



Role of Nutrition in Egyptian Multiple Sclerosis Patients and its Relation to Different Clinical Types

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ABSTRACT

Background: Demyelination, inflammation and oxidative injury are the main pathological hallmarks of multiple sclerosis (MS). Antioxidant factors in the diet may regulate the activation of immune-inflammatory cells, decreasing inflammation. They may also mitigate oxidative stress, preventing chronic demyelination and axonal damage. **Aim of work:** Evaluate of the consumption rate of nutrients between patients with relapsing-remitting and progressive multiple sclerosis. We are also trying to determine the role of deficiencies in dietary factors considered antioxidants or anti-inflammatory in the course of the disease. **Patients and Methods:** Across-Sectional Analytical study among (86) relapsing-remitting MS (RRMS) and (33) progressive MS (SPMS, PPMS). Patients attending Kasr Al Ainy Multiple Sclerosis Research Unit (KAMSRU), the Multiple Sclerosis Clinic of the Neurology department, Cairo University. The sample consisted of both genders aged ≥ 18 years, who had been diagnosed with MS for at least one year. The Data were collected using a structured interview questionnaire including reliable Socioeconomic Status Scale (SES), anthropometric measurements, Expanded Disability Status Scale (EDSS), the food frequency papers and 24- hour recall questionnaire to evaluate the actual daily intake of nutrients. **Results:** The mean age of all patients was (33.49 ± 9.8) years; females represented more than (76.4%) of all patients, with a significant higher of females among RRMS than Prog MS, younger age was also significantly associated with RRMS patients (P. values = 0.01, 0.001 respectively). Our results point to statistically significant differences between patients with RRMS and Prog MS in their intake of Potassium and Iron (P. values = 0.015, 0.01 respectively), where most patients with prog MS have a higher mean daily intake of potassium and iron than patients with RRMS. There were no significant differences between RRMS and Prog MS in their daily intake of calories, water, protein, fat, carbohydrate, fiber, sodium, calcium, magnesium, phosphorous, zinc, copper, vitamin-A, vitamin C, thiamin and riboflavin. **Conclusion:** High daily intake of potassium and iron were associated with Prog MS more than RRMS, so this must be taken into account during diet planning.

Keywords: Multiple sclerosis, Nutrients, Antioxidants, Anti-Inflammatory.

1. Introduction

Multiple sclerosis (MS) is one of the most common neurological disabling disorders among young adults. MS is a neurodegenerative disease characterized by a variable clinical course and diverse pathophysiology, including nitrative oxidative stresses and inflammation as well as loss of blood-brain barrier (BBB) integrity (Wigner *et al.*, 2022) Oxidative stress is an important component of the inflammatory processes leading to demyelination and axonal damage. Oxidative stress and inflammation are present in relapsing-remitting, primary and secondary progressive MS (Riccio and Rossano, 2018). The early stage of MS (RRMS) lasts about 10 years, and is dominated by inflammatory processes, whereas the chronic stage is associated with neurodegenerative axonal and

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neuronal loss (Miller *et al.*, 2019). Nutrition and dietary factors affect the mechanisms of MS pathology, its development and degree of activity (Stoiloudis *et al.*, 2022).

Diet can induce the production of inflammatory factors such as tumor necrosis factor, interleukins, prostaglandins and leukotrienes, leading to inflammation and oxidative stress (Esposito *et al.*, 2021). On the other hand, Anti-Inflammatory dietary molecules are able to downregulate inflammatory processes by inhibiting proinflammatory transcription factors, or by modulating the activity of enzymes involved in inflammatory events (Riccio and Rossano, 2018). Also, Dietary antioxidant factors can dampen oxidative stress, may help against chronic demyelination and neuronal or axonal damage (Katz Sand, 2018). The hypothesis that low daily intake of some nutrients that are considered as antioxidants or anti-Inflammatory may be associated with different stages of MS and increased neurological disability was investigated.

2. Subjects and Methods:

2.1 Study setting and design

A cross-sectional study in which Multiple Sclerosis patients recruited by convenience from the Kasr Al Ainy Multiple Sclerosis Research Unit (KAMSRU), the Multiple Sclerosis Clinic of the Neurology department, Cairo University.

2.2 Sample size and sampling technique

This study was conducted on 119 patients whose diagnosed with MS according to 2017 revision of McDonald's criteria (diagnosed with Relapsing Remitting MS (RRMS), Secondary Progressive MS (SPMS) or Primary Progressive MS (PPMS)). The sample size was identified according to "Steven k. Thompson" equation (Thompson, 2012). Our patients were above 18 years old of both sex groups. Patients diagnosed as clinically isolated syndrome (CIS), patients with memory problems or poor reporting, patients with other neurological diseases, patients with diabetes mellitus and pregnant women were excluded from our study. Patients are diagnosed as having Multiple sclerosis by neurologist then they were individually interviewed by the nutritionist to fill the detailed questionnaires; each interview took about 40 minutes.

2.3 Data collection tools

Demographic and socioeconomic status assessment: participants were assessed by valid and reliable socioeconomic status scale for health research in Egypt proposed by El Gilany *et al.*, (2012). The socioeconomic status was classified according to the quartiles of the score into very low, low, middle and high levels (El-Gilany *et al.*, 2012).

