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Dietary Patterns in Mexican Patients With Multiple Sclerosis A Study of Cases and Controls

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ABSTRACT

Introduction: Multiple sclerosis is a demyelinating disease of the central nervous system. Various nutritional factors appear to be involved in the incidence and progression of the disease.

Objective: Identify dietary patterns in patients with multiple sclerosis.

Methods: An analysis of cases and controls was performed in the study "Risk factors associated with multiple sclerosis in Mexico: multicenter study" conducted at the National Institute of Neurology and Neurosurgery. The sample for this study corresponded to 205 prevalent cases and 433 healthy controls, matched by age and sex. Dietary information was obtained from the questionnaire frequency of food consumption, 3 years prior to diagnosis for cases and 3 years before the time of the interview for controls. 23 food groups were formed to generate dietary patterns cluster analysis was used.

Results: Two major dietary patterns were identified: "healthy" 50.16% and "unhealthy" 49.84%. The largest proportion of dietary intake by food groups in a healthy pattern was the consumption of fruits (23.86%) and vegetables (11.05%). While the unhealthy pattern had a high percentage of consumption in soft drinks and sweetened beverages (17.47%) and wheat and derivatives (6.58%). Higher proportion of healthy consumption pattern (58.54%) between cases and a higher proportion of consumption of unhealthy pattern (53.81%) among controls ($p < 0.05$) was observed. The conditional logistic regression analysis showed that MS cases consumed OR 1.85 (95%CI 1.23, 2.80) times the healthy pattern compared to controls.

Conclusion: Increased consumption of healthy dietary pattern among cases possibly associated with the study of prevalent cases that might have already changed their dietary patterns in an attempt to influence the natural course of the disease was found.

INTRODUCTION

Multiple Sclerosis (MS) is a neurodegenerative, demyelinating, inflammatory, chronic disease, of unknown etiology, which affects the Central Nervous System (SNC) [1]. It has a higher incidence among young adults who are between 20 and 40 years old. It

mainly affects women [2]. Most patients present progressive physical disability that limits and disables them in the medium or long term; besides this, the high cost of treatment with therapies to modify the disease makes MS a health problem that has a great social and economic impact [3]. In 2016, an estimated 2, 221,188 people worldwide had multiple sclerosis (95%UI 2, 033,866–2, 436,858), corresponding to a prevalence of 30.1 cases (95%UI 27.5–33.0) per 100000 populatio [4]. In some countries, there has been an increase in prevalence and incidence, in a range going from 80 to 300 cases per 100,000 inhabitants [5]. By contrast, there are low prevalences in regions such as Africa and South America, with around 5 cases per 100,000 inhabitants [6]. Mexico is considered to have a low prevalence, with approximately 1.5 to 12 cases per 100,000 inhabitants [7]. This could possibly be explained by environmental circumstances and the genetic makeup of the population, although underdiagnosis and/or underreporting could also be a determining factor for this low prevalence [7].

Different experimental, epidemiological and clinical studies have proposed that certain dietary patterns could have an influence on its incidence and progress [8]. Diets rich in saturated fats, consumption of red meat, cow's milk, alcohol, tobacco, candy, smoked products, coffee and tea, have been related to a greater risk and progression of MS [9-11]. While proteins of vegetable origin, a diet rich in fiber, polyunsaturated fats (fish, oils), skim milk, fruits, vegetables, rice and an adequate intake of certain micronutriments such as: vitamin D [12], vitamin B12 [13,14], vitamin E [15,16], vitamin A [17], folates [14], seem to be related to the disease in a protective way. However, these associations between certain dietary patterns and MS etiology and development are still inconsistent [18-20]. Based on prior studies on the association between certain dietary patterns and a greater risk of developing or modifying the course and prognosis of multiple sclerosis, in the present study we set forth as our objective, to identify dietary patterns in Mexican patients with multiple sclerosis.

