Original Communication

Association between dietary inflammatory index and risk of demyelinating autoimmune diseases

A cross-sectional study

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Abstract: *Background:* Considering limited data on the association between dietary inflammatory index (DII) and demyelinating autoimmune diseases, here, we studied this issue in the early diagnosed patients [e.g., preceding Multiple Sclerosis (MS) diagnosing level (Clinically Isolated Syndrome (CIS), and Radiologically Isolated Syndrome (RIS), MS, and Neuromyelitis Optica Spectrum Disorder (NMOSD)] using a case-control study among the Iranian population. *Methods:* A total of 291 subjects were selected as the cases (Patients with demyelinating autoimmune diseases including CIS, RIS, MS, and NMOSD, who were diagnosed less than six months before recruitment) and 297 others as controls. A 117-item semi-quantitative food frequency questionnaire (FFQ) was obtained from all of the participants and DII was calculated. *Results:* After controlling for potential confounders, adherence to a pro-inflammatory diet was associated with a higher risk of demyelinating autoimmune diseases (OR=2.05, 95% CI: 0.51, 3.58), EDSS (OR=2.02, 95% CI: 0.51, 3.53), active plaque (OR=1.90, 95% CI: 0.08, 3.71), higher lesion load (OR=2.11, 95% CI: 0.58, 3.64), LETM (OR=2.19, 95% CI: 0.27, 4.11), higher number of plaques (OR=2.11, 95% CI: 0.58, 3.64), and brain atrophy (OR=2.12, 95% CI: 0.57, 3.67). *Conclusion:* Our study suggests a possible link between the inflammatory potential of the diet and demyelinating autoimmune disease; however, further prospective cohort studies are needed to draw a causal link on this issue.

Keywords: diet, multiple sclerosis, neuromyelitis optica spectrum disorder, inflammation

Introduction

Accumulating data indicate a steady rise in autoimmune diseases over the last decades [1]. Several examples, among others, include Celiac Disease (CD), Systemic Lupus Erythematosus (SLE), Inflammatory Bowel Diseases (IBD), Neuromyelitis Optica Spectrum Disorder (NMOSD), Multiple Sclerosis (MS), and Type 1 Diabetes Mellitus (T1DM) [1]. Autoimmune diseases cause significant morbidity and disability; however, their impact on health services delivery appears to be underestimated, although many of these diseases are chronic and require intensive medical interventions [2]. Therefore, it is strongly warranted to optimize treatment strategies and stop the increase in incidence using simple and cost-effective approaches.

Various modifiable (smoking, tobacco [3], and vitamin D deficiency [4], as well as high body mass index (BMI) [5]) and non-modifiable (genetic and female sex factors) have been suggested as risk factors for developing the demyelinating autoimmune disease [6]. Previous studies have investigated the effect of specific nutrients on the risk of MS, though, their findings were mixed. For instance, fish consumption was suggested to be associated with a lower risk of MS [7, 8]; however, other studies did not support this fact [9]. Moreover, red meat was reported as a protective [9] and risk factor [10] regarding MS risk. Other nutrients also revealed mixed results [11, 12, 13]. There is also evidence of a positive association between MS incidence and consumption of meat, milk, and animal fat [14, 15]. However, a potentially better approach for investigating the diet-disease

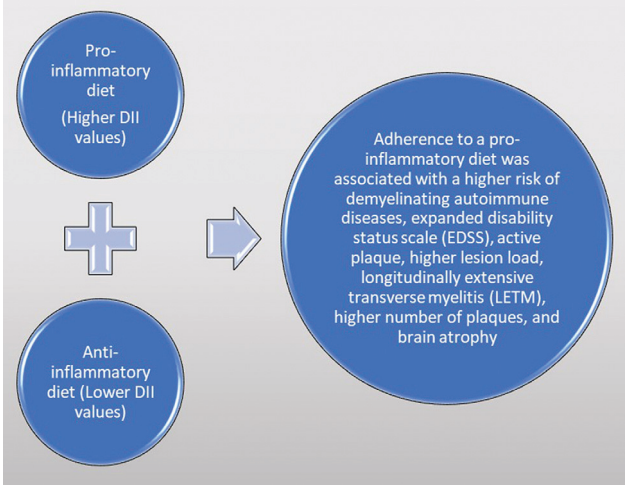

Figure 1. Summary of the present study findings.

associations is to determine the overall quality of the diet, as an alternative for nutritional groups [16]. Dietary indices studied in association with autoimmune conditions promote autoimmunity through enhancing obesity, metabolic syndrome, and cardiovascular disease [17, 18]. In one study, a new hypothesis was proposed concerning the influence of dietary total antioxidant capacity (TAC) on the odds of NMOSD. A diet rich in foods with high TAC can be effective in the modification of the NMOSD risk [19].

