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Nutritional assessment status of adult patients with multiple sclerosis: A nationally representative survey

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Abstract

No previous research has assessed the nongenetic factors, especially the nutrition status of MS patients in Arab countries. Hence, this study aims to assess the nutritional status of MS patients among Arab adults. This study is a nationally representative cross-sectional study using a structured, online self-administered, validated quantitative food frequency questionnaire (FFQ) from 13 Arab countries. All data analyses were performed using STATA 16.0 and R for statistical computing version 4.0.4. A total of 813 participants were surveyed, most of the MS participants were female (68.4%), married (58.5%), non-smoker (72.6%) and 53.3% were diagnosed with MS for up to five years. MS participants did not consume the DRI of both the macro and the micronutrients including the energy requirements, except the dietary intake of the sodium which was insignificantly different from the DRI. Results also showed that most participants rarely consumed the main food items including bread, cereals, and most types of meat. While, more than 50% of the participants consumed fruit, vegetables, all types of chicken, fish, fresh soup, rice, and egg up to 3 times per month. On the other hand, milk and milkshake were consumed rarely; while, tea and herbal teas were the most common beverages. Nutrient deficiencies are very common among MS Arab patients. The finding of this study can establish a base for the development of a nutritional program for MS patients in accordance with the recommended DRI.

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Introduction

Multiple sclerosis (MS) is defined as a chronic inflammatory condition of the central nervous system (CNS) that is considered as one of the most prevalent causes of non-traumatic disability in young and middle-aged adults. There are four main phenotypes of MS and they are clinically isolated syndrome (CIS); Relapsing-remitting MS (RRMS); Secondary progressive MS (SPMS); Primary progressive MS (PPMS). The RRMS account for 90% of the cases in Jordan (El-Salem *et al.*, 2006).

In addition to its adverse health effects, MS-related health care costs burden numerous countries around the world leading to losses estimated by billions of dollars annually. The effect of MS on the CNS is primarily characterized by the degradation of the myelin sheath, which results in electrical nerve impulses transmission impairment. MS is encountered in many areas of the optic nerves, spinal cord, and brain, whereby myelin is replaced by sclera or scar tissue that causes motor and cognitive symptoms. No single diagnostic test to date can decide whether a patient has MS or not; instead, physicians rely on several diagnostic criteria for its detection (Polman *et al.*, 2011).

The signs and symptoms of MS are easy to distinguish and can recur through the course of this disease naturally. In the advance and severe stages, MS patients can lose the ability to speak, write or walk and eventually succumb to death due to the disease's complications. To date, there is no validated medication to alter the path of MS, avoid future incidents, or stop the deterioration of the myelin sheet. It is possible to achieve initial recovery from relapses, but over time, neurologic deficits can continue to manifest (van der Vuurst de Vries *et al.*, 2018).

The prevalence of MS differs by geographic location and remains unclear whether it is due to environmental influence, genetic difference, or other variable reasons (Moss, Rensel and Hersh, 2017). MS is thought to be the outcome of a combination of genetic susceptibility and environmental influences (Hedström, Alfredsson and Olsson, 2016), such as low vitamin D levels (Munger *et al.*, 2006), sun exposure (van der Mei, 2003), smoking (Hedström, Olsson and Alfredsson, 2016) and viral exposures (Thacker, Mirzaei and Ascherio, 2006). Other important factors such as obesity have been reported as a risk factor for MS during adolescence (Hedstrom *et al.*, 2014). Besides their potential impact on the MS onset, these various environmental factors may further influence the clinical disease course that significantly varies among MS patients. These findings have resulted in the exploration of adaptive environmental factors that can be adjusted to relieve MS symptoms, delay progression, and increase recovery rate (van der Vuurst de Vries *et al.*, 2018).

Diet appears to be a possible co-factor in the inflammatory process, influencing molecular pathways and gut microbiota (Esposito *et al.*, 2018). The European Society for Clinical Nutrition and Metabolism (ESPEN) recommends a diet low in saturated fatty acids and high in polyunsaturated fatty acids, as well as adequate vitamin D intake and sunlight exposure, to prevent MS. However, n-3 fatty acid, vitamin C, and B12 supplements are not suggested to reduce the frequency and number of relapses in people with MS. (Burgos *et al.*, 2018).