METHODS

Study design and patients

This study corresponds to a case and control design that was observational and analytical. A secondary analysis was carried out of a data base obtained from the original study entitled "Risk factors associated with multiple sclerosis in Mexico: A multicentric study" which took place during 2010-2013 (CONACyT. Salud 2008 CO1-87366). A total of 205 prevalent cases was included, with a diagnosis of multiple sclerosis, according to the current McDonald critera, at the National Institute of Neurology and Neurosurgery (INNN). For each case, there were 2 healthy controlsfrom the outpatient clinic at the INNN (total 433), paired by age and sex. The studied population corresponded to 205 prevalent cases of multiple sclerosis, who were older than 18 years old, and 433 controls for whom we had complete dietary, clinical and anthropometric data. The protocol was approved by the Ethics and Research Committee of the National Institute of Public Health of Mexico (INSP) and the National Commission of Scientific Research of the Mexican Institute of Social Security (IMSS). Dietary information. The information on food and nutrient consumption was obtained through the "Food consumption frequency" questionnaire, which includes 100 foods, divided into 9 sections. Here, the portion size was specified and the frequency of consumption for each food: never, less than once a month, times per month (1-3), times per week (1-6), times per day (1-6). Respondents were asked to recall the consumption frequency of foods, three years prior to the diagnosis, for cases, and 3 years prior to the interview, for controls. This questionnaire was validated and adapted to the Mexican diet [21] and has been used in several studies in Mexico [22].

The amount of nutrients obtained from the daily consumption of each food was calculated using the computerized program: "Evaluation System for Nutritional Habits and Nutriment Consumption (SNUT 3.0)" [23]. The nutriment values obtained through the SNUT program were compared to the corresponding values in the Dietary Reference Intake (DRI) tables of the Institute of Medicine, National Academy of Sciences. USA and Canada [24]. Dietary patterns. To identify dietary patterns, foods and beverages were classified in previously defined groups. 23 food groups were formed, according to nutriment composition and other components (for example carbohydrate or fiber content) (Appendix 1). Some foods (e.g. coffee and tea) were in a separate group. Intake of food groups was converted to grams or milliliters consumed

daily. To generate Dietary Patterns (DP), a cluster analysis was performed, using the K-means method [25]. Two to four clusters were tested and analyzed, which maximized the euclidean distance between clusters and, finally, the two best characterized patterns were selected. The clusters were named according to the food groups contributing the highest percentages of daily intake - "healthy" and "unhealthy".

Other variables of the study. Anthropometry. A self-report was obtained of participants' weight and height. The nutritional state was evaluated, according to WHO criteria, using the Body Mass Index (BMI) [26]. This was figured as the weight in kilograms divided by the height in meters, squared (kg/m2). The definition of low weight was BMI ≤ 18.5, normal weight was BMI > 18.5 to < 25, overweight was BMI ≥ 25 to <30, and obesity was BMI ≥ 30. Marital status was defined as: single, married (or living with a partner), divorced (or separated) and widowed.Educational level was defined as the highest educational level achieved. Occupation was considered to be any work or activity in which the subject invested a certain amount of time and for which he/she may or may not get financial remuneration. A history of alcohol consumption was defined by the questions, "Have you ever drunk alcohol?". Those who answered "yes", were asked, "How frequently did you drink alcohol last year?" A history of alcohol consumption was considered for those who said they had consumed 3 or more glasses/drinks (daily, weekly, bi-weekly, monthly). A history of tobacco consumption was defined by the question, "Have you ever smoked tobacco?" It was considered to be positive for those who answered "yes".

Statistical analysis

After an exploratory analysis, the final data base was defined. Descriptive statistics were used: for continuous variables, mean ± SD, and for categorical variables, percentages. The cluster analysis resulted in mutually exclusive dietary patterns, based on the percentage contribution (±SD) to the total dietary intake, in grams and/or milliliters. The t Student statistical test was used to compare the 23 food groups to each of the 2 dietary patterns obtained from the cluster analysis. For the rest of the covariables, chi square or Fisher exact tests were performed. A value of $p<0.05$ was considered to establish statistical significance. The odds ratios (OR) were estimated with 95% confidence intervals, using the conditional logistic regression models, adjusting by covariables (educational level, marital status, occupation and BMI). All the analyses were developed using the Stata statistical program, version 13.0 [27].

RESULTS

Table 1: Socio-demographic characteristics of multiple sclerosis cases and controls in Mexico, 2010-2013.

