# Nutritional status and anthropometric measurements of patients with multiple sclerosis

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## ABSTRACT

**الأهداف:** تحديد الحالة الغذائية والقياسات البشرية للمرضى الذين يعانون من مرض التصلب العصبي المتعدد.

**الطريقة:** شملت هذه الدراسة ما مجموعه 37 حالة (15 ذكر، و22 أنثى) من المرضى المصابين بمرض التصلب العصبي المتعدد الذين راجعوا مستشفى نومونا للتدريب والبحوث، أنقرة، تركيا خلال الفترة من يونيو إلى أغسطس 2011م. لقد تم تحديد الحالة الغذائية للمرضى بواسطة السجلات الغذائية على مدى 24 ساعة لمدة 3 أيام، وتم تحديد السلوك الغذائي للمرضى عن طريق استبيان تواتر الغذاء. وقد تم قياس وزن وطول الجسم وحساب مؤشر كتلة الجسم. وتم تحليل مكونات الجسم من خلال تحليل المعاوقة الكهربائية الإحيائية، فيما استخدم برنامج قاعدة البيانات الغذائية لتقييم الكميات المأخوذة من الطاقة والمواد الغذائية للمرضى بالمقارنة مع توصيات مرجع الكميات الغذائية. كما تم تحليل مستويات سكر الغلوكوز، والدهون، ومجموع البروتينات، والألبومين، ومجموع الكالسيوم، والمغنيسيوم، وفيتامين ب12، وفيتامين د.

**النتائج:** لقد عانى 5.4% من المرضى من نقص في الوزن، و54.1% منهم كان وزنهم طبيعي، و24.3% يعانون من زيادة في الوزن، و16.2% يعانون من فرط في الوزن. وكانت كمية الطاقة المأخوذة يومياً 2730±840.97 كيلو كالوري عند الذكور، و1967±647.24 كيلو كالوري لدى الإناث. ولقد كانت نسبة الكربوهيدرات 46.9%، والبروتينات 14.6%، والدهون من مجموع الطاقة الكلي 38.4%. وكانت مستويات مصل فيتامين د لنسبة 16.7% من المرضى ومصل فيتامين ب12 لنسبة 6.7% من المرضى أقل من المستويات المرجعية المنصوح بها.

**خاتمة:** لقد تبين من خلال هذه الدراسة بأن المرضى الذين يعانون من مرض التصلب العصبي المتعدد يعانون من زيادة في مؤشر كتلة الجسم وحالة غذائية متردية. وثبت أيضاً بأن تغيير نمط الحياة مع وجود العادات الغذائية المتوازنة يعد من الأمور الهامة بالنسبة لمرضى التصلب العصبي المتعدد.

**Objectives:** To determine the nutritional status and anthropometric measurements of patients with multiple sclerosis (MS).

**Methods:** This research was conducted on 37 (15 men, 22 women) new diagnosed MS patients who applied to Ankara Numune Education and Research Hospital, Ankara Turkey, from June to August 2011. The nutritional status of patients was determined by a 3-day and 24-hour dietary record and a food frequency questionnaire. Body composition was analyzed by bioelectrical impedance analyzer, and body mass index was calculated. The Nutrient Data Base (BEBIS) program was used to evaluate the energy and nutrient intakes of patients and compared with Dietary Reference Intakes recommendations. Blood samples were collected and serum glucose, lipid profiles, total protein, albumin, total calcium, magnesium, vitamin B12, and vitamin D levels were analyzed.

**Results:** Approximately 5.4% of patients were underweight, 54.1% were normal weight, 24.3% were overweight and 16.2% were obese. Daily mean energy intakes were 2730±840.97 kcal in men and 1967±647.24 kcal in women. The percentage of the carbohydrates was 46.9%, proteins was 14.6%, and fats of the total energy was 38.4%. Approximately 16.7% of the patients' serum vitamin D, and 6.7% of the patients' serum vitamin B12 levels were below than the reference ranges.

**Conclusion:** Multiple sclerosis patients have high body mass index values and poor nutritional status. It was verified that life style modification with adequate and balanced nutritional habits is very important in MS patients.