Numerous MS reports showed conflicting findings among different populations, implying the need for more confirmation studies (Moss, Rensel and Hersh, 2017; Pakdel *et al.*, 2019). Most of these reports also did not investigate MS patient's dietary intake to suggest the optimal daily intakes required for the prevention and/or the management of MS disease. Moreover, literature evidence assessing the relationship between the macro and micronutrient intakes and MS disease in the Arab Countries is limited. Hence the current study aims to assess the nutritional status of MS patients among Arab adults.

Materials and methods

Study design and Setting

This multinational, observational, cross-sectional study was conducted to assess the nutritional status of MS patients in Arab countries. The current study was conducted consecutively between October and December 2020.

The data were collected using an online self-administered questionnaire from 13 Arab countries. The straightening of the reporting of observational studies in epidemiology- nutrition (STROBE -nut) was used to improve the study design structure and quality (Hörnell *et al.*, 2017). A convenience sample of MS adults aged 18-60 years was assessed for their dietary intakes using a validated quantitative food frequency questionnaire (FFQ); that has been frequently used in patients with the central nervous disorder (Jahrami *et al.*, 2020).

Participants

A total of 813 participants were surveyed using convenience self-selection sampling. The inclusion and exclusion criteria of this study are shown in Table 1.

Table 1. Pre-defined inclusion and exclusion criteria for nutritional assessment of MS study selection.

Inclusion criteria	Exclusion criteria
Diagnosed MS patients of any type, from both genders.	Healthy or undiagnosed MS patients.
Able to write and speak Arabic language, aged between 18-60 years.	Unable to write and speak the Arabic language.
Willing to participate and write about nutritional intake, symptoms, and lifestyle habits in the study.	
MS: multiple sclerosis	

Before starting the recruitment process, the authors discussed all potential approaches and sources to reach the targeted participants from the population. The recruiting process of MS participants was done by sending an electronic invitation through social media platforms (Facebook, WhatsApp, Twitter, Snapchat, and Instagram). MS associations and centers in the targeted 13 Arab countries were also approached via email or/ and direct phone calling to encourage their MS members/patients to participate in this study. Furthermore, participants were kindly asked to share the questionnaire link with other MS patients who met the inclusion criteria via their social networks. The advantages of these recruitment approaches include; covering larger and widespread demographic/geographic areas, time-saving, lower cost, and lower effort compared to the face-to-face recruitment process. All questions in our questionnaire were translated into Arabic language and were made simple and clear to answer. Participants willing to write about their nutritional intake, symptoms, health, and lifestyle habits were free to fill-up the questionnaire confidentiality within their own free time. All collected data were stored in a secured Google Drive and were only accessible by the principal investigator and coded for the research team.

Instruments

A structured questionnaire was used to collect the data. The questionnaire was available in Arabic language and consisted of three main parts. The first part contained general questions, including sociodemographic and anthropometric measures, which were gender, marital status, education level, nationality, body weight (kg), and height (cm). Body mass index (BMI) was calculated by dividing body weight in kg by the squared height in meter and was used to classify the participants into the four BMI categories in accordance to the World Health Organization (WHO); underweight, normal, overweight, or obese; BMI < 18.5; BMI <24.9; BMI ≥ 25.0 and <29.9; BMI ≥ 30.0, respectively. A recent cohort study concluded that BMI calculated from self-reported weight and height is valid for both genders across various socio-demographic groups (Hodge *et al.*, 2020). The second part of the questionnaire was made of general health questions regarding smoking, sleeping hours, working schedule (regular vs. irregular) and hours, and the age being diagnosed as MS patient. While the third part of the questionnaire was a quantitative food and beverage frequency questionnaire consisting of 37 items corresponding to 102 food/ beverages from the seven main food groups (Jahrami *et al.*, 2020). The frequency intake has been divided into six choices (1 time/day, ≥2 times/day, 1-2 times/week, 3-6 times/week, 1-3 times/month, rarely or never) based on the average intake of a specific standard serving food/ beverage item during the past month. The determination of standard unit for each portion was standardized using food photos of specific serving sizes (Bell and Brammer, 2017). The responses of the participant's dietary intake were analyzed using nutrition and fitness software (ESHA

Food Processor SQL, version 10.1.1, Salem, OR, USA). ESHA Food Processor® Nutrition Analysis software.

