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Healthy eating index and risk of multiple sclerosis: a case-control study

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ABSTRACT

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Background and Objective: Diet quality indices a provide unique approach to studying relations between diet and disease. Our objective was to investigate the relationship between Healthy Eating Index (HEI) and risk of multiple sclerosis (MS).

Methods: We recruited 68 subjects with MS and 140 healthy subjects in a case-control study. Dietary intake was collected using a valid and reliable food frequency questionnaire. The HEI was calculated. Logistic regression was used to evaluate the relationship between HEI score and MS, after adjustment for season of the birth, daily stress, total energy intake, and age.

Results: In comparison to controls, cases had lower mean scores for total HEI (68.4 vs 72.5, p = 0.04), vegetable (7.5 vs 8.8, p = 0.006), fruit (6.3 vs 8.0, p = 0.02), and food variety (8.0 vs 10, p = 0.008). When comparing the highest and the lowest quintiles of HEI, we observed a significant decreasing trend in the risk of MS (p for trend = 0.04). Although insignificant (p > 0.05), MS risk was reduced when comparing each quintile to the reference quintile (Q2: OR = 0.95, 95% CI: 0.37-2.38; Q3; OR = 0.62, 95% CI: 0.24-1.62; Q4: OR = 0.36, 95% CI: 0.12-1.14; and Q5: OR = 0.38, 95% CI: 0.13-1.19).

Conclusions: Our study suggests that a high-quality diet assessed by HEI may decrease the risk of MS.

key words:
Healthy Eating Index,
Multiple Sclerosis,
diet quality

Introduction

Multiple sclerosis (MS) is a chronic demyelinating disease that usually occurs in early adulthood [1]. The prevalence of MS varies from 2 to 125 per 100 000 population among different populations and geographic areas [2]. Previously, Iran was considered to have a low MS prevalence. However, MS epidemiology has changed in recent years. A recent study showed the MS prevalence and incidence in Iran to be respectively 54.51 and 5.87 per 100 000 population, which constitutes a medium to high prevalence [3]. The disease is triggered by a combination of genetic and environmental risk factors, with environmental factors exerting a predominant impact [4, 5]. Among environmental risk factors, nutrition is one of the most important ones because it is ecologically associated with certain dietary patterns (e.g., the Mediterranean diet) [6]. The beneficial and harmful effects of nutrients have been investigated in previous studies [7-10],

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but methodological constraints limit definite conclusions. Furthermore, the evaluation of the associations between foods and nutrients need large sample sizes. Researchers have proposed measures and indices such as the Healthy Eating Index (HEI) to assess the overall dietary pattern in many diseases [11, 12]. Geographically, Iran is situated in the Eastern Mediterranean region; however, it is considered a high-risk area for MS, as the disease incidence has dramatically increased over the last 20 years [1]. In addition, Iran is experiencing a nutrition shift toward a Western or unhealthy dietary pattern, which is an underlying cause of chronic diseases [2]. Therefore, given the definite role of environmental factors, such as diet, in MS development, and limited studies conducted in this area, it seems necessary to investigate nutritional factors related to MS. The studies in developing countries can provide unique opportunities to test the association between diet and disease [6]. Where economic resources are severely restricted, food intake is strongly linked to income so that even small economic differences are directly reflected in the diet. This linkage would tend to increase between-person variations [3]. Therefore, the aim of the present study was to assess the association between the HEI and MS disease in a hospital-based case-control study.

Materials and methods

Subjects

In this 1:2 matched case-control study, 70 incident cases aged from 20 to 60 years who were admitted to the major neurological clinics of Tehran were included, with the response rate of 85%. Cases were diagnosed with neurologically confirmed MS within the past six months. Controls (n = 142) were selected from patients admitted to the same facilities as the cases, for a variety of acute conditions unrelated to smoking, alcohol consumption, and long-term modification of diet (participation rate 85%). Controls were frequency-matched with cases by sex and age (5-year age groups). Also, participants were selected using convenience sampling. Two controls were excluded due to poor response to dietary questions. Furthermore, we excluded two patients from the analysis because their log-transformed total energy intake values were either less than or greater than 3 standard deviations from the mean, indicating errors in their responses to the dietary questions. Finally, the data were available for 68 cases with MS and 140 controls.