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Multiple sclerosis (MS), is a chronic disease of central nervous system, affecting young adults, with a female predominance. The course is usually relapsing-remitting for approximately 10 years, followed by a secondary progressive phase.[1] Different pathomechanisms, immune-mediated inflammation, oxidative stress, and excitoxicity, are involved in the immunopathology of MS.[2] The etiology of MS is unknown. It is regarded as a complex multicausal disease. The etiological factors comprise genetic factors, dysfunction of the immune system and environmental factors. Autoimmune responses to myelin components may play an important role in the initiation of MS. Environmental etiological factors for MS are infection by a latent virus, possibly by a human herpes virus or rotavirus. Other environmental factors, contributing for MS, are sunlight and nutrition.[3] Diet is a commonly postulated factor because strong associations have been observed between increased MS prevalence and diets high in meat and dairy products and low in fish.[4] A large number of different diet compounds were also associated with MS.[5] There are some evidence from studies that a high consumption of saturated animal fats is associated with an increased incidence of MS.[6] Conversely, findings from the population-based case-control studies that have examined dietary fat intake and foods contributing to dietary fat in relation to the risk of MS have been inconsistent; most of them suggest a null association with intakes of fat, meat and dairy products. In 2 large cohorts of women, there were no evidence that higher intake of saturated fat or lower intakes of polyunsaturated fat and fish omega-3 fatty acids were associated with an increased risk of MS.[7] Nervous tissue contains large amount of lipids; therefore, particular attention has been directed to the role of dietary fat and their possible therapeutic effects in patients with MS. Findings from such studies indicate that supplementation with unsaturated fatty acids, particulary omega-3 fatty acids, could positively influence the course of MS. Diets and dietary supplements are much used by people with MS in the belief that they might improve disease outcomes.[6,8] A role of vitamin D in the immunopathogenesis of MS is biologically plausible.[1] Holmoy was the first to propose that poor vitamin D status modulates the immune response to Epstein-Barr virus in a way that increases the risk of developing MS.[9-11] Low blood level of vitamin D (<50 nmol/L) have been reported in 50-70% of patients in different MS populations.[12] Obesity and malnutrition in MS are frequently observed. Weight gain was related to reduced mobility and low energy expenditure and fatigue. Weight loss was related to dysphagia, reduced cognition, poor appetite, poor sight and so forth.[13] The objective of the present study was to determine the nutritional status and anthropometric measurements of patients with multiple sclerosis (MS).

**Disclosure**. Authors have no conflict of interests, and the work was not supported or funded by any drug company.

**Methods.** The investigation was carried out in 37 (15 men, 22 women) MS patients ages between 20-55 years from the Ankara Numune Training and Research Hospital, Ankara, Turkey from June to August 2011. All patients were new diagnosed and non-smoker. Also, none of them were using any vitamin-mineral supplementations. The patients with other metabolic diseases and mental disabilities were excluded from the study. All subjects gave their written informed consent and the study was approved by the Ethics Committee of the Ankara Numune Training and Research Hospital (2011-178). Demographic characteristics and knowledge related with MS were administrated with questionnaire by face to face interview. The body weight, height, and waist circumferences were measured and body mass index (BMI) was calculated [(BMI=weight (kg)/height ($m^2$)]. Body mass index values were evaluated using the World Health Organization (WHO) classification. The patients were grouped into 4 categories, underweight (<18.5 kg/$m^2$), normal-weight (18.5 to 24.9 kg/$m^2$), overweight (25-29.9 kg/$m^2$) and obese (>30kg/$m^2$) in accordance with the cut-off points.[14] Waist circumferences values were evaluated using the WHO cut-off points (>$10^2$ cm for men, >88 cm for women).[15] Body composition was analyzed with bioelectrical impedance analyze (BIA). Some biochemical parameters (serum glucose, total cholesterol, triglyceride, high density lipoprotein (HDL-C), low density lipoprotein (LDL-C), total protein, albumin, total calcium, magnesium, vitamin B12, vitamin D) of the patients were analyzed. The biochemical parameters were determined by using conventional autoanalysers. The nutritional behavior of the patients was determined by a food frequency questionnaire. The nutritional status of the patients was determined by a three days 24-hour dietary record. Nutrient Data Base (BEBIS) Program was used to evaluate the energy and nutrient intakes of the patients. Dietary vitamin and mineral intakes were compared with DRI (Dietary Reference Intake) recommendations.[16]

