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Dietary Inflammatory Index Scores Are Associated with Pressure Pain Hypersensitivity in Women with Fibromyalgia

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Abstract

Objective. Pain hypersensitivity has been described as one of the most disabling symptoms of fibromyalgia syndrome (FMS). Here we analyzed the relationship between an anti-inflammatory diet profile and the pressure pain thresholds (PPTs) of tender point sites and other fibromyalgia-related symptoms in patients with FMS. **Methods.** This cross-sectional study included 95 women diagnosed with FMS and 98 menopause-status matched controls. The Dietary Inflammatory Index (DII) was calculated by conducting a 24-hour diet recall interview. The PPTs of tender point sites and self-reported global pain levels were evaluated by algometry and the visual analog scale, respectively. Disease severity, fatigue, sleep anxiety, and central sensitization were also evaluated. **Results.** Linear regression analysis revealed that the PPTs of tender point sites including the occiput ($\beta = 0.234$, 95% confidence interval [CI] = 0.016–0.452, $P = 0.036$), trapezius ($\beta = 0.299$, 95% CI = 0.083–0.515, $P = 0.007$), zygapophyseal joint ($\beta = 0.291$, 95% CI = 0.022–0.559, $P = 0.035$), second rib ($\beta = 0.204$, 95% CI = 0.060–0.348, $P = 0.006$), gluteus ($\beta = 0.591$, 95% CI = 0.110–1.072, $P = 0.017$), greater trochanter ($\beta = 0.379$, 95% CI = 0.016–0.742, $P = 0.041$), and knee ($\beta = 0.482$, 95% CI = 0.117–0.850, $P = 0.011$) were associated with DII score after adjustments for the age, menopausal status, and global energy levels reported by the patients with FMS. No significant differences were found for the cases or controls between the DII score and the remaining clinical symptoms. Analyses of covariance showed that the PPTs of the aforementioned tender point sites were also significantly associated ($P < 0.05$) with the DII score quartiles in patients with FMS, but no significant differences were found between these quartiles and the other clinical symptoms. **Conclusions.** A pro-inflammatory diet was associated with pain hypersensitivity in patients with FMS.

Key Words: Dietary Inflammatory Index; Pressure Pain Threshold; Pressure Algometry; Fibromyalgia

Introduction

Fibromyalgia syndrome (FMS) is a complex, chronic, and generalized pain condition characterized by several symptoms including fatigue, sleep disturbance, anxiety, and impaired cognition [1]. The constellation of comorbidities linked to FMS can lead to debilitation in the performance of daily life activities among patients affected by it [2]. Therefore, FMS is considered a public health concern and is associated with a substantial economic cost [3]. The prevalence of FMS is 2.7% worldwide, and women are more likely to have the disease than men [4].

The underlying mechanism of FMS remains unknown, but the available data suggest that a genetic predisposition and environmental factors may promote its development [5]. Recent studies have highlighted a role for the immune system, and especially inflammatory cytokines, in the development and maintenance of this disease [6,7]. In fact, elevated levels of pro-inflammatory cytokines

have been observed in patients with FMS [8–10]. Interestingly, Wallace et al. found that interleukin (IL)-1, IL-6, and IL-8 are dysregulated in FMS and that, consequently, strategies for targeting inflammatory cytokines may be of special interest in its management [11]. Indeed, it has been suggested that an imbalance in pro- and anti-inflammatory cytokines might be linked to the diverse clinical processes involved in this disease, such as pain, fatigue, and sleep loss [12].

Recent guidelines suggest that a multifaceted treatment approach including both pharmacological and nonpharmacological interventions is the most effective way to ameliorate the symptoms of FMS [13–16]. Among the available nonpharmacological options, nutritional interventions appear to be a promising strategy for these patients [13,15–19]. A recent review reported that specific dietary modifications may lead to clinical improvements in the symptoms of FMS [16], and similarly, an association between dietary habits and psychosocial outcomes has been revealed in women with FMS [13]. There is also limited and contradictory evidence that such dietary interventions may be associated with the clinical symptoms of FMS, including disease severity, fatigue, sleep, and anxiety [18–20]. Kaartinen et al. showed that a vegan diet rich in lactobacteria reduced pain levels and improved sleep quality among patients with FMS [19], and Donaldson et al. noted an improvement in disease severity after patients followed a vegetarian diet plan [18]. However, Azad et al. were unable to link vegetarian diets to improvements in fatigue, insomnia, nonrestorative sleep, or pain in relation to FMS [20]. Of note, the association between diet and pain hypersensitivity—the main symptom of FMS—has never been investigated. Therefore, more research is still required to explore the relationships between diet and fibromyalgia-related symptoms.