Anthropometric measurements: (namely; weight, height, and accordingly the body mass index (BMI)) were conducted for the patients (Nuttall, 2015). Hemoglobin level and White blood cells count were obtained for (74.78%) of patients by the physician. The Serum hemoglobin level was checked to define the most common nutritional deficiency worldwide (Iron Deficiency Anemia). The hemoglobin level to diagnose anemia is less than 13 g/dl in males and less than 12 g/dl in females according to the WHO reference (WHO, 2018). The WBC differential count is a popular biomarker for evaluating the presence of systemic inflammations, an infection and Allergic reaction (Hasselbalch *et al.*, 2018).

Complete medical assessment: was be done for all patients, according to MS sheet of KAMSRU, which included questions related to MS phenotype, Age at Onset, duration of disease, annual relapse rate and Expanded Disability Status Scale (EDSS) which is the most common tool for assessing clinical disability in people with MS (Meyer-Moock *et al.*, 2014). Scoring is based on an examination by a neurologist. It has 10 available levels that describe progressive disability ranging from 0 (normal) to 10 (death due to MS) (Meyer-Moock *et al.*, 2014).

2.4 Dietary intake assessment

The 24- hour recall questionnaire is one of the most valid and widely used tools in nutritional assessment (Castell *et al.*, 2015). The 24 hours dietary recall consists of record all foods patient eats, drink, use of vitamins & minerals, number of meals & snacks and drinking coffee or any caffeine beverages. Nutritionist asked each patient about all the foods and drinks he consumed during the past 24 hours, three recalls were taken, the actual food intake of each respondent is evaluated with a high

degree of reliability and validity according to Food and Agriculture Organization (FAO, 2018). Average of the three days was taken and it entered into a computer program of food analysis based on food composition tables of Egyptian National Nutrition Research Institute (NNI, (2006). Then, percentage (%) of the mean daily intake of nutrients was calculated from the next formula:

$$\text{formula: } \frac{\text{The Mean Food Intake}}{\text{The Dietary Reference Intakes}} \times 100$$

Factors such as age and gender were taken into account when assigning Dietary Reference Intakes (DRI) values for each subject (Mahan, 2004).

Food frequency sheets (FAO, 2018) were used to evaluate the consumption of foods, drinks, and food groups which consumed daily, monthly and weekly; according to aim of study we used a closed and adjustable list contain local foods and foods supposed to be associated to MS.

2.5 Statistically analysis

Results were analyzed by the statistical package for social science (SPSS) version 21 (IBM, 2012). χ^2 test (chi-square) was used for comparison among proportions and Independent T-test was used to compare between the two sample means with the assumption that variables are normally distributed, P- value was considered a significant when P was 0.05 or less, and descriptive statistics such as arithmetic mean and standard deviation were used for quantitative variables; Pearson correlation was used to identify the extent to which two variables are linearly correlated.

3. Results

The patients were divided according to the type of disease into Relapsing Remitting MS (RRMS) and Progressive MS (Prog MS) including both (SPMS, PPMS). Regarding participants in our study, (72.3%) had an RRMS, (22.7%) had an SPMS and (5%) reported an PPMS disease course.

Table (1) shows the Demographic and Socioeconomic status of all patients and compares them in RRMS and Prog MS. The mean age of all patients was (33.49 ± 9.8) years; females represented more than (76.4%) of them, and there were a significant higher of females with younger age among RRMS than Prog MS patients (P. values = 0.01, 0.001 respectively). While there were no significant differences in the socioeconomic level or marital status between RRMS and Prog MS patients, which means that more than two thirds of all patients (73.1%) had middle socioeconomic level and (69.7%) were married.

Table 1: Demographic and Socioeconomic characteristics of patients with RR MS and patients with Prog MS.

Variables		Total (N =119)		Relapsingremitting MS (n=86)		Progressive MS (n=33)		Test of sig.	P value
		N	%	N	%	N	%		
Gander	Male	28	23.6	15	17.4	13	39.4	X ² = 6.3	0.01*
	Female	91	76.4	71	82.6	20	60.6		
Age groups	Range	18-56		18- 56		28 - 56		Z=-4.5	0.001*
	Mean ±SD	33.49 ± 9.8		30.89 ± 8.5		40.2 ± 7.9			
	Median	33		29.5		40			
Socioeconomic Status	Very low	1	0.8	1	1.2	0	0.0	X ² = 5.4	0.13
	Low	28	23.6	17	19.8	11	33.3		
	Middle	87	73.1	67	77.9	20	60.6		
	High	3	2.5	1	1.2	2	6.1		
Marital status	Married	83	69.7	58	67.4	25	75.8	X ² = 4.1	0.24
	un Married	32	26.9	26	30.2	6	18.2		
	widow	3	2.5	2	2.4	1	0.0		

SD= Standard Deviation χ^2 = chi square test z = z score of Mann Whitney U test *=significant $p < 0.05$

Table (2) Our results showed a significant increase in anemia, an abnormal level of white blood cells, and obesity among RRMS patients more than in prog MS patients ($P = 0.001, 0.05, 0.03$ respectively). While both the duration of the disease and EDSS were significantly higher among prog MS patients more than in RRMS patients ($P = 0.022, 0.001$ respectively). Figure (1) shows the percentage of obesity and underweight among RR MS and prog MS.

