” one of the post-hoc tests, was applied to determine the difference in the comparison of more than two groups. When analyzing categorical variables, χ^2 test was applied to evaluate the relationship between number (*n*) and percentage (%) distribution. In cases where χ^2 assumptions were not met, Fischer test was used if appropriate conditions were met. In the comparison of more than 2 ratios, the appropriate post-hoc test was applied to determine the difference.

In order to evaluate the statistical relationship between 2 quantitative variables, Pearson Correlation Coefficient was used when 2 of the variables met the normal distribution assumptions, and Spearman Correlation Coefficient was used when at least 1 of the variables did not meet the normal distribution assumptions. In all statistical tests, the confidence interval was accepted as 95.0% and evaluated at a significance level of $P < .05$. Overall DII scores were analyzed as both continuous and categorized variables. The outcome variables included pain, FIQ-R and uric acid/creatinine ratio. Variables with moderate correlation and no multicollinearity

with the independent variable have been added as potential confounders. Potential confounders were also identified as a result of the literature review.^{38–44} Linear regression models were adjusted for confounding variables including ages (years), gender (male, female), educational status (secondary school and above), BMI (kg/m^2), body fat (%), fat free mass (kg), cholesterol (mg/day), fiber (g/day), β -caroten (mg/day), iron (mg/day), magnesium (mg/day), and vitamin C (mg/day).

In all statistical tests, the confidence interval was accepted as 95.0%; it was evaluated at the $P < .05$ significance level.

Results

Sample characteristics

The general characteristics of FM patients are shown in Table 1. The mean age of the patients was 48.8 ± 12.6 years. Among the participants, 17 were male and 67 were female. Half of the patients were secondary school graduates. The supplement usage ratio was 39.0%. Additionally, 27.3% of individuals used vitamin D, and 51.4% used cobalamin. Menopause was reported in 50.7% of the patients, and 42.9% had chronic diseases. The mean body weight was 74.4 ± 14.0 kg, the BMI was 27.6 ± 4.7 kg/m^2 , the waist circumference was 93.6 ± 13.1 cm, and the body fat mass was 31.5 ± 7.4 %. The mean FIQ-R was 54.0 ± 23.4 , and the mean VAS pain score was 5.8 ± 2.2 cm.

Energy and nutrients intake

The DII scores were divided into quartiles according to the following cutoff points: Q1: -1.65 to ≤ -0.60 ; Q2: > -0.6 to ≤ 0.17 ; Q3: > 0.17 to ≤ 0.73 ; Q4: > 0.73 to 1.46 . The energy and nutrient intakes of patients according to the quartiles of the DII scores are shown in Table 2. There were no statistically significant differences in energy, macronutrient, cholesterol, and caffeine intakes between quartiles. However, fiber, thiamine, folate, vitamin C, vitamin A, beta-carotene, iron, and magnesium intakes were statistically significantly different between quartiles ($P < .05$).

Table 1. General characteristics of participants.

	Total (<i>n</i> = 84)
Age, y	48.8 ± 12.6
Gender (female) <i>n</i> (%)	67 (79.7)
Secondary school education, <i>n</i> (%)	42 (50.0)
Use of supplement <i>n</i> (%)	33 (39.3)
Use of antidepressant <i>n</i> (%)	52 (62.9)
Menstrual status (menopause) <i>n</i> (%)	34 (50.7)
Chronic disease (yes) <i>n</i> (%)	36 (42.9)
Weight (kg)	74.4 ± 14.0
BMI (kg/m^2)	27.6 ± 4.7
Waist circumference (cm)	93.6 ± 13.1
Body fat mass (%)	31.5 ± 7.4
FIQ-R	54.0 ± 23.4
VAS pain (cm)	5.8 ± 2.2
CRP	2.3 ± 1.7
Uric acid/creatinin	5.0 ± 1.2
DII	0.05 ± 0.76

Abbreviations: BMI, body mass index; CRP, C-reactive protein; DII, Diet Inflammatory Index; FIQ-R, Revised Fibromyalgia Impact Questionnaire; VAS, visual analog scale.

Table 2. Energy and nutrients intake of participants across quartiles (Q) of the Dietary Inflammatory Index (DII) scores.

