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Assessing the Relationship between Dietary Phytochemical Index and Fatigue Severity in Multiple Sclerosis Patients

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Abstract

Background: Phytochemical-rich foods have anti-inflammatory effects and play a role in the prevention and control of inflammatory diseases such as Multiple Sclerosis (MS). Although some aspects of a diet high in phytochemicals promoting health and preventing chronic diseases are known, further studies are required to confirm the previous findings.

Methods: This cross-sectional study investigated the relationship between Dietary Phytochemical Index (DPI) and fatigue severity in patients with MS. A total of 240 patients aged 18 to 65 years were selected from the MS Association center of Golestan province. A valid and reliable food frequency questionnaire was used to evaluate the diet, and fatigue severity was assessed using the Fatigue Severity Scale (FSS) questionnaire. DPI was calculated using the formula [daily energy from foods rich in phytochemicals (*kcal*) divided by total daily energy intake (*kcal*)] and was calculated as 100.

Results: After controlling for potential confounding factors, the highest tertile of DPI had a lower prevalence of fatigue symptoms (odds ratio (OR: 0.27; 95%CI: 0.03-0.36; p=0.012) compared to those in the lowest tertile. The average age of the study participants was 31.9±7.7 years, and the fatigue score scale among the participants was 39.31±11.62.

Conclusion: In conclusion, a significant inverse relationship between DPI and fatigue severity was observed in patients with MS. Further prospective studies are needed to confirm these findings.

Keywords: Fatigue, Multiple sclerosis, Phytochemical

Introduction

Multiple Sclerosis (MS) is an autoimmune disease that affects the Central Nervous System (CNS) by causing inflammation and demyelination. It is a major cause of disability in young adults and affects more women than men (1). The disease is characterized by damage to the myelin coating of the nervous system, which causes inflammation and injury to the nerve sheath and ultimately to the nerve fibers. The complete etiology of this disease is not fully known yet, but it seems that repeated autoimmune attacks on the central nervous system are responsible for axonal inflammatory damage and subsequent disability in people with this disease (2). MS disease is divided into four forms according to the way it occurs and progresses (3). Patients with chronic debilitating diseases such as MS also face problems related to their disease, and these problems limit the patients' participation in health promotion activities, and as a result, cause an increase in secondary complications and limitations in independent living (4). Fatigue is a common symptom of MS, affecting 53 to 90% of patients. It is often ranked by patients as one of the most important symptoms of disability, with a great impact on the quality of life (5). Fatigue can be described as apathy, lack of energy, or an uncontrollable feeling of tiredness that cannot be fully explained by depression or myasthenia. In two-thirds of patients with MS, fatigue is one of the three main symptoms and is ranked as one of the most difficult symptoms of this disease (6). Fatigue in MS can be attributed to two primary factors: primary and secondary causes. The primary contributors to this symptom are intricately tied to the disease's progression and stem from central nervous system impairments, including demyelination, axonal reduction, and inflammation (7). It is noteworthy that fatigue stands as a significant factor affecting the quality of life for individuals with MS, irrespective of concurrent factors such as depression or disability levels.

Symptoms caused by MS disease can have devastating effects on roles, job duties, and daily life activities. Fatigue threatens the patient's independence and ability to participate effectively in the family and society. In addition to the fatigue caused by this disease, it limits a person's ability to take care of himself, and as a result of these problems, patients suffer from mental and emotional disorders. There is no definitive treatment for this disease, but measures can be used to reduce symptoms, including fatigue, and support patients (8).

Various mechanisms have been stated for the pathogenesis of this disease, the most important of which may be inflammation, stress, dysfunction of the body's immune system, infectious agents, and even abnormal flora. Cytokines and chemokines appear to play a role in regulating (9,10). Cytokines and chemokines appear to play a role in many of the cellular interactions that occur in MS. Th1 pro-inflammatory cytokines including Interleukin-2 (IL-2), Tumor Necrosis Factor alpha (TNF-α), Interferon gamma (IFN-γ) play a key role in activating and maintaining immune responses that can directly damage oligodendrocytes or myelin membrane, and this disease is referred to as an inflammatory disease (10). Also, various studies agree that the indicators of metabolic syndrome and the type of nutrition of a person have a great impact on the incidence and severity of MS symptoms (11). Recent studies have shown that insulin resistance and abdominal obesity through disturbances in the plasma levels of adipokines, changes in the metabolism of fatty acids, and dysfunction of blood vessels cause procoagulation and systemic inflammation, as well as disruption of the oxidant and antioxidant balance in the body, or in other words, it becomes oxidative stress, which can play a key role in the pathogenesis of various neurodegenerative diseases, including MS (12,13).

