Adherence to healthy dietary pattern is associated with lower risk of multiple sclerosis

Journal of Central Nervous System Disease
Volume 14: 1–9

DOI: 10.1177/11795735221092516
SAGE

Fatemeh Keykhaei[1], Somayeh Norouzy[2], Mohsen Froughipour[3], Mohsen Nematy[1], Morteza Saeidi[2], Lida Jarahi[4], Fatemeh Amiri[1], Mahsa Malek Ahmadi[1] and Abdolreza Norouzy[1]

[1]Department of Nutrition, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. [2]Department of Management and Medical Information, Kerman University of Medical Sciences, Kerman, Iran. [3]Department of Neurology, Ghaem Hospital, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. [4]Department of Community Medicine, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

ABSTRACT

BACKGROUND: Different studies have confirmed the role of nutritional factors in the etiology of Multiple sclerosis (MS). However, dietary patterns associated with the risk of MS remain unknown.

OBJECTIVES: This study aimed to investigate the possible relationship between the existing dietary patterns and the risk of MS.

METHODS: This case-control study was conducted in Mashhad city, Iran in 2015. In total, 197 MS patients and 200 control subjects (matched in terms of age, gender, education level, and body mass index) were enrolled in this study. The required data were collected through interviews and questionnaire completion. Moreover, the data on the usual dietary intake of each participant during the past year were evaluated using a valid and reliable semi-quantitative food frequency questionnaire (160 items). Logistic regression analysis was applied to discover the associations between dietary patterns and the risk of MS.

RESULTS: Four major dietary patterns were identified in this study, including Unhealthy, Western, Healthy, and Traditional. After adjustment for smoking habits, the family history of autoimmune diseases and the duration of breastfeeding, the highest tertile of Healthy dietary pattern was found to be associated with the reduced risk of MS by 74% (OR = .26; $P < .001$), whereas the Unhealthy dietary pattern was associated with a three-fold increased risk of MS (OR = 3.04; $P < .001$). However, no correlation was observed between the Western and Traditional dietary patterns and the risk of MS.

CONCLUSION: According to the results of this study, a healthy diet may reduce the risk of MS, whereas an unhealthy dietary pattern may.

KEYWORDS: multiple sclerosis, dietary pattern, food frequency questionnaire

RECEIVED: December 18, 2020. **ACCEPTED:** March 21, 2022.

TYPE: Original Research Article

DECLARATION OF CONFLICTING INTERESTS: The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

FUNDING: The authors received no financial support for the research, authorship, and/or publication of this article.

CORRESPONDING AUTHOR: Abdolreza Norouzy, Metabolic Research Center, Mashhad University of Medical Sciences, Azadi Square, University Paradise, Mashhad 91779-48564, Iran. Email: norouzyA@mums.ac.ir

Multiple sclerosis (MS) is a chronic progressive, inflammatory, neurodegenerative disorder of the central nervous system (CNS). It is the leading cause of disability in young adults, especially women aged 20–40 years. MS is characterized by axonal injury and demyelination.[1] Currently, 2.8 million people are diagnosed with MS across the world.[2]

According to the international MS prevalence categorization, Iran is located in a low-risk region for this disease (5–25 cases per 1,00,000 individuals); however, the prevalence of MS has increased to 35.5–51.9 cases per 1,00,000 individuals in the central areas of our country.[3] Furthermore, epidemiological studies in different countries indicated that the interactions of genetic and environmental factors are strongly involved in the incidence of MS.[4,5]

More recently, epidemiologic research, preclinical models, a small number of prospective studies, and limited prospectively followed cohorts provide preliminary evidence that dietary factors influence MS incidence, the course of the disease, and symptomatology.[6]

Several studies addressed the association between dietary habits and the incidence of MS, the results of which have pointed to the relationship between the consumption of animal saturated fats, dairy products, fruits, and vegetables with the risk of MS.[7-10] Some researchers believe that consuming fruits and vegetables could lower the risk of MS, possibly due to the effect of antioxidants.[11,12] On the other hand, some studies demonstrated that consuming smoked or processed meat (containing nitrate) raises the risk of MS. Smoked or processed meat has been associated with the higher odds of MS, while consuming fish could exert protective effects against MS.[7]

The individual component approach could reveal several significant associations between dietary parameters and the incidence of MS. However, it might overlook the complexity of the proper relationship between dietary habits and the disease.[13] Dietary patterns refer to the combined effects of foods exploring beyond the results explained by single foods or nutrients.[14]

Dietary patterns diverge across different genders, races, cultures, and geographical ethnicities. The general nutritional habits of every country and the associations with health and the disease status of the people need further research in different populations.[15] Investigating dietary patterns reflect the nutritional habits and behaviors of individuals, yielding detailed information about nutritional etiology.[3]

Although considering the effects of macro or micronutrients and singular foods or food groups, it is essential to note that these individual components are not ingested in isolation. Instead, the diet comprises many members eaten together as part of an overall program, and there are likely significant interactions. Therefore, examining the effects of global dietary patterns is very important[6]

Considering the scientific evidence about nutrition and MS incidence, as well as the possible role of this parameter in the etiology of the disease, the present study aimed to evaluate the possible association between dietary patterns and MS to discover the details of the nutritional etiology of MS. Further studies and clinical trials are warranted to advance this line of research.