Energy and nutrients	DII				P
	Q1 (n: 21) x̄ ± SS/median (min–max)	Q2 (n: 21) x̄ ± SS/median (min–max)	Q3 (n: 22) x̄ ± SS/median (min–max)	Q4 (n: 20) x̄ ± SS/median (min–max)	
Energy (kcal)	1566.4 (1016.5–2415.2)	1368.4 (1092.3–2456.0)	1387.5 (1098.4–2338.4)	1545.8 (1156.7–2488.4)	.336 ^μ
Carbohydrate (%)	46.6 ± 10.0	44.8 ± 11.4	45.6 ± 1.6	43.4 ± 10.4	.804*
Protein (%)	14.1 ± 3.8	13.2 ± 1.9	15.3 ± 4.0	13.9 ± 4.3	.310*
Fat (%)	38.2 ± 10.2	41.5 ± 11.5	39.3 ± 11.0	42.0 ± 9.2	.596*
Saturated fat (g)	18.3 ± 7.0	18.1 ± 7.1	19.8 ± 8.0	22.2 ± 12.3	.429*
Monosaturated fatty acids (g)	25.3 ± 9.3	24.7 ± 9.9	23.1 ± 10.0	21.3 ± 13.7	.684*
Polyunsaturated fat (g)	15.3 ± 9.0	13.0 ± 5.8	10.4 ± 5.4	11.9 ± 6.5	.122*
Omega-3 fatty acids (g)	0.8 (0.4–3.7)	0.8 (0.3–2.0)	0.8 (0.2–3.1)	0.8 (0.2–4.5)	.751 ^μ
Omega-6 fatty acids (g)	13.8 ± 8.0	11.8 ± 5.7	9.0 ± 5.2	10.5 ± 5.7	.095*
Cholesterol (mg/day)	225.7 (35.7–438.0)	220.1 (3.0–544.5)	263.6 (55.0–623.7)	248.7 (73.1–6476.4)	.158 ^μ
Fiber (g/gün)	21.8 (7.8–45.9) ^a	19.4 (8.4–29.1) ^{a, b}	14.5 (8.3–25.1) ^{b, c}	10.2 (4.6–26.7) ^c	<.001 ^μ
Caffeine (mg/day)	60.0 (0.0–396.0)	80.0 (0.0–320.0)	60.0 (0.0–780.0)	40.0 (0.0–160.0)	.156 ^μ
Thiamine (mg/day)	0.9 (0.4–1.7) ^a	0.7 (0.3–1.1) ^{a, b}	0.6 (0.3–1.2) ^{a, b}	0.5 (0.3–0.9) ^b	.001 ^μ
Riboflavin (mg/day)	0.9 (0.3–1.7)	0.7 (0.4–1.5)	0.9 (0.4–1.5)	1.0 (0.3–5.9)	.430*
Niacin (mg/day)	8.2 (2.6–83.7)	6.5 (1.2–12.4)	7.5 (2.6–22.4)	6.3 (1.8–30.4)	.134 ^μ
Pridoxin (mg/day)	1.0 (0.4–2.2)	0.9 (0.2–1.3)	0.7 (0.4–1.5)	0.6 (0.2–2.2)	.068 ^μ
Folate (μg/day)	288.0 (122.7–638.0) ^a	271.7 (118.0–553.0) ^a	194.0 (134.1–462.6) ^{a, b}	158.7 (61.4–1205.0) ^b	.002 ^μ
Cobalamin (μg/day)	1.3 (0.0–208.1)	1.2 (0.0–4.0)	2.5 (0.6–6.7)	2.5 (0.5–117.2)	.173 ^μ
Vitamine C (mg/day)	134.0 (8.6–208.1) ^a	65.0 (6.4–213.0) ^b	45.7 (11.3–159.6) ^b	51.3 (0.0–156.8) ^b	<.001 ^μ
Vitamine A (μg/day)	1091.9 (32.8–2147.3) ^a	635.8 (149.8–1216.2) ^{a, b}	628.5 (161.8–1540.0) ^b	453.4 (190.2–3254.9) ^b	.001 ^μ
Beta carotene (mg/day)	5.0 (0.2–10.9) ^a	1.6 (0.5–4.5) ^{a, b}	1.2 (0.1–8.6) ^b	0.5 (0.0–3.6) ^b	<.001 ^μ
Iron (mg/day)	10.4 (5.4–24.2) ^a	7.1 (3.7–11.3) ^{a, b}	6.6 (5.1–10.8) ^b	5.4 (2.8–18.1) ^b	<.001 ^μ
Magnesium (mg/day)	267.4 ± 99.6 ^a	215.6 ± 75.9 ^b	192.8 ± 59.6 ^c	155.3 ± 54.6 ^c	<.001 ^μ
Zinc (mg/day)	7.0 (3.9–13.6)	5.9 (3.3–9.9)	6.2 (3.8–9.7)	5.3 (2.7–17.0)	.159 ^μ

* One-way ANOVA; γ: χ^2 ; μ: Kruskal-Wallis.

Different letters in the row indicate statistically significant difference between groups.

Table 3. Anthropometric measures and biochemical parameters of participants across quartiles (Q) of the Dietary Inflammatory Index (DII) scores.