Variables	Cases n=205 (%)	Controls n=433 (%)	p value
Sex			0.811¥
Female	132 (64.39)	283(65.36)	
Male	73 (35.61)	150(34.64)	
Age (years, mean±SD)	34.27 ± 10.35	34.19±10.74	0.926*
< 20	4 (1.95)	17 (3.93)	0.444¥
20 – 40	152 (74.15)	303 (69.98)	
41 – 60	43 (20.98)	103 (23.79)	
> 60	6 (2.93)	10 (2.31)	
Marital status			<0.001¥
Single	108 (52.68)	158 (36.49)	
Married	75 (36.59)	251 (57.97)	
Divorced	17 (8.29)	16 (3.70)	
Widowers	5 (2.44)	8 (1.85)	
Education			<0.001¥
Elementary or les	9 (4.39)	75 (17.32)	
Junior High School	24 (11.71)	113 (26.10)	
Senior High School	85 (41.46)	108 (24.94)	
Collegue or Masters degree	87 (42.44)	137 (31.64)	
Ocupation			0.010¥
Home maker	69 (33.66)	139 (32.10)	
Student	23 (11.22)	72 (16.63)	
Red neck	16 (7.80)	66 (15.24)	
Profesional	39 (19.02)	63 (14.55)	
Unemployed	58 (28.29)	93 (21.48)	
BMI (mean±SD)	24.29±4.17	25.86±5.18	0.0002*
<25.0 kg/m^2	124 (60.49)	211 (48.73)	0.007¥
25.0-29.9.0 kg/m^2	64 (31.22)	148 (34.18)	
≥ 30.0 kg/m^2	17 (8.29)	74 (17.09)	
Smoking			0.835¥
Yes	122 (59.80)	254 (58.93)	
No	83 (40.20)	179 (41.07)	
Alcoholism			0.911¥
Yes	166 (80.98)	349 (80.60)	
No	39 (19.02)	84 (19.40)	

¥Square chi test. *Student´s t test. BMI: Body Mass Index; SD: Standard Deviation

The distribution by female sex was similar among MS cases (64.39%) and their controls (65.36%). The average age for cases and controls was 34.27±10.35 and 34.19±10.74, respectively. A greater proportion of single people was observed (52.68%) among cases, and a greater proportion of married people (57.97%) among controls ($p<0.05$). 42.44%

of cases had an educational level that was equal to a bachelor's degree or higher, while in the controls a lower educational level was observed (p <0.05). With respect to occupation, a greater proportion of professionals was observed (19.02%) among cases than in controls (14.55%) (p <0.05). The body mass index was greater among controls (25.86 ± 5.18) than among cases (24.29±4.17). This statistically significant difference was maintained in the different BMI categories, with predominance of the normal nutritional status in the cases (60.49%) and overweight/obesity in the controls (51.27%) (p <0.05). A statistical significance was not observed among cases and controls with respect to a history of tobacco and alcohol consumption (Table 1).

Table 2: Clinics characteristics of multiple sclerosis cases in Mexico, 2010-2013 n = 205.

Variables	
Type of Multiple Sclerosis Relapsing remitting,n (%)	174 (84.88)
Secondary progressive, n (%)	11 (5.37)
Primary progressive, n (%)	18 (8.78)
Progressive relapsing, n (%)	2 (0.98)
Subclinical time[1]	3.48 ± 4.96
Diagnostic time[1]	3.05 ± 3.97
EDSS score[1]	3.67 ± 2.22
Subclinical time by dietary pattern	
Unhealthy[1]	3.57±4.20
Healthy[1]	3.41±5.49
Diagnostic time by dietary pattern *	
Unhealthy[1]	2.32 ± 2.81
Healthy[1]	3.57 ± 4.55
EDSS score by dietary pattern *	
Unhealthy[1]	3.30 ± 2.17
Healthy[1]	4.04 ± 2.24

*Statistically significant differences in the Student´s t test (p value <0.05).

[1]Values are means ± standard deviation.