Methods

The sample size was calculated by the sample size formula in correlation studies and according to a survey conducted by Jahromi et al,[16] which stated that the relationship between the traditional diet score and the risk of MS was .27 (r)

$$n = \left[\frac{Z_\alpha + Z_\beta}{c}\right]^2$$

$$c = 0.5 * Ln[(1+r)/(1-r)]$$

This case-control study was conducted on 197 relapsing-remitting MS (RRMS) patients within the age range of 18–65 years selected from Mashhad MS Association Registry (the North East of Iran) in 2015. The study was conducted after the approval of the Mashhad University of Medical Sciences Ethics Committee with numbers A-748, and each individual entered the study with fully informed consent. The research population consisted of the MS patients registered within the past six months and the newly registered patients reporting no change in diet.[17]

Moreover, 200 healthy controls were enrolled in the study. The control group included the interested healthy participants with no neurological diseases. They filled and signed the written informed consent. They were also selected according to the following inclusion criteria: coming from the same hospital as cases to reduce the risk of bias in demographics, for various acute conditions unrelated to pregnancy, and long-term dietary modifications. They matched age (10-year groups), gender, education level, and body mass index (BMI).

The exclusion criteria for both groups were as follows: (1) adherence to a specific diet during the past year, (2) consumption of food supplements, and (3) under- or over-estimation of energy intake (<800 or >4200 kcal/day).

Demographic information and other relevant information about smoking habits, a family history of autoimmune diseases, and duration of exposure to breastfeeding (0-6 months or ≥7 months), were obtained with the help of skilled interviewers.

Anthropometric measurements

Anthropometric measurements for each individual were recorded by trained health professionals following CDC's recommendations given in the anthropometry procedures manual 2007 by National Health and Nutrition Examination Survey.[18]

Body composition and weight were measured while the subjects were minimally clad and barefoot. The obtained data were analyzed using a bioelectrical impedance analyzer (Tanita BC-418 Body Composition Analyzer) and recorded to the nearest 100 g. The participants' height was measured in a standing position without shoes using a tape measure with shoulders in a normal situation. The obtained data were recorded to the nearest .5 cm. The waist circumference was measured in duplicate at a level midway between the lowest rib and iliac crest to the nearest millimeter using a flexible tape. BMI was calculated using the following formula: the weight in kilograms/[height in meters] ̂2). Based on the BMI classification of the World Health Organization, the subjects were categorized as underweight (<18.5 kg/m^2), healthy weight (18.5-24.9 kg/m^2), overweight (25-29.9 kg/m^2), and obese (≥30 kg/m^2) in accordance with the predetermined cut-off points.[19]

Assessment of dietary intake

In this study, subjects' routine dietary intake was assessed using the semi-quantitative Food Frequency Questionnaire (FFQ), with 160 Iranian food items, developed, and validated in Mashhad University of Medical Sciences.[20] In this study, FFQ was completed during face-to-face personal interviews conducted by expert dietitians. The interviewers used photographs of household portions to confirm the precise food intake as household measures.

Table 1. Categorization of food groups in dietary pattern analysis.

FOOD GROUP	
Breads	Different types of bread: Barbaric, barley, sangak, milk-mixed, machine-baked, lawash, taftan, fatir, French loaves and toasts
Rice	Simple and different types of kata
Low-fat dairy	Low-fat milk, low-fat yogurt, cocoa milk and cheese
High-fat dairy	High-fat milk, high-fat yogurt, cream cheese and a variety of dairy ice creams
Butter	Butter
Red meat and viscera	Traditional food Koobida or loqma kebab, shishlik or barg kebab, bakhtiari kebab, fried meat such as: pan meat, meat mixed with muscle, qurma and steak, cutlet, shami kebab, tass kebab, roast beef, Turkish kebab, hamburger, lamb tongue, legs, parotid, meat roulette, donut or samosa, liver, heart or kidney, rumen, brain, mixed liver
Processed meat, canned	(Hamburger, sausages, corned beef, beef jerky meat)
Poultry	Grilled chicken, fried chicken and pachin (traditional food)
Fish	Fried fish and grilled fish
Tuna	Tuna fish
Stews	Chicken stew, meat and vegetable stew, split pea stew, celery stew, fesenjan stew, succinic stew, eggplant stew, yatimcha, bamia stew
Soups and porridges	Barley soup, noodle soup, other kinds of soups Noodle aash, wheat or rice aash, yogurt aash, shola qalamkar aash Mashhadi shola, halim, kashk ishkana, egg ishkana
Egg	Poached egg, scrambled eggs and omelets
Fruits	Apples, bananas, grapes, lemons, oranges, and strawberries, …
Fruit juice	Types of fruit juices
Nuts	Walnuts, almonds, pistachios, seeds, …
Vegetables	Tomato, carrot, cucumber and herbs, …
Tea	Tea
Coffee	Bitter coffee or nescafe, sweet coffee or nescafe
Soft drinks	Coke, diet coke, beer
Broth	Broth, lamb head and leg savory
Potato	Mashed potatoes, potatoes and yogurt
French fries	French fries, chips
Bean	Lentils, mixed peas, different types of bean
Pizza	Vegetables pizza, meat pizza
Spaghetti	Macaroni, lasagna
Salads	Olivier, macaroni salad, green salad, cabbage salad, shirazi salad
Desserts	Milk pudding, caramel cream, jelly, honey, jam, halva, rice and milk, maqut, sweet halva
Sugars and sweets	Sugar cubes or balls, poolaki, sugar, rock candy, sohan, gaz, sugar floss, candies, gummy candy, chewing gum, cream cake or cookies, non-creamy cakes and cookies, jalebi, bamia, ice pop, shirazi faloodeh, canned fruits, different types of syrup
Pickles	Different types of pickle
Snacks	Biscuit, chips, corn snack, Mexican corn, fruit bar, black kashk, tamarind