Overall, various aspects of the effect of diet on modulating the condition of various neurodegenerative diseases such as MS, inflammation, and oxidative stress, modulating the immune system have been investigated. It has been shown that the Western diet is associated with a higher prevalence of MS due to the higher content of pro-inflammatory foods such as red meat, fat, and refined grains and the lower content of anti-inflammatory foods and phytochemicals in these foods such as fruits and vegetables (14,15). It has also been shown that vegetarian diets have been useful in reducing the potential risks of this disease due to the high content of vitamins, minerals with antioxidant properties, unsaturated fatty acids, vegetable protein, fiber, and other phytochemicals

(16). However, considering that the evaluation of a food composition or a special nutrient alone cannot express the inflammatory or anti-inflammatory power of the diet and reflect the synergistic and possible interaction effects of the diet, hence recently various dietary indicators have been used to investigate these effects (17).

One of these nutritional indices is the Dietary Phytochemical Index (DPI). DPI evaluates the quality of the diet based on the percentage of daily energy intake from foods rich in phytochemicals in relation to the total energy intake (18). Based on this index, the vegetarian diet will have the highest score, and the Western diet will have a score of less than 20. This index is a simple method to evaluate the intake of DPI, and despite some limitations, it can have clinical applications. In a cross-sectional study, the DPI had an inverse relationship with body fat mass and oxidative stress (19). Recently, in a study, the relationship between DPI and plasma concentration of C-reactive protein as an index of systemic inflammation and oxidized LDL-C plasma levels has been proven (20). Also, in another study, the consumption of DPI found in fruits and vegetables has been associated with reducing the risk of neurodegenerative diseases (21). Several epidemiological studies have shown a relationship between DPI and cardiovascular disease risk factors including obesity and blood sugar (19,22-27). The DPI is a new scale that evaluates the quality of the diet based on the percentage of daily energy intake from foods rich in phytochemicals in relation to the total energy intake. Despite some limitations, it can have clinical applications, and several studies have demonstrated its inverse relationship with body fat mass and oxidative stress (19). However, the relationship between DPI and MS disease and related problems has not been studied enough. Therefore, we conducted the present study to investigate the potential relationship between DPI and MS disease and to evaluate the possible association of DPI with some clinical aspects of MS disease, such as fatigue and anthropometric indices.

Materials and Methods

Study design and participants

In this cross-sectional study, 240 people who referred to the MS Association center of Golestan province were examined. The files of the patients who were members of the MS Association Center were reviewed, and all the patients who met the inclusion criteria were selected. Eligible individuals were invited to participate in this research if they wanted to, and if the answer was positive, they were given a consent form. They had to be approved by a neurologist and be between 18 and 65 years old, have a Body Mass Index (BMI) of 18.5 to 40, and have the ability to write and answer the questions. Individuals with chronic conditions such as hypertension, cardiovascular disease, dyslipidemia, kidney or liver defects, stroke, food allergies, Parkinson's disease, pulmonary defects, or thyroid defects, as determined by a physician or self-reported by the participant, were excluded from the study. Furthermore, the participants who adhere to a special diet were also excluded from the study to minimize the influence of the dietary factors that may impact the results. Written informed consent was provided to the patients, and they entered the study by completing the consent form.

Dietary assessment

In this study, dietary assessment was conducted utilizing a well-established 168-item semi-quantitative Food Frequency Questionnaire (FFQ), which had previously undergone rigorous evaluation for reliability and validity (28). Trained nutritionists administered the FFQs through face-to-face interviews with the participants. To ensure the accuracy, household measurements were used to convert the reported portion sizes of consumed foods into grams. Subsequently, mean energy and nutrient intakes were computed using a customized adaptation of NUTRITIONIST IV software. This approach ensured precise evaluation of dietary intake in the research cohort.