Expanded Disability Status Scale was used to evaluate for assessment disability and disability scales in MS patients. Expanded Disability Status Scale scores are changing between 0 and 10. Expanded Disability Status Scale scores increase when the severity of the MS increases. The results were expressed as the mean ±

standard deviation (± SD) and percentages (%). Pearson chi-square ($x^2$) test was used to compare the percentage of risk factors among men and women. The statistical analyses were performed with SPSS version 13.0 for Windows. Differences were considered significant with a probability value of $p<0.05$.

**Results.** As shown in **Table 1**, the mean age of the patients was 33.3±9.72 years and the mean duration of MS were 49.1±42.31 months in women and 30.7±25.54 months in men. The percentage of the patients with MS history in their family was 31.8% in women, 13.3% in men. The mean Expanded Disability Status Scale (EDSS) of patients were 1.9±1.43 in women 2.2±2.15 in men.

The mean BMI of women were 24.8±5.41 kg/m$^2$ and men 25.6±5.32 kg/m$^2$. The 5.4% of patients were underweight, 54.1% were normal, 24.3% were overweight and 16.2% were obese. The mean waist circumference of the men was 87.2±13.85 cm and women 76.0±13.39 cm. The percentages of the body fat in women was 30% and 22.1% in men (**Table 2**).

**Table 1 -** The variables related with multiple sclerosis by gender (N=37).

| Variables | Men (n=15) | | Women (n=22) | | Total (n=37) | | *P*-value |
|---|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | Mean | SD | |
| Age (years) | 31.4 | 5.76 | 34.6 | 11.63 | 33.3 | 9.72 | 0.320 |
| Multiple sclerosis age (months) | 30.7 | 25.54 | 49.1 | 42.31 | 41.8 | 37.22 | 0.120 |
| Expanded disability status scale score | 2.2 | 2.15 | 1.9 | 1.43 | 2 | 1.72 | 0.617 |
| Family history (%) | 2.0 | 13.3 | 7.0 | 31.8 | 9 | 24.3 | |
| $X^2$= 1.656, $p$=0.198 | | | | | | | |

**Table 2 -** Anthropometric measurements of multiple sclerosis patients (N=37).

| Anthropometric measurements | Men (n=15) | | Women (n=22) | | Total (n=37) | | *P*-value |
|---|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | Mean | SD | |
| Height, cm | 1.74 | 0.08 | 1.58 | 0.03 | 1.6 | 0.09 | 0.000* |
| Weight, kg | 77.5 | 15.17 | 62.4 | 12.38 | 68.5 | 15.35 | 0.002* |
| Waist circumference, cm | 87.2 | 13.85 | 76.0 | 13.39 | 80.4 | 14.46 | 0.022* |
| Body fat, % | 22.1 | 10.91 | 30.0 | 10.36 | 26.9 | 11.12 | 0.051 |
| Lean body mass, kg | 56.6 | 6.82 | 42.1 | 5.36 | 47.6 | 9.26 | 0.000* |
| Body water, L | 58.4 | 7.00 | 48.3 | 5.75 | 52.2 | 7.89 | 0.002* |
| Body mass index, kg/m$^2$ | 25.6 | 5.32 | 24.8 | 5.41 | 25.2 | 5.34 | 0.674 |
| ***Body mass index*** | **n** | **(%)** | **n** | **(%)** | **n** | **(%)** | |
| <18.5 | 2 | (13.3) | - | - | 2 | (5.4) | |
| 18.5-24.9 | 6 | (40.0) | 14 | (63.6) | 20 | (54.1) | |
| 25.0-29.9 | 5 | (33.3) | 4 | (18.2) | 9 | (24.3) | |
| ≥30 | 2 | (13.3) | 4 | (18.2) | 6 | (16.2) | |
| $X^2$= 4.826, p=0.185 | | | | | | | |
| *$p$<0.05 | | | | | | | |