In FFQ, the average food intake is based on the typical portion sizes among the Iranian population. To elaborate on the exact amount of participants' use of food, standard units were set based on the typical servings by most individuals (e.g., a bowl of yogurt and chips, a glass of beverage, and a plate of rice). Because similar dishes have different sizes, to establish the average use, a food photo album was placed at the beginning of the FFQ with ten photos showing the average uses of foods.

Moreover, the participants were inquired about the frequency of consuming several food items within the past month. The frequency of consuming each food item was evaluated in different categories, as follows: never or less than once a month, monthly (1–3 times a month), weekly (once a week, 2–4 times a week, 5–6 times a week), and daily (once a day, 2–3 times a day, 4–5 times a day, six times or more a day).

Portion sizes were classified as small (half of the persistent moderate use or less), medium (equal to the determined average use), and large (one and a half times more than the modarate use or more). The recorded frequency of consuming each food was converted to daily intake, and the serving size of the consumed items was converted to grams using household measures.

Due to the variety of the recorded food items, the food items were classified into 32 food categories (Table 1). This classification was made based on the similarity of the nutrient content of each food item.

Some food items that had unique nutrient profiles (e.g., eggs), if consumed, could indicate a particular food pattern (e.g., French fries or pizza). These were taken as a separate food category.

Statistical analysis

The dietary intakes were converted into grams per day. All data analyses were done in SPSS (version 16; SPSS Inc, Chicago, IL). We classified the 160 food items in the FFQ into 31 food groups (Table 1), because of the variety of the recorded food items. This classification was made based on the similarity of the nutrient content of each food item and also in the light of the related literature.[21] Factor analysis was used to determine the significant dietary patterns based on 31 food categories, because the factor analysis is a proper multivariable statistical method to determine dietary patterns.[22,23] This data reduction method identifies the independent vectors of variables in a correlation matrix. It provides scores that allow individuals to be ranked in terms of how closely they conform to the total pattern.[24] The factors were rotated by orthogonal transformation. In addition, we used the eigenvalue threshold of 1.2 and scree plots to select the number of factors to retain. The eigenvalues declined after the fourth factor and remained similar.

To achieve a simple and explainable matrix and detect food patterns, a varimax rotation was used. To define food groups in each pattern and simplify food pattern tables, factor loads under .2 were omitted. The factor load shows the correlation between dietary patterns and food groups that varies from −1 to +1. A positive load indicates a positive association with the factor, whereas a negative load shows an inverse relationship. The larger a load of a given food item or group relative to the factor, more significant the contribution of that food item or group to a specific factor.[22,23,25,26] Subsequently, the dietary patterns were identified according to the consumed food items placed in these patterns. The defined dietary patterns (i.e., factors) were labeled based on our interpretation of the content and previous manuscripts.[17,25,26]

Each participant received a factor score for each identified pattern. Afterward, they were divided into three groups based on a tertile distribution of dietary pattern scores using logistic regression models. The lowest tertile of each dietary pattern was used as the reference. To assess the trend across the tertiles, we assigned median values to each tertile of the dietary pattern scores as a continuous variable.[27-29] In addition, conditional multivariate logistic regression was used to assess the associations between dietary patterns and the risk of MS. The first tertile of dietary pattern score was determined as the reference. Since the initial model was unadjusted, it was further adjusted for smoking habits, the family history of autoimmune diseases, and the duration of breastfeeding.

Results

In total, 197 patients with MS based on the diagnosis of a specialist who met the inclusion criteria were enrolled in this study. In addition, 200 healthy subjects were taken as the control. The patients' demographic characteristics and their peers in the control group are presented in Table 2.

The majority of MS patients in this study were female (77.7%) with a mean age of 32.5 ± 8 years. The known risk factors significantly associated with MS were smoking habits, family history of autoimmune diseases, and duration of breastfeeding. Correspondingly, smoking habits (OR = 3.22; $P < .001$) and family history of autoimmune diseases (15.2%) showed to increase the odds of MS (OR = 4.70; $P < .001$), whereas the duration of breastfeeding was associated with the reduced odds of MS (OR = .48; $P = .006$) (Table 3).

The mean BMI of the two groups (case and control) was 24.77 ± 5.42 and 25.25 ± 5.02 kg/m^2, respectively ($P = .36$). In terms of the classification of BMI, 8% of the patients were underweight, 48.7% were healthy weight, 28.4% were overweight, and 14.6% were obese ($P = .74$).