Data analysis

The data were visualized using Shapiro-Wilk test which is a normality test in frequentist statistics, and it was used to establish the normality assumption. Data were summarized using descriptive statistics; the mean and standard errors were calculated for continuous data and the frequency counts, as well as proportions, were reported for categorical data. The 95% Confidence Intervals (95% CI) were used to establish population estimates. The estimated energy requirement (EER) for each participant was calculated based on the Institute of Medicine's (IOM) formulas as per sex, weight, and height (Jahrami *et al.*, 2020). Independent samples t-test was used to compare the dietary intake based on gender (male vs female); Cohen's d was according calculated to estimate effect size and results of <0.2 were interpreted as low, and 0.5 as moderate and >0.8 as large effect size. All data analyses were analyzed using R for statistical computing version 4.0.4.

Results

Participants demographic characteristics

A total of 813 participants (65.4%females) were approached in this current study. Table 2 shows that 44.8% of the participants have normal BMI (18.5-24.9 kg/m2). The marital status data showed that more than half of the participants were married (58.5%). As for the educational level, 64.6% of the participants of this study held an undergraduate degree, while the rest either had secondary school or less educational level (24.5%) or possessed a postgraduate degree (10.9%). Furthermore, most of the participants (99.1%) were from Arab-speaking countries. Approximately 54.0% of the participants reported sleeping between 6 to 8 hours daily, and around two-thirds of the participants were non-smokers. Regarding the participants' occupations, 26.4% were housewives/ homemakers and 19.1% and 16.2% were governmental and private employees, while 17.1% were unemployed. Moreover, around two-thirds (72.3%) of the study participants worked irregular jobs for a duration range of 4-8 hours/day. Patients diagnosed with MS for around one to five years were 53.3%, whereas and the rest of the sample populations have been diagnosed with MS for more than 6 years.

Table 2. Sociodemographic characteristics of the MS participants, n=813.

Characteristics	Categories	N (%)
BMI	Normal	364 (44.8)
	Obese	166 (20.4)
	Overweight	248 (30.5)
	Underweight	35 (4.3)
Gender	Male	257 (31.6)
	Female	556 (68.4)
Status	Widowed	17 (2.1)
	Single	269 (33.1)
	Married	476 (58.5)
	Divorced	51 (6.3)
Education level	Secondary school or less	199 (24.5)
	Undergraduate degree	525 (64.6)
	Postgraduate degree	89 (10.9)
Nationality	Arabic speakers	806 (99.1)
	*Other	7 (0.9)
Sleeping hours	<4 hours/day	32 (3.9)
	>8 hours/day	123 (15.1)
	4-6 hours/day	217 (26.7)
	6-8 hours/day	441 (54.2)
Smoking	Yes	223 (27.4)
	No	590 (72.6)
Disease onset (years)	1-5 years	433 (53.3)
	6-10 years	185 (22.8)
	More than 10 years	195 (24.0)
Type of work	Free business	59 (7.3)
	Housewife/ Homemaker	215 (26.4)
	Student	73 (9.0)
	Unemployed	139 (17.1)
	Retired	40 (4.9)
	Employee (private)	132(16.2)
	Employee (government)	155 (19.1)
Style of work	Regular (morning)	96 (27.7)
	irregular (shifts)	250 (72.3)
Hours of work	4-8 hours/ day	261 (75.4)
	8-12 hours/ day	85 (24.6)

*Other: Arabic speakers from non-Arabic countries.

Dietary intake of the macronutrients and micronutrients of MS participants compared to dietary reference intakes (DRI) for healthy adults

The results in Table 3 showed a significant difference between the DRI and the average dietary intake of the macronutrients (p-value ≤0.001). The mean carbohydrate percentage (38.9%) was lower than recommended minimum intake (45- 65%). Meanwhile, the mean percentages of both protein (16.92%) and fat (22.74%) intake were within the recommended range (10-35%) and (20-35%), respectively.

