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Evaluation of Ultra-Processed Food Intake and Inflammatory Dietary Pattern in Adults With Fibromyalgia Syndrome. A Case-Control Study

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Abstract: Background: Fibromyalgia Syndrome (FMS) is a chronic disorder marked by widespread pain, fatigue, and sleep disturbances. Recent studies suggest that low-grade inflammation and oxidative stress play key roles in FMS pathophysiology. Ultra-processed foods (UPFs), high in inflammatory ingredients, may exacerbate these mechanisms. **Objective:** This study aims to evaluate the relationship between UPF intake and inflammatory dietary patterns in FMS patients compared to healthy controls. **Methods:** A cross-sectional case-control study was conducted with 89 participants: 45 FMS patients and 44 healthy controls. The study was approved by the institutional ethics committee of the Complejo Hospitalario Universitario de Canarias (CHUC_2024_27). Data collection took place from January 17, 2025 to April 9, 2025. Dietary intake was assessed using the NOVA classification system for UPF consumption and the Dietary Inflammatory Index (DII) for inflammatory dietary patterns. Symptoms were evaluated using the Visual Analog Scale (VAS) for pain and the Fatigue Severity Scale (FSS). **Results:** FMS patients consumed significantly more UPFs (34.5%) than controls (26.7%) ($p < 0.001$). FMS participants also reported higher pain (VAS: 6.8 ± 1.9) and fatigue (FSS: 5.1 ± 1.1) compared to controls (VAS: 1.2 ± 0.5, FSS: 4.8 ± 1.0). Inflammatory dietary patterns were more pronounced in FMS patients, who consumed higher levels of saturated fats (29.4 ± 6.1 g/day vs. 24.8 ± 5.7 g/day; $p = 0.02$) and lower levels of anti-inflammatory nutrients like magnesium (240.5 ± 36.7 mg/day vs. 278.9 ± 40.2 mg/day; $p < 0.001$) and vitamin C (58.2 ± 12.9 mg/day vs. 74.6 ± 13.5 mg/day; $p < 0.001$). **Conclusions:** This case-control study demonstrates that adults with FMS exhibit a more pro-inflammatory dietary profile compared to healthy controls, characterized by greater consumption of ultra-processed foods and reduced intake of anti-inflammatory nutrients such as magnesium, vitamin C, and polyphenols.

Keywords: FMS; ultra-processed foods; dietary inflammatory index; chronic pain; systemic inflammation; gut microbiota; NOVA classification; fatigue; nutrition

1. Introduction

Fibromyalgia Syndrome (FMS) is a chronic condition characterized by widespread musculoskeletal pain [1,2], persistent fatigue [3], and significant sleep disturbances [4], with an estimated prevalence of 2–4% in the general population [5,6]. As a multifaceted disorder, it impacts patients' quality of life [7], often limiting daily functioning and contributing to considerable psychological distress [8], including symptoms of anxiety [9] and depression [10]. The condition predominantly affects women, with a female-to-male ratio of approximately 3:1 [11,12], suggesting underlying hormonal and genetic components in its pathophysiology [13].

Although the precise etiology of FMS remains elusive, recent evidence points to a multifactorial origin [14]. Low-grade systemic inflammation [15], oxidative stress [16], and gut microbiota

alterations [17,18] have been identified as potential contributors to disease mechanisms. Central sensitization, wherein the nervous system exhibits heightened responsiveness to sensory stimuli, is also considered a key mechanism underlying the chronic pain experienced by FMS patients [19]. Moreover, the imbalance of neurotransmitters such as serotonin, dopamine, and glutamate contributes to the worsening of symptoms, especially those related to pain amplification, fatigue, and cognitive impairment [20–22].

Given the growing burden of FMS and its significant public health implications, identifying modifiable risk factors and effective therapeutic strategies remains a pressing priority [23]. With this regard, current pharmacological treatments—including antidepressants, anticonvulsants, and analgesics—typically offer only partial relief and are frequently accompanied by undesirable side effects [24,25]. Consequently, non-pharmacological interventions such as physical activity [26,27], cognitive-behavioral therapy [28], and dietary modification [29] have garnered increasing attention as complementary approaches in the management of FMS. Among these, diet has emerged as a pivotal factor, given its influence on systemic inflammation [30], oxidative balance [31], and the gut microbiome [32]—elements that may collectively shape the course and severity of FMS.

Ultra-processed foods (UPFs), in particular, have attracted scrutiny for their detrimental effects on metabolic, inflammatory, and neurological health [33]. As defined by the NOVA classification, UPFs are industrially manufactured products composed of refined ingredients, chemical additives, and synthetic compounds that may provoke inflammatory responses and disrupt gut microbiota homeostasis [34–36]. These products are typically high in added sugars, hydrogenated fats, and artificial preservatives—all linked to increased oxidative stress [37,38] and chronic low-grade inflammation [39], both of which may intensify FMS symptoms. Epidemiological evidence has associated high UPFs consumption with elevated risks of obesity [40], type 2 diabetes [41], and cardiovascular diseases [42], as well as heightened levels of systemic inflammatory markers such as C-reactive protein and interleukin-6 [43–45] These pro-inflammatory effects may contribute to FMS pathophysiology via mechanisms involving mitochondrial dysfunction [46], neuroinflammation [47], and altered energy metabolism [48].

