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Dietary Food Groups and Nutrient Intake in Association with Multiple Sclerosis: A Case-Control Study

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ABSTRACT

Introduction: It has been proposed that dietary intake is associated with multiple sclerosis (MS). The present case-control study was conducted to investigate the relationship between intake of different food groups and occurrence of MS among the recently diagnosed adult patients in Yazd City, Iran.

Materials and Methods: In the current study, a group of 45 patients who have recently been diagnosed with MS and 100 healthy controls were investigated in this research. Participants were matched regarding their gender. Dietary intakes were assessed using a self-administered semi-quantitative food frequency questionnaire (FFQ). Participants also completed a demographic questionnaire including information such as age, gender, marital status, job, education, sun exposure, smoking, sunscreen, body mass index (BMI), economic status, as well as their spouses' occupations and education. Logistic regressions in crude and multivariable-adjusted models were used to investigate the relationship between food groups and the odds of developing MS.

Results: The findings showed that participants with high consumption of fruits, potatoes, refined grains, pickles, and fibers had a significantly lower chance for developing MS after adjustment for the maximum possible confounding variables ($P < 0.05$).

Conclusion: The present study revealed that several food groups or nutrients are associated with the development of MS. Further multi-central prospective studies including more participants are needed to confirm these results.

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Introduction

Multiple Sclerosis (MS) is one of the common neurological disorders, which occurs among young adults [1]. In this disease, the immune system attacks the myelin that protects the central nervous system cells. Consequently, destruction of myelin leads to some disorders in the transmission of nerve signals from the brain and the spinal cord to other parts of the body. The disease also has social and economic consequences [2, 3]. In fact, treatment of MS, as a chronic autoimmune and inflammatory disease is costly and includes management of the disease symptoms. The incidence of this disease is more frequent among women than men and it is more prevalent within the age range of 20-40 years. According to the International Federation of Medical Insights, the average outbreak of MS has risen from 30 per 100000 in 2008 to 33 per 100000 in 2013. The highest prevalence of this disease was observed in North America (140 per 100000) and Europe (108 per 100000); whereas, the lowest rates were attributed to Sub-Saharan Africa (1.2 per 100000) and East Asia (2.2 per 100000). Based on the World Health Organization, Iran has a moderate outbreak with regard to this disease (20 to 60 in per 100000) [4]. Although the etiology of MS has remained unclear [5], various risk factors were mentioned for this disease such as environmental causes, infections, genetic problems, viruses, toxins, metabolic problems, and exposure to nitric oxide. Furthermore, researchers believe that nutritional factors might affect the incidence or severity of the disease [6]. The previous studies investigated the role of several dietary factors such as vitamin D status, unsaturated fatty acids, especially omega-3 and omega-6, antioxidants such as vitamin C, dietary fiber, plant proteins, fish, whole fruit juices, whole grains, and liquid oils in preventing MS. Other risk factors such as saturated, solid, and animal fats, red meat, high-fat dairy, and soda were also checked out [6-10].

Although nutrition plays a vital role in healthy living, evidences indicate that the dietary patterns in Iran have changed towards the western or unhealthy pattern over the past two decades [11], which is the one of the main causes of chronic diseases [12]. A literature review over the Mediterranean diet indicated that that the whole and refined grains had an inverse relationship with incidence of MS [13, 14]. It was also reported that high consumption of animal fats, processed meat, sugars, and hydrogenated fats increased the risk of developing MS [15]. Contrary to these findings, a case-control study based on the Mediterranean diet showed a positive correlation between consumption of refined grains and incidence of MS [16]. In addition, in a prospective study, the researchers pointed out that the risk of MS had no association with reception of dairy products, poultry, fish, red meat, and processed meat [17].

Considering the role of nutritional factors in the prevalence of MS, a number of investigations were conducted in this field, which led to contradictory and analogous findings. The present study targeted at investigating the relationship of consuming different food groups and nutrients with MS in a case-control study.

Materials and Methods

An international board affiliated with the US MS Society has provided some criteria for the diagnosis of MS, including the relapsing-remitting period and the progressive period in which the patient experiences the progressive MS from the beginning with no periods of recovery. Application of the magnetic resonance imaging (MRI) for brain, spinal cord imaging, as well as clinical and paraclinical diagnostic techniques help the physicians to observe the plaques and scars caused by the disease in the white matter around the cerebral ventricles, the optic nerve pathway, the posterior region of the brain, and the spinal cord. Moreover, examination of the cerebrospinal fluid (CSF) helps the disease diagnosis regarding the presence of immunoglobulin G (IgG), which is used as a definitive diagnosis of MS.

Sample size

The sample size was determined based on the census sampling method in a pilot study. Consequently, researchers referred to the MS Society of Yazd City and interviewed the participants. The patients were explained about the study outline and goals. Finally, all patients who met the inclusion criteria entered the study after signing the informed consent forms. The case group members were selected using the following inclusion criteria:

1- Having confirmed diagnosis of MS by a neurologist and pass of two years (in maximum) since the diagnosis.

2-Having the consent to participate in the study.

3- Lack of having congenital, metabolic, or chronic diseases other than MS based on the patient’s reports.

4- Having no family history of MS.
5- Being in the age range of 20-50 years.