**Table 3 -** Some biochemical parameters of the multiple sclerosis patients (N=37).

| Biochemical parameters | Men (n=15) | | Women (n=22) | | Total (n=37) | | Reference ranges | *P*-value |
|---|---|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | Mean | SD | | |
| Glucose, mg/dl | 82.4 | 10.83 | 89.7 | 17.27 | 86.7 | 15.21 | 70 - 115 | 0.171 |
| Total cholesterol, mg/dl | 159.1 | 34.71 | 174.4 | 29.53 | 168.3 | 32.12 | 110 - 200 | 0.171 |
| Triglyceride, mg/dl | 103.6 | 61.35 | 75.6 | 30.90 | 86.8 | 46.85 | 50 - 200 | 0.083 |
| HDL-C, mg/dl | 33.5 | 5.24 | 48.4 | 11.41 | 42.5 | 11.91 | 35 - 85 | 0.000* |
| LDL-C, mg/dl | 104.6 | 32.22 | 110.9 | 28.16 | 108.4 | 29.55 | 0 - 130 | 0.544 |
| Total protein, g/L | 68.2 | 3.82 | 70.8 | 5.43 | 69.8 | 4.95 | 61 - 79 | 0.128 |
| Albumin, g/L | 41.9 | 2.89 | 39.8 | 3.39 | 40.7 | 3.33 | 35 - 48 | 0.065 |
| Total calcium, mg/dl | 9.5 | 0.29 | 9.4 | 0.40 | 9.5 | 0.37 | 8.5 - 10.6 | 0.300 |
| Magnesium, mg/dl | 2.1 | 0.10 | 2.0 | 0.16 | 2.1 | 0.14 | 1.8 - 2.5 | 0.284 |
| Vitamin $B_{12}$, pg/ml | 257.7 | 129.32 | 267.1 | 118.33 | 263.3 | 120.94 | 126.5 - 505 | 0.833 |
| Vitamin D, ng/ml | 15.5 | 7.09 | 8.3 | 3.24 | 11.3 | 6.22 | 6.3 - 46.4 | 0.000* |
| HDL-C - high density lipoprotein cholesterol, LDL-C - low density lipoprotein cholesterol, *$p$<0.05 | | | | | | | | |

Some biochemical parameters results of patients with MS were shown in **Table 3**. The serum lipids of the patients were in normal ranges. Serum total calcium and magnesium mean values of patients were in normal ranges. The mean serum vitamin D was 11.3±6.22 ng/ml and vitamin B12 levels of patients was 263.3±120.94 pg/ml. The 16.7% of patients' serum vitamin D and 6.7% of vitamin B12 levels were below the reference ranges.

The mean daily dietary energy intakes of patients were 2730±840.97 kcal in men and 1968 ±647.24 kcal in women. The percentage of carbohydrates, proteins, and fats of the total energy were 49.5%, 14.8% and 35.7% in men; 45.1%, 14.6% and 40.3% in women, respectively. The percentages of the total energy from saturated fatty acids were 11.6% in men and 13.4% in women. The percentages of the total energy from polyunsaturated and monounsaturated fatty acids was 10.6% and 11.5% in men; 9% and 13.7% in women. The mean omega-3 fatty acid intakes were 2.1±0.79g in men, 1.7±0.77g in women (**Table 4**).

**Table 5** demonstrates the mean dietary vitamin and mineral intakes of patients and comparison by Dietary Reference Intake recommendations. The 32.4% of patients' dietary vitamin B12, 13.5% of patients' vitamins E and C, 8.1% of patients' vitamin A intakes were insufficient. More than half of (51.4%) the patients' dietary iron intakes were insufficient. The patients' dietary calcium (Ca) (29.7%), magnesium (24.3%), and zinc (10.8%) intakes were insufficient. The mean vitamin E and iron intakes of patients were statistically different between gender ($p$=0.047 and $p$=0.000).