On the other hand, micronutrients have shown a significant difference between DRI and the actual dietary intake for all analyzed micronutrients (p-value ≤0.001), with the exception for sodium (p-value = 0.09; Table 4). In other words, MS participants did not consume the DRI of both the macro and the micronutrients including the energy requirements, except the dietary intake of the sodium which was insignificantly different from the DRI. Among the macronutrients, the total energy (kcal) and the fiber (g) intakes of the MS participants were less than the recommended DRI. Whereas the protein (g) and carbohydrates (g) intakes exceeded the recommended DRI. Following the same pattern, various dietary intake of the micronutrients by the study participants was detected. Iron (mg), vitamin B3 (niacin; mg), vitamin B6 (mg), omega-6 (g), and vitamin A (RE), were higher than the DRI. While the other micronutrients including calcium (mg), magnesium (mg), phosphorous (mg), potassium (mg), zinc (mg), in addition to vitamin B1 (thiamin; mg), vitamin B2 (riboflavin; mg), omega- 3 (g), vitamin C (mg), and vitamin D (mg) intake were significantly less than the DRI for healthy adults. The differences in dietary intake of macronutrients and micronutrients between males (n=257) and females (n=556) were determined by running independent-samples t-test (Table A1). The macronutrients and micronutrients for each level of gender were normally distributed, as assessed by Shapiro-Wilk's test (p > 0.05). The results indicated that there was no statistically significant difference in the macronutrients and micronutrients among MS males and females (Table A2). Data are mean ± standard deviation, unless otherwise stated.

Table 3. Average daily intakes of energy and macronutrients for MS participants compared with DRI for healthy adults.

Variable	DRI	Mean± SD	Std. Err.	95%CI for the mean
Energy [kcal]	2000-2500	1820±1207	42	1737, 1903
Protein [g]	56	77±55	2	73, 81
Protein [%]*	10-35	16.92	ND	ND
Carbohydrate [g]	130	177±119	4	169, 186
Carbohydrate [%]*	45- 65	38.90	ND	ND
Fiber [g]	38	18±15	1	17, 19
Cholesterol [mg]	<300	266±195	7	252, 279
Total Fat [g]	31	46±33	1	44, 48
Total Fat [%]*	20-35	22.74	ND	ND
Saturated Fat [g]	25	23±17	1	22, 24
Saturated Fat [%]	<10	11.37	ND	ND
Monounsaturated Fat [g]	ND	17±12	0	16, 17
Monounsaturated Fat [%]	15-20	8.40	ND	ND
Polyunsaturated Fat [g]	14	10±8	0	10, 11
Polyunsaturated Fat [%]	5-10	4.94	ND	ND

DRI: Dietary Reference Intakes, Food and Nutrition Board, Institute of Medicine. ND: not detected. * Macronutrients percentages were calculated from means range of total energy (2000-2500kcal).

Table 4. Average daily intakes of essential micronutrients for the study participants compared with DRI for healthy adults.

Variable	DRI	Mean± SD	Std. Err.	95%CI for the mean
Calcium [mg]	1200	464±363	13	439, 489
Iron [mg]	18-25	27±21	1	26, 29
Magnesium [mg]	420	333±249	9	316, 350
Sodium [mg]	1500	1567±1110	39	1491, 1644
Phosphorous [mg]	700	588±1503	15	559, 617
Potassium [mg]	4700	2380±1506	53	2277, 2484
Zinc [mg]	11-15	6±5	0	6, 7
Vit B3 (Niacin) [mg]	1.3	14±10	0	13, 15
Vit B1 (Thiamin) [mg]	1.2	1±1	0	1, 1
Vit B2 Riboflavin [mg]	2.0-2.5	1±1	0	1, 1
Vit A [RE]	10	702±510	18	667, 737
Vit B6 [mg]	1.7	2±1	0	1, 2
Vit C [mg]	90	71±54	2	68, 75
Omega-3 [g]	1.59	1±0	0	1, 1
Omega-6 [g]	15	37±1	0	37, 37
Vitamin D [IU]	400	241±87	3	235, 247

DRI: Dietary Reference Intakes, Food and Nutrition Board, Institute of Medicine.

Food and beverages frequency intake

The intake frequency of the 30 most common and frequently consumed food items are shown in Table 5. Results of the FFQ showed that the highest percentage of the participants rarely consumed the main food items such as bread (more than half of the participants rarely consumed brown bread and 36.5% rarely consumed the white type), cereals, and most types of meat. Around one-third of the sample rarely consumed seafood and 20.7% consumed it 1-3 times per month. More than half of the participants consumed fruit, vegetables, all types of chicken, fish, fresh soup, rice, and egg around 1-3 times per month. Table 6 shows the

beverage frequency intake of the study participants for seven different beverage types. The results indicated that more than half of the participants (63.3%) rarely consumed milk and milkshake, while almost all study participants rarely drank alcohol (92.4%). Tea and herbal teas were relatively the common beverages consumed, where merely 21% of the study participants seldom consumed them.

Table 5. The percent of food frequency intake of the study participants for 30 food items (MS patients), n= 813, percentages are given in brackets.