The Dietary Inflammatory Index (DII) is a validated dietary index that was developed to predict patient inflammation levels [21]. DII scores are associated with several inflammatory markers, including C-reactive protein, IL-1, IL-2, IL-6, homocysteine, and fibrinogen [22–25]. Given that inflammatory cytokines may be involved in the mechanism underlying FMS and that nutritional interventions seem to improve the symptomology of the disease, we hypothesized that an anti-inflammatory diet would improve pain hypersensitivity and other symptoms associated with FMS. Anti-inflammatory diets are characterized by the consumption of an abundance of vegetables and fruits, a moderate intake of low-fat protein sources such as chicken and fish, as well as monounsaturated fats including olive oil and nuts, and a restricted consumption of bread and grains, especially refined grain products [26,27]. In this context, we examined whether an anti-inflammatory diet is associated with any changes in the DII score, pressure pain thresholds (PPTs) of tender point sites, or other FMS-related symptoms including self-reported global pain levels, disease severity, fatigue, sleep, and anxiety in a population of women with FMS.

Methods

Participants

Between January 2018 and July 2018, 95 women diagnosed with FMS and 98 menopause-status matched healthy female controls, all aged between 30 and 70 years, were enrolled in this case–control study. Menopausal status was matched because the menopausal transition is associated with an increased risk of anxiety [28] and midlife women approaching and passing through menopause are more likely to suffer sleep disturbances [29]. We wrote to the two fibromyalgia associations in Spain (AGRAFIM and AFIXA), which agreed to help us to identify, approach, and recruit women with FMS to participate in this study. The controls were volunteers recruited from among the friends, relatives, and colleagues of the patients or from the Faculty of Health Sciences at the University of Granada.

The criteria for inclusion of patients with FMS in this study were 1) a diagnosis of FMS from a rheumatology specialist; 2) the presence of symptoms consistent with the 1990 American College of Rheumatology criteria for FMS; 3) the absence of any acute or terminal illnesses. The exclusion criteria for entire sample cohort were 1) a history of drug or alcohol abuse; 2) women who were pregnant or breastfeeding; 3) use of vasoactive drugs, contraceptives, anticoagulants, or antithrombotic therapies; 4) participants with an active tumor. A total of 225 individuals were approached to participate in the study and were screened for eligibility; after applying the inclusion and exclusion criteria, a total of 193 women were included.

The study was explained to each person, and any questions they had were answered. We then obtained their informed consent to participation in this research, which was performed in strict compliance with the international code of medical ethics established by the World Medical Association and the Declaration of Helsinki. The study was also approved by the Ethics Committee at the University of Granada. Each participant completed a structured questionnaire that included items about their medical history and menopausal status. There were no financial incentives for participation in this study, but every participant received information promoting healthy eating habits.

Visual Analog Scale for Pain

The patients' global level of pain was assessed using the visual analog scale (VAS) pain score (0–100 mm, with higher scores indicating more pain). The VAS has been shown to be an important instrument in evaluating pain

levels and is sensitive and specific in the assessment of pain among patients with FMS [30].

Fibromyalgia Impact Questionnaire

The Spanish version of the Fibromyalgia Impact Questionnaire (FIQ-R) was used to assess the effect of FMS symptoms on the physical and mental health of patients. This self-reported questionnaire comprises 21 items that assess physical impairment, the number of days feeling good, amount of work missed, ability to work, and levels of pain, fatigue, rest, stiffness, anxiety, and depressive symptoms. The total score is the sum of all the subscales (0 to 100 points), and higher scores indicate a more negative impact [31].