Dietary inflammatory index (DII) is another population-based summary measure that captures the inflammatory potential of individuals' diets. There are few studies that have reported on the potential role of DII in the risk of MS [20, 16] and also other autoimmune diseases including RA [21], IBD [22], T1DM [23], and MS [16]. No datasets were found regarding other diseases including NMOSD. Considering limited data in this area, here, we studied the association between DII and risk of demyelinating autoimmune diseases in the early diagnosed patients [e.g., preceding MS diagnosing level (Clinically Isolated Syndrome (CIS)), and Radiologically Isolated Syndrome (RIS)), MS, and NMOSD using a population-based case-control study among the Iranian population.

Methods and materials

Study design and participants

In the present hospital-based case-control study, 588 subjects were selected by sequential sampling from December 2018 to February 2020. Of the patients referred to the Kashani hospital, affiliated with Isfahan University of Medical Sciences (Isfahan, Iran), 291 subjects were selected as cases and 297 others as control. Patients with demyelinating autoimmune diseases including CIS, RIS, MS, and NMOSD, who were diagnosed less than six months before recruitment, were included. Moreover, patients aged between 20–60 years old; without any changes to the usual dietary habits since diagnosis were included. We enrolled participants, who were diagnosed less than six months of recruitment due to possible disease-related changes in diet.

A total of 297 patients were also selected as the control from the same hospital who were without demyelinating autoimmune diseases. Exclusion criteria for both groups were being pregnant or lactating; diagnosis of gastrointestinal and liver diseases, cancer, endocrine, and metabolic disorders, inflammatory diseases of the peripheral nervous system, immune system disorders, and following a special diet. Patients with reported daily energy intakes higher than 4200 kcal/d (17573 kJ/d) or lower than 800 kcal/d (3347 kJ/d), were also excluded [24]. Written informed consent was obtained from all the participants. The research ethics committee of Semnan University of Medical Sciences (IR.SEMUMS.REC.1398.208) approved the protocol of the current study.

Assessment of demyelinating autoimmune diseases and related parameters

Upon the admission of suspected individuals to the MS clinic of Kashani hospital, they have undergone a clinical examination by an expert neurologist to diagnose RIS, CIS, MS, and NMOSD based on related guidelines [25, 26, 27, 28]. Moreover, the presence of longitudinally extensive transverse myelitis (LETM), active plaque, lesion load, number of plaques, and brain atrophy were assessed through a clinical examination using magnetic resonance imaging (MRI). The disability of participants was examined using an expanded disability status scale (EDSS) which ranged from 0–10, indicating no disability and symptoms to the most disability [29].

Dietary assessment

All of the recruited participants were completed a 117-item semi-quantitative food frequency questionnaire (FFQ) to obtain the dietary habits of patients during the previous year [30]. Through a face-to-face interview by a trained dietitian, participants were asked to report the consumption frequency of each food item on a basis of daily, weekly, or monthly. Subsequently, the portion sizes of consumed foods were transformed into grams using household measures [31]. All of the collected data were analyzed by Nutritionist IV software (First Databank, Hearst Corp, San Bruno, CA, USA).

Calculating DII

The FFQ-derived dietary data of participants was used to calculate the DII score. The DII is a population-based dietary score that was developed to identify the inflammatory

characteristics of the diet. The higher positive DII scores imply a more pro-inflammatory diet while the higher negative DII values represent a dietary habit with anti-inflammatory properties. A detailed description of DII has been published previously by Shivappa et al [32]. At first, the raw dietary components of participants were adjusted by energy intakes using the residual method. The reported dietary intake of participants in terms of the 45 dietary parameters is subtracted from the global average intake of that dietary parameter and divided by its global standard deviation to calculate z-score. Z-score is a multiplier that expresses participants' exposure relative to the standard global mean. Then z-score is converted to percentile and multiplied by 2 and then subtracted from the number one. The obtained score is multiplied by the inflammatory score related to that food parameter and the numbers obtained from the 45 dietary parameters for each person are summed together to obtain the total DII score for each person [32]. A total of 27 food items were available from the 117-item FFQ and hence was used to calculate DII. These 27 food items were protein, carbohydrate, fiber, total fat, saturated fat, cholesterol, mono- and poly-unsaturated fat, omega-3, omega-6, vitamin B1, B2, B3, B6, B12, folic acid, vitamin A, C, D, E, magnesium, iron, zinc, selenium, beta carotene, pepper, and onion.