The mean waist circumference of the case and control subjects was 83.42 ± 12.51 and 82.48 ± 12.71 cm, respectively ($P = .46$). Moreover, the body fat percentage of the case and control subjects was 28.81% and 26.48%, respectively ($P = .007$). The mean lean body mass in MS patients and control subjects was 42.56 ± 7.98 and 47.46 ± 9.10, respectively ($P < .001$) (Table 4).

Our findings identified four main dietary patterns via factor analysis, as follows:

Table 2. Participants characteristics of in multiple sclerosis and healthy control groups.

PARTICIPANTS CHARACTERISTICS		MULTIPLE SCLEROSIS (*N* = 197)	HEALTHY CONTROL (*N* = 200)	*P*-VALUE
		N (%)		
Gender				
Male		44 (22.3)	36 (18)	.26*
Female		153 (77.7)	164 (82)	
Education Level				
Elementary		23 (11.6)	20 (10)	.50*
Secondary		90 (45.2)	82 (41)	
Post-secondary		83 (42.1)	97 (48.5)	
Occupational status				
Student		30 (15.22)	54 (27)	.007*
Practitioner		56 (28.42)	62 (31)	
Home/domestic duties		108 (54.82)	79 (39.5)	
Retired		2 (1.01)	3 (1.5)	
Positive family history of autoimmune diseases		30 (15.2)	8 (4)	<.001*
Cigarettes smoking habits		46 (23.4)	21 (10.5)	<.001*
Duration of breastfeeding				
0-6 months		58 (29.4)	40 (20)	.006*
>6 months		139 (70.6)	160 (80)	
BMI category	<18.5	16 (8)	13 (6.5)	.74*
	18.5-24.9	96 (48.7)	92 (46)	
	25-29.9	56 (28.4)	59 (29.5)	
	≥30	29 (14.6)	36 (18)	
Age (year, mean ± SD)		32.54 ± 8.85	31.72 ± 8.39	.33**

*Chi square test, **T-test.

Table 3. Anthropometric measurements of subjects in multiple sclerosis participants and healthy control.

ANTHROPOMETRIC INDICES	MULTIPLE SCLEROSIS (*N* = 197)	HEALTHY CONTROL (*N* = 200)	*P*-VALUE*
	MEAN ± SD		
Waist circumference (cm)	83.42 ± 12.51	82.48 ± 12.71	.46
Body fat percentage	28.81 ± 7.84	26.48 ± 12.71	.007*
Lean body mass (kg)	42.56 ± 7.98	47.46 ± 9.10	<.001*
Body mass index	24.77 ± 5.42	25.25 ± 5.02	.36

*T-test.

1. Unhealthy dietary pattern (consumption of desserts, coffee, sugar and sweets, pickles, red meat, and soft drinks).
2. Western dietary pattern (consumption of pizza, poultry, snacks, processed meat, and tuna).
3. Healthy dietary pattern (consumption of fruits and vegetables, salads, stews, bread, and low-fat dairy).
4. Traditional dietary pattern (consumption of broth, nuts, eggs, fruit juice, high-fat dairy products, and fish).

Table 4. Factor-loading matrix and the explained variances for major dietary patterns and food groups identified in study participants.

FOOD GROUPS	LOADING COEFFICIENT			
	DIETARY PATTERNS			
	UNHEALTHY	WESTERN	HEALTHY	TRADITIONAL
Desserts	.74	.16	.07	.06
Coffee	.64	.11	.22	−.06
Sugars and sweets	.61	.06	.04	.14
Pickles	.61	−.05	−.06	.14
Red meat	.55	.32	.08	.23
Soft drinks	.44	.31	.06	−.02
Pizza	.07	.76	−.08	−.09
Poultry	.22	.69	.45	.01
Snacks	.88	.53	.08	.27
Processed meat	.49	.53	−.04	.14
Tuna	.05	.49	.25	.11
Vegetables	−.08	−.01	.73	−.02
Salads	.18	.04	.71	.01
Stews	.08	.12	.42	.06
Fruits	.01	.01	.37	−.02
Bread	.02	.03	.32	.01
Low-fat dairy	.03	−.07	.20	.14
Soups and porridges	.18	.03	.02	.68
Broth	.19	.02	.03	.62
Nuts	−.05	.03	.10	.49
Eggs	−.02	.09	.05	.46
Fruit juice	.16	.02	−.08	.25
High-fat dairy	.06	−.01	.19	.20
Fish	.13	.19	.12	.20
Percent of variance explained	17.19	6.60	5.94	4.74

Total variance explained by four factors: 34.47. Values <.20 were excluded for simplicity. Bartlett's test of sphericity was <.001.

The correlation of the food groups consumed and dietary patterns are shown in Table 5.

The odds ratios of MS across the tertiles of dietary patterns are presented in Table 5. After adjustment for tobacco use, breastfeeding duration, and the family history of autoimmune diseases, the highest tertile of Healthy dietary pattern was associated with the reduced odds of MS by 74% (OR = .26; 95% CI: .14–.46) ($P < .001$).

On the other hand, the Unhealthy dietary pattern was associated with a 3-fold increase in the odds ratio of MS, and individuals in the second (OR=2.09, 95% CI: 1.19–3.67, P<.001) and third tertiles (OR=3.04; 95% CI: 1.71–5.41) (P<.001) had higher odds ratios of MS.