Phytochemical index calculation

The calculation of the DPI followed the established methodology developed by McCarty, expressed as DPI = (daily energy obtained from foods rich in phytochemicals in *kcal* divided by total daily energy intake in *kcal*)×100 (18). Within this framework, foods classified as rich sources of phytochemicals encompassed fruits, vegetables, legumes, nuts, whole grains, soy products, seeds, and olive oil. Notably, potatoes were excluded from this category due to their limited phytochemical content. Furthermore, natural fruit and vegetable juices, along with tomato sauces, were incorporated into the fruit and vegetable groups due to their substantial phytochemical content. This comprehensive approach to assessing dietary phytochemical intake ensured a thorough evaluation of the participants' dietary habits in relation to phytochemical-rich foods.

Fatigue severity assessment

The severity of fatigue in the patients was evaluated using the Iranian version of the fatigue severity questionnaire. The validity and reliability of this questionnaire have been demonstrated in previous studies (29). Cronbach's alpha coefficient is 0.96. The FSS questionnaire measures individuals' personal perception of their fatigue through a set of 9 items and an eye analogy that illustrates how fatigue impacts movement, motivation, exercise, physical performance, daily activities, and interferes with work, family, and social life. To complete the questionnaire, the participants were instructed to read all the statements and select the number that best represents their level of disagreement, ranging from 1 (strongly disagree) to 7 (strongly agree). The minimum possible score on this questionnaire was 9, and the maximum score was 63. A score between 9 and 18 indicates low fatigue, a score between 18 and 45 shows moderate fatigue, and a score above 45 represents high fatigue.

Assessment of other variables

Demographic information, including age, marital status (married or single), employment status (employed or unemployed), education level (less than diploma, diploma, or university), dietary supplement consumption (yes or no), smoking status (yes or no), and presence of other diseases besides MS (yes or no), was obtained using a demographic information questionnaire. Body weight was measured with precision to the nearest 0.1 *kg*, with participants wearing minimal clothing and no shoes. A digital weighing scale manufactured by SECA in Hamburg, Germany, was used for this purpose. Height was carefully measured to the nearest millimeter using an unyielding measuring rod. BMI was calculated as weight in kilograms divided by height in meters squared. Waist circumference was measured using an inflexible tape measure with an accuracy of 0.5 *cm*, without applying any pressure, at the midpoint between the last rib and the tip of the sternum at the end of natural exhalation. Hip circumference was measured using an inflexible tape measure with an accuracy of 0.5 *cm*, without applying any pressure, at the widest part of the hips, and the Waist-to-Hip Ratio (WHR) was calculated by dividing waist size by hip circumference. Physical activity was determined by metabolic equivalents× hr.d (METhr.d) by recording 24 *hr* physical activity, and the individual's level of physical activity was calculated as METhr.d (30).

Statistical analysis

The general characteristics within the different DPI tertiles were presented as means with Standard Deviations (SDs) for continuous variables and as numbers with corresponding percentages for categorical variables. To assess disparities among the tertiles, we employed an Analysis of Variance (ANOVA) for continuous variables and a Chi-square test for categorical variables. Dietary consumption patterns of the study participants across the DPI tertiles were compared using analysis of covariance (ANCOVA), with all values adjusted for energy intake. Binary logistic regression models were employed to estimate Odds Ratios (ORs) and their associated 95% Confidence Intervals (CIs) for psychological profiles across the DPI tertiles, in both unadjusted and multivariable-adjusted models. The adjusted model accounted for factors such as age, total energy intake, BMI, physical activity level, and marital status (married or single). The trend in the relationship between DPI tertiles and the psychological profile was evaluated by treating the tertiles of DPI as ordinal variables in the logistic regression analysis. Statistical analyses were conducted using the Statistical Package for Social Sciences, version 21 (SPSS Inc. IBM Corp., Armonk, NY, USA), and statistical significance was defined as $p<0.05$.