Confounders

Using the Seca scale (Seca Scale with Height Rod, Hamburg, Germany), weight and height were measured to the nearest 0.1 kg and 0.1 cm, respectively. BMI was computed using the height (m^2) and weight (kg) by the related equation. Sun exposure status of participants was also examined using a validated questionnaire and subjects categorized as low, moderate, and high, accordingly [33, 34]. The physical activity (PA) status was determined using a reliable and valid version of the International Physical Activity Questionnaire (IPAQ) and patients categorized as low, moderate, and high [35]. Moreover, patients were assessed by an expert physician regarding the presence of drug addiction, hypertension (blood pressure>140/90 mmHg) [36], anemia (hemoglobin level of less than 13 g per dL [130 g per L) in men and less than 12 g per dL (120 g per L) in women], migraine [37], and sexual disability [38].

Statistical analysis

Categorical and continuous variables were expressed as number (percent) and mean±standard deviation (SD), respectively. The normality of continuous variables was assessed using skewness statistic, Q-Q plot, and Kolmogorov-Smirnov test. The Chi-square test was used for assessing the distribution of categorical data between the case and the control group and also between the anti- and pro-inflammatory groups. The independent samples t-test was implemented to compare participants' dietary intake between the case and the control group. To explore the association between the DII with the risk of demyelinating autoimmune diseases and related parameters, logistic regression analysis was performed in different models. First, we adjusted for total energy intake and sex. In the next model further adjustment was made for age, economic status, BMI, and physical activity. Statistical analyses were done using the SPSS version 20.0 (SPSS, Inc., Chicago, IL, USA), and $P<0.05$ was considered statistically significant.

Results

A total of 291 patients with demyelinating autoimmune diseases (mean age of 33.64 years) and 297 controls (mean age of 34.98 years) make up our study population. General characteristics of the study population across case and control are presented in Table 1. Patients' age, height, weight, and BMI were significantly higher in the control group compared to the case group. Moreover, subjects in the control group were more likely to be female, live with family, with low economic status, and without anemia (all P-values <0.05).

General characteristics and clinical findings of patients diagnosed with demyelinating autoimmune diseases (n=291) according to the DII status (anti-inflammatory/pro-inflammatory) are shown in Table 2. Subjects with the anti-inflammatory potential of the diet were less likely to be anemic and with low physical activity (all P-values <0.05).

Dietary intakes of patients in the case and control group are indicated in Table 3. Patients with demyelinating autoimmune diseases consumed higher amounts of energy, protein, cholesterol, saturated fat, total fiber, vitamin A, β-carotene, vitamin B2, B3, B6, B9, B12, and magnesium, as well as, lower amounts of polyunsaturated fats (all P-values <0.05).

OR and 95% confidence interval for the association between DII, demyelinating autoimmune diseases, and its clinical findings are shown in Table 4. In the crude model, patients with a pro-inflammatory diet had a higher risk of demyelinating autoimmune diseases compared to those with an anti-inflammatory diet (OR=1.02, 95% CI: 0.03, 2.01). Further adjustment for total energy intake, sex, age, physical activity, economic status, and body mass index intensifies the association between DII and the risk of demyelinating autoimmune diseases (OR=2.05, 95% CI: 0.51, 3.58). Adherence to a pro-inflammatory diet was associated with a lower risk of EDSS (OR=0.98, 95% CI: 0.02,