Despite growing recognition of the interplay between diet and chronic pain disorders, the specific impact of UPF consumption on individuals with FMS remains insufficiently explored. Preliminary studies suggest that diets rich in minimally processed, anti-inflammatory foods—such as those containing omega-3 fatty acids, polyphenols, and dietary fiber—may alleviate FMS symptoms by modulating inflammatory pathways and promoting gut microbial diversity [49–51]. Conversely, excessive intake of UPFs may exacerbate neuroinflammation, heighten pain perception, and impair mitochondrial function—hallmarks of FMS pathology. Additionally, UPFs have been linked to dysbiosis and increased intestinal permeability [52], both of which may foster systemic inflammation and amplify nociceptive responses [53]. Given that many FMS patients report frequent gastrointestinal disturbances, the connection between dietary patterns, gut health, and symptom severity merits deeper investigation.

Given the current lack of robust, large-scale epidemiological research on the role of UPFs in FMS, this case-control study seeks to address a critical gap in the literature. The objective is to examine the association between UPF consumption and the severity of FMS-related symptoms by comparing dietary patterns and clinical profiles between individuals diagnosed with FMS and matched controls without the condition.

2. Methodology

2.1. Study design

This cross-sectional case-control study was conducted following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [54]. A non-probability convenience sampling method was employed to compare UPF consumption between individuals diagnosed with FMS and asymptomatic controls. The study was conducted from January 17, 2025 to

April 9, 2025, at the Asociación de Fibromialgia y Fatiga Crónica de Tenerife (Santa Cruz de Tenerife, Spain), following approval from the institutional ethics committee of Complejo Hospitalario Universitario de Canarias, Santa Cruz de Tenerife, Spain (CHUC_2024_27). All participants provided written informed consent, which was obtained by S.M.P. prior to inclusion in the study. Data collection was conducted anonymously, with oversight by I.M.M.P. to ensure compliance with ethical and data protection standards.

2.2. Participants

After signing the informed consent form, participants underwent a medical history review and dietary assessment to determine eligibility based on predefined inclusion and exclusion criteria. The study included (1) adults aged 18 years or older (2) who had been diagnosed with FMS according to the 2016 criteria of the American College of Rheumatology (ACR, 2010) [55]. Eligible participants (3) had no major dietary restrictions that could influence UPF consumption patterns and (4) no severe comorbidities that might affect dietary intake or metabolism. Individuals actively (5) engaged in structured dietary interventions or (6) weight-loss programs were excluded to minimize potential confounding effects.

Exclusion criteria included being (1) under 18 years of age, (2) having undiagnosed chronic pain conditions, (3) or presenting with major gastrointestinal disorders such as inflammatory bowel disease or celiac disease, which could impact nutrient absorption and digestion. Participants with (4) severe psychiatric disorders that could interfere with dietary reporting, as well as those taking dietary supplements that significantly altered nutrient intake, were also excluded. Following the initial screening of 112 candidates, 45 were excluded due to lack of informed consent, and 24 were excluded for not meeting the eligibility criteria. The final study sample comprised 89 participants, divided into the case group (*FMS patients*) and the control group (*healthy individuals*). See details in **Figure 1**. Participants selection process.
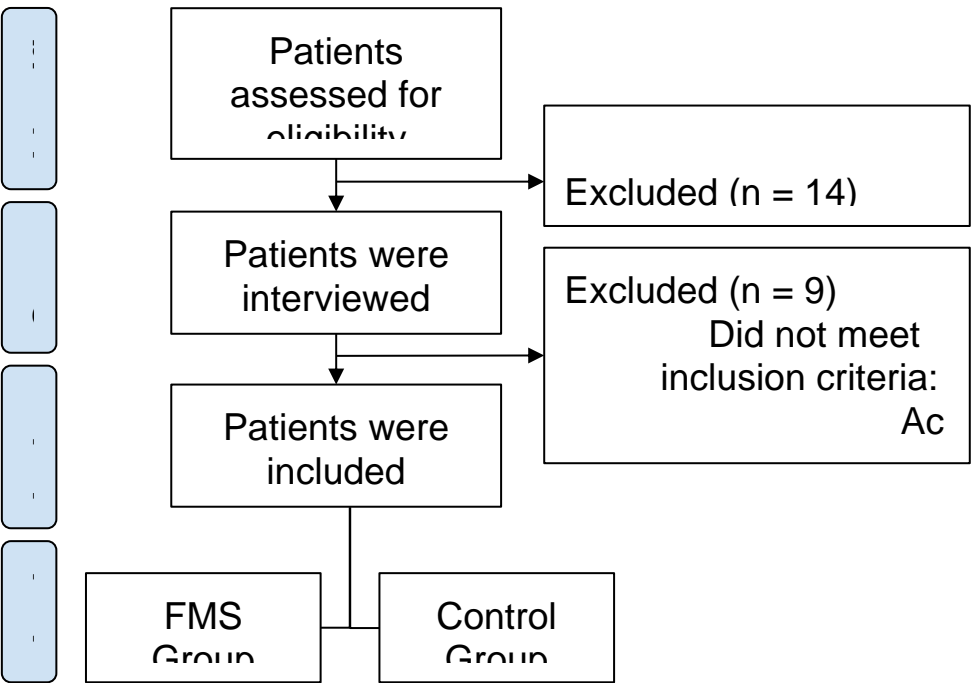

Figure 1. STROBE participants selection process.

2.3. Sample Size calculation

Sample size was calculated using G*Power software (version 3.1.9.7; Düsseldorf University, Germany) [56] based on an expected medium effect size (Cohen's d = 0.65), derived from preliminary data on dietary intake differences between individuals with FMS and healthy controls. With a

significance level of α = 0.05 and power (1 − β) of 0.80 for two-tailed comparisons, a minimum of 84 participants (42 per group) was required to detect statistically significant differences. The final sample included 89 participants (45 with FMS and 44 controls), exceeding the minimum requirement and ensuring adequate power for the analyses conducted.