Anthropometric measures	DII				P
	Q1 (n : 21) x̄ ± SS/median (min-max)	Q2 (n : 21) x̄ ± SS/median (min-max)	Q3 (n : 22) x̄ ± SS/median (min-max)	Q4 (n : 20) x̄ ± SS/median (min-max)	
Body weight (kg)	68.5 ± 11.5 ^a	72.7 ± 13.8 ^{a, b}	75.1 ± 12.1 ^{a, b}	81.6 ± 16.1 ^b	.023*
Body mass index (kg/m ²)	25.8 ± 4.0 ^a	26.7 ± 3.6 ^{a, b}	27.6 ± 4.4 ^{a, b}	30.2 ± 5.6 ^b	.018*
Normal	47.6 (10)	38.1 (8)	27.3 (6)	20.0 (4)	.067 ^γ
Overweight	38.1 (8)	28.6 (6)	54.5 (12)	30.0 (4)	
Obese	14.3 (3)	33.3 (7)	18.2 (4)	50.0 (10)	
Waist circumference (cm)	90.0 ± 14.6 ^a	101.4 ± 14.0 ^b	93.0 ± 7.44 ^a	89.9 ± 12.8 ^a	.013*
Normal	28.6 (6) ^a	9.5 (2) ^{b, c}	4.5 (1) ^c	35.0 (7) ^a	.033 ^γ
Risk	71.4 (15) ^{a, b}	90.5 (19) ^{b, c}	95.5 (21) ^c	65.0 (13) ^a	
Body fat mass (%)	26.3 ± 6.9 ^a	32.3 ± 4.7 ^b	32.8 ± 6.6 ^b	34.8 ± 8.5 ^b	.010*
Fat free body mass (kg)	48.5 (38.0–71.3)	43.8 (38.7–65.3)	45.5 (36.8–68.1)	46.2 (31.9–63.0)	.302 ^μ
Body fluid (%)	49.5 (41.1–60.8) ^{a, b}	49.0 (30.2–52.8) ^a	48.6 (35.0–57.0) ^a	52.8 (42.1–60.7) ^b	.015 ^μ
Biochemical parameters					
CRP (mg/L)	1.5 (0.3–5.7)	3.1 (0.3–4.5)	1.8 (0.0–10.2)	2.4 (0.1–6.8)	.167 ^μ
Neutrophil (10 ³ /μL).	58.7 (34.0–79.0)	58.5 (39.6–76.9)	58.5 (40.1–71.9)	58.6 (43.0–72.6)	.429 ^μ
Lymphocyte (10 ³ /μL).	33.0 (20.3–41.5)	30.2 (15.3–45.7)	29.7 (6.5–48.9)	36.5 (17.3–48.7)	.300 ^μ
HDL-C (mg/dL)	54.0 (42.0–76.0)	49.0 (32.0–88.0)	50.5 (36.0–77)	50.5 (30.0–80.0)	.124 ^μ
Urea (mg/dL)	25.0 (12.0–58.0)	24.0 (6.0–58.0)	24.3 (7.0–48.0)	24.5 (6.0–46.0)	.970 ^μ
Uric acid (mg/dL)	3.8 (2.7–6.4)	4.2 (2.7–7.5)	3.9 (2.1–7.0)	4.2 (2.7–6.6)	.629 ^μ
Creatinine (mg/dL)	0.8 (0.5–3.4)	0.8 (0.5–1.7)	0.8 (0.5–1.1)	0.8 (0.5–1.8)	.599 ^μ
Neutrophil/lymphocyte ratio	1.7 ± 0.5	1.9 ± 0.5	2.0 ± 0.7	2.0 ± 0.8	.447*
Uric acid/HDL-C	0.1 (0.0–0.1)	0.1 (0.1–0.2)	0.1 (0.0–0.2)	0.1 (0.1–0.2)	.016 ^μ
Uric acid/creatinine	4.4 (1.1–6.5) ^a	4.7 (2.7–6.8) ^{a, b}	5.3 (6.8–3.6) ^b	5.5 (4.3–7.5) ^b	<.001 ^μ

* One way ANOVA; γ: χ^2 ; μ: Kruskal-Wallis.

Different letters in the row indicate a statistically significant difference between groups.

Abbreviations: CRP: C-reactive protein, HDL-C: High Density Lipoprotein Cholesterol.

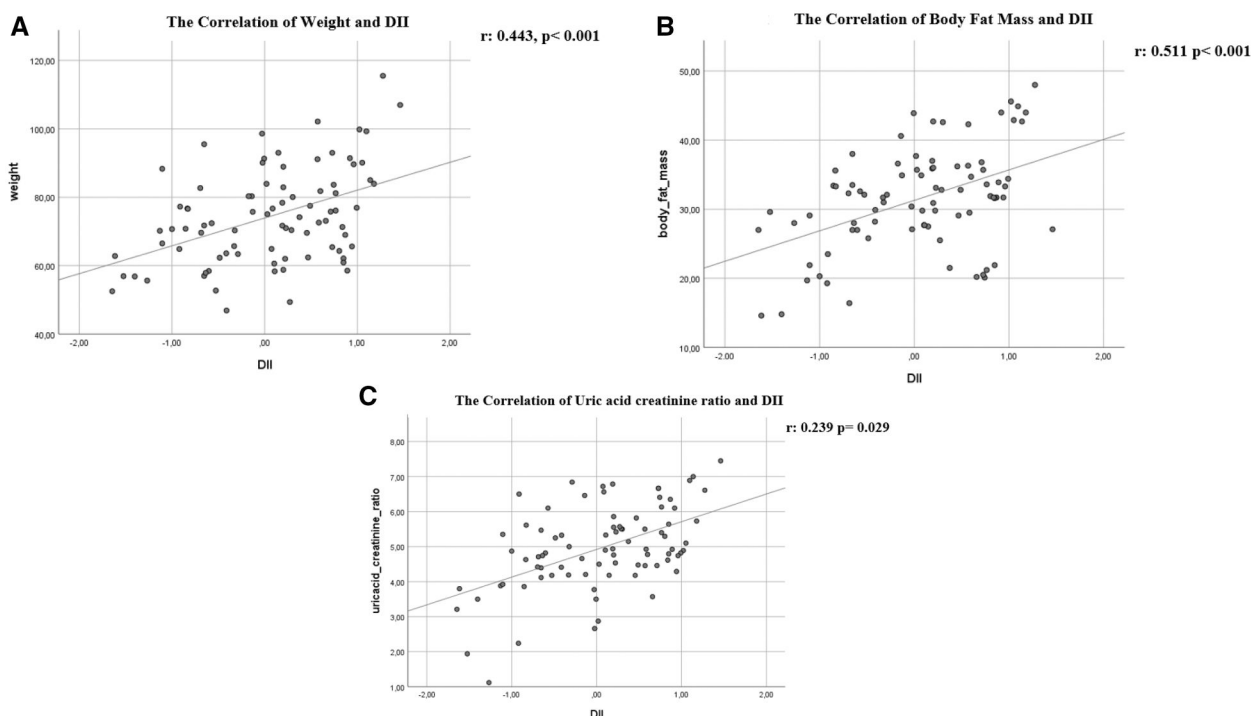


Figure 2. The correlations of weight, body fat mass, and uric acid creatinine ratio and DII.