Table 1. General characteristics of participants

Variables	Control (n=297)	Case (n=291)	P-value
Age (years)	34.98±0.42	33.64±0.52	0.01[1]
Height (cm)	165.78±0.54	165.36±0.49	0.04[1]
Weight (kg)	69.69±0.80	65.95±0.74	0.001[1]
BMI (kg/m^2)	25.29±0.24	24.68±0.17	<0.001[1]
Sex			
Female	271 (91.2)	249 (85.6)	0.03[2]
Male	26 (8.8)	42 (14.4)	
Living status			
Alone	46 (15.48)	98 (33.67)	<0.001[2]
With family	251 (84.52)	193 (66.33)	
Education level			
Under diploma	121 (40.74)	131 (45.03)	0.39[2]
Diploma	136 (45.80)	117 (40.20)	
University education	40 (13.46)	43 (14.77)	
Physical activity level			
Low	212 (71.39)	219 (75.27)	0.53[2]
Moderate	74 (24.91)	64 (21.99)	
High	11 (3.70)	8 (2.74)	
Economic status			
Low	58 (19.52)	48 (16.49)	<0.001[2]
Moderate	187 (62.98)	149 (51.21)	
High	52 (17.50)	94 (32.30)	
Sun exposure level			
Low	183 (61.62)	205 (70.46)	0.06[2]
Moderate	75 (25.25)	60 (20.61)	
High	39 (13.13)	26 (8.93)	
Drug addiction			
No	288 (96.97)	274 (94.16)	0.09[2]
Yes	9 (3.03)	17 (5.84)	
Hypertension			
No	285 (95.96)	282 (96.91)	0.53[2]
Yes	12 (4.04)	9 (3.09)	
Anemia			
No	286 (96.30)	263 (90.38)	0.004[2]
Yes	11 (3.70)	28 (9.62)	
Migraine			
No	265 (89.23)	253 (86.95)	0.39[2]
Yes	32 (10.77)	38 (13.05)	
Sexual disability			
No	265 (89.23)	253 (86.95)	0.39[2]
Yes	32 (10.77)	38 (13.05)	

Data are presented as mean±standard deviation or number (percent); P<0.05 considered statistically significant. [1]Calculated by Independent-Samples T test. [2]Calculated by Chi-square test.

Table 2. General characteristics of patients diagnosed with demyelinating autoimmune diseases according to the dietary inflammatory index (DII)

Variables	Anti-inflammatory	Pro-inflammatory	P-value
Types of demyelinating autoimmune diseases			
CIS	7 (30.4)	59 (22.0)	0.73
RIS	0 (0.0)	3 (1.1)	
RRMS	15 (65.2)	168 (62.7)	
SPMS	0 (0.0)	15 (5.6)	
PPMS	0 (0.0)	4 (1.5)	
NMOSD	1 (4.3)	19 (7.1)	
LETM			
Yes	4 (17.4)	20 (7.5)	0.09
No	19 (82.6)	248 (92.5)	
Demyelinating autoimmune diseases attack			
No	20 (87.0)	206 (76.9)	0.26
Yes	3 (13.0)	62 (23.1)	
EDSS			
No disability	6 (26.1)	90 (33.6)	0.49
Low to moderate	17 (73.9)	170 (63.4)	
Moderate to high	0 (0.0)	8 (3.0)	
Familial history of demyelinating autoimmune diseases			
Yes	6 (26.1)	50 (18.7)	0.38
No	17 (73.9)	218 (81.3)	
Active plaque			
Yes	3 (13)	27 (10.1)	0.65
No	20 (87)	241 (89.9)	
Lesion load			
No	1 (4.3)	4 (1.5)	0.67
Low	14 (60.9)	187 (69.8)	
Medium	5 (21.7)	48 (17.9)	
High	3 (13)	29 (10.8)	
Brain atrophy			
No	22 (95.7)	247 (92.2)	0.48
Mild	0 (0.0)	14 (5.2)	
Moderate	1 (4.3)	7 (2.6)	
Migraine			
Yes	2 (8.7)	36 (13.4)	0.51
No	21 (91.3)	232 (86.6)	
Hypertension			
Yes	0 (0.0)	9 (3.4)	0.37
No	23 (100)	259 (96.6)	
Anemia			
Yes	5 (21.7)	23 (8.6)	0.04
No	18 (78.3)	245 (91.4)	
Sleep disorders			
Yes	17 (73.9)	173 (64.6)	0.36
No	6 (26.1)	95 (35.4)	

(Continued on next page)

1.95); however, controlling for potential confounders changed the findings in such a way that a pro-inflammatory diet was linked with a higher odd of EDSS (OR=2.02, 95% CI: 0.51, 3.53). After adjustment for total energy intake, sex, age, physical activity, economic status, and body mass index, adherence to a pro-inflammatory diet was significantly associated with higher risk of active plaque (OR=1.90, 95% CI: 0.08, 3.71), higher lesion load (OR= 2.11, 95% CI: 0.58, 3.64), LETM (OR=2.19, 95% CI: 0.27,

Table 2. (Continued)