2.4. Outcomes

2.4.1. Anthropometric and Clinical Measurements

To begin with, anthropometric parameters such as body weight, height, and body mass index (BMI) were measured. BMI was calculated using the standard formula (*weight in kilograms divided by the square of height in meters*, kg/m²). These data were obtained using calibrated digital scales and wall-mounted stadiometer (Harpedem, Holtain Ltd., Crymych, United Kingdom), following standardized measurement protocols to ensure consistency and reliability across participants. Subsequently, body composition was assessed using bioelectrical impedance analysis (BIA), specifically with the InBody 770 multi-frequency analyzer (InBody Co., Ltd., Seoul, South Korea) [57], a device widely validated for use in clinical populations. This non-invasive method estimates key components of body composition, including fat mass, lean mass, and total body water, by analyzing the resistance and reactance of electrical currents as they pass through body tissues.

In terms of clinical symptom assessment, the Fibromyalgia Impact Questionnaire (FIQ) [58] was employed to evaluate the overall impact of FMS. This validated instrument captures multiple symptom domains, including pain, fatigue, physical functioning, and quality of life, providing a comprehensive measure of disease severity [59]. Additionally, pain intensity was quantified using the Visual Analog Scale (VAS), a sensitive and widely adopted tool in clinical research for measuring subjective pain experience [60]. Moreover, fatigue levels were evaluated using the Fatigue Severity Scale (FSS) [61], which assesses the impact of fatigue on physical, social, and cognitive functioning. The FSS has demonstrated high reliability and validity in both general and clinical populations, including patients with fibromyalgia [62].

2.3.2. Dietary Assessment

UPFs consumption was categorized using the NOVA classification system [35], which stratifies foods into four groups based on their degree of processing. These groups include unprocessed or minimally processed items (e.g., *fresh fruits*, *vegetables*, and *whole grains*), processed culinary ingredients (e.g., *oils, salt*, and *sugar*), processed foods (e.g., *canned vegetables* and *cheese*), and ultra-processed foods (e.g., s*ugary beverages*, *ready-to-eat meals*, *packaged snacks*, and i*ndustrially processed bakery products*). Participants reported their UPF consumption frequency, and their total UPF intake was expressed as a percentage of their overall energy intake.

In addition, the Dietary Inflammatory Index (DII) [63] was employed as a validated measure to assess the inflammatory potential of the participants' diets. By examining the intake of specific nutrients and food items, the DII generates a score indicating whether a diet tends toward a pro-inflammatory or anti-inflammatory profile.

2.4. Statistical Analysis

Statistical analyses were conducted using SPSS v.29.0.2.0 (IBM Corp., Armonk, NY, USA) [64]. Dietary intake and clinical data were entered into an electronic database, with a second researcher performing double data entry to ensure accuracy and data integrity. Descriptive statistics—including mean, median, standard deviation, minimum, and maximum values—were calculated for all study variables.

Afterwards, the normality of data distribution was assessed using the W Shapiro–Wilk test with p-values > 0.05 indicating normal distribution. For intergroup comparisons, independent samples t-tests were used for variables with normal distribution, while the Mann–Whitney U test was applied for non-normally distributed variables. Lastly, effect sizes were calculated to assess the magnitude of

differences between groups: Cohen's d was used for parametric analyses, and the biserial correlation coefficient was applied for nonparametric tests. Statistical significance was set at p < 0.05.

3. Results

3.1. Description of sample

A total of 89 participants were included in the study, with 45 individuals assigned to the FMS group and 44 to the control group. Specifically, the FMS group consisted of 33 women and 12 men, with a mean age of 50.1 ± 8.5 years, whereas the control group included 30 women and 14 men, with a mean age of 48.7 ± 9.1 years. Notably, age was normally distributed in both groups, as confirmed by the Shapiro–Wilk test (FMS: W = 0.973, p = 0.293; Control: W = 0.976, p = 0.348).

In relation to the anthropometric characteristics, participants in the FMS group exhibited higher body weight (72.5 ± 10.3 kg) and BMI (27.5 ± 4.2 kg/m²) compared to those in the control group (68.9 ± 9.7 kg and 24.9 ± 3.8 kg/m², respectively). It is worth noting that BMI did not follow a normal distribution in either group (FMS: W = 0.945, p = 0.014; Control: W = 0.951, p = 0.018), while body weight was marginally non-normal. In contrast, height was similar between groups (FMS: 1.62 ± 0.08 m; Control: 1.63 ± 0.07 m), and the distribution was normal in both cases.

In addition, the waist-to-hip ratio (WHR) was slightly higher in the FMS group (0.89 ± 0.05) than in the control group (0.85 ± 0.04). Despite this difference, WHR followed a normal distribution in both groups (FMS: W = 0.970, p = 0.182; Control: W = 0.975, p = 0.225). Regarding body composition, the analysis revealed significantly higher fat mass in the FMS group (34.5 ± 5.3%) compared to controls (28.1 ± 4.7%). Conversely, fat-free mass (FMS: 65.5 ± 5.3% ; Control: 71.9 ± 4.7%) and muscle mass (FMS: 47.5 ± 4.8% ; Control: 49.3 ± 4.2%) were lower in the FMS group. Importantly, all body composition variables demonstrated non-normal distributions in both groups (p < 0.05).

Furthermore, participants in the FMS group reported significantly greater pain intensity, as measured by the Visual Analog Scale (VAS: 6.8 ± 1.9), in contrast to the control group (1.2 ± 0.5). Similarly, fatigue symptoms—assessed using the Fatigue Severity Scale (FSS)—were markedly elevated in the FMS group across all subdomains, including daily interference, task initiation, motivation, post-effort fatigue, and social engagement. All clinical variables exhibited highly significant deviations from normality (p < 0.001 in all cases). The anthropometric and clinical characteristics of the FMS and control groups are presented in **Table 1**.