**Discussion.** Multiple sclerosis is an immune-mediated, demiyelinating, and neurodegenerative disease of the central nerves system that causes neurological disability in young adults especially women, between 20 and 40 years of age.[17] The etiology of MS is still unknown but genetic predisposition, altered immune response, and environmental (infectious and/or nutritional) factors are possible causative agents.[18] Dietary factors have been suggested as a possible cause of MS, but without hard evidence.[5]

**Table 5 -** Evaluation of dietary micronutrient intakes of the multiple sclerosis patients by Dietary Reference Intake (DRI) recommendations (N=37).

| Insufficient intake (<67% DRI) | Men (n=15) | | Women (n=22) | | Total (n=37) | | *P*-value |
|---|---|---|---|---|---|---|---|
| | n | (%) | n | (%) | n | (%) | |
| *Vitamins* | | | | | | | |
| Vitamin A, IU | 1 | (6.7) | 2 | (9.1) | 3 | (8.1) | 0.791 |
| Vitamin E, mg | - | - | 5 | (22.7) | 5 | (13.5) | 0.047* |
| Vitamin C, mg | 2 | (13.3) | 3 | (13.6) | 5 | (13.5) | 0.979 |
| Vitamin $B_{12}$, mcg | 3 | (20.0) | 9 | (40.9) | 12 | (32.4) | 0.182 |
| *Minerals* | | | | | | | |
| Zinc, mg | 1 | (6.7) | 3 | (13.6) | 4 | (10.8) | 0.503 |
| Iron, mg | - | - | 4 | (18.2) | 19 | (51.4) | 0.000* |
| Calcium, mg | 2 | (13.3) | 9 | (40.9) | 11 | (29.7) | 0.072 |
| Magnesium, mg | 3 | (20.0) | 6 | (27.3) | 9 | (24.3) | 0.613 |

*$p$<0.05

**Table 4 -** Dietary energy and macronutrient intakes of the multiple sclerosis patients (N=37).

| Energy and Macronutrients | Men (n=15) | | Women (n=22) | | Total (n=37) | | *P*-value |
|---|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | Mean | SD | |
| Energy, kcal | 2730.0 | 840.97 | 1967.0 | 647.24 | 2276.0 | 814.59 | 0.004* |
| Carbohydrates, g | 340.4 | 146.66 | 219.5 | 97.04 | 268.6 | 132.21 | 0.005* |
| Carbohydrates, % TE | 49.5 | 8.49 | 45.1 | 10.40 | 46.9 | 9.79 | 0.186 |
| Protein, g | 98.0 | 35.86 | 67.8 | 26.44 | 1.5 | 0.51 | 0.006* |
| Protein, % TE | 14.8 | 2.43 | 14.6 | 2.87 | 14.6 | 2.67 | 0.934 |
| Fat, g | 104.9 | 25.82 | 84.2 | 31.49 | 92.7 | 30.72 | 0.043* |
| Fat, % TE | 35.7 | 8.4s1 | 40.3 | 8.67 | 38.4 | 8.76 | 0.114 |
| Polunsaturated fatty acids, g | 31.5 | 10.45 | 19.4 | 8.84 | 9.6 | 3.54 | 0.001* |
| Polunsaturated fatty acids, % TE | 10.6 | 2.52 | 9.0 | 3.67 | 9.7 | 3.32 | 0.149 |
| Monounsaturated fatty acids, g | 33.3 | 9.75 | 30.0 | 12.80 | 31,4 | 11,64 | 0.397 |
| Monounsaturated fatty acids, % TE | 11.5 | 3.46 | 13.7 | 4.53 | 12.8 | 4.23 | 0.119 |
| Saturated fatty acids, g | 33.3 | 7.29 | 29.6 | 12.34 | 31.1 | 10.63 | 0.311 |
| Saturated fatty acids , % TE | 11.6 | 3.21 | 13.4 | 3.63 | 12.7 | 3.55 | 0.120 |
| Omega-3 fatty acid, g | 2.1 | 0.79 | 1.7 | 0.77 | 1.8 | 0.79 | 0.458 |

TE - total energy, *$p$<0.05

The findings suggest that weight loss and cachexia are often present in patients with MS. Malnutrition has been connected to impairment of the immune system; it affects mental function, respiratory muscle strength and increases as a risk of specific nutrient deficiencies. Dysphagia, a potential contributing factor to malnutrition, is a frequent symptom in degenerative, chronic illness such as multiple sclerosis. Such impairments contribute muscle wasting and weakness, fatigue, and muscle spasms. The proportion of malnutrition and weight loss increases with disability. Weight gain and obesity have also been reported in MS.[17] There are many factors contributing to overweight in patients with MS, including immobility, low energy expenditure, steroids and inactive daily life. Obesity and unhealthy eating pattern may worsen disabilities already existing.[17] In the present study, the 5.4% of the patients were underweight, 40.4% were overweight and obese. The 27.3% of the women patients' waist circumference was >88 cm, 14.3% of the men patients' waist circumference was >102 cm. There were significant positive correlations between EDSS score and body weight and waist circumferences in women (data not shown).