The main type of MS wasrelapsing remitting (84.88%). On average, subclinical time to diagnostic, diagnostic time and EDSS score (Expanded Disability Status Scale) at the time of the study was 3.48 ± 4.96 years, 3.05 ± 3.97 years and 3.67 ± 2.22 points on the scale, respectively.With respect to diagnostic time by healthy and unhealthy dietary pattern was 3.57 ± 4.55and 2.32 ± 2.81 years, respectively (p <0.05).EDSS scoreby healthy dietary pattern was 4.04 ± 2.24 compared to unhealthy 3.30 ± 2.17points on the scale (p <0.05). Subclinical time analysis by dietary pattern was not statistical significance (Table 2).

Table 3: Cluster analysis. Percentage dietary contribution to the intake of total diets in grams and /or milliliters from food groups by dietary patterns of Multiple Sclerosis cases and controls in Mexico, 2010-2013.

Food groups	Healthy n = 320 (50.16%) % ± SD	Unhealthy n = 318 (49.84%) % ± SD
Fruits*	23.86 ± 9.42	14.26 ± 7.85
Milk	13.49 ± 9.16	14.39 ± 11.14
Vegetables*	11.05 ± 4.75	6.48 ± 3.18
Soda and sugary drinks *	7.42 ± 8.15	17.47 ± 15.33
Wheat and wheats products*	5.98 ± 3.55	6.58 ± 3.86
Mexican dishes	5.45 ± 4.39	4.15 ± 3.82
Water*	5.18 ± 6.17	2.74 ± 4.01
Cereals	4.05 ± 2.19	4.37 ± 2.73
Legumes*	3.78 ± 2.85	2.73 ± 2.11
Natural fruit juices	3.33 ± 4.05	3.90 ± 4.28
Coffee and herbal infusions*	2.44 ± 5.20	5.77 ± 7.83
Red meats*	2.01 ± 1.32	3.19 ± 2.42
Chicken*	2.73 ± 1.57	2.23 ± 1.57
Tortillas*	2.32 ± 1.32	1.33 ± 0.98
Vegetable oils*	1.98 ± 1.02	1.19 ± 0.69
Fish and seafood	1.63 ± 1.23	1.51 ± 1.35
Eggs*	1.03 ± 0.94	1.29 ± 1.13
Drinks and spirits*	0.41 ± 1.17	1.79 ± 3.67
Saturated fats*	0.69 ± 0.56	1.38 ± 1.16
Delicatessen*	0.49 ± 0.48	1.01 ± 0.85
Low calories Sodas*	0.13 ± 0.92	0.89 ± 3.21
Desserts and chips *	0.22 ± 0.29	0.71 ± 0.83
Candy*	0.24 ± 0.32	0.54 ± 0.69

¥Values in percent (%) ± standard deviation (SD).

*Statistically significant differences in the Student´s t test by food groups according to dietary patterns (p value <0.05).

Two main dietary patterns were found: healthy (DP1) and unhealthy (DP2). 50.16% of individuals consumed DP1, while 49.84% consumed DP2. The dietary intake by food groups in DP1 was characterized by a high fruit and vegetable consumption, a greater intake of water, legumes – mainly beans – chicken, tortilla and vegetal oils, compared to DP2 which had a greater percentage of soda and sweetened beverage consumption, wheat and its derivatives - mainly bread - coffee and tea, red meats, eggs, alcohol, foods with a high content of saturated fats such as "chicharron" (fried pork skin), bacon, "chorizo" (spicy pork sausage), "carnitas" (fried pork), cold cuts, desserts, appetizers and candy. The proportion of consumption of these food groups was statistically different among the dietary patterns (p<0.05) (Table 3).

Table 4: Daily energy and nutrient intake compared to the dietary reference intakes by Multiple Sclerosis cases and controls in Mexico, 2010-2013.