Table 1. Anthropometric and clinical characteristics of FMS and control groups.

Characteristics	FMS Group (n = 45)	W	*p*-value	Control Group (n = 44)	W	*p*-value
Gender (Female/Male)	33/12			30/14		
Age (years)	50.1 ± 8.5	0.973	0.293	48.7 ± 9.1	0.976	0.348
Weight (Kg)	72.5 ± 10.3	0.958	0.057	68.9 ± 9.7	0.963	0.064
Height (m)	1.62 ± 0.08	0.979	0.481	1.63 ± 0.07	0.981	0.507
BMI (Kg/m²)	27.5 ± 4.2	0.945	**0.014***	24.9 ± 3.8	0.951	**0.018***
WHR	0.89 ± 0.05	0.970	0.182	0.85 ± 0.04	0.975	0.225
BIA (%)						
Fat mass (%)	34.5 ± 5.3	0.942	**0.011***	28.1 ± 4.7	0.946	**0.015***
Fat-free mass (%)	65.5 ± 5.3	0.940	**0.02***	71.9 ± 4.7	0.911	**0.021***
Muscle mass (%)	47.5 ± 4.8	0.943	**0.019***	49.3 ± 4.2	0.905	**0.020***
VAS - Visual Analog Scale						
Pain intensity (0-10 scale)	6.8 ± 1.9	0.882	**<0.001***	1.2 ± 0.5	0.911	**<0.001***
FSS - Fatigue Severity Scale						
Total score	5.1 ± 1.1	0.894	**<0.001***	4.8 ± 1.0	0.905	**<0.001***
Daily Interference	6.1 ± 1.2	0.890	**<0.001***	2.3 ± 0.8	0.907	**<0.001***
Task Initiation	5.8 ± 1.4	0.888	**<0.001***	2.0 ± 0.7	0.904	**<0.001***
Motivation	5.7 ± 1.3	0.891	**<0.001***	2.2 ± 0.9	0.902	**<0.001***
Post-effort Fatigue	6.0 ± 1.5	0.889	**<0.001***	1.9 ± 0.6	0.903	**<0.001***
Social Engagement	6.0 ± 1.5	0.886	**<0.001***	1.9 ± 0.6	0.904	**<0.001***

Table 1. *Anthropometric and clinical characteristics of FMS and control groups.* **Abbreviation**: BMI: Body Mass Index; WHR: Waist-to-Hip Ratio; BIA: Bioelectrical Impedance Analysis; VAS: Visual Analog Scale for pain intensity (0 = no pain, 10 = worst pain imaginable); FSS: Fatigue Severity Scale. *p < 0.05; **p < 0.01; ***p < 0.001 indicates statistically significant differences between groups. Several variables showed a non-normal distribution, as determined by the Shapiro–Wilk test.

3.2. Inflammatory Dietary Intake and Ultra-processed Food Consumption

3.2.1. Ultra-processed Food Consumption (NOVA Classification)

According to the NOVA classification system [35], the FMS group consumed significantly fewer unprocessed or minimally processed foods (35.1 ± 9.2%) than the control group (45.3 ± 8.7%; $p < 0.001$). Likewise, processed culinary ingredient consumption was slightly lower in the FMS group (14.3 ± 5.6%) than in controls (16.7 ± 4.9%; $p = 0.04$). In contrast, the intake of processed foods (16.1 ± 5.3%) was higher in the FMS group compared to controls (11.3 ± 4.6%; $p < 0.01$). Notably, UPF consumption was significantly elevated in the FMS group (34.5 ± 8.9%) relative to the control group (26.7 ± 7.1%; $p < 0.001$), underscoring the potential role of industrial food products in modulating symptomatology in FMS.

3.3.2. Inflammatory Dietary Intake (DII/E-DII)

- Pro-inflammatory components

After the application of DII/E-DII [63] participants with FMS exhibited significantly higher intake of pro-inflammatory dietary components compared to controls (45.3 ± 8.7% vs. 35.1 ± 9.2%, $p < 0.001$), with a large effect size ($d = 1.14$). This suggests a more pro-inflammatory dietary pattern in the FMS group. Regarding macronutrient intake, individuals in the FMS group consumed significantly more saturated fats (29.4 ± 6.1 g/day) than controls (24.8 ± 5.7 g/day), with a large effect size ($d = 0.97$, $p = 0.02$). Conversely, the intake of trans fats was lower in the FMS group (3.2 ± 1.0 g/day) compared to controls (4.1 ± 1.1 g/day), although the effect size was small ($d = –0.48$, $p = 0.045$).

Cholesterol intake was also higher among participants with FMS (210.5 ± 35.4 mg/day) compared to controls (187.6 ± 30.7 mg/day), with a small effect size ($d = 0.42$, $p = 0.04$). Additionally, refined carbohydrate intake was greater in the FMS group (220.4 ± 35.2 g/day vs. 198.7 ± 32.4 g/day; $p = 0.01$), corresponding to a medium effect size ($d = 0.64$). Interestingly, sodium intake was significantly lower in the FMS group (1850.0 ± 320.0 mg/day) than in the control group (2040.0 ± 340.0 mg/day; $p = 0.039$), with a medium effect size ($d = –0.56$).