Table 2: Clinical features of patients and Anthropometric Measurements.

Variables		Relapsing remitting MS (n=86)		Progressive MS (n=33)		Test of sig.	P value
Anemia	Male	0	0	2	15.38	X ² =7.569	0.001*
	female	31	43.66	5	25		
WBCs 10 ³ \mm	Normal	51	75	18	85.71	X ² =1.345	0.05*
	Abnormal	17	25	3	14.28		
Body Mass Index (BMI)	Underweight	1	1.1	4	12.2	χ ² =6.6	0.03*
	Normal	27	31.4	11	33.3		
	Overweight	33	38.4	13	39.4		
	Obesity	25	29.1	5	15.1		
Duration of the disease:	Range	1-15		1-37		Z =10.86	0.022*
	Mean ±SD	4.6+4.6		10.3+6.1			
	Median	4.0		8.0			
Annual relapse rate	Range	0-4		0-3		Z =0.99	0.32
	Mean ±SD	1.5+1.01		1.06+0.88			
	Median	1.0		1.0			
Expanded Disability Status Scale (EDSS)	Range	0 – 7		2 – 8		Z=-8.37	0.001*
	Mean ±SD	2.8 ± 1.9		5.7 ± 1.2			
	Median	2.5		6.0			

SD= Standard Deviation χ^2 = chi square test z = z score of Mann Whitney U test *=significant $p < 0.05$

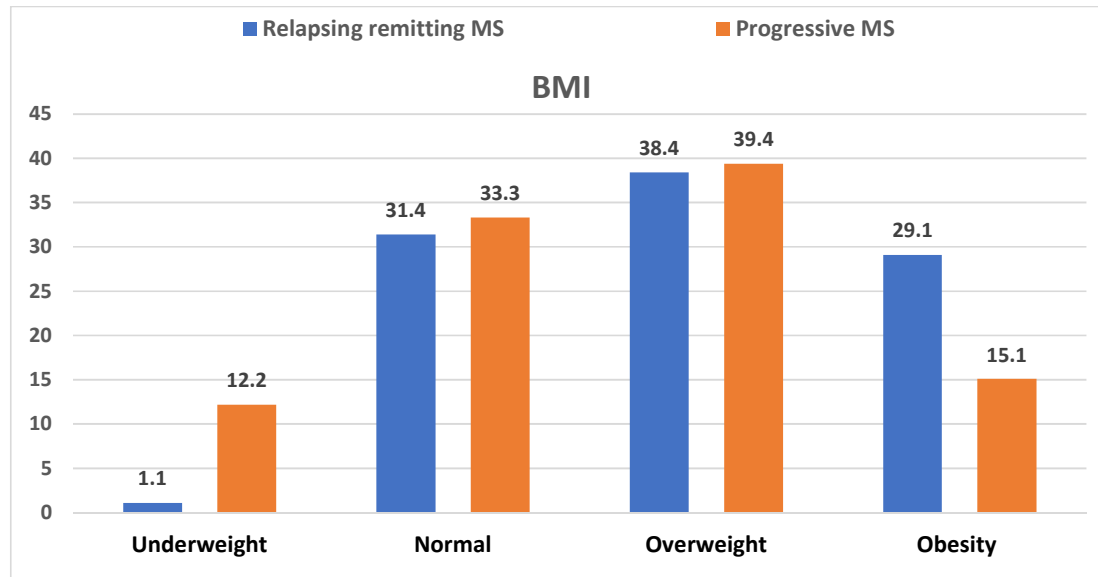


Fig. 1: The BMI categories among RR MS and Prog MS patients.

Tables (3,4) indicate that there were no significant differences between patients with RRMS and Prog MS in their intake of macronutrients or vitamins. In contrast, Tables (5) points to statistically significant differences between patients with RRMS and Prog MS in their intake of

Potassium and Iron (P. values = 0.015, 0.01 respectively), where most patients with prog MS have a higher mean daily intake of potassium and iron than patients with RRMS.

Table 3: The mean daily intake of macronutrients by patients with RRMS and patients with Prog MS.

Variables	Relapsing remitting MS (n=86)	Progressive MS (n=33)	P value
	Mean \pm SD	Mean \pm SD	
Energy (kcal)	1804.7 \pm 881.9	1867.1 \pm 665.0	0.452
Protein(gm)	62.9 \pm 18.2	69.7 \pm 18.3	0.203
Fat(gm)	48.1 \pm 15.4	54.8 \pm 20.9	0.481
Carbohydrate(gm)	285.6 \pm 101.6	276.9 \pm 92.5	0.429
Water(ml)	2178.4 \pm 491.7	2073.2 \pm 437.2	0.737
Fibers(gm)	5.7 \pm 2.4	6.6 \pm 3.2	0.21

SD= Standard Deviation

*=significant p<0.05

Table 4: The mean daily intake of vitamins by patients with RR MS and patients with Prog MS.