Variables	Anti-inflammatory	Pro-inflammatory	P-value
BMI			
Underweight	2 (8.7)	35 (13.1)	0.73
Normal	19 (82.6)	219 (81.7)	
Overweight	2 (8.7)	12 (4.5)	
Obese	0 (0.0)	2 (0.7)	
Physical activity level			
Low	12 (52.2)	207 (77.2)	0.02
Moderate	10 (43.5)	54 (20.1)	
High	1 (4.3)	7 (2.6)	
Sexual disability			
No	1 (4.3)	32 (11.9)	0.27
Yes	22 (95.7)	236 (88.1)	
Economic status			
Low	3 (13.0)	45 (16.8)	0.74
Moderate	11 (47.8)	138 (51.5)	
High	9 (39.1)	85(31.7)	
Sun exposure level			
Low	16 (69.6)	189 (70.5)	0.26
Moderate	3 (13)	57 (21.3)	
High	4 (17.4)	22 (8.2)	
Number of plaques			
0	15 (65.2)	191 (71.3)	0.67
1–3	5 (21.7)	48 (17.9)	
>3	3 (13)	29 (10.8)	

Data are presented as number (percent); P<0.05 considered statistically significant. CIS: Clinically Isolated Syndrome; RIS: Radiologically Isolated Syndrome; RRMS: Relapsing-remitting multiple sclerosis; SPMS: Secondary-progressive multiple sclerosis; PPMS: Primary-progressive multiple sclerosis; NMOSD: Neuromyelitis optica spectrum disorder; BMI: Body Mass Index; LETM: longitudinally extensive transverse myelitis; EDSS: expanded disability status scale. [1]Calculated by Chi-square test.

Table 3. Dietary intake of patients diagnosed with demyelinating autoimmune diseases and the control group

Variables	Control (n=297)	Case (n=291)	P-value[1]
Total ENERGY intake (kcal/d)	1777±40.4	1854±42.1	0.18
Carbohydrate (g/d)	250±6.42	259±6.92	0.34
Fat (g/d)	62.4±1.95	64.3±1.76	0.45
Protein (g/d)	69.0±1.60	78.1±2.09	<0.001
Cholesterol (mg/d)	181±5.06	211±5.79	0.03
Saturated Fat (g/d)	19.1±0.63	21.8±0.77	0.01
MUFA (g/d)	18.3±0.59	18.3±0.49	0.94
PUFA (g/d)	12.0±0.49	11.1±0.33	<0.001
Total Fiber (g/d)	25.4±0.75	27.9±0.91	0.01
Vitamin A (μg/d)	555±21.7	684±37.2	0.03
β-carotene (μg/d)	4393±207	5639±417	<0.001
Vitamin C (mg/d)	208±9.37	228±12.1	0.19
Vitamin E (mg/d)	9.26±0.32	9.55±0.32	0.52
Vitamin B1 (mg/d)	1.38±0.03	1.48±0.04	0.06
Vitamin B2 (mg/d)	1.76±0.05	2.09±0.07	<0.001
Vitamin B3 (mg/d)	16.4±0.41	17.7±0.54	0.04
Vitamin B6 (mg/d)	1.63±0.03	1.87±0.05	<0.001
Vitamin B9 (μg/d)	461±12.0	510±15.7	0.01
Vitamin B12 (μg/d)	3.43±0.11	4.12±0.16	<0.001
Vitamin D (μg/d)	1.67±0.09	1.91±0.11	0.10
Zinc (mg/d)	10.4±0.30	11.3±0.32	0.09
Selenium (μg/d)	68.2±1.99	71.3±1.99	0.27
Magnesium (mg/d)	349±10.0	389±12.3	0.02
Iron (mg/d)	12.3±5.38	13.0±6.47	0.16

Data are presented as mean±standard deviation. P<0.05 considered statistically significant. MUFA: mono-unsaturated fatty acids; PUFA: poly-unsaturated fatty acids. [1]Calculated by Independent-Samples T test. [2]Calculated by Chi-square test

4.11), higher number of plaques (OR=2.11, 95% CI: 0.58, 3.64), and brain atrophy (OR=2.12, 95% CI: 0.57, 3.67).

Discussion

This case-control study showed that those with higher DII scores had a higher risk of developing inflammatory auto-immune diseases. This result confirms our hypothesis that having a pro-inflammatory diet is associated with an increased risk of inflammatory auto-immune conditions (Figure 1).

Few observational studies have directly assessed the association between DII and inflammatory auto-immune diseases, with the main focus being on MS. Similar to our study, Shivappa et al. [39] confirmed that subjects with higher DII scores were at increased risk of developing MS. However, the generalizability of its finding to the target population is limited because of the hospital-based nature of their study. Also, a longitudinal MRI study conducted in a large MS cohort recently reported the potential inflammatory character of the diet. Lower intake of dietary fiber, raw fruit, and vegetables, along with higher consumption of processed red meat and sweetened beverages increased MS lesion accrual [40]. Lastly, in 2020, Abdollahpour et al. [41] proved that a pro-inflammatory diet elevates the possibility of MS diagnosis. However, in contrast with our study and also previous datasets, a cross-sectional analysis in the Brazilian northeast failed to show any modification of clinical course by DII in 137 MS cases [42]. As to other diseases including CIS and RIS, or NMOSD, no datasets were found to make comparisons, making the results of the present study more interesting.