The inclusion criteria to select the control group members were:

1- Having consent to participate in the study
2- Having no congenital metabolic or chronic diseases based on the patient's reports
3-Having the same sex as the patient
4- Having no family history of MS
5- Being healthy and living in the same neighborhood (near the intervention group members).

Based on the census results, 50 people were selected as members of the intervention group, but a final number of 45 participants completed the study.

Participants

The present case-control study included 45 patients with MS recently diagnosed by a neurologist (MS was confirmed by a neurologist and a maximum of two years have passed since the diagnosis). The case group included the patients who had been dealing with the disease for a maximum of two years and referred to the MS Society in Baghaei Pour clinic, Yazd. A neurologist diagnosed and confirmed the MS by imaging the brain and spinal cord using the magnetic resonance imaging (MRI) as well as the criteria set by McDonald et al. However, if MS diagnosis was not known, "probability of MS" was reported [18].

Moreover, 100 healthy individuals were selected as the control group (the ratio of the case to control group members was 2:1). The control group participants were selected from the same residence area where the patients lived. In addition, the control and intervention group members were matched in terms of gender.

Assessment of Semi-Quantitative Feed Frequency Questionnaire

The Semi-Quantitative Feed Frequency Questionnaire (FFQ), developed by Mirmiran et al [19] was administered after minor modifications. The FFQ employed in this study consisted of a list of 168 food items including the items of a previously used questionnaire with confirmed validity and reliability [19]. The revised questionnaire included 10 added food items commonly consumed in Yazd. Which was modified to a multiple-choice questionnaire [20]. The participants were asked to report their food consumption frequency based on the provided measurement units during the previous year. Although the consumption frequency of each food item was considered for one year, the researcher asked the participants to mention their consumption in terms of day, week, or month depending on the food item under question. Later, the consumption amounts of each food item were converted into grams per day using the Home Scale Guide.

Given the general information questionnaire, valid related studies were reviewed and a general information questionnaire was prepared based on the participants' economic and social status. The reported intakes were converted to grams per day using the manual of home scales. The food items were also classified into pre-defined food groups based on the similarity of food profiles.

Data analysis and evaluation of anthropometric

The participants' height and weight measures were collected based on their oral self-reports.

Later, the participants were asked to report their demographic information such as age (year), gender (male or female), as well as household economic status (house ownership status, number and type of the cars available at home, and total family income), smoking, medical history, medication use, and family history of MS (Yes-No) using a self-administered questionnaires.

The significance level of 0.05 was considered for identifying the relationship between food groups and MS. The collected data were analyzed by SPSS version 21. Chi-square test was performed to compare the qualitative variables between the case and control groups.

Data analysis and evaluation of other variables

In order to compare the quantitative variables, their normal distribution was evaluated using Kolomogorov-Smirnov test before selection of the statistical tests. The covariance (ANCOVA) tests were also run to compare the quantitative variables with normal distribution between the two groups.

Later, nonparametric tests of Mann-whithney and Kruskal-wallis were utilized to compare the non-normal quantitative variables. In the case that the chi-square assumptions were not met, Fisher test was run. In addition, 95% confidence interval and odds ratio were calculated for variables studied in the logistic regression. Comparisons of the means and ratios among the intake tertiles of the extracted dietary patterns were conducted by ANOVA and Chi-square tests, respectively. Logistic regression was used to find the association of dietary intakes with MS disease. Participants were divided into three groups based on their dietary intakes and nutrients. Later, the odds of MS incidence in the second and third tertiles were calculated and compared with that of the first tertile. The p value was also calculated considering the median of each tertile as a continuous variable. Furthermore, in the adjusted model, the effect of age, gender, energy, marital status, economic status, education, occupation, smoking, sun exposure, sunscreen, body mass index, spouse's education, and spouse's occupation were considered. Moreover, mean intakes of the reported food groups were compared before and after adjusting for the confounding and contextual variables using ANOVA and ANCOVA tests, respectively.

Ethical issue

The protocol of this study was approved by the Ethics Committee of the School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran with the registry code of IR.SSU.SPH.REC.1396.24.

Results

In total, 45 patients with MS aged 34.51 ± 8.53 years and 100 healthy gender-matched controls aged 40.14 ± 12.45 were included in the present study. The mean BMI for the case and control groups were 24.29 ± 4.19 and 25.32 ± 3.74, respectively.

The demographic and lifestyle characteristics of the participants are presented in table 1. The mean age (P = 0.002), physical activity (P = 0.030), and sunlight exposure (P = 0.009) were significantly lower in the case group compared to the control group (P < 0.05). Moreover, the number of people with average income was significantly higher in the case group than the control group; whereas, members of the control group had higher incomes (P = 0.031). No significant difference was observed between the case and control groups in terms of other variables.

Table 1: General characteristics of the study participants.