Results

The general information of the study subjects is shown as a percentage in table 1. Out of the 240 study subjects, 204 were female and 36 were male. 195 individuals were married, and 45 were single. 106 individuals were unemployed, and other 134 were employed. Additionally, 19 individuals had an under-diploma education, 76 had a diploma, and 145 had a university education. The average DPI is shown in table 2, with the lowest rate being 3.65 and the highest being 45.24. The average score of the dietary phytochemical profile was 13.58. The anthropometric characteristics of the patients are shown in table 2. Table 3 shows the comparison of the average DPI according to the demographic information of the study subjects. It was found that the average phytochemical profile of the diet in women was higher than that of men, and a significant difference was observed between the two groups (p=0.003). Single individuals had a higher average DPI than married ones, and a significant difference was observed between the two groups (p=0.013). The unemployed individuals had higher DPI than the employed ones, but no significant difference was found between the two groups (p=0.4). It was demonstrated that individuals with less than a diploma had a higher average dietary phytochemical profile than the diploma group and university education group, and a significant difference was observed (p=0.009).

Table 4 shows the comparison of anthropometric variables at different tertiles of DPI in the studied subjects. The Welch test was used to compare

Table 1. Overview of demographic characteristics of the study participants

Variable	Number (percentage)	Mean (SD)
Age	-	38.08±7.01
Gender		
Male	36(15)	-
Female	204(85)	-
Marital status		
Single	45(18.8)	-
Married	195(81.2)	-
Occupation		
Unemployed	106(44.2)	-
Employed	134(55.8)	-
Level of education		
Less than a diploma	19(7.9)	-
Diploma	76(31.7)	-
College education	145(60.4)	-

Table 2. Dietary phytochemical index of the participants and central/dispersion indices of anthropometric characteristics

Variable	Minimum	Maximum	Mean (SD)
Height (*cm*)	154	185	163.17±6.08
Weight (*kg*)	55	105	73.28±10.34
BMI	20.17	37.34	27.43±3.05
Waist (*cm*)	67	128	94.14±13.05
Hip (*cm*)	90	149	111.67±10.41
WHR	0.7	0.95	0.84±0.05
DPI *	3.65	45.24	13.58±6.34

* Body Mass Index (BMI), Waist to Hip Ratio (WHR), Dietary Phytochemical Index (DPI).

Table 3. Comparison of mean DPI with respect to the participants' demographic information (Mean values and standard deviations)

Variable	Mean (SD)	p-value
Gender		
Male	11.24±3.25	0.003*1
Female	13.99±6.66	
Marital status		
Single	14.88±6.26	0.013*1
Married	13.28±6.33	
Occupation		
Unemployed	14.01±6.75	0.40[1]
Employed	13.24±5.99	
Education		
Less than a diploma	15.83±11.73	0.009*2
Diploma	12±3.75	
College education	14.2±6.31	

*1) The obtained p-value was calculated using a two-sample t-test. A p-value less than 0.05 is considered statistically significant.
*2) p-value <0.05 considered as significant based on one-way ANOVA test.

Table 4. Anthropometric characteristics of the participants across the Tertiles (T) of the Dietary Phytochemical Index (DPI) Mean values and standard deviations

Variable	Total		T1 <10.89 (n=80)		T2 10.89 ≤ to 14.41 (n=80)		T3 ≥14.41 (n=80)		p-value*
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Age (year)	38.08	7.01	40.125	7.22	38.38	7.11	35.72	6.01	0.001
Weight (*kg*)	73.28	10.34	80.513	10.28	73.66	7.41	65.66	7.12	0.001
BMI	27.43	3.05	29.51	2.67	27.79	2.108	24.96	2.436	0.001
Waist (*cm*)	94.14	13.05	101.787	10.74	95.66	11.26	84.97	11.255	0.001
Hip (*cm*)	111.67	10.41	117.96	9.23	112.337	8.61	104.725	8.87	0.001
WHR	0.84	0.05	0.8604	0.0454	0.847	0.0513	0.8078	0.051	0.001

* One-way ANOVA was applied and p-value <0.05 considered as significant, Body Mass Index (BMI), Waist to Hip Ratio (WHR).