Variables	Relapsing remitting MS (n=86)	Progressive MS (n=33)	Variables
	Mean \pm SD	Mean \pm SD	
Vitamin A	357.9 \pm 848.4	239.8 \pm 245.3	0.997
Vitamin C	36.7 \pm 34.9	43.7 \pm 51.9	0.527
Thiamine	0.51 \pm 0.31	0.56 \pm 0.34	0.124
Riboflavin	0.52 \pm 0.34	0.60 \pm 0.33	0.520

SD= Standard Deviation

*=significant p<0.05

Table 5: The mean daily intake of minerals by patients with RR MS and patients with Prog MS.

Variables	Relapsing remitting MS (n=86)	Progressive MS (n=33)	Variables
	Mean \pm SD	Mean \pm SD	
Sodium(mg)	2565.4 \pm 801.7	3073.4 \pm 911	0.216
Potassium(mg)	1934.9 \pm 739.3	2099.9 \pm 826	0.015*
Calcium(mg)	427.3 \pm 174.9	517 \pm 237.7	0.440
Phosphorus(mg)	776.6 \pm 331.8	867.3 \pm 355.4	0.174
Magnesium(mg)	72.3 \pm 28.8	82.3 \pm 45.5	0.128
Iron(mg)	11.3 \pm 3.4	13.9 \pm 4.9	0.01*
Zinc(mg)	8.08 \pm 3.7	9.8 \pm 3.2	0.12
Copper(mg)	0.67 \pm 0.2	0.94 \pm 0.6	.168

SD= Standard Deviation

*=significant p<0.05

Nutrient intake was classified according to the level of consumption compared to the FAO, WHO and United Nations University (UNU) 2001 human energy requirements and the FAO and WHO 2001 human vitamin and mineral requirements, where < 50% was considered unsafe level of consumption, > 50–75% considered needs improvement, > 75–120% considered acceptable level of consumption, and > 120% considered over consumption (UNU, 2004; UNU/WHO, 2004).

Results of this study indicates that no significant differences between RRMS patients and Prog MS patients in their daily intake of water, energy, protein, fat, carbohydrates, fiber and vitamins. Despite this, we noticed that (18.2%) of Prog MS patients compared to (8.1%) of RRMS patients consumed unsafe amounts of water while (54.7%) of RRMS patients compared to (33.3%) of Prog MS patients consumed unsafe amounts of protein. We also noticed that (36%) of patients in both groups had overconsumption energy intake. This was because of overconsumption of carbohydrates in RRMS patients, while in Prog MS patients was because of overconsumption of fat. Almost all of the

participants in both study groups had a severe deficiency in the intake of fiber and more than half of them consumed Unsafe amounts of vitamins A, C, thiamin and riboflavin.

Table 6: Comparison between RRMS and Prog MS patients regarding Percentage of the main daily dietary intake of macronutrients.

Nutrients		Relapsing remitting MS		Progressive MS		Sig. test	P. value
		n	%	n	%		
Water	Un safe	7	8.1	6	18.2	2.799	0.424
	Un acceptable	35	40.7	11	33.3		
	Acceptable	33	38.4	11	33.3		
	Overconsumption	11	12.8	5	15.2		
Energy	Un safe	1	1.2	0	0.0	0.653	0.884
	Un acceptable	10	11.6	5	15.2		
	Acceptable	44	51.2	16	48.5		
	Overconsumption	31	36.0	12	36.4		
Protein	Un safe	47	54.7	11	33.3	6.376	0.095
	Un acceptable	15	17.4	6	18.2		
	Acceptable	20	23.3	15	45.5		
	Overconsumption	4	4.7	1	3.0		
Fat	Un safe	3	3.5	0	0.0	2.842	0.417
	Un acceptable	14	16.3	5	15.2		
	Acceptable	44	51.2	14	42.4		
	Overconsumption	25	29.1	14	42.4		
Fiber	Un safe	86	100.0	32	97.0	2.628	0.105
	Un acceptable	0	0.0	1	3.0		
	Acceptable	0	0.0	0	0.0		
	Overconsumption	0	0.0	0	0.0		
Carbohydrate	Un safe	4	4.7	1	3.0	5.172	0.160
	Un acceptable	8	9.3	4	12.1		
	Acceptable	27	31.4	17	51.5		
	Overconsumption	47	54.7	11	33.3		

*Unsafe < 50%, Unacceptable 50–75%, Acceptable 75–120%, Overconsumption ≥ 120% of RDA

*Statistically significant

Table 7: Comparison between RR MS and Prog MS patients regarding Percentage of the main daily dietary intake of vitamins.