Food/frequencies	Rarely	1-3 times/month	1-2 times/week	3-6 times/week	1 time/day	2+ times/day
White "Lebanese/ Arabic" bread (30 g)	297 (36.5)	258 (31.7)	6 (0.7)	99 (12.2)	73 (9)	80 (9.8)
Brown "Lebanese/ Arabic" bread (30 g)	442 (54.4)	227 (27.9)	0	66 (8.1)	46 (5.7)	32 (3.9)
Biscuits, rusks, cookies (30 g)	289 (35.5)	390 (48.0)	4 (0.5)	59 (7.3)	45 (5.5)	26 (3.2)
Cereals, cereals bar (30 g/1 bar)	642 (79.0)	126 (15.5)	1 (0.1)	22 (2.7)	18 (2.2)	4 (0.5)
Beef (steak or cubes) (150 g)	329 (40.5)	400 (49.2)	4 (0.5)	41 (5.0)	30 (3.7)	9 (1.1)
Burgers, meatballs, minced meat (75 g)	416 (51.2)	335 (41.2)	5 (0.6)	30 (3.7)	19 (2.3)	8 (1.0)
Chicken (all types of preparation) (150 g)	75 (9.2)	535 (65.8)	8 (1.0)	109 (13.4)	63 (7.7)	23 (2.8)
Lamb, goat, deer, rabbit, lamb (150 g)	475 (58.4)	275 (33.8)	1 (0.1)	39 (4.8)	16 (2.0)	7 (0.9)
Fish (150 g)	271 (33.3)	455 (56.0)	4 (0.5)	57 (7.0)	16 (2.0)	10 (1.2)
Seafood (octopus, squid, shrimps) (150 g)	602 (74.0)	168 (20.7)	0	26 (3.2)	13 (1.6)	4 (0.5)
Lentils, beans, chickpeas (150 g/1 cup)	204 (25.1)	508 (62.5)	4 (0.5)	52 (6.4)	33 (4.1)	12 (1.5)
Fresh soup (250 ml/ cup)	315 (38.7)	415 (51.0)	4 (0.5)	45 (5.5)	26 (3.2)	8 (1.0)
Soup with pasta (e.g. noodles) (250 ml/ cup)	448 (55.1)	298 (36.7)	3 (0.4)	42 (5.2)	15 (1.8)	7 (0.9)
Rice (all types) (1 cup/medium plate))	133 (16.4)	494 (60.8)	8 (1.0)	92 (11.3)	68 (8.4)	18 (2.2)
Boiled potatoes, mashed potatoes (1 medium)	324 (39.9)	391 (48.1)	9 (1.1)	56 (6.9)	25 (3.1)	8 (1.0)
French fries regular portion	267 (32.8)	447 (55.0)	6 (0.7)	54 (6.6)	30 (3.7)	9 (1.1)
Fresh Vegetables (any kind) (1 piece)	106 (13.0)	478 (58.8)	12 (1.5)	99 (12.2)	59 (7.3)	59 (7.3)
Fresh Fruits (any kind) (1 piece)	87 (10.7)	454 (55.8)	5 (0.6)	120 (14.8)	81 (10.0)	66 (8.1)
Dried fruits (¼ cup)	510 (62.7)	215 (26.4)	0	53 (6.5)	23 (2.8)	12 (1.5)
Dried nuts, nuts (¼ cup)	304 (37.4)	380 (46.7)	1 (0.1)	69 (8.5)	41 (5.0)	18 (2.2)
Yoghurt complete or light (170 g)	350 (43.1)	345 (42.4)	2 (0.2)	71 (8.7)	37 (4.6)	8 (1.0)
Cream cheese "Glasses" (25 g)	481 (59.2)	249 (30.6)	2 (0.2)	49 (6.0)	24 (3.0)	8 (1.0)
Feta, white cheese, hard cheese (25 g)	385 (47.4)	327 (40.2)	4 (0.5)	57 (7.0)	28 (3.4)	12 (1.5)
Egg (boiled, fried, omelet) (1 medium egg)	157 (19.3)	464 (57.1)	5 (0.6)	93 (11.4)	56 (6.9)	38 (4.7)
Pies (e.g. cheese pie, spinach pie) (1 pie)	436 (53.6)	316 (38.9)	2 (0.2)	37 (4.6)	13 (1.6)	9 (1.1)
Ice cream, milk shake, pudding (1 scoop)	459 (56.5)	289 (35.5)	3 (0.4)	40 (4.9)	17 (2.1)	5 (0.6)
Honey, jam (10 ml)	407 (50.1)	293 (36.0)	4 (0.5)	51 (6.3)	43 (5.3)	15 (1.8)
Olives (10 drupes)	276 (33.9)	389 (47.8)	1 (0.1)	71 (8.7)	46 (5.7)	30 (3.7)
Chocolate (any type) (60 g)	265 (32.6)	400 (49.2)	3 (0.4)	77 (9.5)	44 (5.4)	24 (3.0)
Chips packs, popcorn (70 g)	386 (47.5)	325 (40.0)	2 (0.2)	59 (7.3)	27 (3.3)	14 (1.7)