Multidimensional Fatigue Inventory

The Multidimensional Fatigue Inventory (MFI) was used to evaluate the severity of fatigue among patients with FMS [32]. This questionnaire contains five subscales: general fatigue, physical fatigue, mental fatigue, reduced activity, and reduced motivation. Each subscale includes four questions scored from 1 to 5 points, with higher scores indicating a higher degree of fatigue. The test–retest analysis of reliability for the MFI showed excellent correlation between the domains, ranging from 0.64 to 0.91 [33].

Pittsburgh Sleep Quality Index

The Pittsburgh Sleep Quality Index (PSQI) comprises 24 items and was used to evaluate the participants' quality of sleep; they responded to 19 of these items, and a person living in the same home (or hospital room) responded to the remaining five. The PSQI evaluates seven subdimensions: subjective quality of sleep, sleep latency, sleep duration, sleep efficiency, sleep disturbances, sleep medication, and diurnal dysfunction. Each dimension is scored from 0 points (no problem) to 3 points (serious problem); the total score ranges from 0 to 21 points, and higher scores represent poorer sleep quality [34]. A previous study showed that the PSQI has good reliability and a Cronbach alpha of 0.805 [35].

Beck Anxiety Inventory

The Beck Anxiety Inventory (BAI) was used to evaluate the psychological aspects and common symptoms of anxiety [36]; this questionnaire contains 21 items that assess the severity of patient anxiety, with a score range from 0 points (no anxiety) to 3 points (high levels of anxiety). The total score ranges from 0 to 63 points, and higher scores indicate a higher degree of anxiety [36]. The test–retest reliability analysis of the BAI showed that it has excellent internal consistency, with a Cronbach alpha of 0.91 [37].

Central Sensitization Inventory

The Spanish version of the Central Sensitization Inventory (CSI) was used to assess the frequency of health-related symptoms associated with central sensitivity syndromes [38]. The CSI is a 25-item survey, and individuals were asked to rate their answer to each question on a five-point Likert scale, with 0 meaning "never" and 4 meaning "always." The CSI score is obtained by summing the responses, with a total possible score of 100; higher CSI scores represent greater self-reported symptomology. The test–retest reliability analysis of this questionnaire showed a correlation of 0.91 [38].

Pressure Pain Threshold

Pressure algometry is a quantitative method commonly used in clinical practice to assess tenderness [39]. The pressure pain threshold (PPT) is defined as the minimum amount of pressure required for a feeling of pressure to first change to one of pain [40]. A digital pressure algometer was used to bilaterally measure the PPT at the 18 tender points defined by the American College of Rheumatology for an FMS diagnosis: the occiput, trapezius, zygapophyseal joint, supraspinatus, second rib, epicondyle, gluteus, greater trochanter, and knee. The device comprises a 1-cm^2 rubber disk attached to a strain gauge, which displays values in kPa (Storz Medical AG, Tagerwilen, Thurgau, Switzerland). The PPTs of the participants were determined by gradually increasing the pressure provided by the algometer (at a rate of 1 kg/s) until the sensation reported by the individual first became painful (participants were instructed to say "stop" at this point). The mean of three trials was calculated and used for the main analysis, and a 30-second resting period was allowed between each recording. The same-day [39] and four-day [41] reliability of pressure algometry is high (intraclass correlation coefficients = 0.91 and 0.94 to 0.97, respectively).

Dietary Assessment

Dietary habits were assessed using a face-to-face interview with trained investigators, who asked the participants to recall all the food they had consumed in the preceding 24 hours, including nutritional supplements and beverages. When necessary, standard household measurements and pictorial food models were used to define the quantities consumed. These food records were subsequently studied using nutrient analysis software (Nutriber 1.1.5).