The correlation of Western and Traditional dietary patterns is adjusted, but no correlation is observed between western dietary pattern (OR = 1.22; 95% CI: .7–2.12) (P = .47) and traditional dietary pattern (OR = 1.41; 95% CI: .81–2.46) (P = 2.22) with MS (ORs are for the third tertile vs the reference).

Smoking habits increased the odds of MS (OR = 3.22; 95% CI: 1.72–6.03) ($P < .001$). Similarly, a family history of autoimmune diseases was associated with an increased odds of MS

Table 5. Multivariate adjusted odd ratios for multiple sclerosis across tertiles of dietary patterns.

TERTILE OF DP SCORE		MULTIPLE SCLEROSIS (*N* = 197)	CONTROL (*N* = 200)	BEFORE ADJUSTMENT			ADJUSTED		
		N (%)		OR (95% CI)	*P*-VALUE	*P*-VALUE FOR TREND	OR (95% CI)	*P*-VALUE	*P*-VALUE FOR TREND
Unhealthy	T1	47 (23.8)	85 (42.5)	1.00		<.001*	1.00		.001*
	T2	70 (35.5)	63 (31.5)	2 (1.22–3.28)	.006*		2.09 (1.19–3.67)	<.001	
	T3	80 (40.6)	52 (26)	2.78 (1.69–4.58)	<.001*		3.04 (1.71–5.41)	<.001	
Western	T1	63 (31.9)	69 (34.5)	1.00		.50	1.00		.47
	T2	63 (31.9)	70 (35)	.98 (.60–1.59)	.95		.86 (.50–1.50)	.60	
	T3	71 (36)	61 (30.5)	1.27 (.78–2.06)	.32		1.22 (.70–2.12)	.47	
Healthy	T1	87 (44.1)	45 (22.5)	1.00		<.001*	1.00		<.001*
	T2	62 (31.4)	71 (35.5)	.45 (.27–.74)	.002*		.35 (.19–.62)	<.001	
	T3	48 (24.3)	84 (42)	.29 (.17–.49)	<.001*		.26 (.14–.46)	<.001	
Traditional	T1	64 (32.4)	68 (34)	1.00		.35	1.00		.21
	T2	61 (30.9)	72 (36)	.90 (.55–1.45)	.66		.86 (.50–1.50)	.61	
	T3	72 (36.5)	60 (30)	1.27 (.78–2.06)	.32		1.41 (.81–2.46)	.22	

Adjusted for smoking habits, family history of autoimmune diseases and duration of breastfeeding (0-6 months or >6 months).
$^*P < .01$.

(OR = 4.70; 95% CI: 1.99–3.17) ($P < .001$), whereas a higher duration of breastfeeding was associated with a reduced odds of MS (OR = .48; 95% CI: 0.28–.80) ($P = .006$). The multivariate logistic regression was used, and each factor was explored after adjusting the other confounding factors.

Discussion

The present study indicated that Healthy dietary patterns, including the consumption of fruits, and vegetables, salads, stews, bread, and low-fat dairy, was associated with a 74% of reduced odds of MS in the second, and third tertiles compared with the first tertile as the reference, and the Unhealthy dietary pattern, including the consumption of desserts, coffee, sugar, and sweets, pickles, red meat, and soft drinks, was associated with a 3-fold increased risk of MS, and subjects in the second and third tertiles vs the reference had higher odds ratios of MS.

In this regard, Razeghi Jahromi et al stated that adherence to vegetarian (high in green leafy vegetables, hydrogenated fats and fruit juice), lacto-vegetarian (high in nuts, fruits, sweets and desserts, vegetables, and high-fat dairy products) and traditional dietary patterns (use of meat, high in low-fat dairy products, vegetable oil, whole, and refined grains, soy, organ meats, coffee, and legumes) is inversely correlated with the risk of MS. Moreover, researchers maintained that the prevalence of MS was higher in individuals with animal fat dietary patterns (high in animal fats, meat products, sugars and hydrogenated fats, and low in whole grains)[16,30] and that there is a significant association between consuming fruit, vegetable and healthy fat and MS[30,31] It is also shown that high-fat and high-sugar lead to an increased systematic inflammation which ends in MS incidence incensement.[31] In a previous study by Hosseini et al conducted in Tehran, two dietary patterns were identified, and it was shown that adhering to the healthy dietary pattern (Whole vegetable, Whole grains, legumes, fruits, low-fat dairy products) was significantly associated with a 70% lower risk of MS, while a marginally significant positive association was found when evaluating the effect of the Western dietary pattern (potato chips, pickles, high-fat dairy products, processed meats, sugar, hydrogenated fats, and red meat) on MS risk.[17]

In a previous study by Black L et al, two major dietary patterns were identified: healthy (fish, eggs, high in poultry, vegetables, and legumes) and Western (high in meat, full-fat dairy; low in whole grains, nuts, fresh fruit). A one-standard-deviation increase in the healthy pattern score was associated with a 25% reduced risk of a first clinical diagnosis of central nervous system demyelination. There was no statistically significant association between the Western dietary pattern and the risk of a first clinical diagnosis of central nervous system demyelination.[32]