The effect of pro-inflammatory diet on the levels of various inflammatory cytokines, such as Vascular Cellular Adhesion Molecule (VCAM), and T and B lymphocytes is one possible explanation for the observed direct association of the DII with inflammatory auto-immune diseases like MS; all of these are important components in the development of MS. When the lymphocyte integrin α4 β1 (VLA-4) binds to VCAM-1 on the brain vascular endothelium, the transmigration of leucocytes (including T lymphocytes,

Table 4. Odds ratios and 95% confident interval for the association between demyelinating autoimmune diseases and dietary inflammatory index

	Anti-inflammatory diet	Pro-inflammatory diet	P-value
Diagnosis of demyelinating autoimmune disease			
Crude	Ref	1.02 (0.03 – 2.01)	0.04
Model	Ref	2.05 (0.51 – 3.58)	0.009
EDSS			
Crude	Ref	0.98 (0.02 – 1.95)	0.04
Model	Ref	2.02 (0.51 – 3.53)	0.009
Active plaque			
Crude	Ref	0.87 (−0.52 – 2.27)	0.22
Model	Ref	1.90 (0.08 – 3.71)	0.04
Lesion load			
Crude	Ref	1.08 (0.10 – 2.07)	0.03
Model	Ref	2.11 (0.58 – 3.64)	0.007
LETM			
Crude	Ref	1.09 (−0.35 – 2.54)	0.13
Model	Ref	2.19 (0.27 – 4.11)	0.02
Number of plaques			
Crude	Ref	1.08 (0.10 – 2.07)	0.03
Model	Ref	2.11 (0.58 – 3.64)	0.007
Brain atrophy			
Crude	Ref	1.06 (0.06 – 2.06)	0.03
Model	Ref	2.12 (0.57 – 3.67)	0.007

Data are presented as odds ratio (95% confidence interval). Crude: Unadjusted. Model: Adjusted for total energy intake, sex, age, physical activity, economic status, and body mass index. [1]Calculated by Multinomial logistic regression

but also monocytes and other immune cells) into the CNS occurs. Upon entering CNS, new inflammatory demyelinating lesions are formed through these lymphocytes [43]. Based on another new hypothesis about the regulation of the host immune responses, gut commensal microorganisms are able to elicit pro-inflammatory responses. As such, gut homeostasis might be substantially influenced by specific healthy dietary habits, leading to both local and systemic low-grade inflammation [44].

This is the first study in Iran and the world to survey the inflammatory properties of diet in relation to a number of inflammatory auto-immune diseases, including CIS, RIS, and NMOSD, which is considered as the study strength. However, some important limitations need to be considered as well. First, self-reported dietary intake may lead to some errors, which could distort the results. Second, disease-specific recall bias and selection bias are common in case-control studies, which might influence the findings. A total of 27 food items were available from the 117-item FFQ and hence was used to calculate DII. Since the original method for the calculation of DII uses 45 food items, this modification might be a limitation for this study. Also, we did not assess the medication of participants which can play a role as a confounder and need to be controlled in future studies. Moreover, biochemical indicators of systemic inflammation were missed in our study and should be measured in future attempts.

In conclusion, results revealed that subjects with a more pro-inflammatory diet were at increased risk of demyelinating autoimmune diseases compared to those who consumed a more anti-inflammatory diet. However, more longitudinal studies are warranted to investigate the protective role of an anti-inflammatory diet on the risk of demyelinating autoimmune diseases.