The Dietary Inflammatory Index

The Dietary Inflammatory Index (DII) is based on the literature published up until 2010 linking diet to inflammatory markers [21]. To calculate the DII score for our study participants, we first linked their dietary data to the regionally representative world database to obtain a robust mean and standard deviation estimate for each

parameter. These then became the multipliers for expressing each individual's exposure relative to the "standard global mean" as a *z*-score (by subtracting the standard global mean from the amount reported by each participant and dividing this value by the standard deviation). To minimize the effect of "right skewing," this value was then converted to a centered percentile score by multiplying it by the respective food parameter effect score derived from the original literature review [21] for each food parameter and each individual to obtain food parameter–specific DII scores; these were then summed to obtain each participant's global DII score. Overall, 23 food parameters including beta carotene, carbohydrates, cholesterol, energy, fiber, folate, iron, magnesium, monounsaturated fatty acid, niacin, polyunsaturated fatty acid, protein, riboflavin, saturated fatty acid, thiamine, total fat, vitamin A, vitamin B12, vitamin B6, vitamin C, vitamin D, vitamin E, and zinc were used to calculate the global DII scores. Lower scores represent more anti-inflammatory dietary profiles and higher scores more pro-inflammatory profiles.

Statistical Analysis

The data were analyzed with SPSS, version 22.0 (IBM Corporation, Armonk, NY, USA). The Kolmogorov-Smirnov test was used to verify the normality of the data distribution, and data were expressed as mean ± SD. To compare two groups, Mann-Whitney *U* tests were used; Student *t* tests were employed for continuous data, and χ^2 tests for categorical data. The DII scores were analyzed both as a continuous and a categorized variable based on their quartiles. Linear regression analyses were used to determine the association between continuous DII scores, the PPTs of tender point sites, and clinical symptoms adjusted for the following confounding factors: age, menopausal status, and overall energy levels. The results are reported as the percent change (β) with 95% confidence intervals (CIs). In the categorized DII score analysis, generalized linear models were developed by including the mean value of each DII quartile, the PPTs of tender point sites, and clinical symptoms after adjustment for the same aforementioned confounding factors. Comparisons of nutrient intake across the DII quartiles were analyzed by one-way ANOVA. Probabilities exceeding 95% (alpha *P* values < 0.05) were used as the threshold cutoff for statistical significance.

Results

The clinical symptoms and PPTs of tender point sites recorded for the 95 cases and 98 controls are summarized in Table 1. The mean DII score was 0.28 ± 0.90 units and ranged from −2.57 (the maximum anti-inflammatory profile) to 1.95 (the maximum pro-inflammatory profile) in the FMS group. No significant differences were observed between the cases and controls for DII score ($P = 0.475$). Of note, FMS patients weighed more than the control group ($P = 0.005$); 76.2% of the overall cohort were postmenopausal women, and 23.8% were premenopausal. As expected, patients with FMS had significantly higher levels of global pain and clinical symptoms including fatigue, sleep, anxiety, and central sensitization than the controls ($P < 0.001$). The mean FIQ score was 72.09 ± 16.26 in women with FMS, and all the PPTs of tender point sites were significantly lower in these patients than in the controls (<0.001).

Table 1. Clinical symptoms and pressure pain thresholds of most tender point sites among cases (women with fibromyalgia) and controls (healthy women)

	Cases (N = 95)	Control (N = 98)	*P* Value
Age, y	55.76±7.96	56.08±10.33	0.808
Height, cm	158.76±5.91	158.72±5.91	0.969
Weight, kg	71.94±13.32	66.75±11, 84	0.005
FIQ-R	72.09±16.26	–	–
VAS pain, cm	7.38±1.80	1.40±2.22	<0.001
MFI	79.46±9.89	43.26±14.06	<0.001
PSQI	15.35±3.77	6.07±3.83	<0.001
BAI	32.53±9.88	9.70±9.25	<0.001
CSI	68.43±11.91	24.47±11.18	<0.001
PPT			
Occiput	0.87±0.68	3.33±1.35	<0.001
Trapezius	0.97±0.66	3.41±1.54	<0.001
Zygapophyseal joint	1.03±0.78	3.30±2.01	<0.001
Supraspinatus	1.25±0.82	3.94±2.04	<0.001
Second rib	0.85±0.44	2.64±1.24	<0.001
Epicondyle	0.95±0.58	3.51±1.48	<0.001
Gluteus	1.87±1.39	6.49±2.48	<0.001
Greater trochanter	2.05±1.09	6.05±2.49	<0.001
Knee	1.71±1.14	5.94±2.42	<0.001
DII	0.32±0.89	0.23±0.91	0.475

Variables are shown as mean ± SD.