	Case N = 45	Control N = 100	Total N = 145	P-value
Age (year)	34.51 ± 8.53	40.14 ± 12.45	38.39 ± 11.64	0.002
Weight (Kg)	65.36 ± 12.04	68.03 ± 10.52	67.20 ± 11.04	0.225
BMI (Kg/m2)	24.29 ± 4.19	25.32 ± 3.74	25.002 ± 3.90	0.197
Sex [n (%)]				
Male	8(17.8)	29(29.0)	37(25.5)	0.216
Female	37(82.2)	71(71.0)	108(74.5)	
Marital status [n (%)]				
Single	8(17.8)	17(17.0)	25(17.2)	1.00
Married or widowed	37(82.2)	83(83.0)	120(82.8)	
Education [n (%)]				
High school diploma lower	20(44.4)	46(46.5)	66(45.80)	0.858
University or college	25(55.6)	53(53.5)	78(54.2)	
Occupation [n (%)]				
Government employed	17(40.5)	42(42.0)	59(41.5)	0.920
Self employed	7(16.7)	14(14.0)	21(14.8)	
Housekeeper or not employed	18(42.9)	44(44.0)	62(43.7)	
Economic statues [n (%)]				
Low income	12(31.6)	27(31.8)	39(31.7)	0.031
Middle income	17(44.7)	20(23.5)	37(30.1)	
High income	9(23.7)	38(44.7)	47(38.2)	

	Case N = 45	Control N = 100	Total N = 145	P-value
Smoking status [n (%)]				
Current or ex-smoker	3(6.7)	11(11.0)	14(9.7)	0.550
Non-smoker	42(93.3)	89(89.0)	131(90.3)	
Physical activity [n (%)]				
Yes	5(11.1)	27(28.4)	32(22.9)	0.030
No	40(28.6)	68(48.6)	108(77.1)	
Sunlight exposure [n (%)]				
Low 15min	15(34.1)	13(13.3)	28(19.7)	
5-15min	19(43.2)	38(38.8)	57(40.1)	0.009
15-30min	4(9.1)	19(19.4)	23(16.2)	
Up 30min	6(13.6)	28(28.6)	34(23.9)	
Sunscreen use [n (%)]				
Yes	19(43.2)	35(35.0)	54(37.5)	0.357
No	25(56.8)	65(65.0)	90(62.5)	
Spouse education [n (%)]				
High school diploma or lower	19(51.4)	45(51.7)	64(51.6)	1.00
University or college	18(48.6)	42(48.3)	60(48.4)	
Spouse occupation [n (%)]				
Government employed	11(30.6)	38(44.7)	49(40.5)	
Self-employed	19(52.8)	31(36.5)	50(41.3)	0.230
Housekeeper or not employed	6(16.7)	16(18.8)	22(18.2)	

The findings indicated higher consumption of processed meat in the case group than the control group (P < 0.001). By adjusting the effects of maximum possible confounding variables including age, gender, energy, marital status, occupation, education, sunlight exposure, smoking, sunscreen use, BMI, spouse education, and spouse occupation in model 2, the difference remained significant (P = 0.004). People in the case group consumed more amounts of butter, tomato, and red meat than the control group and the difference between the two groups was significant (P < 0.04). However, after adjusting for the confounding variables, no significant difference was observed (P > 0.05). The results revealed that consumption of potato was significantly lower, while consumption of confectioneries and soft drinks was significantly higher in the case group compared to the controls (P < 0.04). The association remained significant after adjusting for the confounders in model 1and 2 (P < 0.05).

The consumption of saturated fatty acids in the raw state was lower in the control group in comparison with the case group and the difference was significant (P = 0.025), but after adjusting for the confounding variables, we observed no significant difference (P > 0.05). Furthermore, the amount of total fat and monounsaturated fat consumption was significantly higher in the case group than the control group (P < 0.001); the difference remained significant even after adjusting for the maximum number of confounding variables in model 2 (P < 0.05). No significant difference was observed between the mean intake rates of other food groups.

Table 2 represents the odds of MS regarding intake of dietary food groups. The incidence chance of MS was five times higher in participants who consumed processed meat more than others and the association remained significant after adjusting for the confounders in models 1and 2 (P < 0.001). The incidence of MS was lower in individuals with a higher intake of pickles (P < 0.05); this relationship remained significant after adjusting for the confounding variables. In addition, higher consumption of fruits, potatoes, and refined grains was associated with a lower chance of developing MS in model 1. High consumption of solid and hydrogenated fats as well as soft drinks increased the incidence of MS and the relationship remained significant after adjusting for the confounding variables in models 1 and 2.

Table 2: Odds ratio for developing Multiple Sclerosis used on tertiles of dietary food group's intake (for the dietary food P trend ≤ 0.05).