Nutrients		Relapsing remitting MS		Progressive MS		Sig. test	P. value
		n	%	n	%		
Vitamin A	Un safe	77	89.5	28	84.8	1.503	0.682
	Un acceptable	4	4.7	3	9.1		
	Acceptable	1	1.2	1	3.0		
	Overconsumption	4	4.7	1	3.0		
Vitamin C	Un safe	57	66.3	21	63.6	2.040	0.564
	Un acceptable	13	15.1	4	12.1		
	Acceptable	10	11.6	3	9.1		
	Overconsumption	6	7.0	5	15.2		
Thiamin	Un safe	57	66.3	20	60.6	0.929	0.818
	Un acceptable	19	22.1	10	30.3		
	Acceptable	7	8.1	2	6.1		
	Overconsumption	3	3.5	1	3.0		
Riboflavin	Un safe	57	66.3	18	54.5	1.706	0.636
	Un acceptable	18	20.9	9	27.3		
	Acceptable	8	9.3	5	15.2		
	Overconsumption	3	3.5	1	3.0		

*Unsafe < 50%, Unacceptable 50–75%, Acceptable 75–120%, Overconsumption ≥ 120% of RDA

*Statistically significant

Table (8): Results pointing to significant differences between patients with RRMS and patients with Prog MS in their daily consumption of Iron. (44.2%) of RRMS patients consumed Unsafe amounts of iron, while (48.5%) of Prog MS patients had Overconsumption of iron (P. values = 0.02).

Although there were no significant differences between RRMS and Prog MS patients in their intake of phosphorous, we noticed it was slightly Overconsumption in (51.5%) of Prog MS patients compared to (32.6%) of RRMS patients. We also noticed that all patients in both groups consumed Unsafe amounts of magnesium and copper and over amounts of Sodium. Also, more than half of them consumed Unsafe amounts of Calcium.

Table 8: Comparison between Relapsing remitting MS and Progressive MS patients regarding percentage of the main daily dietary intake of minerals.

Nutrients		Relapsing remitting MS		Progressive MS		Sig. test	P. value
		n	%	n	%		
Sodium	Un safe	0	0.0	0	0.0	2.628	0.105
	Un acceptable	0	0.0	0	0.0		
	Acceptable	0	0.0	1	3.0		
	Overconsumption	86	100.0	32	97.0		
Potassium	Un safe	3	3.5	2	6.1	4.059	0.255
	Un acceptable	25	29.1	4	12.1		
	Acceptable	36	41.9	18	54.5		
	Overconsumption	22	25.6	9	27.3		
Calcium	Un safe	60	69.8	18	54.5	3.635	0.162
	Un acceptable	21	24.4	10	30.3		
	Acceptable	5	5.8	5	15.2		
	Overconsumption	0	0.0	0	0.0		
Phosphorous	Un safe	8	9.3	1	3.0	4.982	0.173
	Un acceptable	8	9.3	4	12.1		
	Acceptable	42	48.8	11	33.3		
	Overconsumption	28	32.6	17	51.5		
Magnesium	Un safe	86	100.0	32	97.0	2.628	0.105
	Un acceptable	0	0.0	1	3.0		
	Acceptable	0	0.0	0	0.0		
	Overconsumption	0	0.0	0	0.0		
Iron	Un safe	20	23.3	3	9.1	15.154	0.002*
	Un acceptable	38	44.2	7	21.2		
	Acceptable	13	15.1	7	21.2		
	Overconsumption	15	17.4	16	48.5		
Zinc	Un safe	5	5.8	1	3.0	2.548	0.467
	Un acceptable	18	20.9	6	18.2		
	Acceptable	50	58.1	17	51.5		
	Overconsumption	13	15.1	9	27.3		
Copper	Un safe	86	100.0	33	100.0	—	—
	Un acceptable	0	0.0	0	0.0		
	Acceptable	0	0.0	0	0.0		
	Overconsumption	0	0.0	0	0.0		

*Unsafe < 50%, Unacceptable 50–75%, Acceptable 75–120%, Overconsumption ≥ 120% of RDA

*Statistically significant

Current study showed the relationship between the frequency of certain foods and both annual relapse rate and the disability of patients. It found a positive relationship between the annual relapse rate and the frequency intake of white bread, and a negative relationship with the frequency intake of some legumes (beans and falafel). Also, there was a positive relationship between disability and the frequency intake of margarine, and a negative relationship with the frequency intake of butter, juice, and very cold drinks.

Table 9: Correlation between annual relapse rate at last year and EDSS and food frequency for patients with multiple sclerosis.

Correlation		Annual relapse rate at last year	Disability Status Scale (EDSS)
Black bread	R	-0.022	0.068
	P	0.811	0.464
White bread	R	0.200*	-0.031
	P	0.029	0.741
Rice/Pasta	R	0.030	-0.144
	P	0.742	0.117
	P	0.609	0.080
Butter	R	0.058	-0.214*
	P	0.528	0.019
Oil	R	0.004	-0.030
	P	0.964	0.750
Margarine	R	0.013	0.262**
	P	0.890	0.004
Beans / falafel	R	-0.180*	0.099
	P	0.050	0.284
Other legumes (cowpeas / beans...)	R	-0.087	-0.116
	P	0.347	0.209
Meat	R	0.096	-0.069
	P	0.301	0.458
Poultry	R	-0.106	-0.051
	P	0.250	0.582
Meat Products	R	-0.090	-0.007
	P	0.328	0.943
Fish	R	-0.038	0.011
	P	0.683	0.909

r= Spearman's rho correlation coefficient

**Indicates to significance level ≤ 0.01 , * Indicates to significance level ≤ 0.05

Table 10: Correlation between annual relapse rate at last year and EDSS and food frequency for patients with multiple sclerosis.