Anthropometric measures and biochemical parameters

The anthropometric characteristics and biochemical parameters of participants according to the quartiles of the DII scores are shown in Table 3. Significant differences were observed between the quartiles of DII scores for mean body weight, BMI, body fat mass, body fluid, waist circumference, and waist circumference category ($P < .05$). Additionally, correlations of body mass index and anthropometric measurements with outcomes are shown (Table S1). There was a linear trend toward increasing weight and body fat mass with increasing DII scores ($P < .001$) (Figure 2).

The biochemical markers of patients according to the quartiles of the DII scores are also shown in Table 3. Only the uric acid/creatinine ratio was statistically significant ($P < .001$), and there was a linear trend toward increasing uric acid/creatinine ratio with higher DII scores (Figure 2).

Linear regression analysis

Table 4 summarizes the study's primary and secondary outcomes using linear regression analysis (Table 4). High DII [β (95% CI) = 1.98 (1.52–2.40), $P < .001$] was independently positively associated with the VAS pain score, explaining 47.0% of its variance. The VAS pain score was positively associated with DII after full adjustment [β (95% CI) = 1.72 (0.90–2.55), $P < .001$], with a coefficient of determination of 48.6%.

Additionally, linear regression analysis revealed that high DII was positively associated with the FIQ-R score, explaining 44.7% of its variance. The FIQ-R score was positively associated with DII after full adjustment [β (95% CI) = 5.62 (0.14–11.09), $P < .001$], with a coefficient of determination of 41.2%. Furthermore, high DII was positively associated with the uric acid/creatinine ratio, explaining 25.8% of its variance. The uric acid/creatinine ratio was positively

associated with DII after full adjustment [β (95% CI) = 0.21 (–0.10 to 0.52), $P < .001$], explaining 29.5% of its variance.

Discussion

This study examined the possible relationships between DII score and pain and fibromyalgia-related symptoms severity and inflammatory markers in a population of women with FM. As a result of our study, we found that pro-inflammatory diet were significantly associated with higher pain, disease severity and inflammatory marker especially uric acid/creatinine ratio. These results support the hypothesis that diet-induced inflammatory potential is associated with pain and disease severity and inflammatory in people with FM.

Current evidences suggest that dietary interventions may have promise as complementary therapies in FM.^{45,46} We also hypothesize that anti-inflammatory diets may reduce the levels of pain, FM disease severity and inflammatory markers.^{45,47} To evaluate the anti-inflammatory properties of the diet, we assessed the inflammatory status of the diet using DII, which, as mentioned, has a strong relationship with inflammatory markers in the literature. It was found that anti-inflammatory diet was associated with lower pain and disease severity in our study. Similarly, it has been shown that an anti-inflammatory diet has been shown to be associated with reduced pressure pain thresholds.²⁴ Kaartinen et al. (2000) has also been shown that FM patients on a vegan diet for three months improved pain and quality of life compared with omnivores.⁴⁸ Moreover, in another study, it was shown that a vegetarian dietary intervention over a seven-month period reduced symptoms of pain, fatigue, depression and anxiety in patients.⁴⁹ It has been reported that vegetarian, vegan, and Mediterranean diets may help alleviate FM symptoms due to their anti-inflammatory properties.⁴⁵ A recent

Table 4. Linear regression analysis of the relationship between scores of Pain, FIQ-R, Uric acid/creatinin and DII.

		Pain				FIQ-R				Uric acid/creatinine ratio			
		β	SE	%95 CI	R2	β	SE	%95 CI	R2	β	SE	%95 CI	R2
DII	Crude	1.98	0.23	1.52–2.40	0.470*	20.47	2.52	5.47–25.48	0.447*	0.53	0.11	0.50–1.10	0.258*
	Model 1	1.89	0.24	1.41–2.37	0.468*	21.83	2.58	16.69–26.97	0.470*	0.73	0.15	0.43–1.04	0.248*
	Model 2	1.72	0.42	0.90–2.55	0.486*	15.72	4.47	6.80–24.64	0.471*	0.45	0.26	–0.08 to 0.97	0.295*
DII Quartile	Crude	1.31	0.16	0.99–1.63	0.440*	12.21	1.82	8.47–15.95	0.331*	0.49	0.28	0.29–0.70	0.214*
	Model 1	1.22	0.17	0.88–1.57	0.432*	12.49	1.97	8.56–16.42	0.363*	0.45	0.11	0.24–0.66	0.454*
	Model 2	0.97	0.24	0.48–1.45	0.477*	5.62	2.74	0.14–11.09	0.412*	0.21	0.15	–0.10 to 0.52	0.285*

Abbreviations: DII, Diet Inflammatory Index; FIQ-R, Revised Fibromyalgia Impact Questionnaire; 95% CI, 95% confident interval; SE, Standart Error. Beta coefficient, standard error, 95% confidence interval, R squared and P value calculated from linear regression analysis
 $P < .001$.