Table 6. The percentage of beverage frequency intake for 7 different beverage types for MS patients, n= 813, percentages are given in brackets.

Beverage/frequencies	Rarely/ never	1-2 times/week	3-6 times/week	1-2 times/day	3-4 times/day	More than 5 time/day
Fruit juice (Packs) 1 cup/pack	305 (37.5)	355 (43.7)	87 (10.7)	55 (6.8)	4 (0.5)	7 (0.9)
Soft (carbonated) drinks 1 can	471 (57.9)	233 (28.7)	63 (7.7)	43 (5.3)	3 (0.4)	0
Milk, milk shake 1 glass	517 (63.6)	173 (21.3)	58 (7.1)	52 (6.4)	4 (0.5)	9 (1.1)
Coffee in a cup (e.g. Americano) 1 cup	335 (41.2)	144 (17.7)	110 (13.5)	163 (20.0)	35 (4.3)	26 (3.2)
Arabic Coffee 1 shot	381 (46.9)	169 (20.8)	93 (11.4)	114 (14.0)	33 (4.1)	23 (2.8)
Tea, other herbal teas 1 cup	167 (20.5)	220 (27.1)	179 (22.0)	154 (18.9)	53 (6.5)	40 (4.9)
Alcoholic drinks (e.g. wine, beer, whisky) 1 unit	751 (92.4)	30 (3.7)	26 (3.2)	4 (0.5)	0	2 (0.2)

Discussion

The current study assessed the prevalence of certain vital nongenetic factors, in particular the nutritional status among MS patients residing in 13 Arab countries. The study findings revealed that the majority of the study participants were of normal body weight, however, when combining MS participants from overweight and obese categories; these categories made-up 50% of the population study.

This result is consistent with Guerrero-García *et al.* (2016) review, which indicated that several studies showed an increase in overweight and obesity prevalence among MS patients due to reduced mobility, fatigue, low energy expenditure, and the use of certain fluid-retention medications (Guerrero-García *et al.*, 2016). Most of the study's participants were female, married, and had at least a college degree. These findings align with previous reports where an increased prevalence of MS was observed among females (Greer and McCombe, 2011; Harbo, Gold and Tintora, 2013; Schriefer *et al.*, 2020), and a bidirectional correlation coexisted between the marital status and MS prevalence (Coles *et al.*, 2006; Landfeldt *et al.*, 2018).

As for the educational status, most studies reported a higher MS prevalence among participants with lower educational levels (Patti *et al.*, 2007; Nielsen *et al.*, 2013). On the other hand, one study found that individuals with higher educational level were the predominant percentage in the studied MS population (Kurtzke and Page, 1997), which was consistent with our current study findings. This can be attributed to the hygiene hypothesis occurrence; where individuals with higher educational levels have higher socioeconomic status, more hygienic conditions, which in turn result in less exposure to infections and therefore more abnormal immune responses and higher MS prevalence (Pakdel *et al.*, 2019). Our data also showed that study participants either worked as government employees or were housewives or unemployed. Moreover, the majority of the participants worked shifts (irregular jobs) with a working duration of 4-8 hours/ day.

This finding was consistent with previous studies that showed a positive association between working shifts and MS occurrence (Hedström *et al.*, 2015; Olsson, Barcellos and Alfredsson, 2017). On the contrary to most studies (Hedström, Alfredsson and Olsson, 2016; van der Vuurst de Vries *et al.*, 2018), the majority of the present MS participants were nonsmokers. This may be attributed to participants' high educational status as well as their awareness regarding the positive correlation between smoking and MS manifestations (Jahrami *et al.*, 2020).