DII = Dietary Inflammatory Index; BAI = Beck Anxiety Inventory; CSI = Central Sensitization Inventory; FIQ-R = Revised Fibromyalgia Impact Questionnaire; MFI = Multidimensional Fatigue Inventory; PPT = pressure pain threshold; PSQI = Pittsburgh Sleep Quality Index; VAS = visual analog scale.

*Significance level $P < 0.05$.

The β estimates and 95% CIs for clinical symptoms and the PPTs of tender point sites, as well as the DII scores for cases and controls, are presented in Table 2. Linear regression analysis revealed that the occiput ($\beta = 0.350$, 95% confidence interval [CI] = 0.089–0.611, $P = 0.009$), trapezius ($\beta = 0.397$, 95% CI = 0.134–0.660, $P = 0.004$), zygapophyseal joint ($\beta = 0.254$, 95% CI = 0.039–0.469, $P = 0.0021$), second rib ($\beta = 0.503$, 95% CI = 0.117–0.889, $P = 0.011$), epicondyle ($\beta = 0.315$, 95% CI = 0.010–0.621, $P = 0.043$), gluteus ($\beta = 0.147$, 95% CI = 0.029–0.265, $P = 0.015$), greater trochanter ($\beta = 0.193$, 95% CI = 0.036–0.350, $P = 0.017$), and knee ($\beta = 0.217$, 95% CI = 0.067–0.366, $P = 0.005$) PPTs were significantly associated with the DII after adjusting for age, menopausal status, and overall energy in patients with FMS but not in controls. No significant differences were found between the DII

Table 2. Beta estimates and confidence intervals for the association between DII and clinical symptoms and pressure pain thresholds of most tender point sites among cases (women with fibromyalgia) and controls (healthy women)

	DII (Continuous)					
	Cases			Controls		
	β	95% CI	*P* Value	*β*	95% CI	*P* Value
VAS pain	0.012	−0.096 to 0.121	0.823	0.048	−0.071 to 0.166	0.422
FIQ-R	0.004	−0.007 to 0.016	0.470	–	–	–
MFI	−0.001	−0.020 to 0.017	0.870	0.013	−0.002 to 0.029	0.089
PSQI	0.035	−0.016 to 0.086	0.177	0.002	−0.064 to 0.068	0.949
BAI	−0.011	−0.029 to 0.007	0.220	0.017	−0.006 to 0.040	0.152
CSI	−0.006	−0.022 to 0.011	0.489	0.018	−0.003 to 0.038	0.088
PPT						
Occiput	0.350	0.089 to 0.611	0.009	−0.086	−0.259 to 0.088	0.326
Trapezius	0.397	0.134 to 0.660	0.004	−0.083	−0.227 to 0.060	0.250
Zygapophyseal joint	0.254	0.039 to 0.469	0.021	−0.075	−0.193 to 0.042	0.204
Supraspinatus	0.208	−0.001 to 0.417	0.051	−0.113	−0.234 to 0.008	0.066
Second rib	0.503	0.117 to 0.889	0.011	−0.118	−0.301 to 0.065	0.202
Epicondyle	0.315	0.010 to 0.621	0.043	−0.134	−0.289 to 0.021	0.089
Gluteus	0.147	0.029 to 0.265	0.015	−0.074	−0.173 to 0.026	0.143
Greater trochanter	0.193	0.036 to 0.350	0.017	−0.062	−0.158 to 0.035	0.205
Knee	0.217	0.067 to 0.366	0.005	−0.089	−0.193 to 0.015	0.090

Beta represents the regression coefficient. Adjusted for age, menopause status and total energy.

BAI = Beck Anxiety Inventory; CI = confidence interval; CSI = Central Sensitization Inventory; DII = Dietary Inflammatory Index; FIQ-R = Revised Fibromyalgia Impact Questionnaire; MFI = Multidimensional Fatigue Inventory; PPT = pressure pain threshold; PSQI = Pittsburgh Sleep Quality Index; VAS = visual analog scale.

scores and the remaining clinical symptoms for cases or controls.