	Cases (n=205)	Controls (n=433)	Dietary Reference Intakes (DRI´s)¢
Variable	**means ± SD**	**means ± SD**	
Total energy intake (Kcal)*	1956.61 ± 623.88	2177.69 ± 810.48	1762 - 2080 Kcal
Vitamine B12, µg	4.36 ± 2.9	4.78 ± 5.74	2.4 - 3.6 µg
Vitamine D, IU*	209.10 ± 138.03	171.15 ± 121.91	600 UI
Vitamine A, IU*	771.94 ± 464.72	687.64 ± 474.35	700 - 900 UI
Folate, µg	318.38 ± 182.45	321.73 ± 158.27	400 µg
Vitamine E, mg	4.19 ± 2.02	4.25 ± 1.59	15 mg
Linolenic Acid, g	0.613 ± 0.27	0.615 ± 0.27	0.6 – 1.2 g
Linoleic acid, g*	5.60 ± 2.50	6.30 ± 2.90	5 - 10 g
Magnesium, mg*	343.44 ± 164.40	381.91 ± 162.86	310 – 420 mg
Calcium, mg*	959.96 ± 475.72	1041 ± 481.71	1000 - 1200 mg
Iron, mg*	13.36 ± 5.71	14.44 ± 5.27	8 - 18 mg
Fiber, g	27.15 ± 15.37	29.65 ± 13.02	25 – 38 g

Kcal: Kilocalories, µg: micrograms; IU: International Units; mg: milligrams; g: grams; SD: standard deviation

¢DRI´s= Dietary Reference Intakes. Estimated Average Requirements. Food and Nutrition Board, Institute of Medicine, National Academies.

*Statistically significant differences in the Student´s t test between cases and controls (pvalue <0.05).

The total energy intake was, on average, significantly lower (1956.61± 623.88 Kcal) among the cases, compared to their controls (2177.69 ± 810.48 Kcal). By contrast, average consumption of vitamin D (209.10 ± 138.03 IU) and vitamin A (771.94 ± 464.72 IU), was greater in the cases, compared to their controls (171.15 ± 121.91 IU) (687.64 ± 474.35 IU) respectively (p<0.05). On average, among the cases, a lower daily intake of linoleic acid was observed (5.60 ± 2.50 g), as well as of magnesium (343.44 ± 164.40 mg), calcium (959.96 ± 475.72 mg), and iron (13.36 ± 5.71 mg), compared to their controls (6.30 ± 2.90 g), (381.91 ± 162.86 mg), (1041 ± 481.71 mg) and (14.44 ± 5.27 mg) respectively (p<0.05). No statistical significance was found among cases and controls, with respect to average intake of vitamin B12, folate, vitamin E, linoleic acid and fiber. When comparing recommended daily intake, we observed, in cases as well as in controls, a lower average intake of vitamin D, E and folate, as well as a greater average intake of vitamin B12. Calcium intake was lower in cases only, as opposed to total energy intake, which was greater only in controls, compared to the recommended daily intake (Table 4).

With respect to the proportion of consumption in the dietary patterns of cases and controls, we observed a greater difference in the healthy pattern consumption (58.54%) among cases and a greater proportion of consumption of the unhealthy pattern (53.81%) among the controls, being this difference statistically significant (p<0.05). (Table V).The conditional logistic regression analysis in the crude model showed that cases with multiple sclerosis consumed the healthy pattern more OR 1.70 (95%CI 1.16, 2.49) compared to their controls. We observed an increase OR 1.85 (95%CI 1.23, 2.80) in the adjusted modelby BMI, educational level, marital status and occupation (Table 5).

DISCUSSION

Using cluster analysis, two main dietary patterns were found in this population – the one called "healthy" was characterized by greater average intake of fruits, vegetables, water, legumes, chicken, tortilla and vegetal oils, with a greater proportion of MS cases following this consumption pattern. On the other hand, the "unhealthy" pattern prevailed among the controls, which was characterized by greater consumption of sodas and sweetened beverages, wheat and its derivatives, coffee, tea, red meats, eggs, alcohol, foods with a high content of saturated fats, cold cuts, desserts, appetizers and candies.

The authors believe that this finding could be explained by the fact that the study is based on the analysis of prevalent cases. The studied sample included MS cases that had an average 3.48 ± 4.96years in the sub-clinical phase, that is since the onset of symptoms until the final MS diagnosis; this was aside from an average of 3.05± 3.97 years since diagnosis, to the time of the study. They also had an average of 3.67± 2.22 points on the EDSS scale [28], which means they were going through some degree of clinical disability, between low and moderate, which at the time of the dietary study, could have led them to modify their dietary patterns towards a healthier consumption; this was geared towards achieving a symptomatic improvement and/or avoiding the progression of the disease, in an effort to have an influence on the natural course of the disease.This was observed when analyzing the time of

diagnosis and the EDSS score by type of dietary pattern in which we found that the cases with the longest time of diagnosis and the highest EDSS score at the time of the study had a healthy dietary pattern.