A study which was designed to assess the importance of abnormal fat distribution and deposition and plasma lipid profile changes in MS patients, the results showed that total subcutaneous fat stores of the body were diminished in male MS patients. Truncal and lower body fat of MS patients was reduced and upper body fat was increased when compared to the controls, and plasma levels of VLDL-C and triglycerides were also found to be higher in MS patients. It is considered that lipid metabolism can be influenced by MS.[18] In our study, the body fat percentage of patients was more than the standards in both genders. The dietary habit of patients with MS has not been properly investigated. Beneficial effects from any particular diet have not been proven in MS. There is some evidence from epidemiological studies that a high consumption of saturated animal fat is associated with an increased incidence of MS.[6] According to the American Heart Association guidelines, individuals, including those with MS, should follow the guidelines below for their total fat intake on a daily basis.[19] In this study, the percentages of energy from total fat and saturated fatty acids were higher than DRI recommendations in both genders.

The findings from such studies indicate that supplementation with unsaturated fatty acids, in particular omega-3 fatty acids, could positively influence the course of MS. However, controlled studies did not show clear beneficial effects from polyunsaturated fatty acids.[6] In a randomized double-blind, placebo controlled trial of a high dose and low dose 18:3 n-6 rich oil and placebo control, high dose had significantly decreasing the relapse rate and the progression of disease.[20] In the present study, the percentage of PUFA from total energy was lower than the recommendations in MS patients. A study was performed to investigate whether supplementation with fish oil given influenced the clinical outcome in newly diagnosed MS patients. There was a significant reduction in the mean exacerbation rate and the mean Expanded Disability Status Scale (EDSS) as compared to pre-study values. The plasma total phospholipids n-3 fatty acids increased and n-6 fatty acids decreased significantly. The results suggest that fish oil supplementation can improve clinical outcome in patients with newly diagnosed MS.[21]

In acute and chronic phases of MS, n-3 PUFAs appear to have beneficial actions by suppressing inflammation, inhibiting the production of pro-inflammatory cytokines, mediating the beneficial actions of granulocyte colony-stimulating factor, granulocyte-macrophage colony-stimulating factor and transforming growth factor-β and preventing neuronal death.[22] A pilot study suggests that a low fat diet with supplemental n-3 was associated with beneficial effects on quality of life, clinical and immunological parameters in relapsing-remitting MS patients.[4] On the other hand, the results of a study do not support relations between intakes of total fat or major specific types of fat and the risk of MS.[7] In this study, omega-3 fatty acid intake of the patients were met the recommendations. Antioxidant nutrients may reduce the risk of MS. In a recent case-control study, vitamin C intake was significantly inversely associated with MS risk among women. However, the authors found no associations between intakes of fruits and vegetables and risk of MS.[23] Vitamins A, C, and E may decrease free radical induced cellular injury and this is the rationale for their use in MS. However, until now there is no evidence found which supports the role of these vitamins in etiology of MS.[17] Antioxidants are considered as important in MS as they are necessary to inhibit oxidation of EFAs by free radicals in membrane phospholipids and protect the integrity of myelin. There is a growing interest in dietary antioxidants and disease activity in MS. Antioxidant deficiencies may develop during the course of MS as a result of chronic inflammation that is accompanied by increased oxidative stress.[2] Levels of antioxidants (α-tocopherol, beta-carotene, retinol, ascorbic acid) were decreased in the serum or cerebrospinal fluid of MS patients during an attack. In MS patients during an attack, a significant increase lipid oxidalibility for plasma and a strong decrease in plasma total antioxidant capacity were detected.[24] Low antioxidant activity in white matter may lead to increased lipid peroxidation by reactive oxygen species and subsequent damage. In a prospective

study, no significant associations were found sbetween intakes of vitamins C or E, carotenoids or fruits, and vegetables and risk for MS.[25] In this study, we observed an approximately 90% of patients' antioxidant vitamin intakes that met the DRI recommendations.