	T_1	T_2	T_3	P-trend
Processed meat[c]				
Participants	12	1	32	-
Median intake (IQR) (gr/day)	0(0)	1.02(0.66-1.55)	1.68(1.68-151)	-
Crude	1.00	0.62(0.07-5.47)	5.00(2.27-11.02)	< 0.001
Model 1[a]	1.00	0.48(0.05-4.52)	5.46(2.33-12.75)	< 0.001
Model 2[b]	1.00	0.69(.06-7.41)	7.82(2.57-23.76)	< 0.001
Fruit				
Participant	18	17	10	-
Median intake (IQR) (gr/day)	238.42(23.72-426.39)	616.66(442.90-774.73)	1206.28(808.32-5466.14)	-
Crude	1.00	0.89(0.39-2.03)	0.44(0.18-1.09)	0.080
Model 1[a]	1.00	0.77(0.31-1.91)	0.16(0.05-0.50)	0.003
Model 2[b]	1.00	0.78(0.25-2.47)	0.20(0.04-0.98)	0.066
Potatoes				
Participant	20	13	12	-
Median intake (IQR) (gr/day)	4.008(0.36-7.02)	13.86(7.40-21.91)	40.11(23.09-277.62)	-
Crude	1.00	0.49(0.21-1.15)	0.44(0.18-1.05)	0.059
Model 1[a]	1.00	0.39(0.15-0.98)	0.34(0.13-0.87)	0.023
Model 2[b]	1.00	0.22(0.06-0.81)	0.19(0.05-0.71)	0.013
Refrains grain				
Participant	17	17	11	-
Median intake (IQR) (gr/day)	106.58(11.06-149.56)	207.94(151.14-293.28)	362.16(295.09-1631.33)	-
Crude	1.00	0.97(0.42-2.23)	0.54(0.22-1.33)	0.187
Model 1[a]	1.00	0.49(0.19-1.27)	0.27(0.09-0.78)	0.016
Model 2[b]	1.00	0.62(0.18-2.12)	0.32(0.08-1.28)	0.067
Hydrogenated Fats				
Participant	7	13	25	-
Median intake (IQR) (gr/day)	0.18(0.00-0.31)	1.18(0.36-2.41)	7.84(2.45-90.33)	-
Crude	1.00	2.61(0.94-7.27)	6.99(2.63-18.56)	< 0.001
Model 1[a]	1.00	2.51(0.88-7.16)	6.99(2.48-19.75)	< 0.001
Model 2[b]	1.00	3.14(0.78-12.59)	11.30(2.60-48.99)	0.001
Soft drink				
Participant	8	15	22	-
Median intake (IQR) (gr/day)	4.08(0.00-4.08)	16.08(6.12-25.20)	68.64(32.16-514.32)	-
Crude	1.00	2.88(1.08-7.68)	4.08(1.60-10.40)	0.003
Model 1[a]	1.00	3.27(1.19-9.02)	4.40(1.59-12.16)	0.004
Model 2[b]	1.00	2.72(0.73-10.20)	3.50(0.87-14.03)	0.057
Yogurt drink				
Participant	24	11	10	-
Median intake (IQR) (gr/day)	6.63(0.00-17.42)	37.18(34.84-74.36)	111.54(111.54-1560)	-
Crude	1.00	0.57(0.24-1.35)	0.43(0.18-1.02)	0.049
Model 1[a]	1.00	0.63(0.25-1.56)	0.14(0.16-1.03)	0.053
Model 2[b]	1.00	1.01(0.28-3.60)	.036(0.10-1.29)	0.148
Pickles				
Participant	20	17	8	-
Median intake (IQR) (gr/day)	1.91(0.00-4.81)	8.06(5.43-13.26)	39.81(13.94-985.72)	-
Crude	1.00	0.79(0.35-1.81)	0.29(0.11-0.75)	0.012
Model 1[a]	1.00	0.63(0.25-1.56)	0.13(0.04-0.41)	< 0.001
Model 2[b]	1.00	0.66(0.19-2.32)	0.06(0.01-0.34)	0.001

[a] Model 1: adjusted for age, energy, sex

[b] Model 2: adjusted for marital status, job, education, sun exposure, smoking, sunscreen, BMI, spouse education, spouse job, economic status

[c] Not adjusted for economic situation

In tables 3, 4, and 5, the average nutrient intakes of the study groups and their relationship with the incidence of MS is indicated. Participants with higher consumption rates of saturated fatty acids had a higher chance of developing MS and the confounding variables did not make any significant difference in models 1 and 2. High intake of mono-unsaturated fatty acids increased the odds of MS and this relationship remained significant after adjusting for the confounding variables. Poly-unsaturated fatty acids were also associated with the incidence of MS, but the relationship did not remain significant after adjusting for the confounding factors in models 1 and 2. However, consumption of fibers decreased the chance for developing MS after adjusting for the confounding variables in Model 1.

Table 3: Odds ratio for developing Multiple Sclerosis used for nutrients intake

	T_1	T_2	T_3	P trend
Energy (Kcal)				
Participant	11	15	19	-
Median intake (IQR) (gr/day)	1662.74(914.49-1956.90)	2369.72(1960.44-3081.71)	4137.39(3100.57-6196.12)	-
Crude	1.00	1.48(0.60-3.67)	2.20(0.91-5.35)	0.080
Model 1	1.00	1.22(0.48-3.14)	2.02(0.79-5.12)	0.123
Model 2	1.00	1.23(0.37-4.06)	1.45(0.43-4.88)	0.551
Total fat (g/day)				
Participant	9	15	21	-
Median intake (IQR) (gr/day)	46.76(24.88-61.64)	81.91(61.91-100.33)	138.02(100.80-290.74)	-
Crude	1.00	0.30(0.12-0.75)	0.57(0.25-1.30)	0.009
Model 1	1.00	0.28(0.07-1.03)	0.51(0.18-1.39)	0.055
Model 2	1.00	0.09(0.01-0.65)	0.33(0.07-1.49)	0.017
Saturated fat (g/day)				
Participant	10	15	20	-
Median intake (IQR) (gr/day)	14.46(7.97-18.98)	23.00(19.08-30.17)	39.53(30.62-91.86)	-
Crude	1.00	1.68(0.66-4.22)	2.71(1.10-6.69)	0.029
Model 1	1.00	1.46(0.53-4.01)	2.03(0.65-6.37)	0.222
Model 2	1.00	1.63(0.43-6.27)	2.44(0.51-11.78)	0.268
Monounsaturated fat (g/day)				
Participant	8	14	23	-
Median intake (IQR) (gr/day)	13.40(6.51-18.67)	24.38(18.74-29.54)	39.19(29.80-97.29)	-
Crude	1.00	2(0.75-5.33)	4.60(1.78-11.86)	0.001
Model 1	1.00	2.13(0.74-6.13)	5.29(1.43-19.62)	0.013
Model 2	1.00	2.32(0.59-9.06)	7.48(1.22-45.75)	0.031
Polyunsaturated fat (g/day)				
Participant	10	16	19	-
Median intake (IQR) (gr/day)	10.79(4.62-15.18)	22.41(15.67-29.52)	42.65(29.86-625.07)	-
Crude	1.00	1.84(0.74-4.61)	2.49(1.01-6.16)	0.049
Model 1	1.00	1.52(0.55-4.20)	1.91(0.65-5.68)	0.250
Model 2	1.00	1.43(0.39-5.25)	2.93(0.72-11.92)	0.122
Protein (g/day)				
Participant	11	15	19	-
Median intake (IQR) (gr/day)	58.09(32.90-71.73)	91.24(72.44-118.34)	162.93(120.13-412.79)	-
Crude	1.00	1.48(0.60-3.68)	2.20(0.91-5.35)	0.080
Model 1	1.00	1.08(0.40-2.94)	1.56(0.38-6.52)	0.572
Model 2	1.00	0.81(0.22-3.02)	2.60(0.39-17.33)	0.482