Other studies in this regard have mainly evaluated the effects of single foods or nutrients on the risk of MS.[11,12,21,33] Additionally, several studies pointed to the fact that a sufficient intake of vitamin D, polyunsaturated fatty acids, vegetables, vegetable protein, fruits, fiber, low-fat milk, antioxidants, vitamins A, C, B, particularly vitamin B12, folate, calcium, and potassium can exert protective effects against MS.[7,11,12,21,31,34]

According to a systematic review, consuming vegetable protein, dietary and cereal fiber, thiamin, vitamin C, riboflavin, potassium, and calcium (abundantly found in plants and different vegetables, fruits and grains) is negatively correlated with the risk of MS.[7] The findings of the current study indicated that adherence to a dietary pattern low in animal fat and high in vegetables, salads, and fruits could decreased the risk of MS. Similarly, a prospective pediatric MS study revealed an increased risk of relapse relating to an increased saturated fat intake, and a reduction in the relapse rate with an increased intake of vegetables.[31]

A body of research showed the possible effect of antioxidants on reducing MS risk.[7,12,35] Vitamins are the antioxidants playing a protective role in the prevention of MS.[21] In this regard, the results of a case-control study in Canada confirmed the protective effects of consuming fruits and vegetables much to fight back MS, and a significant negative association between vitamin C consumption and the risk of MS.[8]

According to the literature, proinflammatory dietary factors include the saturated fatty acids of animal origin, unsaturated fatty acids in trans-configuration, meat, sweetened drinks; hypercaloric diets rich in refined (low-fiber) carbohydrates, increased dietary salt, and the intake of proteins in cow milk fat globule membrane.[36]

According to Swank and Goodwin, high-fat diets lead to the synthesis of storage lipids, and cholesterol, managing to reduce membrane fluidity, possible capillary obstruction, and inflammation[37] Recent studies indicated that the effect of saturated fats is controlled at the transcriptional level, influencing gene expression, and cell metabolism, development and differentiation.[35]

A high sugar intake rapidly increases the amount of calories and glucose level. Subsequently, it is likely to increase insulin production, upregulation of biosynthetic pathways, and production of arachidonic acid and its pro-inflammatory derivatives.

Non-processed meat is an important dietary source of protein, zinc, iron, vitamin B12, other minerals, and vitamins.[38] However, epidemiological studies have linked higher meat consumption with an increased risk of chronic diseases, including obesity, cardiovascular diseases, type 2 diabetes and cancers. Findings are mainly to the fat content of meat, and the possible formation of carcinogenic compounds when cooked at a high temperature.[39]

Recent national studies reported the nutritional transition from the Iranian dietary patterns toward western or unhealthy dietary patterns during the past two decades, which is considered an important underlying cause of chronic diseases in Iran.[25,26,40]

The traditional Iranian diet consists of foods like cooked rice, mixed pilaf, rice, and stew, rice, high-protein dishes, and stuffed vegetables.[41]

In the present study, it was also shown that MS occurs more frequently in women. The findings of the current studies indicated that MS prevalence is at least two times as high in women as in men.[42] This has led to extensive studies of differences in the immune system or nervous system between women and men, which might be caused by the effects of gonadal hormones, genetic differences, and different environmental exposures, and men's and women's modern lifestyles. We review the impact of sex from a genetic, immunological, and clinical point of view.[43]

In the current study, the duration of breastfeeding was found to decrease the risk of MS. Other studies in this regard investigated the role of breastfeeding in the incidence of MS, proposing inconclusive results. Breastfeeding for at least four months is associated with a reduced risk of MS.[44,45] Human milk and breastfeeding duration may affect the development of the white matter of the brain[46] The protective effect of breastfeeding in MS pathogenesis may be related to components with antimicrobic activities, such as immunoglobulins, lysozyme, oligosaccharides (human milk oligosaccharides, HMO), fatty acids, lactoferrin, polyamines, and other glycoproteins and peptides.[45]

Since dietary patterns broadly vary depending on gender, race, culture, and geographical diversity, the existing research needs to be replicated in different populations.

Limitations of study

One limitation of this study is that the dietary patterns explored are just one component of a lifestyle, but nutritional behaviors such as time and the frequency of meals and snacks were not evaluated though they play a crucial role in predicting dietary patterns. Also, the result of dietary pattern assessment mostly depends on the target population, and discrepancies were reported concerning to race, culture, and geographical districts. We also suggested the assessing eating behaviors, consumption of snacks, and meal patterns,[47] and a need for a longitudinal study of this topic. Moreover, the factor analysis method has certain limitations due to the theoretical or arbitrary decisions that a researcher makes that can influence the findings. Finally, the possibility of recall bias to evaluate dietary patterns by FFQ assessment should not be overlooked. Another limitation is susceptibility to bias in recollection about exposure, and reverse causality.[48]

It is also noteworthy that the effects of the potential confounding variables, such as Epstein–Barr virus infection, sun exposure, and residual dietary factors on the incidence of MS, were not evaluated and adjusted in this study. There is a need for longitudinal investigations and the limitations of the case-control design, including susceptibility to bias in recollection about exposure and reverse causality.

Still, another limitation is that we do not provide any data about the disability status of MS patients and physical activity. In this study, MS patients have significantly higher body fat percentages. This can be due to disability.