Correlation		Annual relapse rate at last year	Disability Status Scale (EDSS)
Egg	R	-0.042	0.148
	P	0.650	0.109
Full Fat Milk	R	0.015	0.024
	P	0.868	0.797
Skimmed Milk/Yogurt	R	-0.034	-0.039
	P	0.716	0.673
Fresh Vegetables	R	-0.002	0.119
	P	0.979	0.198
Cooked Vegetables	R	-0.062	-0.052
	P	0.500	0.577
Fruits	R	0.122	-0.141
	P	0.185	0.125
Tea	R	-0.039	0.011
	P	0.672	0.908
Coffee	R	-0.142	-0.054
	P	0.123	0.561
Juice	R	0.130	-0.275**
	P	0.160	0.003
Carbonated Water	R	0.018	0.030
	P	0.847	0.747
Cold Drinks	R	0.150	-0.180*
	P	0.103	0.050
Nuts	R	-0.077	0.050
	P	0.405	0.589

r= Spearman's rho correlation coefficient

**Indicates to significance level ≤ 0.01 , * Indicates to significance level ≤ 0.05

4. Discussion

It is known that MS is much more common in women than in men, significantly higher prevalence of RRMS and a somewhat lower prevalence of PPMS (Gilli *et al.*, 2020; Luetic *et al.*, 2022). Which corresponds with our results, that indicated more than two-thirds of the patients (76.4%) were females, (72.3%) of them were Relapsing–Remitting MS (RRMS) and (22.7%) were Secondary Progressive MS (SPMS), while Just (5%) were Primary Progressive MS (PPMS), with significantly higher prevalence of females among RRMS patients compare to Prog MS patients; $P=0.01$. This can be interpreted in several ways, such as a deleterious role of estrogens or progesterone in women, a protective role of testosterone in men (Collongues *et al.*, 2018).

Patients were aged between 18-56 years with mean age (33.49, SD: 9.8 \pm) our results in accordance with Previous Egyptian study (Afifi *et al.*, 2023). Prog MS Patients had higher Mean age (40.2 \pm 7.9) than RRMS Patients (30.89 \pm 8.5). This agrees with another study found that Mean age at disease onset was (31.6) for relapsing-onset and (42.7) for progressive-onset (Wilson *et al.*, 2023). Also, it consistent with the observation that age is one of the greatest risk factors for progressive MS (Miller *et al.*, 2019).

For dietary macronutrients assessment, the intake of energy, carbohydrates, fats and protein was compared between RRMS and Prog MS patients. We did not find any significant differences. However, we noticed overconsumption of fat in Prog patients, While in RRMS MS patients there was overconsumption of carbohydrates. Which agree with recently study in a southern European cohort showed that patients with the first episode of demyelinating had a higher consumption of simple carbohydrates (Cavalla *et al.*, 2022). Increased amount of consumed calories is believed that associated with inflammation. As results from studies caloric restriction revealed a reduction in oxidative stress in patients with relapsing and progressive MS, leading to a better quality of life (Stoiloudis *et al.*, 2022). Also, High animal fat intake may trigger the inflammatory cascade since they activate inflammatory toll-like receptors and disrupt the blood-brain barrier integrity (Katz Sand, 2018; Matveeva *et al.*, 2018). Although fiber have role in reducing the elevated level of serum C-reactive protein and the elevated oxidative and systemic inflammatory status (Xie *et al.*, 2015). Our

results revealed almost All patients in both groups consumed Unsafe amount of fiber, So High-fiber dietary intake that is, fruits, vegetables, legumes and whole grains, and poorer in simple sugars (sugar-sweetened sweets and drinks) may reduce disease severity and suppress inflammatory conditions in patients with MS. Furthermore, energy intake and dietary fibers are good predictors for EDSS (Afifi *et al.*, 2023).

Vitamins, as essential micronutrients, seem to be crucial in the pathogenesis of MS, and particularly vitamins A and C were found to have a protective role in MS development or progression as they reduce the levels of proinflammatory cytokines, increase the total antioxidant capacity and reduces the levels of oxidative stress markers (Sanchez *et al.*, 2022). Our Patients in both groups had a severe deficiency in the intake of vitamin C and vitamin A, also this accordance with previous studies (Navidhamidi *et al.*, 2022). Our Results of dietary minerals assessment showed a significant association between Prog MS and the high mean daily intake of Potassium and iron. Where Overconsumption of iron was observed in Prog MS patients, RRMS patients consumed Unsafe amounts of iron. Inadequate iron levels (both low and high) may be harmful in MS since iron excess might increase free radicals, which may elevate oxidative stress, while iron reduction could decrease immune system function and cause an energy deficit due to loss of mitochondria membrane potential (Armon-Omer *et al.*, 2019) Sodium was consumed in very large amounts by both RRMS and prog MS patients: (2565.4±801.7 and 3073.4±911mg/day respectively). This was higher than recommended by 2020–2025 Dietary Guidelines (HHS and USDA, 2020) but less than the mean sodium intake reported in Egyptian study (Afifi *et al.*, 2023). Despite that, a recent research show the dietary salt intake does not affect activity and the course of MS (Zielińska and Michońska, 2022).