- Anti-inflammatory components

1. Macronutrient Intake

The FMS group showed a significantly lower protein intake (68.4 ± 12.7 g/day) compared to the control group (74.3 ± 11.8 g/day; $p = 0.04$). Although fat consumption was slightly higher in the FMS group (82.6 ± 15.1 g/day) than in controls (76.5 ± 13.9 g/day), the difference was not statistically significant ($p = 0.09$). Notably, carbohydrate intake was significantly elevated in the FMS group (220.4 ± 35.2 g/day) versus the control group (198.7 ± 32.4 g/day; $p = 0.03$). Fiber intake tended to be lower in the FMS group (18.6 ± 4.5 g/day) compared to controls (21.3 ± 5.2 g/day; $p = 0.05$), which may contribute to altered gut microbiota and inflammatory response.

2. Micronutrient Intake

Significant group differences were also found in micronutrient intake. Vitamin C consumption was markedly lower in the FMS group (58.2 ± 12.9 g/day) compared to the control group (74.6 ± 13.5 g/day; $p < 0.001$), with a large effect size (Cohen's $d = -1.24$). Similarly, magnesium intake was significantly reduced among individuals with FMS (240.5 ± 36.7 g/day) in comparison to controls (278.9 ± 40.2 g/day; $p < 0.001$; $d = -1.00$). Iron intake was also lower in the FMS group (10.3 ± 2.1 g/day) versus the control group (11.2 ± 2.3 g/day; $p = 0.021$). Although zinc intake showed a similar trend—

being lower in the FMS group (8.1 ± 1.6 g/day) than in controls (9.4 ± 1.7 g/day)—this difference did not reach statistical significance (*p* = 0.234).

3. Bioactive Compounds

In terms of bioactive compounds, significant differences were observed between groups. Alcohol consumption was lower in the FMS group (2.4 ± 1.1 g/day) compared to the control group (3.7 ± 1.4 g/day; *p* = 0.01). Similarly, caffeine intake was reduced in individuals with FMS (182.3 ± 45.2 mg/day) relative to controls (219.7 ± 52.8 mg/day; *p* = 0.03). Notably, the intake of flavonoids and polyphenols was significantly lower in the FMS group (185.2 ± 38.6 mg/day) than in the control group (229.4 ± 41.3 mg/day; *p* = 0.009), which suggests a diminished dietary exposure to these anti-inflammatory phytochemicals.

4. Food-Based Items

In the analysis of specific food-based components, garlic intake was slightly lower in the FMS group (1.6 ± 0.7 g/day) compared to controls (2.1 ± 0.9 g/day; p = 0.05). Interestingly, curcumin intake was significantly higher in the FMS group (5.8 ± 2.3 g/day vs. 4.1 ± 1.9 g/day; p = 0.03), which may reflect a higher prevalence of supplement use or dietary adjustments in response to chronic pain symptoms. Piperine intake was also higher in the FMS group (1.3 ± 0.6 g/day vs. 0.9 ± 0.5 g/day; p = 0.06), though the difference did not reach statistical significance. A detailed comparison of UPFs consumption and pro-inflammatory dietary intake between individuals diagnosed with FMS and healthy controls is provided in **Table 2**.

Table 2. Difference in dietary intake and UPF consumption in FMS and control groups.

Characteristics	FMS Group	Control Group	Statistic	*p*-value	Size effect
NOVA - Ultra-Processed Food Classification System					
Unprocessed/minimally processed foods	35.1 ± 9.2%	45.3 ± 8.7%	**264.0**	**<0.001*****	**-1.14**
Processed culinary ingredients	14.3 ± 5.6%	16.7 ± 4.9%	**272.0**	**0.04***	**-0.46**
Processed foods	16.1 ± 5.3%	11.3 ± 4.6%	**675.0**	**<0.01****	**0.97**
Ultra-processed foods	34.5 ± 8.9 %	26.7 ± 7.1 %	**695.0**	**<0.001*****	**0.97**
DII/E-DII-Dietary Inflammatory Index					
Energy-adjusted score	14.3 ± 5.6	16.7 ± 4.9	348.0	**0.013***	**-0.46**
Pro-inflammatory components (%)	45.3 ± 8.7	35.1 ± 9.2	162.0	**<0.001*****	**1.14**
Macronutrients *(g/day)*					
Saturated Fats	29.4 ± 6.1	24.8 ± 5.7	530.0	**0.02***	**0.97**
Trans Fats	4.1 ± 1.1	3.2 ± 1.0	488.0	**0.045***	**-0.48**
Cholesterol (mg/day)	210.5 ± 35.4	187.6 ± 30.7	**606.0**	**0.04***	**0.42**
Refined carbohydrates / sugar	220.4 ± 35.2	198.7 ± 32.4	**777.0**	**0.01***	**0.64**
Sodium	1850.0 ± 320.0	2040.0 ± 340.0	**502.0**	**0.039***	**-0.56**
Anti-inflammatory components (%)	16.1 ± 5.3	11.3± 4.6	595.0	**0.03***	**0.97**
Macronutrients *(g/day)*					
Proteins	68.4 ± 12.7	74.3 ± 11.8	316.0	**0.048***	**-0.48**
Fats	82.6 ± 15.1	76.5 ± 13.9	487.0	0.058	0.42
Carbohydrates	220.4 ± 35.2	198.7 ± 32.4	777.0	**0.01***	0.64
Fibers	18.6 ± 4.5	21.3 ± 5.2	357.0	0.17	-0.56
Micronutrients *(g/day)*					
Vitamine C	58.2 ± 12.9	74.6 ± 13.5	**186.0**	**<0.001*****	**-1.24**
Magnesium	240.5 ± 36.7	278.9 ± 40.2	**223.0**	**<0.001*****	**-1.0**
Iron	10.3 ± 2.1	11.2 ± 2.3	**294.0**	**0.021***	**-0.41**
Zinc	8.1 ± 1.6	9.4 ± 1.7	**369.0**	**0.234***	**-0.79**
Bioactive compounds *(g/day)*					
Alcohol	2.4 ± 1.1	3.7 ± 1.4	**198.0**	**0.01***	**-1.03**
Caffeine (mg/day)	182.3 ± 45.2	219.7 ± 52.8	**216.0**	**0.03***	**-0.76**
Flavonoids / Polyphenols	185.2 ± 38.6	229.4 ± 41.3	**204.0**	**0.009****	**-1.08**
Food-based items *(g/day)*					
Turmeric	5.8 ± 2.3	4.1 ± 1.9	**574.0**	**0.03***	**0.81**
Garlic and onion	1.6 ± 0.7	2.1 ± 0.9	220.0	0.05	-0.62
Ginger	1.6 ± 0.7	2.1 ± 0.9	220.0	0.05	-0.62
Piperine	1.3 ± 0.6	0.9 ± 0.5	**574.0**	0.06	0.72