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	T_1	T_2	T_3	P trend
Carbohydrate (g/day)				
Participant	17	9	19	-
Median intake (IQR) (gr/day)	231.56(106.46-277.63)	329.41(277.63-439.82)	584.91(444.32-1091.93)	-
Crude	1.00	0.41(0.16-1.04)	1.20(0.52-2.73)	0.659
Model 1	1.00	0.32(0.11-0.88)	0.46(0.10-2.17)	0.132
Model 2	1.00	0.18(0.04-0.74)	0.13(0.01-1.35)	0.029
Dietary fiber intake (g/day)				
Participant	15	17	13	-
Median intake (IQR)(gr/day)	13.20(4.93-17.45)	22.02(17.80-27.64)	39.78(27.83-113.07)	-
Crude	1.00	1.17(0.50-2.73)	0.82(0.34-1.97)	0.659
Model 1	1.00	0.68(0.26-1.80)	0.19(0.05-0.77)	0.023
Model 2	1.00	0.69(0.20-2.41)	0.30(0.04-2.19)	0.259

[a] Model 1: adjusted for age, energy, gender

[b] Model 2: adjusted for marital status, job, education, sun exposure, smoking, sunscreen, BMI, spouse education, spouse job, economic status

[c] Not adjusted for economic situation

Table 4: Comparison of dietary food groups intake between patients with multiple sclerosis and healthy individuals

	Case	Control	P. value
Processed meat (g/day)[d]			
Crude	14.27 ± 2.72[c]	1.33 ± 1.82	< 0.001
Model 1[a]	13.56 ± 2.71	1.52 ± 1.80	< 0.001
Model 2[b]	14.21 ± 3.49	1.50 ± 2.20	0.004
Organ meats (g/day)			
Crude	9.85 ± 2.68	5.66 ± 1.80	0.196
Model 1	9.96 ± 2.70	5.61 ± 1.77	0.188
Model 2	12.57 ± 3.78	5.59 ± 2.39	0.136
Fish (g/day)			
Crude	9.84 ± 2.40	11.87 ± 1.61	0.484
Model 1	10.17 ± 2.42	11.72 ± 1.60	0.599
Model 2	11.11 ± 3.33	12.64 ± 2.11	0.709
Poultry (g/day)			
Crude	61.32 ± 13.16	59.27 ± 8.83	0.897
Model 1	53.98 ± 12.09	62.58 ± 8.00	0.560
Model 2	61.06 ± 13.35	57.40 ± 8.45	0.824
Eggs (g/day)			
Crude	28.74 ± 3.16	22.53 ± 2.12	0.105
Model 1	28.09 ± 3.25	22.82 ± 2.15	0.185
Model 2	31.48 ± 4.24	22.71 ± 2.69	0.096
Butter (g/day)			
Crude	3.85 ± 0.64	2.30 ± 0.43	0.045
Model 1	3.70 ± 0.66	2.37 ± 0.43	0.095
Model 2	3.59 ± 0.86	2.67 ± 0.55	0.390
Margarine (g/day)			
Crude	1.30 ± 0.40	0.61 ± 0.27	0.148
Model 1	1.28 ± 0.41	0.62 ± 0.27	0.183
Model 2	1.43 ± 0.59	0.76 ± 0.37	0.355
Low-fat dairy product (g/day)			
Crude	78.75 ± 20.35	83.37 ± 13.65	0.850
Model 1	76.30 ± 19.90	84.47 ± 13.17	0.736
Model 2	95.14 ± 27.38	81.26 ± 17.32	0.681
High-fat dairy product (g/day)			
Crude	164.68 ± 37.97	189.11 ± 25.47	0.594
Model 1	137.30 ± 34.85	201.43 ± 23.06	0.133