The DII scores were divided into quartiles (Qs) according to the following cutoff points: Q1: −2.57 to ≤−0.19; Q2: >−0.19 to ≤0.41; Q3: >0.41 to ≤1.01; Q4: >1.01 to 1.95. Table 3 shows the clinical symptoms and PPTs of tender point sites according to these quartiles in patients with FMS. After adjusting for confounding factors, the occiput ($P = 0.015$), trapezius ($P = 0.005$), zygapophyseal joint ($P = 0.012$), second rib ($P = 0.009$), greater trochanter ($P = 0.017$), and knee ($P = 0.011$) PPTs, but not the remaining clinical symptoms, were significantly associated with the DII score quartiles in patients with FMS. Table 4 shows macro- and micronutrient intakes in patients with FMS according to the DII quartiles. Beta carotene, energy, fiber, folate, iron, magnesium, niacin, polyunsaturated fatty acid, riboflavin, thiamine, vitamin B6, vitamin C, vitamin E, and zinc were found to be significantly higher in Q1 (the most anti-inflammatory quartile) in all cases ($P < 0.05$).

Discussion

This study examined, for the first time, the possible relationships between DII score and the PPTs of tender point sites and other fibromyalgia-related symptoms including self-reported global pain, disease severity, fatigue, sleep, and anxiety in a population of women with FMS. Although no significant differences in these factors were associated with an anti-inflammatory dietary profile, pro-inflammatory diets were significantly associated with lower PPTs for most tender point sites. These results support the hypothesis that diet-related inflammatory potential was associated with pain hypersensitivity in individuals with FMS.

Current evidence suggests that dietary interventions may be a good therapeutic approach to reduce FMS symptoms [15,16,18,19,42,43]. Interestingly, eating a mostly raw, vegan diet [18] or a strict low salt, uncooked vegan diet rich in lactobacteria [19] had beneficial effects on these symptoms. Similarly, relationships between dietary habits and psychosocial outcomes such as mental health, depression, and optimism were identified in a population of women with FMS [13]. However, most previous work has focused on restrictive diets, isolated nutrients, or supplements, and the association between dietary inflammatory potential and symptoms of FMS has never been investigated.

The available literature shows that sensory stimulation of healthy tissues in patients with FMS can result in pain hypersensitivity [44]. Here, we provide the first insights into the association between dietary inflammatory potential and PPTs—an accurate technique for assessing pain hypersensitivity in individuals with FMS [39]. In a similar context, patients with rheumatoid arthritis who followed a Mediterranean diet (well known for its anti-inflammatory properties) reported a reduction in pain levels [45]. Interestingly, and in agreement with our results, Tian et al. found evidence that tumor necrosis factor alpha, a widely recognized mediator in many cytokine-dependent inflammatory events, increases in

Table 3. Clinical symptoms and pressure pain thresholds among women with fibromyalgia according to quartiles of the DII

	Q1 (N = 20)		Q2 (N = 22)		Q3 (N = 23)		Q4 (N = 20)		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	*P* Value
VAS pain	7.20	1.64	7.91	1.57	7.48	2.10	7.40	1.14	0.355
FIQ-R	70.50	13.33	79.90	10.45	69.17	20.09	71.90	15.37	0.056
MFI	77.75	9.46	80.55	9.83	80.17	11.04	79.90	8.92	0.669
PSQI	15.40	3.41	16.89	2.37	15.00	3.59	15.32	4.51	0.311
BAI	29.70	10.45	34.50	9.59	33.96	9.64	33.60	9.53	0.166
CSI	67.55	7.71	69.45	13.89	70.61	12.54	69.25	9.65	0.592
PPT									
Occiput	1.18	0.79	0.94	0.75	0.72	0.44	0.57	0.37	0.015
Trapezius	1.37	0.84	0.97	0.65	0.83	0.41	0.73	0.45	0.005
Zygapophyseal joint	1.50	1.12	0.97	0.72	0.90	0.53	0.80	0.53	0.012
Supraspinatus	1.61	1.14	1.31	0.89	1.08	0.52	0.99	0.51	0.066
Second rib	1.09	0.49	0.87	0.52	0.80	0.37	0.67	0.25	0.009
Epicondyle	1.24	0.74	0.95	0.59	0.85	0.43	0.78	0.35	0.059
Gluteus	2.43	1.63	2.12	1.70	1.65	1.32	1.44	0.78	0.075
Greater trochanter	2.39	0.95	2.36	1.47	1.78	0.87	1.65	0.72	0.017
Knee	2.17	1.00	1.91	1.43	1.51	1.05	1.20	0.65	0.011

Adjusted for age, menopause status and total energy.