References

1. Lerner A, Jeremias P, Matthias T. The world incidence and prevalence of autoimmune diseases is increasing. Int J Celiac Dis. 2015;3(4):151–5.
2. Jacobson DL, Gange SJ, Rose NR, Graham NM. Epidemiology and estimated population burden of selected autoimmune diseases in the United States. J Clin Immunol Immunopathol. 1997;84(3):223–43.
3. Abdollahpour I, Nedjat S, Sahraian MA, Mansournia MA, Otahal P, van der Mei I. Waterpipe smoking associated with multiple sclerosis: A population-based incident case-control study. Mult Scler J. 2017;23(10):1328–35.
4. Duan S, Lv Z, Fan X, Wang L, Han F, Wang H, et al. Vitamin D status and the risk of multiple sclerosis: a systematic review and meta-analysis. Neurosci Lett. 2014;570:108–13.
5. Wesnes K, Riise T, Casetta I, Drulovic J, Granieri E, Holmøy T, et al. Body size and the risk of multiple sclerosis in Norway and Italy: the EnvIMS study. Mult Scler J. 2015;21(4):388–95.
6. Van der Mei I, Lucas RM, Taylor B, Valery P, Dwyer T, Kilpatrick TJ, et al. Population attributable fractions and joint effects of key risk factors for multiple sclerosis. Mult Scler J. 2016;22(4):461–69.
7. Bäärnhielm M, Olsson T, Alfredsson L. Fatty fish intake is associated with decreased occurrence of multiple sclerosis. Mult Scler J. 2014;20(6):726–32.
8. Abdollahpour I, Nedjat S, Mansournia MA, Sahraian MA, Kaufman JS. Estimating the marginal causal effect of fish consumption during adolescence on multiple sclerosis: a population-based incident case-control study. Neuroepidemiology. 2018;50(2–3):111–8.
9. Zhang SM, Willett WC, Hernán MA, Olek MJ, Ascherio A. Dietary fat in relation to risk of multiple sclerosis among two large cohorts of women. Am J Epidemiol. 2000;152(11):1056–64.
10. Lauer K. The risk of multiple sclerosis in the USA in relation to sociogeographic features: a factor-analytic study. J Clin Epidemiol. 1994;47(1):43–8.
11. Bredholt M, Frederiksen JL. Zinc in multiple sclerosis: A systematic review and meta-analysis. ASN Neuro. 2016;8(3):1759091416651511.
12. Naghashpour M, Jafarirad S, Amani R, Sarkaki A, Saedisomeolia A. Update on riboflavin and multiple sclerosis: a systematic review. Iran J Basic Med Sci. 2017;20(9):958.
13. AlAmmar WA, Albeesh FH, Ibrahim LM, Algindan YY, Yamani LZ, Khattab RY. Effect of omega-3 fatty acids and fish oil supplementation on multiple sclerosis: a systematic review. Nutr Neurosci. 2021;24(7):569–79.
14. Agranoff BW, Goldberg D. Diet and the geographical distribution of multiple sclerosis. Lancet (London, England). 1974;2(7888):1061–6.