Model 1: Adjusted for age, gender, educational status; **Model 2:** Additionally adjusted for BMI, body fat, fat free mass, cholesterol, fiber, caroten, iron, magnesium, vitamine C.

study revealed that patients adhering to an anti-inflammatory Mediterranean diet experienced improvements in clinical symptoms, particularly regarding overall disability.⁵⁰ On the other hand, Azad et al. (2000) concluded that vegetarian diet wasn't an effective intervention for these patients.⁵¹ A recent systematic review also reported that anti-inflammatory diets positively affect pain. However, it emphasized that due to the small number of studies, limited sample sizes, and short intervention periods, there is currently insufficient evidence to recommend any specific diet for FM patients. More research is necessary to recommend specific diets and investigate potential mechanisms.⁴⁵

The effects of dietary interventions on pain may be mediated through oxidative stress and inflammation. Cytokines and chemokines produced as a result of oxidative stress lead to the production of pro-inflammatory mediators.⁴² Dietary fiber may help prevent inflammation by reducing lipid oxidation and supporting gut flora.⁵² Moreover, thiamine may inhibit pro-inflammatory mediators by suppressing NF- κ B phosphorylation and Toll-like receptor activity, thereby reducing TNF- α , IL-6, IL-1B expression and CRP production.⁵³ Vitamin C may have also anti-inflammatory properties by modulating the binding of NF- κ B to DNA, which causes oxidative stress. This modulation may reduce the production of TNF- α and IL-6, which induce CRP production in the liver.⁵⁴ Due to its antioxidant activity, dietary patterns rich in antioxidants may be associated with inflammatory status. For this reason, diet may play an important role in FM, as evidenced by the improvement of symptoms in individuals following dietary intervention.⁴⁶ Moreover, weight loss as a result of dietary interventions is associated with both reduced inflammation and improved quality of life in FM patients. Therefore, the improvement in symptoms with different dietary strategies may support the hypothesis that both weight loss and the psychosomatic component of the disease may play an important role in the disease.⁵⁵ Due to the cross-sectional nature of our study, changes in body weight were not examined, but anthropometric measures were analysed in our study. In addition, our study found that body weight, BMI, body fat percentage and body fluid percentage were higher in individuals in Q4. Interestingly, people in Q2 had a higher waist circumference than the other quartiles. Individuals in Q1 have low body fat and high lean body mass, which may explain the lower waist circumference of Q1 compared to other quartiles. The differences in Q2 and Q3 may be due to individuals with low muscle mass.

Consistent with the hypothesis that diet modulates inflammation, we found only an association between increased DII and increased uric acid/creatinine ratio. However, there was no statistically significant difference in CRP, neutrophil/lymphocyte ratio, and uric acid/HDL-C ratio. The uric acid/creatinine ratio is associated with BMI, and the metabolic conditions associated with this ratio are responsible for hyperuricaemia.⁵⁶ High levels of uric acid can be an inducer of oxidative stress and ROS production in vascular endothelial cells.⁵⁷ A positive correlation between DII and CRP has been reported in epidemiological studies.³³ However, to the best of our knowledge, the relationship between DII and CRP levels in FM has not been analysed. Since this is the first study to investigate the relationship between DII and CRP in FM patients, it is thought that the results of this study will shed light on the literature.

The ratio of uric acid to HDL-C is a marker that increases with inflammation.⁵⁸ The marker has been shown in the literature to be particularly useful in the diagnosis and progression of metabolic syndrome. Elevated serum uric acid levels can induce oxidative processes in vascular smooth muscle, endothelium, renal tubules, hepatocytes and adipose tissue.¹⁴ In this study, no statistically significant difference was found between uric acid/HDL ratios according to dietary inflammatory index in FM patients. This may be due to the fact that the uric acid and HDL-C levels of the participants, the majority of whom were women, were within the reference range.

The anti-inflammatory effects of the Mediterranean diet and the DASH diet are well known, and these dietary patterns may be associated with the neutrophil/lymphocyte ratio. In the elderly population, higher consumption of vegetables and cereals, especially in women, and higher diet quality have been shown to be associated with lower neutrophil/lymphocyte ratios.⁵⁹ In a middle-aged population (45–70 years), the neutrophil/lymphocyte ratio was shown to decrease with increasing adherence to the Mediterranean diet.⁶⁰ In the literature, fibromyalgia patients have been shown to have a higher neutrophil/lymphocyte ratio than controls.³⁶ In this study, it was observed that the neutrophil/lymphocyte ratio was higher in people with a more pro-inflammatory diet. Although the difference between the groups is not statistically significant, it fills the gap in the literature on the relationship between diet and neutrophil/lymphocyte ratio in FM. The results might have varied depending on the assessment of other variables influencing the neutrophil and lymphocyte ratio in the sample group or the inclusion of confounders.