Table 5: Logistic conditional regression analysis according dietary patterns of Multiple Sclerosis case = 205 and controls = 433 in Mexico 2010-13.

Pattern	Cases n (%)	Controls n (%)	OR crude	95% CI	p value	OR adjusted[1]	95% CI	p value
Unhealthy	85 (41.46)	233 (53.81)	Ref.	-	-	Ref.	-	-
Healthy	120 (58.54)	200 (46.19)	1.7	1.16-2.49	0.006	1.85	1.23-2.80	0.003

This change in diet is a consequence, not of the disease per se, but of associated symptomatology that leads the patients to modify their dietary patterns [29,30]. The healthy dietary pattern found in this study shares similarities with the diet known as theMediterranean diet, which consists of consumption of olive oil, unrefined cereals, legumes, diverse vegetables, fruits, fish and seafood, as well as a low consumption of animal fats or red meats. This is important since it has been proven that this type of diet is associated with lower systemic inflammation and a possible protective effect for MS [31]. Riccio and Rossano suggested that some dietary components need to be controlled, in order to contribute to the MS treatment [32]. The authors proposed that a hypercaloric diet leads to greater systemic inflammation [20]. Another clinical study in Mexican population consistently reported these observations, where a positive associationwas found between the Western dietary pattern, chronic diseases and high concentrations of C-reactive protein [33]. These clinical findings are theoretically sustained, and show that through diverse inflammatory mechanisms, focal injuries are produced in the white matter of the CNS, leading to an increase in the rate of relapses, a greater progression of the disease and finally, a worsening of the degree of disability in individuals with MS [34]. Thus, what was found in our study, where a greater proportion of the healthy consumption pattern was observed among MS cases, has clinical relevance, since it is possible that by modifying the dietary pattern, we could be having an influence on the progression of the disease, delaying it, limiting disability and improving life quality and well-being in the MS patient [35]. Our study's analysis of the total energy consumption pattern and nutrients, revealed a lower total energy consumption, as well as lower consumption of linoleic acid, fiber, magnesium, calcium, iron, and a higher consumption of vitamins D and A in MS cases, when compared to the healthy controls and can be contributing to a common symptom in these subjects, like chronic fatigue from peripheral, instead of central origin. This was observed in the daily clinical practice.

These findings are similar to those reported by Hewson DC et al., in Great Britain, who studied food intake in 142 MS patients, comparing them to a healthy control group. They found that the MS patients had a lower total energy intake; however, the comparison with other nutriments was not significant [36]. Timmerman et al., analyzed the dietary food intake in women with MS, compared to the dietary recommendations for U.S. population, finding a lower consumption of carbohydrates, fiber, vitamin E, calcium and zinc. However, they also had a greater intake of saturated fats, proteins, vitamins A and C, folic acid and iron [37]. Ramsaransing et al., in an exploratory study on dietary patterns in different MS subtypes, compared to population data, found a significantly lower intake of total fats, linoleic acid, magnesium, folic acid and total energy intake; they did not find an association with some micronutrients, such as: vitamin B12, vitamin E, calcium and iron [8]. On the other hand, Williams CM et al., evaluated 20 patients with MS with severe disability and found that the total energy intake, as well as intake of folic acid, iron, vitamin D and zinc, were lower than the recommended values [38]. We must point out that important methodological differences are found among the studies, such as: time and type of sampling, data collection instruments, size of sample and characteristics of the analyzed populations. However, the associations with dietary patterns, total energy consumption and intake of some nutriments found in our study, are consistent with those reported in the analyzed literatura [39,40].