BAI = Beck Anxiety Inventory; CSI = Central Sensitization Inventory; DII = Dietary Inflammatory Index; FIQ-R = Revised Fibromyalgia Impact Questionnaire; MFI = Multidimensional Fatigue Inventory; PPT = pressure pain threshold; PSQI = Pittsburgh Sleep Quality Index; VAS = visual analog scale.

Table 4. Nutrient intake according to the quartiles of the DII in women with fibromyalgia

	Q1		Q2		Q3		Q4		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	*P* Value
DII score	−0.88	0.65	0.15	0.17	0.72	0.19	1.31	0.26	<0.001
Beta carotene, μg	4,481.44	3,041.69	2,280.25	2,744.13	1,746.97	2,021.98	801.30	815.51	<0.001
Carbohydrate, g	165.86	74.15	140.68	68.39	141.85	53.64	128.07	55.71	0.243
Cholesterol, mg	224.77	155.80	268.53	215.59	207.29	129.69	208.08	137.56	0.547
Energy, kcal	1,497.09	515.45	1,284.47	415.33	1,255.75	352.19	1,143.02	371.39	0.041
Fiber, g	27.54	14.19	17.11	9.44	13.16	5.23	10.05	4.57	<0.001
Folate, μg	357.99	238.73	188.59	70.93	150.99	56.62	106.94	47.70	<0.001
Iron, mg	15.17	6.77	11.04	4.88	8.26	2.57	7.03	2.40	<0.001
Magnesium, mg	435.64	183.54	280.33	168.62	257.84	108.41	220.58	94.11	<0.001
Mono-unsaturated fatty acid, g	23.30	10.21	21.84	14.74	21.50	10.71	16.92	1.45	0.285
Niacin, mg	32.19	12.92	27.50	10.87	24.76	13.22	21.82	9.41	0.025
Polyunsaturated fatty acid, g	13.28	7.71	7.87	4.57	8.11	5.27	5.13	3.26	<0.001
Protein, g	79.74	34.11	67.36	23.49	60.60	28.91	63.00	47.01	0.248
Riboflavin, mg	1.51	0.42	1.47	0.95	1.25	0.49	1.06	0.32	0.042
Saturated fatty acid, g	14.83	8.08	15.03	9.98	15.30	7.00	15.46	6.71	0.993
Thiamine, mg	1.43	0.72	1.06	0.42	0.88	0.39	0.72	0.34	<0.001
Total fat, g	57.08	22.65	50.26	27.99	49.57	20.66	42.07	18.75	0.179
Vitamin A, RE	173.81	168.89	178.66	175.02	160.91	113.49	211.05	336.80	0.878
Vitamin B12, μg	3.89	2.62	4.93	7.12	2.83	1.97	2.29	1.66	0.126
Vitamin B6, mg	1.97	0.87	1.49	0.76	1.40	0.59	0.94	0.37	<0.001
Vitamin C, mg	183.90	104.28	127.88	59.54	104.46	53.82	62.72	52.32	<0.001
Vitamin D, μg	3.22	4.80	3.56	4.87	2.11	2.93	0.94	1.58	0.091
Vitamin E, mg	7.73	3.92	5.74	4.32	2.33	1.12	1.79	1.35	<0.001
Zinc, mg	9.10	5.38	7.01	3.31	6.43	2.05	5.74	2.20	0.011

Comparisons of nutrient intake across the quartiles of the DII were analyzed using a one-way analysis of variance.