variables such as age and weight, while the ANOVA test was utilized to investigate waist circumference, BMI, hip circumference, and the waist-to-hip circumference ratio. According to table 4, the results indicate a statistically significant difference in all the anthropometric variables at different tertiles of the DPI (p<0.05). The average age in the first tertile was 40.125±7.22, in the second tertile was 38.38±7.11, and in the third tertile was 35.72±6.01, suggesting that younger individuals have higher DPI. In the first DPI tertile, the average waist circumference of the study subjects was 101.78±10.74, in the second tertile was 95.66±11.26, and in the third tertile was 84.97±11.255, indicating that individuals with a higher waist have a lower DPI. Similarly, in the first DPI tertile, the average hip circumference of the study subjects was 117.96±9.23, in the second tertile was 112.337±8.61, and in the third tertile was 104.725±8.87, suggesting that individuals with a higher hip circumference have a lower DPI. Lastly, in the first DPI tertile, the average waist-to-hip circumference ratio of the study subjects was 0.86±0.04, in the second tertile was 0.847±0.051, and in the third tertile was 0.80±0.05, demonstrating that individuals with a lower waist-to-hip ratio have a higher DPI.

Table 5 shows the comparison of the average dietary indices at different DPI tertiles of the studied subjects. The comparison of the average dietary indices at different phytochemical tertile of the diet in the study subjects was measured using the ANOVA test. According to the results, average of all the dietary indices at different tertiles of the dietary phytochemical profile showed a statistically significant difference (p<0.05). The first tertile of DPI decreased the amount of total energy intake, protein, carbohydrate, fat, SFA, MUFA PUFA, and increased the amount of fiber and cholesterol compared to other levels.

Table 6 represents the comparison of the average intensity of fatigue in different DPI tertiles of the studied subjects according to different genders. The results showed that the average intensity of fatigue at different tertiles of the dietary phytochemical profile had a statistically significant difference (p<0.05). It was suggested that the intensity of fatigue in the first tertile has a higher level, and with the increase in DPI, the intensity of fatigue in the study subjects decreased, specifically in women. The intensity of physical activity at different tertiles of DPI had a statistically significant difference in both genders (p<0.05). With the increase in DPI, the amount of physical activity of the study subjects increased. After adjusting for potential confounders, individuals in the highest tertile of DPI had a lower and statistically significant odds ratio for fatigue intensity (OR: 0.27; 95%CI: 0.03-0.36; p=0.012), compared to those in the lowest

Table 5. Food intake of the participants based on their Dietary Phytochemical Index (DPI) (Mean values and standard deviations)

Variable	Total		T1 <10.89 (n=80)		T2 10.89 ≤ to 14.41 (n=80)		T3 ≥14.41 (n=80)		p-value *
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Total energy	2725.77	393.49	3028.36	319.717	2782.9	239.645	2365.95	285.72	0.001
Protein	84.68	10.98	89.21	12.06	86.808	8.044	78.016	9.1787	0.001
Carbohydrate	452.21	80	508.09	69.53	464.636	52.11	383.89	61.383	0.001
Fat	67.8	11.79	74.195	14.85	67.494	9.723	61.71	5.17	0.001
Cholesterol	169.05	35	21.014	4.88	18.2	3.09	16.37	1.3	0.023
SFA	18.53	3.91	0.8604	0.04544	0.847	0.0513	0.8078	0.051	0.001
MUFA	17.02	3.78	18.88	5.41	16.46	2.29	15.715	1.78	0.001
PUFA	19.2	4.91	21.285	5.8	19.3	4.9	17	3.78	0.001
Fiber	10.63	2.03	9.4	1.58	10.86	2.496	11.64	1.044	0.001

* One-way ANOVA was applied and p-value <0.05 was considered as significant.

Table 6. Mean and standard deviations of fatigue intensity and physical activity participants across the Tertiles (T) of the Dietary Phytochemical Index (DPI) (Mean values and standard deviations)

Variable	Total		T1 <10.89 (n=80)		T2 10.89 ≤ to 14.41 (n=80)		T3 ≥14.41 (n=80)		p-value*
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Male									
Fatigue (FSS)	43	9.19	45.84	7.73	39.55	11.17	40.12	8.91	0.001
Physical activity	316.41	105.21	254.26	50.84	335.22	77.35	419.12	148.22	0.001
Female									
Fatigue (FSS)	38.66	11.9	44.86	9.79	41.52	9.91	30.58	10.94	0.001
Physical activity	397.29	214.34	271.37	77.67	347.49	103.97	553.09	273.65	0.001
Fatigue (FSS)	39.31	11.62	45.1	9.307	41.3	10.004	31.5475	11.08	0.001
All genders									
Physical activity	385.17	203.67	269.687	71.979	346.112	101	539.7	266.241	0.001

* p-value <0.05 was considered as significant based on-way ANOVA.

tertile (Table 7).