Dietary assessment

Dietary intake was assessed by trained dietitians using a valid and reproducible 147-item semiquantitative food frequency questionnaire (FFQ) [4, 5]. The consumption frequency of each food item was obtained on a daily, weekly, or monthly basis. The portion sizes were then converted to grams using household measures [6].

The HEI [7] was developed by Kennedy et al based on the Food Guide Pyramid and dietary guidelines. The index evaluates three major aspects of the usual diet (namely, adequacy, moderation, and variety) by assessing 10 dietary components. The first five components measure the degree to which a person's diet conforms to serving recommendations for the five major food groups, namely, grains (bread, cereal, rice, and pasta), vegetables, fruits, milk (milk, yogurt, and cheese), and meat (meat, poultry, fish, dry beans, eggs, and nuts). The scores were computed proportionately to the number of servings consumed. total fat intake of ≤ 30% of total calories, saturated fat intake of ≤ 10% of total calories, and cholesterol intake of ≤ 300 mg/d were assigned the maximum score of 10 points. Variety component was calculated based on the McCullough method [8]. Because the FFQ does not assess foods consumed on a particular day, the total number of unique foods consumed per month among all participants was divided into quintiles, with the lowest quintile being scored 0 and the highest one being scored 10. For the current study, we applied one modification to the original index. Since we did not have reliable data on table salt intake, we decided to eliminate the sodium component. Therefore, the total score of HEI ranged from 0 to 90, with higher scores indicating a better diet quality.

Other measures

The daily imposed stress was evaluated by the valid and reliable Depression, Anxiety, and Stress Scales (DASS-21) for Iranian population [9]. Body weight was measured to the nearest 0.1 kg on a calibrated balance (Soehnle, Germany).

Statistical analysis

Statistical analyses were conducted using SPSS version 19.0 (SPSS Inc., Chicago, IL, USA). Data were assessed for normality using the Kolmogorov-Smirnov test, and are expressed as mean ± SD (for normally distributed data) or median and interquartile range (for non-normally distributed data). The Mantel-Haenszel chi-square test was used to compare qualitative variables, and the Wilcoxon signed-ranks test was used to compare mean ranks between matched groups. Age, the season of birth, amount of imposed stress during the day, and total energy intake were considered as potential confounders and were included in the models. A p value of < 0.05 was considered statistically significant and all reported p values are two-tailed.

Table 1. Baseline characteristics of multiple sclerosis cases and healthy controls

Characteristics	Cases (n = 68)	Controls (n = 140)	P value
Age, year	29 (23-33)	29 (24-35)	0.901
Body mass index, kg/m2	25.1(22.8-26.1)	23.5 (22.2-25.0)	0.180
Energy intake, kcal	2310 (2013-2745)	2267 (1839-2990)	0.005
Gender			
Male	11 (16.2)	26 (18.6)	0.642
Female	57 (83.8)	114 (81.4)	
Season of birth			
Spring	26 (38.2)	41 (30.4)	0.012
Summer	26 (38.2)	50 (37.0)	
Autumn	11 (16.2)	18 (13.3)	
Winter	17 (25.0)	26 (19.3)	
Smoking status			
Yes	4 (5.8)	10 (7)	0.711
No	64 (94.2)	130 (93)	
Imposed stress			
Normal	3 (4.8)	26 (20.2)	< 0.001
Mild	6 (9.5)	30 (23.3)	
Moderate	15 (23.8)	46 (35.70)	
Severe	29 (46)	21 (16.3)	
Very severe	10 (15.9)	6 (4.7)	

Data are median (IQR) or frequency (%).
**P values are for the comparison between matched groups using the Wilcoxon test or χ^2 test*