Conclusion

In the light of the present findings, adherence to a healthy diet, including the consumption of fruits, and vegetables, salads, stews, bread, and low-fat dairy products, is associated with the reduced risk of MS. On the other hand, an unhealthy dietary pattern, including the consumption of desserts, coffee, sugar and sweets, pickles, meat, and soft drinks, is likely to increase the risk of MS. Therefore, it is recommended that further research be conducted to identify the correlations between other dietary patterns and the incidence of MS to establish a causal relationship between diet and MS.

Acknowledgments

At this moment, we hope to be grateful to the staff of Mashhad MS Organization and the Research Development Center of Ghaem Hospital of Mashhad, Iran, for assisting us in this research project.

ORCID iDs

Fatemeh Keykhaei https://orcid.org/0000-0001-7516-370X
Abdolreza Norouzy https://orcid.org/0000-0001-6740-5502

REFERENCES

1. Farinotti M, Vacchi L, Simi S, Di Pietrantonj C, Brait L, Filippini G. Dietary interventions for multiple sclerosis. *Cochrane Database Syst Rev*. 2012;12:CD004192.
2. Walton C, King R, Rechtman L, et al. Rising prevalence of multiple sclerosis worldwide: Insights from the atlas of MS. *Mult Scler J*. 2020;26(14):1816-1821.
3. Bagheri M, Maghsoudi Z, Fayazi S, Elahi N, Tabesh H, Majdinasab N. Several food items and multiple sclerosis: A case-control study in Ahvaz (Iran). *Iran J Nurs Midwifery Res*. 2014;19(6):659-665.
4. Olsson T, Barcellos LF, Alfredsson L. Interactions between genetic, lifestyle and environmental risk factors for multiple sclerosis. *Nat Rev Neurol*. 2017;13(1):25-36.
5. Jörg S, Grohme DA, Erzler M, et al. Environmental factors in autoimmune diseases and their role in multiple sclerosis. *Cell Mol Life Sci*. 2016;73(24):4611-4622.
6. Sand IK. The role of diet in multiple sclerosis: mechanistic connections and current evidence. *Curr Nutr Rep*. 2018;7(3):150-160.
7. da Silva KRP, Alvarenga RMP, Fernandez y Fernandez O, Alvarenga H, Thuler LCS. Potential risk factors for multiple sclerosis in Rio de Janeiro: A case-control study. *Arq neuropsiquiatr*. 2009;67(2A):229-234.
8. Ghadirian P, Dadgostar B, Azani R, Maisonneuve P. A case-control study of the association between socio-demographic, lifestyle and medical history factors and multiple sclerosis. *Can J Public Health*. 2001;92(4):281-285.
9. Khadilkar SV, Sahni AO, Agarwal S. A case control study of environmental risk factors in Indians with multiple sclerosis. *Neurol Asia*. 2005;10:47-52.
10. Bjørnevik K, Chitnis T, Ascherio A, Munger KL. Polyunsaturated fatty acids and the risk of multiple sclerosis. *Mult Scler J*. 2017;23(14):1830-1838.
11. Pekmezovic TD, Tepavcevic DBK, Mesaros ST, Basuroski IBD, Stojsavljevic NS, Drulovic JS. Food and dietary patterns and multiple sclerosis: A case-control study in Belgrade (Serbia). *Ital J Public Health*. 2012;6(1):81-87.
12. Ascherio A, Munger KL. Environmental risk factors for multiple sclerosis. Part II: Noninfectious factors. *Ann Neurol*. 2007;61(6):504-513.
13. Waijers PM, Ocké MC, van Rossum CT, et al. Dietary patterns and survival in older Dutch women. *Am J Clin Nutr*. 2006;83(5):1170-1176.
14. Hodge AM, English DR, O'Dea K, Giles GG. Dietary patterns and diabetes incidence in the Melbourne collaborative cohort study. *Am J Epidemiol*. 2007;165(6):603-610.
15. Dindyal S, Dindyal S. How personal factors, including culture and ethnicity, affect the choices and selection of food we make. *Internet J Caribb Third World Med*. 2003;1(2):27-33.
16. Jahromi SR, Toghae M, Jahromi MJR, Aloosh M. Dietary pattern and risk of multiple sclerosis. *Iran J Neurol*. 2012;11(2):47-53.
17. Hosseini Z, Behrouz M, Philippou E, Keykhaei F, Nematy M. Dietary patterns and risk of multiple sclerosis: A casecontrol study. *J Nutr Sci Diet*. 2017:3(3):63-70.
18. Control CDC Prevention. *National Health and Nutrition Examination Survey (NHANES): Anthropometry Procedures Manual*. Atlanta, GA: CDC; 2007.
19. World Health Organization. *Obesity: Preventing and Managing the Global Epidemic*. Geneva, Switzerland: World Health Organization; 2000.
20. Ghazizahedi S, Nouri M, Norouzy A, et al. *Scientific: Validity and Reproducibility of Iranian Food Frequency Questionnaire*; 2014.
21. Fitzgerald KC, Tyry T, Salter A, et al. *A Survey of Current Dietary Habits within a Large Population of People with Multiple Sclerosis (S44. 002)*. AAN Enterprises; 2017.