Risk factor which has been associated with MS is vitamin D. Vitamin D might be one of the attractive candidates among various environmental factors that have been proposed to contribute to the development of MS.[12] Hypovitaminosis D may be a candidate for risk-modifying factor of MS. The high level of circulationg vitamin D in the blood are associated with a reduce risk of developing MS.[26] The effect of vitamin D on MS risk has been less studied. Until now, there is only one study which has directly analyzed the risk of MS based on the serum level of 25-hydroxy vitamin D before MS occurred.[1,17] Some studies suggest a relationship between low serum vitamin D levels and disease activity in relapsing-remitting MS, but the causality of this relationship has not been proven. Lower vitamin D levels have been reported during relapses than remission in relapsing-remitting MS patients.[27-29] Serum level of 25 (OH)D were associated with both relapse rate and disability in MS patients.[30-32] Epidemiological studies have shown an increase in MS frequency with increasing distance from the equator, which inversely correlates with duration and intensity of sunlight.[25] The benefits from vitamin D could either be due to its beneficial effects on nervous system or immune system regulation. There is data showing that vitamin D regulates myelin production by oligodendrocytes as well as other neuronal processes.[17] Epidemiological and experimental evidence suggests that high levels of vitamin D, a potent immunomodulator, may decrease the risk of MS.[33] The study was conducted to examine whether levels of 25-OH vitamin D are associated with risk of MS. The result of study suggest that high circulating levels of vitamin D are associated with a lower risk of MS.[33] In this study, the mean serum vitamin D level was 11.3±6.22 ng/ml. The 16.7% of patients' serum vitamin D levels was below the reference ranges. Dietary vitamin D intake was examined directly in relation to risk of MS in 2 large cohorts of women. No association was found between vitamin D from food and MS incidence.[34] Adequate vitamin D intake reduces inflammatory cytokines; thus, inadequate vitamin D intake contributes to inflammation and consequently, development MS. Poor vitamin D status has been associated with increased risk for development of MS.[35] Multiple sclerosis and vitamin B12 deficiency have common inflammatory and neurodegenerative pathophysiological characteristics. Additionally, low levels of vitamin B12 have been demonstrated in MS patients. Recent studies suggest that vitamin B12 has important myelin formation, immunmodulatory and neurotrophic effects. Vitamin B12 deficiency may cause to formation of defective central myelin, which triggers the autoimmune process. These observations suggest further studies of the need to close monitoring of vitamin B12 levels as well as the potential requirement for supplementation of vitamin B12 alone or in combination with the immunotherapy for MS patients.[36] Vitamin B12 deficiencies and MS participate features of soreness and weakness of the legs and arms, difficulty in walking, diminished sensory perception, difficulty in speaking, memory loss, jerking of limbs, fatigue and paralysis. Vitamin B12 anomalies have been linked to people with MS in quite a few studies. Some researchers think B12 deficits are a prime factor in MS.[37] In our study, the 6.3% of the patients' serum vitamin B12 levels was lower than the reference ranges, and the daily vitamin B12 intake of 32.4% of MS patients was lower than the DRI recommendations. In this study, there was a negative correlation between serum vitamin B12 levels and EDSS scores in men (data not shown).

Calcium and Magnesium are important in development structure and stability of myelin. In a study, a group of patients having MS was treated with dietary supplements containing Ca, Mg and vitamin D for period of 1-2 years. The number exacerbations observed during the program was less than one half the number expected from case histories.[38] In this study, dietary Ca intakes were insufficient in 29.7% and Mg in 24.3% of patients.

***Study limitations.*** First, the sample size is small and we included only 37 MS patients. 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. There is no control group. Further study should be carried out as a case-control study and should include hormone tests.

In conclusion, our data demonstrated that nutritional status of patients with MS is poor. Professional consultations are needed for the patients. Dietary management in MS should commence at diagnosis with an assessment of nutritional status and appropriate healthy eating advice. More researches are needed to assess the effect of nutrition onset of MS and the nutritional status of MS patients.

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