	Case	Control	P. value
Model 2	138.97 ± 46.75	199.10 ± 29.58	0.298
Tea (g/day)			
Crude	357.73 ± 54.81	404.49 ± 36.77	0.480
Model 1	357.73 ± 54.81	404.49 ± 36.77	0.480
Model 2	402.35 ± 73.86	426.62 ± 47.04	0.789
Coffee (g/day)			
Crude	6.95 ± 1.89	4.91 ± 1.27	0.373
Model 1	5.90 ± 1.90	5.38 ± 1.26	0.823
Model 2	4.13 ± 2.16	5.77 ± 1.36	0.539
Fruit (g/day)			
Crude	880.79 ± 140.38	846.35 ± 94.17	0.839
Model 1	788.22 ± 119.04	888.01 ± 78.78	0.492
Model 2	779.47 ± 139.74	896.73 ± 88.50	0.497
Fruit juice (g/day)			
Crude	128.51 ± 24.76	79.37 ± 16.61	0.102
Model 1	112.37 ± 22.32	86.63 ± 14.77	0.345
Model 2	82.713 ± 27.30	86.21 ± 17.28	0.917
Tomatoes (g/day)			
Crude	63.93 ± 21.53	105.16 ± 14.44	0.114
Model 1	54.75 ± 20.98	109.29 ± 13.88	0.034
Model 2	49.00 ± 27.76	106.13 ± 17.56	0.098
Vegetables (g/day)			
Crude	238.41 ± 33.00	208.77 ± 22.14	0.457
Model 1	224.97 ± 28.47	214.81 ± 18.84	0.770
Model 2	228.42 ± 32.79	204.50 ± 20.77	0.554
Garlic (g/day)			
Crude	0.59 ± 0.23	0.86 ± 0.15	0.323
Model 1	0.46 ± 0.22	0.92 ± 0.15	0.090
Model 2	0.62 ± 0.25	0.70 ± 0.16	0.786
Potatoes (g/day)			
Crude	15.57±4.72	27.26 ± 3.16	0.041
Model 1	14.13±4.83	27.91 ± 3.19	0.020
Model 2	12.55±3.90	24.83 ± 2.47	0.012
Whole grain (g/day)			
Crude	60.41 ± 12.78	72.50 ± 8.57	0.433
Model 1	54.76 ± 12.44	75.05 ± 8.23	0.182
Model 2	66.33 ± 16.34	75.75 ± 10.34	0.640
Refrains grain (g/day)			
Crude	269.44 ± 30.74	253.82 ± 20.62	0.674
Model 1	247.01 ± 28.14	263.91 ± 18.62	0.623
Model 2	225.91 ± 29.25	262.67 ± 18.51	0.310
Snakes (g/day)			
Crude	4.80 ± 2.09	7.37 ± 0.40	0.310
Model 1	4.34 ± 2.16	7.57 ± 1.43	0.221
Model 2	3.93 ± 3.10	8.35 ± 1.96	0.249
Dried fruit (g/day)			
Crude	10.79 ± 2.37	10.50 ± 1.59	0.918
Model 1	10.83 ± 2.43	10.48 ± 1.61	0.906
Model 2	11.59 ± 3.19	11.18 ± 2.02	0.918
Mayonnaise (g/day)			
Crude	3.71 ± 0.89	1.99 ± 0.60	0.110
Model 1	3.45 ± 0.88	2.11 ± 0.58	0.208
Model 2	2.44 ± 0.84	2.16 ± 0.53	0.782
Nuts (g/day)			
Crude	19.10 ± 2.61	16.77 ± 1.75	0.458
Model 1	16.92 ± 2.43	17.75 ± 1.61	0.778
Model 2	16.70 ± 3.17	18.93 ± 2.00	0.568

	Case	Control	P. value
Olive (g/day)			
Crude	6.65 ± 1.60	4.21 ± 1.07	0.207
Model 1	6.20 ± 1.62	4.41 ± 1.08	0.366
Model 2	5.63 ± 2.28	5.16 ± 1.44	0.868
confectioneries (g/day)			
Crude	64.82 ± 7.20	40.97 ± 4.83	0.007
Model 1	61.47 ± 7.11	42.48 ± 0.70	0.030
Model 2	68.32 ± 8.69	38.12 ± 5.50	0.006
Hydrogenated fats (g/day)			
Crude	9.98 ± 1.50	2.51 ± 1.00	< 0.001
Model 1	9.51 ± 1.50	2.72 ± 0.99	< 0.001
Model 2	7.92 ± 1.90	2.18 ± 1.20	0.015
Vegetable oil (g/day)			
Crude	8.55 ± 1.75	7.65 ± 1.17	0.667
Model 1	7.68 ± 1.77	8.04 ± 1.17	0.865
Model 2	7.99 ± 1.94	7.70 ± 1.23	0.905
Sugars (g/day)			
Crude	32.71 ± 4.76	26.28 ± 3.20	0.263
Model 1	31.82 ± 4.46	26.68 ± 2.95	0.344
Model 2	35.28 ± 5.2	25.15 ± 3.34	0.122
Condiment (g/day)			
Crude	28.60 ± 3.80	23.99 ± 2.55	0.316
Model 1	26.42 ± 3.63	24.97 ± 2.40	0.742
Model 2	29.32 ± 4.85	26.41 ± 3.07	0.627
Soft drink (g/day)			
Crude	83.30 ± 11.69	28.80 ± 7.84	< 0.001
Model 1	78.93 ± 11.28	30.76 ± 7.47	0.001
Model 2	60.40 ± 12.71	28.79 ± 8.04	0.046
Yogurt drink (g/day)			
Crude	60.78 ± 22.30	88.02 ± 14.96	0.312
Model 1	53.61 ± 22.42	91.25 ± 14.84	0.170
Model 2	43.45 ± 30.76	100.17 ± 19.47	0.137
Broth (g/day)			
Crude	41.73 ± 14.10	45.21 ± 9.46	0.838
Model 1	43.42 ± 14.50	44.45 ± 9.60	0.953
Model 2	49.27 ± 20.15	56.28 ± 12.75	0.778
Salt (g/day)			
Crude	6.67 ± 1.18	6.47 ± 0.79	0.887
Model 1	6.21 ± 1.20	6.68 ± 0.80	0.753
Model 2	6.21 ± 1.42	6.65 ± 0.70	0.800
Pickles (g/day)			
Crude	13.34 ± 12.09	28.31 ± 8.11	0.306
Model 1	7.42 ± 12.32	30.97 ± 8.15	0.119
Model 2	11.26 ± 4.15	21.13 ± 2.63	0.056
Legumes (g/day)			
Crude	32.68 ± 8.77	44.08 ± 5.88	0.282
Model 1	28.29 ± 8.16	46.05 ± 5.40	0.076
Model 2	35.74 ± 11.07	41.79 ± 7.00	0.658
Red meats (g/day)			
Crude	85.77 ± 8.30	62.17 ± 5.57	0.020
Model 1	81.10 ± 7.96	64.27 ± 5.26	0.084
Model 2	83.23 ± 9.58	63.42 ± 6.06	0.096