22. Kim J-O, Mueller CW. *Factor Analysis: Statistical Methods and Practical Issues*. London, UK: Sage; 1978.
23. Kleinbaum DG, Kupper LL, Nizam A, Rosenberg ES. *Applied Regression Analysis and Other Multivariable Methods*. Boston, MA: Cengage Learning; 2013.
24. Jacques PF, Tucker KL. *Are Dietary Patterns Useful for Understanding the Role of Diet in Chronic Disease?* Oxford, UK: Oxford University Press; 2001.
25. Hosseyni Esfahani F, Jazayeri A, Mirmiran P, Mehrabi Y, Azizi F. Dietary patterns and their association with socio-demographic and lifestyle factors among Thehrani adults: Tehran lipid and glucose study. *J Sch Publ Health Inst Publ Health Res*. 2008;6(1):23-36.
26. Abdollahi S, Zeinali F, Azam K, Toupchian O, Djafarian K. Identifying major dietary patterns among the elderly in Tehran health homes. *Jundishapur J Health Sci*. 2015;7(4):e30395.
27. Safarian M, Ghayour-Mobarhan M, Esmailie H, Nematy M, Razavi A. Investigation of dietary patterns, healthy eating index and traditional risk factors of cardiovascular disease in 35-65 years old adults of Mashhad. *Med J Mashhad Univ Med Sci*. 2013;56(4):226-235.
28. Rahimi A, Rahimi M, Norouzy A, et al. Association of dietary pattern and body size with early menarche among elementary school girls in west of Iran. *Int J Pediatr*. 2019;7(12):10583-10593.
29. Woo HD, Kim DW, Hong Y-S, et al. Dietary patterns in children with attention deficit/hyperactivity disorder (ADHD). *Nutrients*. 2014;6(4):1539-1553.
30. Azary S, Schreiner T, Graves J, et al. Contribution of dietary intake to relapse rate in early paediatric multiple sclerosis. *J Neurol Neurosurg Psychiatr*. 2018;89(1):28-33.
31. Esposito S, Bonavita S, Sparaco M, Gallo A, Tedeschi G. The role of diet in multiple sclerosis: A review. *Nutr Neurosci*. 2018;21(6):377-390.
32. Black LJ, Rowley C, Sherriff J, Pereira G, Ponsonby A-L, Lucas RM. A healthy dietary pattern associates with a lower risk of a first clinical diagnosis of central nervous system demyelination. *Mult Scler J*. 2019;25(11):1514-1525.
33. Habek M, Hojsak I, Brinar VV. Nutrition in multiple sclerosis. *Clin Neurol Neurosurg*. 2010;112(7):616-620.
34. Shivappa N, Hebert JR, Behrooz M, Rashidkhani B. Dietary inflammatory index and risk of multiple sclerosis in a case-control study from Iran. *Neuroepidemiology*. 2016;47(1):26-31.
35. Zorzon M, Zivadinov R, Nasuelli D, et al. Risk factors of multiple sclerosis: a case-control study. *Neurol Sci*. 2003;24(4):242-247.
36. Riccio P, Rossano R. Nutrition facts in multiple sclerosis. *ASN neuro*. 2015;7(1): 1759091414568185.
37. Swank RL, Goodwin J. Review of MS patient survival on a Swank low saturated fat diet 1 1 (For an additional perspective, see editorial opinions). *Nutrition*. 2003;19(2):161-162.
38. National Health and Medical Research Council. *Australian Dietary Guidelines*.Canberra, Australia: National Health and Medical Research Council; 2013.
39. Bingham SA, Hughes R, Cross AJ. Effect of white versus red meat on endogenous N-nitrosation in the human colon and further evidence of a dose response. *J Nutr*. 2002;132(11):3522S-3525S.
40. Ghassemi H, Harrison G, Mohammad K. An accelerated nutrition transition in Iran. *Publ Health Nutr*. 2002;5(1A):149-155.
41. Karizaki VM. Ethnic and traditional Iranian rice-based foods. *J Ethn Foods*. 2016; 3(2):124-134.
42. Luchetti S, van Eden CG, Schuurman K, van Strien ME, Swaab DF, Huitinga I. Gender differences in multiple sclerosis: Induction of estrogen signaling in male and progesterone signaling in female lesions. *J Neuropathol Exp Neurol*. 2014;73(2):123-135.
43. Magyari M. Gender differences in multiple sclerosis epidemiology and treatment response. *Dan Med J*. 2016;63(3):B5212.
44. Ragnedda G, Leoni S, Parpinel M, et al. Reduced duration of breastfeeding is associated with a higher risk of multiple sclerosis in both Italian and Norwegian adult males: The EnvIMS study. *J Neurol*. 2015;262(5):1271-1277.
45. Fernández L, Langa S, Martín V, et al. The human milk microbiota: Origin and potential roles in health and disease. *Pharmacol Res*. 2013;69(1):1-10.
46. Isaacs EB, Fischl BR, Quinn BT, Chong WK, Gadian DG, Lucas A. Impact of breast milk on intelligence quotient, brain size, and white matter development. *Pediatr Res*. 2010;67(4):357-362.
47. Tseng M. Validation of dietary patterns assessed with a food-frequency questionnaire. *Am J Clin Nutr*. 1999;70:422.
48. Melamed A, Robinson JN. Case–control studies can be useful but have many limitations: Study design: Case-control studies. *BJOG*. 2019;126(1):23-23.