Table 2. *Difference in dietary intake and UPF consumption in FMS and control groups.* Data are presented as mean ± SD. p-values were obtained using Mann-Whitney U tests (p < 0.05 considered significant). ***p < 0.001 indicates highly significant differences between groups. **Abbreviations**: FMS: FMS Syndrome; CTRL: Control; VAS: Visual Analog Scale; FSS: Fatigue Severity Scale; FFQ: Food Frequency Questionnaire; NOVA: Ultra-Processed Food Classification System; SD: Standard Deviation.

4. Discussion

The consumption of UPFs has been linked to various chronic diseases [65], including FMS [66], and may worsen symptoms like fatigue, pain, and inflammation in individuals with FMS through immune activation, neuroinflammation, and the gut-brain axis, potentially leading to systemic inflammation [29,67]. The potential mechanisms through which UPFs may influence the pathophysiology of FMS are illustrated in **Figure 2**.
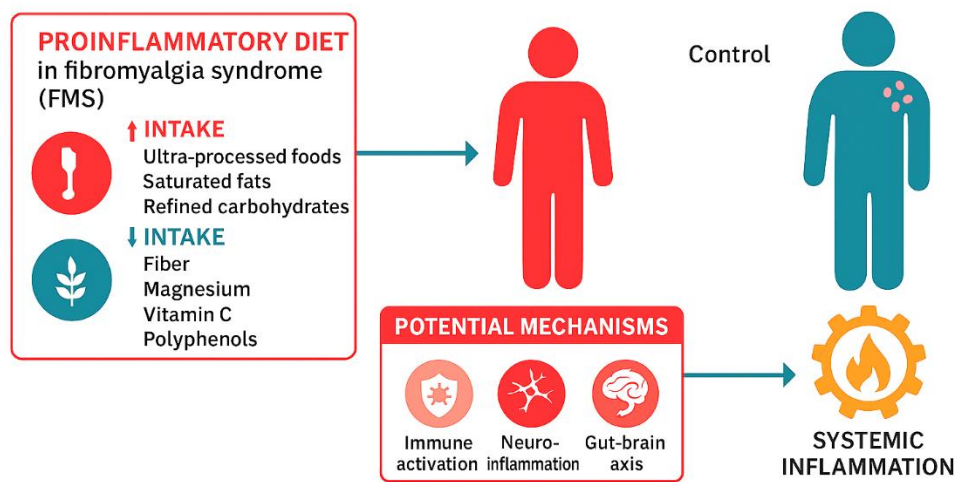

Figure 2. Summary of differences in dietary patterns between individuals with FMS and healthy controls. Compared to controls, participants with FMS showed higher intake of ultra-processed foods, saturated fats, and refined carbohydrates, along with lower consumption of anti-inflammatory nutrients such as vitamin C, magnesium, polyphenols, and fiber. These dietary characteristics may contribute to systemic inflammation, oxidative stress, and central sensitization, which are key mechanisms in the pathophysiology of chronic pain in FMS.

In our study, participants with FMS reported significantly higher UPF consumption than healthy controls. This dietary pattern may worsen overall well-being by increasing systemic inflammation and oxidative stress, thereby exacerbating fatigue and pain which have been identified higher than controls [48]. Furthermore, most individuals with FMS presented with overweight status (BMI = 27.5 ± 4.2), a known risk factor for the development and progression of FMS. These participants also reported moderate pain intensity (VAS = 6.8 ± 1.9) and clinically significant fatigue that interfered with daily activities (FSS = 6.1 ± 1.2). Given the centrality of fatigue in FMS and its established link to chronic inflammation and impaired energy metabolism, these findings highlight the need to explore diet as a modifiable risk factor [68].

The first tool employed in our study was the NOVA classification [35], which categorizes foods into four groups based on processing levels: unprocessed, processed culinary ingredients, processed foods, and ultra-processed foods. Our results showed that participants with FMS consumed fewer unprocessed foods (35.1 ± 9.2%) compared to the control group (45.3 ± 8.7%; *p* < 0.001), and fewer culinary ingredients (14.3 ± 5.6% vs. 16.7 ± 4.9%; p = 0.04). Conversely, their intake of processed foods was slightly higher (16.1 ± 5.3% vs. 11.3 ± 4.6%; *p* < 0.01), and UPF intake was markedly elevated (34.5 ± 8.9% vs. 26.7 ± 7.1%; p < 0.001).