15. Esparza ML, Sasaki S, Kesteloot H. Nutrition, latitude, and multiple sclerosis mortality: an ecologic study. Am J Epidemiol. 1995;142(7):733–7.
16. Abdollahpour I, Jakimovski D, Shivappa N, Hébert JR, Vahid F, Nedjat S, et al. Dietary inflammatory index and risk of multiple sclerosis: Findings from a large population-based incident case-control study. Clin Nutr. 2020;39(11):3402–7.
17. Jahromi SR, Toghae M, Jahromi MJR, Aloosh M. Dietary pattern and risk of multiple sclerosis. Iran J Neurol. 2012; 11(2):47.
18. Manzel A, Muller DN, Hafler DA, Erdman SE, Linker RA, Kleinewietfeld M. Role of "Western diet" in inflammatory autoimmune diseases. Curr Allergy Asthma Rep. 2014; 14(1):1–8.
19. Rezaeimanesh N, Jahromi SR, Moghadasi AN, Rafiee P, Ghorbani Z, Moghadam NB, et al. Dietary total antioxidant capacity and neuromyelitis optica spectrum disorder susceptibility. Nutr Food Sci. 2019;50(4):653–63.
20. 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.
21. Jandari S, Mosalmanzadeh N, Moghadam MRSF, Soleimani D, Shivappa N, Hébert JR, et al. Dietary inflammatory index and healthy eating index-2015 are associated with rheumatoid arthritis. Public Health Nutr. 2021;24(18):6007–14.
22. Lo C-H, Lochhead P, Khalili H, Song M, Tabung FK, Burke KE, et al. Dietary inflammatory potential and risk of Crohn's disease and ulcerative colitis. Gastroenterology. 2020;159(3): 873–83.e1.
23. Shah H, Wolfson E, Yu MG, Adam A, Hu F, King GL. 1543-P: Dietary Inflammatory Index Associated with Complications in Long Duration Type 1 Diabetes. Diabetes. 2020;69(1):1543-P.
24. Estruch R, Martinez-Gonzalez MA, Corella D, Basora-Gallisá J, Ruiz-Gutierrez V, Covas MI, et al. Effects of dietary fibre intake on risk factors for cardiovascular disease in subjects at high risk. J Epidemiol Community Health. 2009;63(7):582–8.
25. Polman CH, Reingold SC, Banwell B, Clanet M, Cohen JA, Filippi M, et al. Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. Ann Neurol. 2011;69(2): 292–302.
26. Wingerchuk DM, Banwell B, Bennett JL, Cabre P, Carroll W, Chitnis T, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015; 85(2):177–89.
27. Thompson AJ, Banwell BL, Barkhof F, Carroll WM, Coetzee T, Comi G, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. Lancet Neurol. 2018;17(2):162–73.
28. Abbara A, Eng PC, Phylactou M, Clarke SA, Hunjan T, Roberts R, et al. Anti-Müllerian hormone (AMH) in the Diagnosis of Menstrual Disturbance Due to Polycystic Ovarian Syndrome. Front. Endocrinol. 2019;10:656.
29. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). Neurology. 1983;33(11):1444–52.
30. Hashemi R, Motlagh AD, Heshmat R, Esmaillzadeh A, Payab M, Yousefinia M, et al. Diet and its relationship to sarcopenia in community dwelling Iranian elderly: a cross sectional study. Nutrition. 2015;31(1):97–104.
31. Ghaffarpour M, Houshiar-Rad A, Kianfar H. The manual for household measures, cooking yields factors and edible portion of foods. Tehran: Nashre Olume Keshavarzy. 1999;7:213.
32. Shivappa N, Steck SE, Hurley TG, Hussey JR, Hébert JR. Designing and developing a literature-derived, population-based dietary inflammatory index. Public Health Nutr. 2014;17(8):1689–96.
33. Køster B, Søndergaard J, Nielsen JB, Allen M, Olsen A, Bentzen J. The validated sun exposure questionnaire: association of objective and subjective measures of sun exposure in a Danish population-based sample. Br J Dermatol. 2017;176(2):446–56.
34. Van der Mei I, Blizzard L, Ponsonby A, Dwyer T. Validity and reliability of adult recall of past sun exposure in a case-control study of multiple sclerosis. Cancer Epidemiol Biomark Prev. 2006;15(8):1538–44.
35. Moghaddam MB, Aghdam FB, Jafarabadi MA, Allahverdipour H, Nikookheslat SD, Safarpour S. The Iranian Version of International Physical Activity Questionnaire (IPAQ) in Iran: content and construct validity, factor structure, internal consistency and stability. World Appl Sci J. 2012;18(8): 1073–80.
36. Umemura S, Arima H, Arima S, Asayama K, Dohi Y, Hirooka Y, et al. The Japanese Society of Hypertension guidelines for the management of hypertension (JSH 2019). Hypertens Res. 2019;42(9):1235–481.
37. Olesen J. Headache Classification Committee of the International Headache Society (IHS) the international classification of headache disorders, asbtracts. Cephalalgia. 2018;38(1):1–211.
38. Drulovic J, Kisic-Tepavcevic D, Pekmezovic T. Epidemiology, diagnosis and management of sexual dysfunction in multiple sclerosis. Acta Neurol Belg. 2020;120(4):791–7.
39. 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.
40. Jakimovski D, Weinstock-Guttman B, Gandhi S, Guan Y, Hagemeier J, Ramasamy DP, et al. Dietary and lifestyle factors in multiple sclerosis progression: results from a 5-year longitudinal MRI study. J Neurol. 2019;266(4):866–75.
41. Abdollahpour I, Jakimovski D, Shivappa N, Hébert JR, Vahid F, Nedjat S, et al. Dietary inflammatory index and risk of multiple sclerosis: Findings from a large population-based incident case-control study. Clin Nutr. 2020;39(11):3402–7.
42. Da Costa Silva BY, De Carvalho Sampaio HA, Shivappa N, Hébert J, Silva Albuquerque LD, Ferreira Carioca AA, et al. Interactions between dietary inflammatory index, nutritional state and multiple sclerosis clinical condition. Clin Nutr ESPEN. 2018;26:35–41.
43. Ciccarelli O, Barkhof F, Bodini B, De Stefano N, Golay X, Nicolay K, et al. Pathogenesis of multiple sclerosis: insights from molecular and metabolic imaging. Lancet Neurol. 2014;13(8):807–22.
44. Ochoa-Repáraz J, Kirby TO, Kasper LH. The gut microbiome and multiple sclerosis. Cold Spring Harb Perspect Med. 2018;8(6):a029017.

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