DII = Dietary Inflammatory Index.

mice fed high-fat diets, resulting in fibromyalgia-like pain behaviors [46]. The relationships between anti-inflammatory diets and decreased tender point site PPTs extends the existing evidence that systemic inflammation lowers PPTs [47]. Thus, our findings suggest that an anti-inflammatory diet might contribute to changes in pain perception in patients with FMS, reducing their pain hypersensitivity.

The mechanisms by which pro-inflammatory diets might decrease PPTs in individuals with FMS remain to be elucidated. Nonetheless, we hypothesize that anti-inflammatory diets may reduce the levels of the pro-

inflammatory cytokines commonly elevated in these patients [8–10], thus reducing their pain hypersensitivity. The same association was not observed in healthy women, which suggests that anti-inflammatory diets only affect pain perception in this way in situations where the individual's inflammatory state is already elevated. The available literature regarding the relationship between diet and other clinical symptoms of FMS is controversial [18–20]. Our results indicate that DII scores were not associated with self-assessed levels of global pain, disease severity, fatigue, sleep, anxiety, or central sensitization as assessed using validated questionnaires. However, estimating FMS symptoms in this way is inherently limited because it is based on subjective patient-reported outcomes. Longitudinal studies will be required to better understand how the inflammatory potential of diets influences pressure pain hypersensitivity in patients with FMS.

In contrast to these findings, a nonrandomized controlled study evaluating the effect of a strict low-salt, uncooked vegan diet rich in lactobacteria on 18 patients with FMS reported that VAS-assessed pain levels and sleep quality improved among patients after a three-month intervention period [19]. Moreover, Donaldson et al. showed that the FIQ but not body pain significantly improved in 30 patients with FMS after a following vegetarian diet plan [18]. On the other hand, after assessing fatigue, insomnia, nonrestorative sleep, and VAS-assessed pain levels, Azad et al. concluded that an exclusively vegetarian diet is a poor option for the treatment of FMS [20]. These contradictory results may be explained by the differences in sample sizes, population characteristics, and methodology used in the assessment of FMS symptoms and dietary intakes in these studies. Given the currently limited evidence and the fact that no previous research has explored the association of these FMS outcomes with DII scores, more research will still be needed to validate our preliminary findings and to elucidate the relationship between dietary intake and objective measures of the clinical symptoms of FMS.

Finally, it is important to note that this study also has potential limitations. First, its cross-sectional design means that no causal conclusions can be drawn. Longitudinal studies are required to analyze the effect of the DII scores and to evaluate the inclusion of anti-inflammatory diet recommendations in the guidelines for clinical management of FMS. Second, although 24-hour diet recall is a reliable method to collect a variety of detailed information about the food individuals consume over a specific period, this tool has the inherent limitation that it may not accurately reflect the interviewee's normal diet at an individual level [48]. To minimize the 24-hour recall bias in this study, the recall was interviewer-driven, it was administered by trained investigators, and standard household measures and pictorial food models were used to improve the accuracy of the food descriptions and quantities. Another limitation was that this study was conducted exclusively in a cohort of women, and therefore further research should also be carried out in men. Furthermore, because the controls included friends and relatives of the patients, they might have had similar dietary patterns to the patient group. Lastly, the DII score was calculated based on only 23 of the 45 food parameters it originally included. However, the missing components (eugenol, flavanols, flavones, flavanones, anthocyanins, isoflavones, garlic, rosemary, saffron, ginger, turmeric, onion, tea, alcohol, and caffeine) are typically consumed in very small quantities, their reported consumption in the 24-hour diet recall was low, and previous research reported that their absence had no effect on DII scores [49]. Despite these limitations, this is the first study to analyze the relationship between DII score and clinical symptoms of FMS, including PPTs. Additionally, the pressure algometry method has been reported to have good discriminating power in FMS and provides objective and direct measures of PPTs [30].

In conclusion, we found that pro-inflammatory diets were associated with lower PPTs for most tender point sites in patients with FMS, suggesting that dietary inflammatory potential might play a relevant role in pain hypersensitivity in these patients. Thus, strategies to promote anti-inflammatory diets should be considered to improve pain hypersensitivity in women with FMS. Furthermore, future intervention studies investigating the effect of dietary inflammatory potential on clinical symptoms of FMS will be required.

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Human and animal rights and informed consent: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

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