An increasing BMI of evidence indicated a significant correlation between diet and MS prevalence, especially since MS is often associated with certain food groups and increased food intake (calories) (Payne, 2001; Saka *et al.*, 2012; Guerrero-García *et al.*, 2016; Titcomb *et al.*, 2020). Accordingly, energy and macronutrients intake may trigger or delay the progression of MS. The dietary intake of the macronutrients and micronutrients in the current study were not compared to reference group. This is because the requirement of some micronutrients especially magnesium, calcium and iron are possibly not be suitable for MS patients due to the direct relation to MS disease progression (49). Instead compared to dietary reference intakes (DRI) which represent the minimum requirement of each nutrient's intake for healthy adults. This type of comparison was also reported in the literature with multiple sclerosis patients (48-50), as well as depression (24). In this study, the participants' mean total energy (kcal) intake was significantly lower than the recommended dietary reference intake (DRI), while participants' mean grams of the macronutrients (proteins, carbohydrates) significantly surpassed the recommended DRI. On the other hand, the lipid profile evaluated by measuring saturated fatty acids (SFA), monounsaturated fatty acids (MUFA), polyunsaturated fatty acids (PUFA), and cholesterol showed higher percentages detected in SFA and cholesterol parameters, while considerably lower percentages for MUFA and PUFA parameters observed in MS patients.

The data also showed a lower fiber intake by the study participants compared to the DRI. These findings are supported by earlier studies, which established a link between simple carbohydrates, SFA, and cholesterol intake and higher MS prevalence and progression. At the same time, lower MS prevalence and progression were seen in diets high in complex carbohydrates (e.g. fiber), MUFA, and PUFA (Bitarafan *et al.*, 2014; Ortí *et al.*, 2020; Titcomb *et al.*, 2020). Our results are consistent with these studies, in which consumption of harmful MS-related foods (SFA and cholesterol) were reported among MS participants. While consumption of beneficial MS-related foods (fiber,

MUFA, and PUFA) were less reported. The finding of this study also showed that both genders have the same proportional intake due to insignificant differences in the macronutrients and micronutrients among MS males and females, hence MS disease is predominant compared to gender.

In an attempt to lessen the progression and diet-related symptoms associate with MS, many patients tend to follow certain diet plans that restrict the consumption of specific food groups (e.g., meat, dairy products, gluten-rich grains), which in turn increases the risk of micronutrient deficiencies (Bitarafan *et al.*, 2014; Titcomb *et al.*, 2020). In our study, the micronutrients findings revealed significantly lower intake of the minerals (calcium, zinc, magnesium, potassium, and phosphorous), vitamins (vitamin D, B1, B2, and vitamin C), and fatty acid (omega 3). This is because magnesium, calcium and iron are possibly linked to MS disease progression (51). On the other hand, iron, vitamin A, vitamin B3, and omega-6 intake were significantly higher than the recommended DRI. These observed patterns of restricting diet to certain food groups may result in diminishing the main natural sources of some of these micronutrients, while expanding others. For example, the omission of dairy products and food rich in lipids can significantly result in calcium, fat- soluble vitamins, and omega-3 deficiencies (40,41). Prolonged low intake of these vital micronutrients will eventually lead to irregular physiological and metabolic body functions, which can further intensify the MS symptoms (12,42).

The variance in MS prevalence based on geographical distribution can be explained by the differences in latitude, lifestyle habits, and dietary patterns (Moss, Rensel and Hersh, 2017; Pakdel *et al.*, 2019). The benefits of Mediterranean and traditional Middle Eastern diets have been recognized in promoting health and reducing the severity of many aliments including MS disease (Dinu *et al.*, 2018). Herein, the food frequency intake results indicated that most MS participants in Arab countries relatively maintained the traditional Middle Eastern diet by incorporating lean proteins, healthy fats, fruits, vegetables and grains in at least one dish per day. However, our data also revealed the presence of some Western diet items in the participants' diet such as eggs, French fries, chocolate, as well as the reduction/ removal of dairy products. The recent shift in eating habits from healthy Middle Eastern and Mediterranean diets to the Western diet, MS patients' unawareness and fear from ingestion of certain food groups thought to be associated with MS progression, and the absence of well-defined diet guidelines and recommendations may explain the rapid increase in MS prevalence in Arab Countries compared to previous decades (Ghafari *et al.*, 2015; Bell and Brammer, 2017; Sahraian *et al.*, 2017). Furthermore, the data from the beverage frequency intake revealed that the study participants rarely consumed dairy drinks (milk and milk shake), soft drinks, and alcohol, instead they moderately consumed tea and herbal teas. A systematic review by Bagur *et al.* (2017), stated that some studies reported higher risk of MS onset and progression among individuals who had a higher intake of milk, whereas a lower risk of MS onset and progression was observed among individuals who had a higher intake of alcohol, coffee, and tea. However, the authors also pointed out that these results are inconsistent with other studies, which mentioned either an inverse or no correlation between beverage type and MS onset and progression (Bagur *et al.*, 2017). Nonetheless, our results indicate participant's preference of specific types of beverages over others. This may be due to possible knowledge among participants of the correlation between specific beverages and MS progression, the drinking habits associated with culture and norms, and the influence of religion, which prohibits alcohol consumption among Muslims including those in Arab countries (Musaiger, 1993; Michalak and Trocki, 2006; Hudaif, Bwardi and Kojan, 2014)