[a] Model 1: adjusted for age, energy, sex
b Model 2: adjusted for marital status, job, education, sun exposure, smoking, sunscreen, BMI, spouse education, spouse job, economic status
[c] All value is reported as a Mean ± Standard error
[d] Not adjusted for economic situation

Table 5: Dietary nutrient intake between patients with multiple sclerosis and healthy individuals

	Case	Control	P. value
Energy (Kcal)			
Crude	3038.73 ± 197.17	2636.61 ± 132.27	0.093
Model 1	3006.11 ± 194.01	2651.29 ± 128.78	0.134
Model 2	2762.97 ± 243.01	2727.65 ± 153.79	0.906
Total fat (g/day)			
Crude	111.61 ± 6.82c	82.44 ± 4.58	0.001
Model 1a	103.05 ± 4.20	86.29 ± 2.78	0.001
Model 2b	102.36 ± 5.28	85.19 ± 3.34	0.010
Saturated fat (g/day)			
Crude	31.15 ± 2.18	25.22 ± 1.46	0.025
Model 1	28.69 ± 1.47	26.33 ± 0.97	0.190
Model 2	28.32 ± 1.73	26.06 ± 1.09	0.292
Monounsaturated fat (g/day)			
Crude	34.87 ± 2.24	24.08 ± 1.50	< 0.001
Model 1	32.19 ± 1.58	25.28 ± 1.04	< 0.001
Model 2	30.77 ± 1.92	24.87 ± 1.22	0.014
Polyunsaturated fat(g/day)			
Crude	42.96 ± 7.79	24.93 ± 5.22	0.057
Model 1	41.41 ± 7.65	25.63 ± 5.06	0.092
Model 2	44.40 ± 10.72	25.98 ± 6.79	0.166
Protein (g/day)			
Crude	116.61 ± 9.41	103.79 ± 6.31	0.259
Model 1	106.42 ± 5.35	108.38 ± 3.54	0.764
Model 2	110.15 ± 5.86	105.16 ± 3.71	0.491
Carbohydrate (g/day)			
Crude	430.84 ± 33.01	396.28 ± 22.15	0.386
Model 1	388.46 ± 11.99	415.35 ± 7.94	0.068
Model 2	380.02 ± 14.53	415.28 ± 9.20	0.052
Dietary fiber intake (g/day)			
Crude	28.38 ± 0.99	28.05 ± 2.01	0.926
Model 1	25.65 ± 1.86	29.27 ± 1.23	0.111
Model 2	26.86 ± 0.27	29.04 ± 1.44	0.436

Discussion

In this case-control study, increased risk of MS was had a significant positive association with hydrogenated fats, mono-unsaturated fats, soft drinks, and processed meat intake. Furthermore, high intake of fruits, potatoes, pickles, dietary fiber, and refined grains decreased the risk of developing MS.

Several epidemiological studies examined the relationship between foods and MS, but their results were contradictory [17]. In a case-control study conducted by Hadgkiss et al., the risk of MS increased with the consumption of saturated fats ($p < 0.001$) and meat ($p = 0.002$) [21]. Moreover, Saka et al. carried out a study on 37 MS patients in Ankara and showed that increased intake of energy ($p = 0.004$), carbohydrates ($p = 0.005$), fats ($p = 0.043$), and polyunsaturated fatty acids ($p = 0.001$) had a significant positive correlation with the increased risk of MS (27). In line with our findings, results of a case-control study indicated that people who consumed high amounts of solid oils and soft drinks were 1.58 and 1.87 times more likely to develop MS, respectively ($p < 0.05$). In contrast, Zhang et al. reported that high intake of saturated fats as well as low intake of unsaturated fatty acids and omega-3 did not have any significant association with the increased risk of MS (20). Besides, it was found that diets with high saturated fats and low levels of poly-unsaturated or omega-3 fatty acids might increase the risk of MS [22].