Discussion

The present cross-sectional analytical study demonstrated that increasing the phytochemical profile of the diet can reduce the severity of fatigue in patients with MS. The study showed that the average phytochemical index of the diet was 13.58±6.34, with the lowest value being 3.65 and the highest value being 45.24. Previous studies have investigated the relationship between foods rich in phytochemicals

Table 7. Fatigue intensity across tertiles of the Dietary Phytochemical Index (DPI) (Multivariable-adjusted odds ratios and 95% confidence intervals)

Variable		T1 <10.89 (n=80)	T2 10.89 ≤ to 14.41 (n=80)	T3 ≥14.41 (n=80)	p-trend *
Fatigue (FSS)	Crude	1	0.55(0.29–1.02)	0.11(0.05–0.23)	0.001
	Adjusted	1	0.61(0.44–1.11)	0.27(0.03–0.36)	0.012

DPI: Dietary Phytochemical Index. Adjusted for age, sex, energy intake, physical activity, marital status, and BMI.
* P-trend <0.05 was considered as significant based one linear regression.

and the risk of certain diseases, such as Alzheimer's disease, and have provided beneficial results and effects (31).

The average age of the patients in this study was 38.08±7.01 years, with an age range of 20-56 years. The study found that the age of the participants decreased with the increase in the DPI score. This result suggests that the consumption of foods rich in phytochemicals was higher in younger participants than in older ones, leading to an increase in the phytochemical score of the diet. Consistent with these results, a cross-sectional cohort study on European adults found that the participants were older in the last quarter of the Dietary Inflammatory Index (DII) (32).

The results associated with food groups in this study showed that the consumption of bread and rolls, margarine, chocolate, butter and fats, vegetable and animal fats, carbonated drinks, meat, cake, biscuits, and sugar, honey, and jam were more pro-inflammatory groups, and they had less consumption of vegetables, fruits, and fish (32).

The study demonstrated that 85% of the patients were female and 15% were male. The phytochemical index score of the diet was higher in women than in men. Visconti *et al* also reported that MS occurs mainly in young adults between the ages of 20-40 years and affects women two times more than men (1). Studies have found that women consume a diet with a higher phytochemical profile than men. This has been observed in several studies. For example, one study found that women consumed more phytochemicals than men (33), while another study conducted in Korea also reported a higher phytochemical index in women compared to men (34). The reasons behind this difference are not entirely clear, but some experts suggest that it may be due to variations in food preferences or cultural norms regarding food choices (35). Furthermore, this gender gap in phytochemical intake may be due to the interaction between phytochemical consumption and the multiple types of phytochemicals that have a similar structure to estrogens, such as isoflavones, and are believed to mimic the role of estrogen in the body (36). Additionally, a study conducted in Iran found that women who had a higher DPI had a lower risk of central obesity (36). Overall, the evidence suggests that women tend to consume a higher amount of phytochemicals than men. This may have important implications for disease prevention and management, given the potential health benefits of phytochemicals.

In the present study, it was shown that the average phytochemical profile of the diet in unmarried patients was significantly higher than that of married patients. The study also demonstrated that there was no statistically significant difference in the average phytochemical profile of the diet in employed or unemployed individuals. According to the current study, 39.6% of the patients had a diploma or less, and 60.4% of them had a university education. The average phytochemical profile of the diet was significantly higher in patients with a literacy level lower than a diploma. The study showed that individuals who had a higher score of DPI had lower average anthropometric indices such as BMI, weight, waist circumference, and the ratio of waist circumference to hip circumference. There was an inverse relationship between the DPI level and the average anthropometrics of the study subjects. Most studies conducted in this regard have demonstrated