Limitations

It is important to note that this study also has potential limitations. First, the cross-sectional design of the study means that no causal conclusions can be drawn. Second, although the 24-hour dietary recall method is a reliable method for determining the nutrients consumed by individuals over the course of a day, it has an inherent limitation due to recall. To minimize 24-hour recall bias in this study, recall was interviewer-guided and a food catalogue was used to improve the accuracy of food descriptions and quantities. In addition, people whose energy intake was <0.9 of their basal metabolic rate were not included in the analysis as this would have been an under-reporting. Third, the majority of the sample is female and not every FM patient is suitable for the indications of prolotherapy, which may not be generalisable to all FM patients. Moreover, physical activity was not questioned in this study. Future research may question physical activity, and it would be useful to measure body mass. In addition, the first quartile of the DII was used as the control group in our study. Finally, the DII score was calculated on the basis of only 26 of the 45 food parameters originally included. However, the missing components (eugenol, flavanols, flavones, flavanones, anthocyanins, isoflavones, garlic, rosemary, saffron, ginger, turmeric, tea, alcohol) were not detected in the nutritional analysis programme used or were consumed in very small amounts or not consumed at all, and previous research has reported that their absence had no effect on DII scores.³³ Despite these limitations, this is one of the few studies analysing the relationship between DII and FMS clinical symptoms. It is also, to the best of our knowledge, the first study to analyze the relationship between the DII and markers of inflammation.

Conclusions

In conclusion, we found that anti-inflammatory diets were associated with lower pain, disease severity and uric acid/creatinine ratio in patients with FM, suggesting that dietary inflammatory potential might play a role in FM symptoms severity in these patients. In this context, a good way to improve the symptoms of the disease may be a combination of different dietary approaches that are tailored to the metabolic changes. In addition, epidemiological studies with large samples and double-blind randomised controlled intervention studies which are involved both genders are needed to investigate the effect of dietary inflammatory potential on clinical symptoms and inflammatory markers in FM.

Supplementary material

Supplementary material is available at *Pain Medicine* online.

Funding

None declared.

Conflicts of interest: None declared.

References

- Wolfe F, Clauw DJ, Fitzcharles M-A, et al. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. *Arthritis Care Res (Hoboken)*. 2010;62(5):600-610.
- Galvez-Sánchez CM, Reyes del Paso GA. Diagnostic criteria for fibromyalgia: critical review and future perspectives. *J Clin Med*. 2020;9(4):1219.
- Fernandez-Feijoo F, Samartin-Veiga N, Carrillo-de-la-Peña MT. Quality of life in patients with fibromyalgia: contributions of disease symptoms, lifestyle and multi-medication. *Front Psychol*. 2022;13:924405.
- Sarzi-Putini P, Giorgi V, Marotto D, Atzeni F. Fibromyalgia: an update on clinical characteristics, aetiopathogenesis and treatment. *Nat Rev Rheumatol*. 2020;16(11):645-660.
- Queiroz LP. Worldwide epidemiology of fibromyalgia. *Curr Pain Headache Rep*. 2013;17(8):356-356.
- Cabo A, Cerdá G, Trillo J. Fibromyalgia: prevalence, epidemiologic profiles and economic costs. *Med Clin*. 2017;149(10):441-448.
- Walitt B, Nahin RL, Katz RS, Bergman MJ, Wolfe F. The prevalence and characteristics of fibromyalgia in the 2012 National Health Interview Survey. *PLoS One*. 2015;10(9):e0138024.
- Bellato E, Marini E, Castoldi F, et al. Fibromyalgia syndrome: etiology, pathogenesis, diagnosis, and treatment. *Pain Res Treat*. 2012;2012:426130.
- Üçeyler N, Hauser W, Sommer C. Systematic review with meta-analysis: cytokines in fibromyalgia syndrome. *BMC Musculoskel Disord*. 2011;12:245.
- Wallace DJ, Gavin IM, Karpenko O, Barkhordar F, Gillis BS. Cytokine and chemokine profiles in fibromyalgia, rheumatoid arthritis and systemic lupus erythematosus: a potentially useful tool in differential diagnosis. *Rheumatol Int*. 2015;35(6):991-996.
- O'Mahony LF, Srivastava A, Mehta P, Ciurtin C. Is fibromyalgia associated with a unique cytokine profile? A systematic review and meta-analysis. *Rheumatology*. 2021;60(6):2602-2614.
- Üçeyler N, Valenza R, Stock M, Schedel R, Sprotte G, Sommer C. Reduced levels of antiinflammatory cytokines in patients with chronic widespread pain. *Arthritis Rheum Offic J Am Coll Rheumatol*. 2006;54(8):2656-2664.
- She D, Xu W, Liu J, et al. Serum uric acid to creatinine ratio and risk of metabolic syndrome in patients with overweight/obesity. *Diabetes Metab Syndr Obes*. 2023;16:3007-3017.
- Yazdi F, Baghaei MH, Baniasad A, Naghibzadeh-Tahami A, Najafipour H, Gozashti MH. Investigating the relationship between serum uric acid to high-density lipoprotein ratio and metabolic syndrome. *Endocrinol Diabetes Metab*. 2022;5(1):e00311.
- Angkananard T, Anothaisintawee T, McEvoy M, Attia J, Thakkinstian A. Neutrophil lymphocyte ratio and cardiovascular disease risk: a systematic review and meta-analysis. *BioMed Res Int*. 2018;2018(1):1.
- Feinberg T, Sambamoorthi U, Lilly C, Innes KK. Potential mediators between fibromyalgia and C-reactive protein: Results from a large US community survey. *BMC Musculoskel Disord*. 2017;18(1):294-212.
- Aktürk S, Büyükcavı R. Evaluation of blood neutrophil-lymphocyte ratio and platelet distribution width as inflammatory markers in patients with fibromyalgia. *Clin Rheumatol*. 2017;36(8):1885-1889.
- Zetterman T, Markkula R, Kalso E. Elevated highly sensitive C-reactive protein in fibromyalgia associates with symptom severity. *Rheumatol Adv Pract*. 2022;6(2):rkac053.
- Beiner E, Brenner Miguel S, Friederich H-C, Tesarz J; PerPAIN Consortium. Elevated high sensitive C-reactive protein in fibromyalgia. *Front Psychiatry*. 2023;14:1237518.
- Khanna D, Khanna S, Khanna P, Kahar P, Patel BM. Obesity: A chronic low-grade inflammation and its markers. *Cureus*. 2022;14(2):e22711.
- Álvarez-Nemegyei J, Pacheco-Pantoja EL, Olán-Centeno LJ, Angulo-Ramírez A, Rodríguez-Magaña FE, Aranda-Muiña JF. Association between fibromyalgia syndrome clinical severity and