Although previous studies found that a healthy lifestyle entailing a diet rich in fruits, vegetables, and dietary fibers along with a low intake of sugar and processed meat, was associated with lower levels of disability in MS patients (Fitzgerald *et al.*, 2018) Our study did not find a relationship between the disability and frequency of eating fruits, vegetables and meat. Also, A prospective study in pediatric MS noted an increased risk of relapse relating to increased saturated fat intake also noted a reduction in relapse rates with increasing intake of vegetables Excluding potatoes and legumes, a one-cup equivalent increase in vegetable intake decreased the risk of relapse by 50% patients (Azary *et al.*, 2018). Despite that, we did not find a relationship between the relapse rate and frequency of eating fats and vegetables.

5. Conclusion

High daily intake of iron was associated with prog MS more than RRMS patients, while, there were no significant differences between RRMS and prog MS patients in their daily intake of water, calories, protein, fat, carbohydrate, fiber, sodium, calcium, magnesium, phosphorous, zinc, copper, iron, vitamin-A, thiamin, riboflavin. So, this must be taken into account during diet planning.

5. Recommendations

Paying attention to diets that provide antioxidants and anti-inflammatories such as vitamins A, C, and D, and omega-3 fatty acids. Managing iron status in diets, reducing sodium intake and increasing fiber intake that is, fruits, vegetables, legumes and whole grains.

6. Study limitations

The current study findings should be interpreted considering the following limitations: First, some defects in 24-hour recall method such as recall bias, inaccurate estimation of portion sizes, possible over/under-reporting of certain foods, Secondly, we did not test the hormones such as insulin, leptin and ghrelin that have important roles in appetite. Finally, the study included only cases. here is no control group.

Competing interests: The authors declare that they have no competing interests.

References

- Afifi, Z., A. Hassan, N. Abdelrahman, A. El Sayed, and M. Salem, 2023. Impact of nutrition counseling on anthropometry and dietary intake of multiple sclerosis patients at Kasr Alainy Multiple Sclerosis Unit, Cairo, Egypt 2019–2020: randomized controlled clinical trial. *Archives of Public Health*, 81(1): 11. DOI: <https://doi.org/10.21203/rs.3.rs-1425231/v1>.
- Armon-Omer, A., C. Waldman, N. Simaan, H. Neuman, S. Tamir, and R. Shahien, 2019. New insights on the nutrition status and antioxidant capacity in multiple sclerosis patients. *Nutrients*, 11(2): 427. doi:10.3390/nu11020427.
- Azary, S., T. Schreiner, J. Graves, A. Waldman, A. Belman, B.W. Guttman, and E. Waubant, 2018. Contribution of dietary intake to relapse rate in early paediatric multiple sclerosis. *Journal of Neurology, Neurosurgery & Psychiatry*, 89(1): 28-33. doi.org/10.1136/jnnp-2017-315936.
- Castell, G.S., L. Serra-Majem, and L. Ribas-Barba, 2015. What and how much do we eat? 24-hour dietary recall method. *Nutricion hospitalaria*, 31(3): 46-48.
- Cavalla, P., P. Golzio, D. Maietta, C. Bosa, M.B. Pasanisi, A. Alteno, and M. Vercellino, 2022. Dietary habits, nutritional status and risk of a first demyelinating event: an incident case-control study in a southern European cohort. *Neurological Sciences*, 43(7): 4373-4380.
- Collongues, N., C. Patte-Mensah, J. De Seze, A.G. Mensah-Nyagan, and T. Derfuss, 2018. Testosterone and estrogen in multiple sclerosis: from pathophysiology to therapeutics. *Expert review of neurotherapeutics*, 18(6): 515-522.
- El-Gilany, A., A. El-Wehady, and M. El-Wasify, 2012. Updating and validation of the socioeconomic status scale for health research in Egypt. *Eastern Mediterranean health journal*, 18(9).
- Esposito, S., M. Sparaco, G.T. Maniscalco, E. Signoriello, R. Lanzillo, C. Russo, and S. Bonavita, 2021. Lifestyle and Mediterranean diet adherence in a cohort of Southern Italian patients with Multiple Sclerosis. *Multiple Sclerosis and Related Disorders*, 47:102636.
- FAO, Food and Agriculture Organization of the United Nation, 2018. *Dietary Assessment: A Resource Guide to Method Selection and Application in Low Resource Setting*. Rom, Italy.
- Fitzgerald, K.C., T. Tyry, A. Salter, S.S. Cofield, G. Cutter, R. Fox, and R.A. Marrie, 2018. Diet quality is associated with disability and symptom severity in multiple sclerosis. *Neurology*, 90(1): e1-e11.
- Gilli, F., K.D. DiSano, and A.R. Pachner, 2020. SeXX matters in multiple sclerosis. *Frontiers in neurology*, 11: 616.
- Hasselbalch, I.C., H.B. S ndergaard, N. Koch-Henriksen, A. Olsson, H. Ullum, F. Sellebjerg, and A.B. Oturai, 2018. The neutrophil-to-lymphocyte ratio is associated with multiple sclerosis. *Multiple Sclerosis Journal–Experimental, Translational and Clinical*, 4(4): 2055217318813183.
- HHS and USDA, 2020–2025. *Dietary guidelines for Americans*. 2020.
- IBM. Corp. (released 2012). *IBM SPSS statistics for windows (version 21.0.)*. Armonk: IBM Corp; 2012.
- Katz Sand, I., 2018. The role of diet in multiple sclerosis: mechanistic connections and current evidence. *Current nutrition reports*, 7(3): 150-160.
- Luetic, G.G., M.L. Menichini, C. Vrech, A. Pappolla, L. Patrucco, E. Cristiano, and J.I. Rojas, 2022. Clinical and demographic characteristics of male MS patients included in the national registry-RelevarEM. Does sex or phenotype make the difference in the association with poor prognosis? *Multiple sclerosis and related disorders*, 58: 103401. <https://doi.org/10.1016/j.msard.2021.103401>.
- Mahan, L.K., 2004. *Krause's food, nutrition, & diet therapy*, 11. S. Escott-Stump (Ed.). Philadelphia: Saunders. <https://trove.nla.gov.au/work/6084784?selectedversion=NBD20212902>.
- Matveeva, O., J.F. Bogie, J.J. Hendriks, R.A. Linker, A. Haghighia, and M. Kleinewietfeld, 2018. Western lifestyle and immunopathology of multiple sclerosis. *Annals of the New York Academy of Sciences*, 1417(1): 71-86.
- Meyer-Moock, S., Y.S. Feng, M. Maeurer, F.W. Dippel, and T. Kohlmann, 2014. Systematic literature review and validity evaluation of the Expanded Disability Status Scale (EDSS) and the Multiple Sclerosis Functional Composite (MSFC) in patients with multiple sclerosis. *BMC neurology*, 14(1): 1-10.