In summary, the current study, to our best knowledge, is considered as the first research examining the nongenetic factors, especially the nutrition status of MS patients in Arab countries. The study findings can add to the current MS literature by examining the nongenetic factors associated with MS prevalence and progression. Furthermore, the results

of this study may provide some direction for future studies aiming to target this patient population. In conclusion, MS patients were characterized by the tendencies of the female percentage with normal BMI, non-smokers and irregular work style for around 4-8 hours daily. The results were found that MS participants are not following the DRI of both macro and micronutrients including the energy requirements, with the exception of the dietary intake of sodium. The daily energy intake and fiber intake of MS patients was less than the DRI. While, carbohydrate and protein intake exceed the DRI. On the other hand, micronutrients including iron and vitamin A were significantly (p-value ≤0.001) exceeding recommendation of DRI, while other micronutrients including calcium and vitamin D were significantly (p ≤0.001) lower than the DRI level. The finding of this study can form the foundation for the development of a nutritional program that can correct the nutritional deficiencies detected in MS patients following the recommended DRI.

Strength and limitations

The present study findings can add to the current MS literature by examining the nongenetic factors associated with MS prevalence and progression. Moreover, among the important observations seen in this study, was the misconceptions among MS patients in Arab countries regarding the MS-related foods translated by their BMI, macronutrients and micronutrients percentages, and food/ beverage frequency intake data. Such valuable results imply the urgent need for educating MS patients' and increasing their awareness regarding food group choices and eating habits that will ultimately improve their well-being, while alleviating MS manifestation and progression.

Similar to other studies, the current study has a number of limitations. The use of cross-sectional design and convenience sample may limit our ability to establish a causal relationship between these nongenetic factors and MS prevalence and progression. In addition, this study design may limit our ability to generalize our findings to MS patient population in Arab countries. More accurate anthropometric parameters (e.g., waist to hip ratio) and serum levels of the examined nutrients were also not measured in this study. Hence, randomized control trials and clinical studies that include these parameters and levels are warranted.

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Data Availability Statement

The data are available from the authors upon reasonable request.

Author contributions

Conceptualization, L.A.; O.A.; and N.E.; methodology, O.A.; L.A.; N.E. and H.J..; formal analysis, H.J.; investigation, O.A.; A.Y.; M.A.; resources, O.A.; A.Y; data curation, O.A.; L.A.; writing-original draft preparation, O.A.; L.A.; N.E.; I.M.; writing-review and editing, O.A.; N.E.; I.M. H.J.; M.A. N.B.; supervision, O.A.; N.B.; project administration, O.A. All authors have read and agreed to the published version of the manuscript.

Conflicts of interest

The authors declare no conflict of interest.

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study. Participants have received explanations about the study aim, methods, time required to fill the survey, and privacy of data. The participation was voluntary, and no monetary or non-monetary incentives were given. Therefore, reading the introduction, willing to write about nutritional intake, completing, and submitting the questionnaire was considered as approval for participating in this study Participants were free to withdraw from the study at any time without any obligation or prior notice.

Ethical approval

The study protocol, including the reuse of data collected and ethical approval was granted by the Research Ethics

Committee of the Faculty of Pharmacy and Medical Sciences, University of Petra, Amman, Jordan (UOP/REC: Q1/11/2020). In the current study, all ethical standards of the Helsinki declaration and its modifications in 1964 were followed.

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