Experimental studies have shown that excessive intake of saturated fatty acids, as an effective factor in the demyelination of neuronal neurons, leads to progression of the disease [23]. In fact, intake of saturated fatty acids might lead to blockage of the central nervous system capillaries and decrease the flexibility of the vessel walls through the accumulation of red blood cells and platelets. This, in turn, creates hypoxia and can ultimately lead to demyelination of the nerves [21].

The results of a retrospective study showed a significant relationship between consuming meat and meat products (p = 0.001) and the risk of MS (9). On the other hand, the findings of a study in Abar City of Croatia, as one of the high risk areas for MS, revealed that consumption of animal fats, sheep, cattle meat, as well as other meat products such as dried meat and sausages (p = 0.007) was associated with an increased risk of MS. The association of consuming red meat, pork, processed meat such as smoked meat and other meat products containing nitrates (bologna and sausage) with the incidence of MS disease was reported [24]. In contrast, two large cohort studies conducted among women showed that receiving dairy products, chicken, fish, red meat, and processed meat was not associated with the risk of MS disease [25]. Application of various forms of nitrates, as preservatives in the meat products, can be justified through biological arguments in the pathogenesis of autoimmune processes. It is revealed that nitrogen oxide units with meat proteins may give rise to severe oxidative damages in biological tissues [26]. In the present study, consumption of fruits, potatoes, pickles, refined grains, and fibers was inversely associated with the odds of developing MS. A case-control study also reported a positive relationship between the intake of refined grains and incidence of MS. Akbulut et al. showed that women with MS had used large quantities of white bread, sugars, and soft drinks before the disease [27]. In addition, the results of a review study indicated that MS patients consumed less bread, cereal products, vegetables, and fruits in comparison with healthy people. Whole grains, such as bran, are a good source of fiber and the role of fiber in preventing the chronic diseases such as MS is based on its biologically active substances with antioxidant and anti-cancer properties [28]. Moreover, high consumption of soft drinks can affect calcium absorption because carbonated drinks contain high amounts of phosphate. Considering that calcium has important effects on the synthesis of myelin sheath and immune system, changes in the calcium concentration might affect its function in the immune system. Some studies highlighted the correlation between low intake of calcium and chance of developing MS [29, 30].

The present research showed that pickles consumption was negatively associated with MS. To the best of our knowledge, no study has ever investigated the relationship between consumption of pickles and MS risk, which may be due to different dietary patterns in different cultures and regions.

A case-control study carried out by Pekmezovic et al. indicated that consumption of various fruits such as cherry had a protective effect on the MS outbreak. In addition, Ghadirian et al. noted that consumption of fruits, diet foods, dietary fiber, cereal fibers, plant proteins, and vitamin C had a protective effect on MS [31]. The study conducted in Croatia also proposed that the outbreak of MS decreased by daily intake of fresh fruits and vegetables. In the study carried out by Hadgkiss et al., the protective effect of herbal protein and fiber was reported on the incidence of MS [21]. Contrary to these findings, Zhang et al., after adjusting for age, latitude, smoking, and energy intake represented that consumption of fruits and vegetables did not find any significant correlation with MS risk [17]. Fruits contain many intrinsic compounds such as phenols, vitamins, and minerals that can influence inflammation and oxidation. Vitamins and antioxidants can neutralize the free radicals and prevent from the peroxidation of lipids in the white matter of brain and demyelination of central nerves in MS [32]. Antioxidant properties of the polyphenols and carotenoids also affect the oxidative balance. In addition, certain polyphenols, such as catechins and quercetin showed anti-inflammatory and immunization properties [33]. In the present study, the control participants were selected from the residence areas where the cases lived. In other words, we did not select the control participants from hospitals, which helped us to control environmental factors that might increase the risk of the disease. Furthermore, the controls might be a representative of the healthy people in Yazd and their lifestyle may be closer to the healthy adults living in the society. In the present study, the association between diet and MS was adjusted for the maximum number of confounding variables.

A number of limitations should be considered while interpreting our results. Considering the retrospective nature of the present study, the causal association between the diet and MS might not be inferred. The case-control studies are prone to rumination bias. Since patients with MS might recall their diet and other factors differently compared to the healthy participants. In the present study, we tried to include newly diagnosed cases, which could decrease the recall bias. Given that the patients with MS might significantly change their diet after diagnosis of the disease. In this retrospective study, the data on dietary intakes of the case group were evaluated during the year before incidence of the disease and information of the control group was collected one year before the interview. Although we applied a validated FFQ, these tools are subject to measurement errors. Measurement error decreases the possibility of finding significant effects and reduces the risk estimates. Furthermore, the patients' physiology status while completing the questionnaires could affect their responses.

Conclusion

In conclusion, the present study revealed that participants with high consumption of fruits, potatoes, refined grains, pickles, and fibers had a significantly lower chance for developing MS. On the other hand, individuals who consumed higher amounts of processed meats, hydrogenated fats, soft drinks, and unsaturated fatty acids showed an increased chance of developing MS. Furthermore, multicentral prospective studies might help to confirm these results.

Abbreviation

MS: Multiple Sclerosis
FFQ: Food Frequency Questionnaire
BMI: Body Mass Index
MRI: Magnetic Resonance Imaging.

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Conflict of interests

The authors of this article declare that there is no conflict of interest.

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