- body composition. A principal component analysis. *Reumatol Clin (Engl Ed)*. 2022;18(9):538-545.
22. Rezaei M, Tajary Z, Esmaily Z, et al. Association between the empirical dietary inflammatory index and musculoskeletal pain in community-dwelling older adults: A cross-sectional study. *Osong Public Health Res Perspect*. 2023;14(1):51-58.
 23. Shin D, Hong SJ, Lee KW, Shivappa N, Hebert JR, Kim K. Pro-inflammatory diet associated with low back pain in adults aged 50 and older. *Appl Nurs Res*. 2022;66:151589.
 24. Correa-Rodríguez M, Casas-Barragán A, González-Jiménez E, Schmidt-RioValle J, Molina F, Aguilar-Ferrández ME. Dietary inflammatory index scores are associated with pressure pain hypersensitivity in women with fibromyalgia. *Pain Med*. 2020;21(3):586-594.
 25. Strath LJ, Brooks MS, Sorge RE, Judd SE. Relationship between diet and relative risk of pain in a cross-sectional analysis of the REGARDS longitudinal study. *Pain Manag*. 2022;12(2):168-179.
 26. Shi Y, Zhang X, Feng Y. Association between the dietary inflammatory index and pain in US adults from NHANES. *Nutr Neurosci*. 2024;27(5):460-469.
 27. Strath LJ, Sims AM, Overstreet DS, et al. Dietary Inflammatory Index (DII) is associated with movement-evoked pain severity in adults with chronic low back pain: sociodemographic differences. *J Pain*. 2022;23(8):1437-1447.
 28. Henriksen M, Lund H, Christensen R, et al. Relationships between the fibromyalgia impact questionnaire, tender point count, and muscle strength in female patients with fibromyalgia: a cohort study. *Arthritis Rheum*. 2009;61(6):732-739.
 29. Ediz L, Hiz O, Toprak M, Tekeoglu I, Ercan S. The validity and reliability of the Turkish version of the Revised Fibromyalgia Impact Questionnaire. *Clin Rheumatol*. 2011;30(3):339-346.
 30. World Health Organization. *Waist circumference and waist-hip ratio*. Report of a WHO Expert Consultation. 2008. Accessed July 21, 2023. <https://www.who.int/publications/i/item/9789241501491>
 31. World Health Organization. Obesity: preventing and managing the global epidemic: report of a WHO consultation. 2000. Accessed July 21, 2023. <https://iris.who.int/handle/10665/42330>
 32. Castell GS, Serra-Majem L, Ribas-Barba L. What and how much do we eat? 24-hour dietary recall method. *Nutricion Hospitalaria*. 2015;31(3):46-48.
 33. Shivappa N, Hébert JR, Rietzschel ER, et al. Associations between dietary inflammatory index and inflammatory markers in the Asklepios Study. *Br J Nutr*. 2015;113(4):665-671.
 34. Hodge AM, Bassett JK, Shivappa N, et al. Dietary inflammatory index, Mediterranean diet score, and lung cancer: a prospective study. *Cancer Causes Control*. 2016;27(7):907-917.
 35. Wirth MD, Burch J, Shivappa N, et al. Association of a dietary inflammatory index with inflammatory indices and metabolic syndrome among police officers. *J Occup Environ Med*. 2014;56(9):986-989.
 36. Al-Nimer MSM, Mohammad TAM. Correlation of hematological indices and ratios derived from them with FIQR scores in fibromyalgia. *Pak J Med Sci*. 2018;34(5):1219-1224.
 37. Moriyama K. The association between the serum uric acid to creatinine ratio and metabolic syndrome, liver function, and alcohol intake in healthy Japanese subjects. *Metab Syndr Relat Disord*. 2019;17(7):380-387.
 38. Nieminen LK, Pyysalo LM, Kankaanpää MJ. Prognostic factors for pain chronicity in low back pain: a systematic review. *Pain Rep*. 2021;6(1):e919.
 39. Ruschak I, Montesó-Curto P, Rosselló L, Aguilar Martín C, Sánchez-Montesó L, Toussaint L, eds. Fibromyalgia syndrome pain in men and women: a scoping review. *Healthcare*. 2023;11(2):223.
 40. Yoo JJ, Cho NH, Lim SH, Kim HA. Relationships between body mass index, fat mass, muscle mass, and musculoskeletal pain in community residents. *Arthritis Rheumatol*. 2014;66(12):3511-3520.
 41. Walsh TP, Arnold JB, Evans AM, Yaxley A, Damarell RA, Shanahan EM. The association between body fat and musculoskeletal pain: a systematic review and meta-analysis. *BMC Musculoskelet Disord*. 2018;19(1):233-213.