UPFs are characterized by poor nutritional quality and are rich in trans fats, refined sugars, highly processed flours, artificial additives, and preservatives [69,70]. These components trigger inflammatory responses through several mechanisms, including NLRP3 inflammasome activation, oxidative stress, and intestinal dysbiosis, all contributing to a persistent proinflammatory state [39,71]. In contrast, a diet based on fresh and minimally processed foods—rich in antioxidants, fiber, polyunsaturated fatty acids, and essential micronutrients—has shown beneficial effects on inflammatory mechanisms and may improve pain, function, and quality of life in individuals with FMS [72].

A second tool used in this study was the DII, which highlighted a dietary pattern rich in proinflammatory nutrients in the FMS group [63]. Among these, cholesterol intake was notably high (210.5 ± 35.4 mg/day), although its role in FMS remains controversial. Some studies suggest a positive association between high cholesterol and fatigue, potentially due to overweight and dyslipidemia-related mitochondrial dysfunction [73]. However, others report no significant correlation between lipid profiles and symptom severity [74], emphasizing the need to consider confounding factors such as familial hypercholesterolemia.

Trans fat intake was also elevated among FMS participants (4.1 ± 1.1 g/day). These fats, mainly produced during industrial food processing, are associated with low-grade inflammation, as evidenced by elevated systemic inflammatory response markers such as hs-CRP, IL-6, and TNF-α [39,75]. Experimental models further support this association; diets rich in fats increase pain sensitivity in animal models of FMS and raise TNF-α levels in plasma, muscle, and dorsal root ganglia [76]. Refined carbohydrate intake was also significantly higher in the FMS group (220.4 ± 35.2 g/day). These nutrients are linked to inflammation and fatigue and have shown a negative correlation with quality of life scores in patients with FMS, as measured by the FIQ [77]. While findings regarding sugar intake are contradictory, the high glycemic index and glycemic load of these carbohydrates contribute to insulin resistance and systemic inflammation [78].

UPFs are also known to increase intestinal permeability [34,53,79]. Studies, such as one conducted in France with 862 adults, have identified associations between UPF intake and biomarkers of intestinal barrier dysfunction [80]. However, these associations were not observed in the PREDIMED-PLUS study, possibly due to lower UPF consumption in the Spanish elderly population [39].

Another critical issue is the nutritional deficiency of anti-inflammatory micronutrients in UPF-based diets. FMS participants showed inadequate intake of magnesium (240.5 ± 36.7 mg/day), vitamin C, vitamin D, zinc, and niacin. Magnesium deficiency is particularly relevant, as it has been linked to increased systemic inflammation, higher levels of substance P and proinflammatory cytokines, poor sleep quality, insulin resistance, and reduced exercise tolerance [81–83].

Magnesium also inhibits NMDA receptor activation in the spinal cord, a key mechanism involved in ascending pain transmission and central sensitization [84]. Its intravenous administration has shown analgesic effects, and estrogen decline after menopause may exacerbate this deficiency [85,86]. Low magnesium levels have been associated with decreased muscle strength and respiratory endurance in FMS patients, alongside greater symptom intensity and impaired ATP production [82,87]. These observations underscore the need to consider micronutrient profiles in FMS dietary interventions.

Our data show higher turmeric consumption among FMS participants (5.8 ± 2.3 g/day) compared to controls (4.1 ± 1.7 g/day). Curcumin, the main active compound in turmeric, has well-documented anti-inflammatory and antioxidant effects via modulation of NF-κB, STAT3, Nrf2, COX-2, and TRPV1 pathways. In preclinical models, curcumin reduced visceral hyperalgesia, TRPV1 receptor expression, oxidative stress, and excitatory neurotransmitter levels (e.g., *substance P*), with effects comparable to those of gabapentinoids [88,89]. These results suggest that while patients may attempt to self-modulate symptoms through functional foods, the potential benefits of compounds like curcumin might be diminished in the context of an overall proinflammatory diet.

Moreover, we found that patients with FMS have a significantly lower intake of flavonoids compared to healthy individuals (185.2 mg/day vs. 229 mg/day; p = 0.009), which may contribute to increased oxidative stress, inflammation, and pain sensitivity, characteristics commonly associated with this condition. It is well established that flavonoids exert their beneficial effects mainly through their antioxidant properties. They act as antioxidants by capturing free radicals through hydrogen donation (protons and electrons), helping to neutralize these harmful compounds [90]. Additionally, their antioxidant activity is due to the presence of the catechol group in ring B. Indirectly, flavonoids can also act as chelators of transition metal ions, such as iron (Fe) and copper (Cu), binding to them and reducing their ability to generate free radicals [91].   Furthermore, they can influence low-density lipoproteins (LDL), decreasing the consumption of antioxidants such as vitamin E and carotenoids, while regenerating oxidized vitamin E in LDL particles [92].

Flavonoids have been shown to possess anti-inflammatory and analgesic properties, modulating molecular pathways such as opioid receptor inhibition, ion channel regulation, and suppression of MAPK and NF-κB pathways, all of which help reduce inflammation and pain [93]. Several flavonoids target key pathways, inhibiting pro-inflammatory cytokines and enzymes, enhancing their pain-relieving effects. They also affect enzyme systems involved in inflammation, particularly tyrosine and serine-threonine protein kinases [94] helping to attenuate chronic inflammation, a hallmark of conditions like FMS.

An effective nutritional intervention for patients with FMS should focus on reducing the consumption of UPFs and increasing the intake of anti-inflammatory nutrients, as this may help attenuate neuroinflammation and central sensitization. However, socioeconomic factors must be taken into account, as individuals from lower-income backgrounds often rely more heavily on UPFs due to economic constraints and the reduced physical and time demands associated with preparing fresh meals [95].