- Miller, E.D., A. Dziedzic, J. Saluk-Bijak, and M. Bijak, 2019. A review of various antioxidant compounds and their potential utility as complementary therapy in multiple sclerosis. *Nutrients*, 11(7): 1528.
- National Nutrition Institute, 2006. Food composition tables in the Middle East for Egypt. "Second Edition". Cairo. A.R.E. <http://nni-egypt.org>.
- Navidhamidi, M., A. Nazari, S. Dehghan, A. Ebrahimpour, R. Nasrnezhad, and F. Pourabdolhossein, 2022. Therapeutic potential of combined therapy of vitamin A and vitamin C in the experimental autoimmune encephalomyelitis (EAE) in Lewis rats. *Molecular Neurobiology*, 59(4): 2328-2347.
- Nuttall, F.Q., 2015. Body mass index: obesity, BMI, and Health: A critical review. *Nutrition Today*, 50(3): 117.128.
- Riccio, P. and R. Rossano, 2018. Diet, gut microbiota, and vitamins D+ A in multiple sclerosis. *Neurotherapeutics*, 15(1): 75-91.
- Sanchez, J.M.S., A.B. DePaula-Silva, J.E. Libbey, and R.S. Fujinami, 2022. Role of diet in regulating the gut microbiota and multiple sclerosis. *Clinical Immunology*, 235: 108379.
- Stoiloudis, P., E. Kesidou, C. Bakirtzis, S.A. Sintila, N. Konstantinidou, M. Boziki, and N. Grigoriadis, 2022. The Role of Diet and Interventions on Multiple Sclerosis: A Review. *Nutrients*, 14(6): 1150.
- Thompson, S.K., 2012. Sampling, 3rd edition. John Wiley and Sons, Inc.
- United Nations University, and World Health Organization. 2004. Human Energy Requirements: Report of a Joint FAO/WHO/UNU Expert Consultation: Rome, 17-24 October 2001, 1. Food & Agriculture Org.
- WHO 2018. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. [cited 2018 July 20]. Available from http://apps.who.int/iris/bitstream/10665/85839/3/WHO_NMH_NHD_MNM_11.1_eng.pdf?ua=1;2011 date of retrieval 20 /7/ 2018.
- Wigner, P., A. Dziedzic, E. Synowiec, E. Miller, M. Bijak, and J. Saluk-Bijak, 2022. Variation of genes encoding nitric oxide synthases and antioxidant enzymes as potential risks of multiple sclerosis development: A preliminary study. *Scientific Reports*, 12(1): 10603.
- Wilson, S., F. Calocer, F. Rollet, M. Fauvernier, L. Remontet, L. Tron, and G. Defer, 2023. Effects of socioeconomic status on excess mortality in patients with multiple sclerosis in France: A retrospective observational cohort study. *The Lancet Regional Health-Europe*, 24: 100542. <https://doi.org/10.1016/j.lanepe.2022.100542>.
- World Health Organization, 2004. Vitamin and mineral requirements in human nutrition. World Health Organization.
- Xie, L.M., Y.Y. Ge, X. Huang, Y.Q. Zhang, and J.X. Li, 2015. Effects of fermentable dietary fiber supplementation on oxidative and inflammatory status in hemodialysis patients. *International Journal Of Clinical And Experimental Medicine*, 8(1): 1363. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4358593/>
- Zielińska, M. and I. Michońska, 2022. Macronutrients, vitamins and minerals in the diet of multiple sclerosis patients. *Advances in Psychiatry and Neurology*, 31 (3): 128-137. DOI: <https://doi.org/10.5114/ppn.2022.121730> 31(1).