Table 2. Comparison of the Healthy Eating Index (HEI) and its components between cases and controls

	Cases (n = 68)	Controls (n = 140)	P value
Total HEI	68.4 (60.9-76.2)	72.5 (63.7-80.6)	0.04
Meat	8.1 (6.9-10.0)	9.3 (6.2-10.0)	0.13
Vegetable	7.5 (5.7-9.9)	8.8 (6.3-10.0)	0.006
Grain	8.5 (5.2-7.2)	7.2 (5.9-10.0)	0.07
Dairy	7.0 (4.3-9.9)	9.1 (5.6-10.0)	0.18
Fruit	6.3 (4.5-8.2)	8.0 (5.1-10.0)	0.02
Total fat	7 (5-10)	8.0 (5.25-10.0)	0.39
Cholesterol	10 (10-10)	10 (10-10)	0.50
Saturated fatty acid	10 (8-10)	9 (6-10)	0.40
Variety	8.0 (4.5-10.0)	10 (8-10)	0.008

Data are median (IQR).
**P values are for the comparison between matched groups using the Wilcoxon test.*

Results

A total of 68 cases and 140 controls were recruited. Characteristics of the participants are shown in Table 1. By design, age and sex distributions were similar in cases and controls. Cases comprised 57 women and 11 men (female to male ratio: 5.2), with the median age of 29 years. Most patients with MS were born in spring (38.2%). The number of subjects reporting severe or very severe stress was greater in cases (61.9%) than controls (21%). Table 2 compares the HEI components between cases and controls. Cases had a lower mean total HEI (68.4 vs 72.5, p = 0.04), vegetable (7.5 vs 8.8, p = 0.006), fruit (6.3 vs 8.0, p = 0.02), and variety score (8.0 vs 10, p = 0.008) in comparison with controls. Table 3 presents the crude and adjusted ORs for MS according to the quintiles of HEI. After adjustment for age and total energy intake, MS risk was reduced when comparing the third, fourth, and fifth quintiles to the reference quintile of HEI (OR = 0.95, 95% CI: 0.37-2.38), (OR = 0.62, 95% CI: 0.24-1.62), (OR = 0.36, 95% CI: 0.12-1.14).), (OR = 0.38, 95% CI: 0.13-1.19) respectively. Although the differences between each quintile and the reference quintile were not significant (p > 0.05), the observed trend was significant (p for trend = 0.02). Further adjustment for daily imposed stress did not change the observed association of HEI with MS risk (p for trend = 0.04).

Discussion

We found that the consumption of a diet consistent with the Food Guide Pyramid and dietary guidelines (higher HEI score) is associated with a lower risk of MS. Among the components of HEI, mean scores of vegetables, fruits, and Food variety were lower in cases than controls.

The association of MS risk with dietary patterns was reported in a recent study by Jahromi et al, indicating a protective association of vegetable-rich dietary patterns with MS. In detail, age-adjusted ORs for risk of MS in the highest tertile of a lacto-vegetarian dietary pattern (high in nuts, fruits, french fries, coffee, sweets and desserts, vegetables, and

Table 3. Odds ratio (OR) and 95% confidence interval (CI) of multiple sclerosis according to quintiles of healthy eating index

	Q1	Q2	Q3	Q4	Q5	P for trend
Case/control (68/140)	17/24	17/25	15/27	9/32	9/32	
Crude OR	1.00 (ref)	1.06 (0.44-2.56)	0.70 (0.28-1.73)	0.57 (0.22-1.45)	0.57 (0.22-1.45)	0.07
Model 1*	1.00 (ref)	0.95 (0.37-2.38)	0.62 (0.24-1.62)	0.36 (0.12-1.14)	0.36 (0.12-1.14)	0.02
Model 2†	1.00 (ref)	0.95 (0.36-2.47)	0.66 (0.24-1.81)	0.38 (0.13-1.12)	0.38 (0.13-1.12)	0.06
Model 3‡	1.00 (ref)	1.45 (0.47-4.45)	0.59 (0.19-1.82)	0.31 (0.09-1.07)	0.31 (0.09-1.07)	0.04