 42. Kaushik AS, Strath LJ, Sorge RE. Dietary interventions for treatment of chronic pain: Oxidative stress and inflammation. *Pain Ther*. 2020;9(2):487-498.
 43. Badaeva A, Danilov A, Kosareva A, et al. Neuronutritional approach to fibromyalgia management: a narrative review. *Pain Ther*. 2024;13(5):1047-1061.
 44. Köroğlu Ö, Adıgüzel KT. The role of nutrition in patients with fibromyalgia: is there an impact on disease parameters? *Gulhane Med J*. 2020;62(3):186-192.
 45. Silva AR, Bernardo A, Costa J, et al. Dietary interventions in fibromyalgia: A systematic review. *Ann Med*. 2019;51(suppl 1):2-14.
 46. Nadal-Nicolás Y, Miralles-Amorós L, Martínez-Olcina M, Sánchez-Ortega M, Mora J, Martínez-Rodríguez A. Vegetarian and vegan diet in fibromyalgia: a systematic review. *Int J Environ Res Public Health*. 2021;18(9):4955.
 47. Holton K. The role of diet in the treatment of fibromyalgia. *Pain Manag*. 2016;6(4):317-320.
 48. Kaartinen K, Lammi K, Hypen M, Nenonen M, Hanninen O, Rauma AL. Vegan diet alleviates fibromyalgia symptoms. *Scand J Rheumatol*. 2000;29(5):308-313.
 49. Donaldson MS, Speight N, Loomis S. Fibromyalgia syndrome improved using a mostly raw vegetarian diet: an observational study. *BMC Complement Altern Med*. 2001;1:7-8.
 50. Casini I, Ladisa V, Clemente L, et al. A personalized Mediterranean diet improves pain and quality of life in patients with fibromyalgia. *Pain Ther*. 2024;13(3):609-620.
 51. Azad KA, Alam MN, Haq SA, et al. Vegetarian diet in the treatment of fibromyalgia. *Bangladesh Med Res Counc Bull*. 2000;26(2):41-47.
 52. Ma Y, Griffith JA, Chasan-Taber L, et al. Association between dietary fiber and serum C-reactive protein. *Am J Clin Nutr*. 2006;83(4):760-766.
 53. Yadav UC, Kalariya NM, Srivastava SK, Ramana KV. Protective role of benfotiamine, a fat-soluble vitamin B1 analogue, in lipopolysaccharide-induced cytotoxic signals in murine macrophages. *Free Radic Biol Med*. 2010;48(10):1423-1434.
 54. Wu X, Schauss AG. Mitigation of inflammation with foods. *J Agric Food Chem*. 2012;60(27):6703-6717.
 55. Pagliai G, Giangrandi I, Dinu M, Sofi F, Colombini B. Nutritional interventions in the management of fibromyalgia syndrome. *Nutrients*. 2020;12(9):2525.
 56. Tao J, Shen X, Li J, et al. Serum uric acid to creatinine ratio and metabolic syndrome in postmenopausal Chinese women. *Medicine (Baltimore)*. 2020;99(17):e19959.
 57. Zhou J, Kim JE, Armstrong CL, Chen N, Campbell WW. Higher-protein diets improve indexes of sleep in energy-restricted overweight and obese adults: Results from 2 randomized controlled trials. *Am J Clin Nutr*. 2016;103(3):766-774.
 58. Kurtkulagi O, Tel BMA, Kahveci G, et al. Hashimoto's thyroiditis is associated with elevated serum uric acid to high density lipoprotein-cholesterol ratio. *Rom J Intern Med*. 2021;59(4):403-408.
 59. Rodríguez-Rodríguez E, López-Sobaler AM, Ortega RM, Delgado-Losada ML, López-Parra AM, Aparicio A. Association between neutrophil-to-lymphocyte ratio with abdominal obesity and healthy eating index in a representative older Spanish population. *Nutrients*. 2020;12(3):855.
 60. Millar SR, Navarro P, Harrington JM, et al. Dietary score associations with markers of chronic low-grade inflammation: a cross-sectional comparative analysis of a middle-to older-aged population. *Eur J Nutr*. 2022;61(7):3377-3390.

© The Author(s) 2024. Published by Oxford University Press on behalf of the American Academy of Pain Medicine.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs licence (<https://creativecommons.org/licenses/by-nc-nd/4.0/>), which permits non-commercial reproduction and distribution of the work, in any medium, provided the original work is not altered or transformed in any way, and that the work is properly cited. For commercial re-use, please contact reprints@oup.com for reprints and translation rights for reprints. All other permissions can be obtained through our RightsLink service via the Permissions link on the article page on our site—for further information please contact journals.permissions@oup.com.

Pain Medicine, 2025, 26, 131–139

<https://doi.org/10.1093/pm/pnae118>

Original Research Article