similar results to the present study (19,22,37-39).
Several mechanisms have indicated the beneficial effects of a diet rich in phytochemicals in preventing obesity. Human studies have suggested that phytochemicals play a key role in adjusting the metabolism of carbohydrates and lipids, regulating appetite, and directly regulating the reproduction, differentiation, and metabolism of adipocytes (19). *In vitro* studies have shown that polyphenols present in fruits and vegetables, such as naringenin, quercetin, hesperidin, and resveratrol, inhibit the proliferation and induce the programmed death of peri-adipocytes (40). Certain additional flavonoids exhibit the capacity to inhibit adipogenesis and promote lipolysis in adipocytes. Studies have reported that increasing the consumption of foods rich in phytochemicals is inversely related to breast cancer, insulin resistance, and high blood pressure. The lower chance of obesity, abdominal obesity, and hypertriglyceridemia, as the main risk factors of cardiovascular diseases, were associated with a higher phytochemical profile (22,24,37,40). In the study conducted by Hislop *et al*, it was shown that the implementation of a diet containing vitamin B12 and iron supplements reduces the neurological and psychological symptoms of patients with MS, and a diet containing antioxidants and unsaturated fatty acids reduces the clinical symptoms of patients, such as movement disorders, depression, and fatigue (41). Phytochemicals, including phenolic compounds (phenolic acids, flavonoids, hydroxycinnamic acids, lignans, stilbenes), isoprenoids, organosulfur compounds (allyl sulfur, isothiocyanates), and natural bioactive compounds, are abundant in fruits, vegetables, whole grains, and legumes and play a key role in modulating the risk factors of chronic diseases, including types of cancer, type 2 diabetes, *etc*. Various studies agree that the indicators of metabolic syndrome and the type of nutrition of a person have a great impact on the incidence and severity of MS symptoms (17,42). The results of recent studies prove that insulin resistance and abdominal obesity through disturbances in the plasma levels of adipokines, changes in the metabolism of fatty acids, and dysfunction of blood vessels cause procoagulation and systemic inflammation, as well as disruption of the oxidant and antioxidant balance in the body, or in other words, oxidative stress can play a role in the pathogenesis of various neurodegenerative diseases, including MS (12,13).
Cytokines and chemokines appear to play a key role in regulating many of the cellular interactions that occur in MS. The pro-inflammatory cytokines including IL-2, TNF-α, and IFN- γ play a key role in activating and maintaining immune responses that can directly damage oligodendrocytes or myelin membrane, and this disease is referred to as an inflammatory disease (10). Dietary phytochemicals induce their beneficial effects mainly due to their antioxidant, anti-inflammatory properties, and regulation of carbohydrate and lipid metabolism (19). Another study demonstrated that phytochemicals significantly reduce oxidative stress (19). Since phytochemicals have been identified as a strong antioxidant source, their consumption can be considered as a reason to reduce oxidative stress. In fact, foods rich in phytochemicals can increase serum phytochemical levels. To provide a more comprehensive picture of the consumption of foods rich in phytochemicals and its relationship with the risk of contracting diseases, the phytochemical index has been regarded (43).

Conclusion

In conclusion, this cross-sectional analytical study found that increasing the phytochemical profile of the diet can reduce the severity of fatigue in patients with MS. The study also showed the DPI score is decreased by an increase in age, and the phytochemical index score of the diet was higher in women than in men. Furthermore, patients who had a higher score of DPI had lower average anthropometric indices such as body mass index, weight, waist circumference, and the ratio of waist circumference to hip circumference. However, as the DPI scale is a relatively new scale in dietary studies, future studies should focus on it. Additionally, since this study is the first to investigate the association between DPI and MS symptoms, more research is required in the future to investigate the mentioned effects.

Ethical approval

Prior to participating in the study, the participants were given written details concerning the background and procedures of the study, and then they provided written informed consent. This study was carried out in compliance with the Declaration of Helsinki, and it was approved by the ethical committee of the Kashan University of Medical Sciences (Ethics Number: IR.KAUMS.MEDNT.REC.1401.079).

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Conflict of Interest

The authors declare that they have no conflict of interest.

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