**Adjusted for age and energy intake*
†Adjusted for age, energy intake, and season of birth
‡ Adjusted for age, energy intake, and daily imposed stress

high-fat dairy products) was 0.31 and in the second tertile of a vegetarian dietary pattern (high in green leafy vegetables, hydrogenated fats, tomato, yellow vegetables, fruit juices, onion, and other vegetables) was 0.42. In contrast, participant with a high-fat dietary pattern (high in animal fats, potato, meat products, sugars, and hydrogenated fats and low in whole grains) had a higher risk of MS [10].

Studies on the association of fruit and vegetable consumption with MS risk are controversial. Zhang et al failed to observe significant association between fruit and vegetable consumption and risk of MS after adjustments for age, latitude of birthplace, smoking, and total energy intake [11]. Studies on the effect of fruits, vegetables, and their components indicate beneficial effect: fiber, plant protein, vitamin C, potassium, and antioxidant compounds have been reported as protective factors against MS [12], with the highest priority being given to vitamin C [13]. In the Nurses' Health Study, the relative risks of MS for women in the highest quintile compared with the lowest quintile of alpha-carotene, beta-carotene, lycopene, total vitamin C, dietary vitamin C, total vitamin E, and dietary vitamin E were 1.1, 1.1, 1.0, 1.4, 1.3, 0.8, and 0.9, respectively [11]. Also, fruits are a rich source of phenols, ditioldion, indols, isoflavons, protease inhibitors, and plant sterols, which effectively attenuate oxidative stress, promote endogenous antioxidant defense system, and modulate oxidant/antioxidant balance [12, 14]. Vitamin C, vitamin E, and other antioxidants inhibit lipid peroxidation in the brain and protect myelin sheath [15, 16]. Therefore, antioxidants may potentially reduce the risk of MS. Recent findings suggest the link between hypercaloric, high-fat, low-fiber diets (low in fruits and vegetables) and changes in gut microbiota profile, which is linked to the development of autoimmune disorders, MS in particular [17]. Reichelt and Jensen suggested that MS might be associated with an increased gut permeability and with an increased uptake of large peptides from the gut, causing the formation of antibodies [17].

Our study has several limitations. Firstly, like other case-control studies, recall bias and selection bias were inevitable. In case-control studies, there is a possibility that cases may recall their diets differently after MS diagnosis. However, our participants had little knowledge about the role of diet and nutrients in MS risk, which might have reduced the possibility of recall bias. Moreover, using hospital controls and administering validated FFQ by trained interviewers in a hospital setting might have further reduced the recall bias and improved comparability of information of cases and controls [18]. Regarding selection bias, high participation rates (85%) in this study minimized the potential for selective participation according to the lifestyle practices (such as diet). Another limitation of the current study was using a semiquantitative FFQ, which, despite its common application to identifying the habitual dietary intakes, is well-recognized for its weakness in characterizing dietary intakes. Using a semiquantitative dietary assessment tool limits our conclusions mostly to comparisons between cases and controls; hence the results are relative and should be interpreted with caution because these types of comparisons generally overestimate or underestimate the true relationship between exposure and outcome [19]. However, a validated FFQ that provides subjects with the option of answering in terms of day, week, or month would enhanced reporting precision considering the fact that frequency of consumption is a truly continuous variable. In our study, data on the sun exposure was not available, which constitutes another limitation. The strength of the study was that we asked incident MS patients diagnosed within 6 month of the interview to recall their diets from 1 year before the diagnosis in order to capture a full cycle of seasons so that responses are representative of habitual long-term intake. Furthermore, the study included cases whose disease diagnosis was less than six months (incident case); therefore, the possibility of diet change was low.

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Contributors

MG and MB conceived and designed the study. All authors collected data, drafted the paper, and revised the manuscript for important intellectual content. ZH, BR, and GA helped in manuscript writing. All the authors approved the final manuscript.

Conflict of interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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