Therefore, any dietary recommendation should not only be evidence-based, but also accessible, affordable, and socially adapted to the realities of FMS patients. Moreover, intergroup differences in UPF consumption may be influenced by socioeconomic status (SES), as highlighted in the cited study, which did not control for these potential confounding factors. It is well established that lower SES is associated with higher UPF consumption, which may affect the observed outcomes and complicate the interpretation of group differences.

4.1. Limitations

This study presents several limitations that should be considered when interpreting its findings. First, the cross-sectional design precludes the ability to infer causality between UPF consumption, pro-inflammatory dietary patterns, and symptom severity in individuals with fibromyalgia (FMS). To establish temporal or causal relationships, longitudinal and interventional studies are warranted.

Second, the use of a non-probability convenience sampling method may have introduced selection bias, potentially limiting the external validity of the findings. Participants were recruited from a single patient association, which may result in a sample with specific sociodemographic characteristics and health-seeking behaviors that do not reflect the general population of individuals with FMS.

Third, dietary intake was assessed via self-reported food frequency questionnaires (FFQs), a method prone to recall bias, underreporting, and social desirability bias. These biases may be especially pronounced in populations experiencing cognitive fatigue or chronic pain, such as individuals with FMS. Although validated tools like the DII/E-DII and the NOVA classification system were used, potential misclassification of food items or inaccuracies in portion size estimation may affect the reliability of dietary assessments.

To gain a more precise understanding of the factors that influence UPF consumption, future studies should conduct subgroup analyses considering variables such as sex, comorbidities (e.g., *gastrointestinal disorders affecting digestion, absorption, synthesis,* or *elimination*), clinical health status (e.g., confirmation of participants as generally healthy or diagnosed), medication use, smoking status,

and specific nutrient intakes. Although the sample size was adequate according to power analysis, such subgroup analyses may have been underpowered to detect small to moderate effects. Therefore, subsequent research should utilize larger, more diverse, and representative cohorts to strengthen the validity and generalizability of findings, and to better understand how socioeconomic and health-related factors influence UPF consumption patterns in this population.

4.2. Recommendations of Clinical practice

Given the well-established associations between ultra-processed food (UPF) consumption, pro-inflammatory dietary components, and increased symptom severity in fibromyalgia (FMS), dietary intervention should be recognized as a key complementary strategy within its clinical management. Healthcare providers and dietitians are strongly encouraged to work collaboratively, using validated instruments—such as the NOVA food classification system and the Dietary Inflammatory Index (DII)—to conduct personalized dietary assessments that can effectively identify and quantify pro-inflammatory dietary patterns.

Patients should be systematically educated on the detrimental effects of UPF consumption and the protective benefits of a diet rich in whole, minimally processed foods—especially those high in antioxidants, dietary fiber, and essential micronutrients. A gradual shift toward an anti-inflammatory dietary profile should be promoted, emphasizing increased intake of unprocessed foods while reducing the consumption of trans fats, refined carbohydrates, and added sugars.

Special attention must be given to identifying and addressing potential micronutrient deficiencies—particularly magnesium, vitamin C, and iron—through targeted supplementation and individualized nutritional counseling. To ensure long-term adherence and optimize clinical outcomes, dietary modifications should be regularly monitored, with ongoing nutritional follow-up integrated into a multidisciplinary care framework.

Incorporating anti-inflammatory nutritional strategies into standard clinical practice holds considerable promise for reducing systemic inflammation, modulating central sensitization, and ultimately improving the quality of life in individuals with FMS. These insights reinforce the urgent need for well-designed clinical trials to rigorously evaluate the efficacy of dietary interventions in managing FMS-related symptoms.

Furthermore, recent evidence supports the value of adopting an integrative therapeutic approach to fibromyalgia—combining pharmacological treatments with complementary strategies such as nutraceuticals (including polyphenols), balanced nutrition, appropriate supplementation, weight management, regular physical activity, and specialized physiotherapy. Together, these interventions may offer a synergistic effect, addressing both the biological and lifestyle dimensions of this complex condition.

5. Conclusions

This case-control study demonstrates that adults with FMS exhibit a more proinflammatory dietary profile compared to healthy controls, characterized by greater consumption of ultra-processed foods and reduced intake of anti-inflammatory nutrients such as magnesium, vitamin C, and polyphenols.

These dietary imbalances may contribute to the chronic inflammation and symptom severity observed in FMS. The findings support the integration of targeted nutritional strategies into multidisciplinary care and highlight the need for future clinical trials to assess the therapeutic impact of anti-inflammatory dietary interventions in this population.

S.E.M.P. and I.M.M.P..;writing—review and editing, S.E.M.P. and I.M.M.P.; visualization, S.E.M.P. and I.M.M.P.; supervision, S.E.M.P. and I.M.M.P.; and project administration, S.E.M.P. and I.M.M.P. All authors have read and agreed to the published version of the manuscript.

Abbreviations

ACR	American College of Rheumatology
ATP	Adenosine Triphosphate
BIA	Bioelectrical Impedance Analysis
BMI	Body Mass Index
DII	Dietary Inflammatory Index
E-DII	Energy-adjusted Dietary Inflammatory Index
FIQ	Fibromyalgia Impact Questionnaire
FMS	Fibromyalgia Syndrome
FSS	Fatigue Severity Scale
IL-6	Interleukin 6
NMDA	N-methyl-D-aspartate
NF-κB	Nuclear Factor Kappa-light-chain-enhancer of Activated B Cells
NOVA	Ultra-Processed Food Classification System
SD	Standard Deviation
SES	Socioeconomic Status
SIR	Systemic Inflammatory Response
TNF-α	Tumor Necrosis Factor Alpha
UPF	Ultra-Processed Food
VAS	Visual Analog Scale
WHR	Waist-to-Hip Ratio

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