The above is important since we consider that a healthy Mediterranean type dietary pattern, with caloric restriction and supplemented with antioxidants, could contribute to counteracting chronic inflammation, decreasing oxidative stress, regulating the synthesis of pro-inflammatory molecules and

achieving a neuroprotective effect that could have an influence on MS progression; this was demonstrated by Piccio L, et al., [41] in an experimental model of autoimmune encephalomyelitis with chronic caloric restriction. These observations were confirmed by Riccio P, et al., [42] in a randomized clinical assay carried out in patients with different MS subtypes, where they proposed that a nutritional intervention based on caloric restriction, a semi-vegetarian diet and administration of vitamin D, with or without other dietary supplements, may contribute to counteracting the chronic inflammation that is common in different MS subtypes. They also showed that the anthropometric parameters improved in the patients. This was similar to what was found in our study, where MS cases followed the healthy consumption pattern to a higher degree, had a lower caloric intake and lower BMI. On the other hand, controls followed the unhealthy consumption pattern, had a greater caloric intake and higher BMI. This last finding is consistent with what was reported by Flores M, et al., [43] in adult Mexican population, where they demonstrated a positive association between Western dietary patterns and a greater energy intake, as well as greater BMI.

Among the strengths of this study are the selection of population-based healthy controls and the use a Mexican validated FFQ instrument to determine the diet. However, at present we face diverse limitations in the interpretation of our results: there is a potential selection bias when studying prevalent cases; for this reason, the subclinical phase, time for diagnosis, physical disability and disease modifying therapies, could have affected the dietary intake in cases and controls in a different manner, introducing a potential information bias (reverse causality). On the other hand, the method used to create food groups and select the number of clusters, involved the researchers' subjective decisions. In conclusion, this study revealed that among the cases, the healthy consumption pattern prevailed (a consequence of the patients' response to the disease), as well as lower intake of calories, linoleic acid, magnesium, calcium, iron and a greater intake of vitamins D, vitamins A and lower BMI. On the other hand, among controls, there was a greater proportion of the unhealthy dietary pattern, a greater caloric intake and higher BMI. Studies have been carried out on the importance of certain dietary patterns and their connection to diverse pro-inflammatory or anti-inflammatory mechanisms in the CNS. These patterns could have an influence on the progression of the disease, and an increase in symptoms such as fatigue; however, these results are still inconclusive. For this reason, we propose carrying out longitudinal studies to confirm the role of diet in the natural history of the disease. The importance of this study is to highlight the clinical relevance of recommending a breakdown of dietary intake, which allows us to show the changes in dietary habits and lifestyles, after the diagnosis of the disease.

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Appendix 1: Food groups used in Multiple Sclerosis case-controls Study. 2010-2013.

Milk	Whole milk, fresh cheesecottage, mozzarella, cream cheese, monterey cheese, cream, yogurt, ice cream.
Fruits	Banana, plump, peach, apple, orange, grapes, strawberries, cantalupe, watermelon, mamey, tangerine, pear, prickle pear, papaya, pineapple, mango
Natural juices	Orange juice, grapefruit juice, pineapple juice
Eggs	Yolk, whole egg from hen
Red meats	Beef liver, beef meat, pork meat, salted beef, ram meet
Delicatessen	Ham, sausages
Chicken	Chicken meat
Fish and seafood	Tuna, sardine, fresh fish and seafood
Legumes	Beans (any kind), lentils, canned peas, green and dry beans
Cereals, rice y potatoes	Corn flakes, rice and potatoes chips
Wheat and derivatives	Flour tortillas, bread buns, bread slices, sweet pastries, cookies, crackers
Corn	Corn tortillas
Mexican dishes	Pozole, tamal, corn starch drink, quesadillas and corn tortillas with beans and meat (“sopes”)
Desserts and snacks	Cake, fried potatoes and “fritos” and nachos
Sweets	Chocolate bars, jam and honey
Vegetables and greens	Cauliflower, broccoli, corn, carrot, spinach, pumpkin, red tomato, pumpkin flower, onion, garlic, lettuce, tomato puree, green bean, squash, purslane, beetroot
Alcohol	Beer, rum, scotch, tequila, red or White wine
Soda and sugary beverages	Different flavor sodas and cola soda
Low-calorie soda	Diet soda
Water	Natural wáter
Saturated fats	Fried pork skin, lard, mayonnaise, butter, margarine, bacon, sausage, deep fried pork meat
Vegetable oils	Vegetal oils, corn oils, corn oils, olive oils
Coffee and tea	Coffee and herbal infusions