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The Association of Dietary Acid Load with Fatigue, Quality of Life, and Nutrient Adequacy Ratio in Multiple Sclerosis Patients

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ABSTRACT

Background: Multiple sclerosis (MS) is associated with many health-related problems and changes in diet were shown to help the patients reduce some symptoms. This cross-sectional study investigated the relationship between dietary acid load with fatigue, quality of life, and nutrient adequacy ratio in MS patients.

Methods: Totally, 283 MS patients were enrolled in Shiraz, Iran between June 2018 and February 2019. Dietary acid load indices including potential renal acid load (PRAL) and net endogenous acid production (NEAP) were determined for the patients. The level of fatigue and quality of life of the individuals were evaluated by the modified fatigue impact scale (MFIS) and the multiple sclerosis quality of life-54 questionnaires (MSQoL-54), respectively. Nutrient intake was determined to calculate the mean adequacy ratio (MAR) using a food frequency questionnaire (FFQ).

Results: The mean score of MAR, NEAP, and PRAL was 0.9±0.18, 87.71±44.86, and 36.27±33.81, respectively. After adjusting for confounders, a significant, negative and very weak association was observed between physical health composite (PHC) of the quality of life and NEAP (p=0.003) and PRAL (p=0.007). Also, a significant, negative, and very weak correlation was found between MAR and NEAP (p=0.006) and PRAL (p=0.028) in a crude model. Furthermore, after adjusting for confounders, the association between MAR and NEAP remained significant (p=0.003).

Conclusion: Our findings revealed that there might be an association between dietary acid load indices, physical dimension of MSQoL-54 and MAR.

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Introduction

Multiple sclerosis (MS) is a chronic inflammatory autoimmune disease characterized by demyelination and destruction of neurons in the central nervous system (1). The global prevalence of MS was estimated 2.8 million in 2020 showing a rise when compared to the prevalence in 2013 (2). Although the etiology of the disease is not clearly known, it seems that the interaction between environmental factors and genetic predisposition plays an important role in the immune system dysregulation (3). Among the clinical symptoms of MS, fatigue is the most prevalent one which can affect the quality of life of these patients (4). It seems that immune, nervous, metabolic, and endocrine systems are involved in the etiology of fatigue (5).

The role of diet as an anti-inflammatory and immunomodulatory agent has been mentioned in alleviating the symptoms and progression of MS disease (6). The positive effects of fruits, vegetables and low-fat dairy products and less meat consumption were demonstrated to reduce disability and fatigue and increase the quality of life in MS patients (7-9). Vegetables, fruits, milk, and yogurt are considered as base producing products, while Western diet, animal proteins, and cheese are regarded as acid producing ones (10). An increase in the intake of acid-producing foods can lead to an increase in hydrogen ions and an acid-base imbalance which can lead to metabolic disorders (11). The results of a cross-sectional study conducted on the elderly women showed that an increase in the dietary acid load was associated with an increase in weakness and a decrease in physical activity (12). In obese adults, the dietary acid load was shown to be related to the nutritional adequacy ratio and the quality of the diet (13). In in MS patients, the effect of dietary acid load on fatigue has been illustrated; but no significant relationship was found between dietary acid load and fatigue (14). As the relationship between dietary acid load with the quality of life and nutrient adequacy ratio in MS patients was not found in literature, and also there was very few evidences regarding the relationship between dietary acid load and fatigue in these patients, the present study was conducted to investigate the relationship between dietary acid load with fatigue, quality of life, and nutrient adequacy ratio in MS patients.

Materials and Methods

In a cross-sectional study, 283 patients with MS referring to Imam Reza Clinic and Shahid Chamran Hospital in Shiraz, Iran between June 2018 and February 2019 were enrolled. All patients were diagnosed by a neurologist according to McDonald's criteria .(15) The sample size was calculated based on the study of Cambil-Martín *et al.* (α=0.05 and 1-β=0.95) (16). Each of the 4 types of MS disease and an age range of 19-75 years were the inclusion criteria of the present study. Patients with other diseases such as renal disorders, cardiovascular diseases, endocrine problems, cancer, and metabolic disorders were excluded. In addition, pregnant or lactating patients were excluded from this study too. The aim of the present research was explained to all patients and a written informed consent was obtained from each patient to be enrolled in the study. The research was approved by the Ethics Committee of Shiraz University of Medical Sciences (IR.SUMS.REC.1397.140) and was carried out according to the Declaration of Helsinki.

Modified fatigue impact scale (MFIS), which is a 21-item questionnaire with three subscales of physical (Nine items), cognitive (ten items) and psychosocial (two items) was used to determine MS-related fatigue. The scale evaluated the impact of fatigue during the past 4 weeks. The total MFIS score ranged from 0 to 84, and a higher score indicated a higher fatigue effect on patient activities (17). In the present study, the valid and reliable Persian version of MFIS was used (18). The health-related quality of life (HRQoL) was assessed using the multiple sclerosis quality of life-54 (MSQoL-54) questionnaire. Two summary scores including physical health composite (PHC) and mental health composite (MHC) scores were derived from MSQoL questionnaire. Each composite score ranged from 0 to 100, and higher scores indicated a better quality of life (19). The reliability and validity of the Persian version of MSQoL-54 were investigated too (20).

The disability status and the disease progression of MS patients were evaluated by expanded disability status scale (EDSS). This scale evaluated the functional systems of the central nervous system, including the pyramidal, cerebellar, brain stem, sensory, visual, intestinal, bladder, cerebral and other functions. Its range was defined from 0 to 13 (with 0.5 increment intervals), and a higher score indicated a greater disability (21). In this study, the EDSS was categorized into three groups of mild: 0–4, moderate: 4.5–5.5 and severe: 6–10 (22).

Body weight was assessed by a digital scale (Seca, Germany) to the nearest 0.1 kg; while wearing light clothing with in absence of any shoes. Height was measured using a wall-mounted stadiometer (Seca, Germany) to the nearest 0.1 cm without shoes. Body Mass Index (BMI) was calculated as weight (in kilogram) divided by the square of height (in meter). A 168-item semi-quantitative food frequency questionnaire (FFQ) with confirmed validity and reliability was used to determine the patients' past year dietary intake (23). The patients were asked to specify the amount and frequency of consumption of each food item on a daily, weekly, monthly, or yearly basis. Then, the reported food intake was converted into grams per day. Nutritionist IV software (San Bruno, CA, USA, version 3.5.2) modified for Iranian foods was employed for nutrients analysis.

Nutrient adequacy ratio (NAR) was used to evaluate the patients' nutrient adequacy (24). It was determined for 14 nutrients including vitamin C, vitamin A, vitamin E, vitamin D, folate, phosphorus, iron, copper, selenium, calcium, magnesium, zinc, sodium, and potassium. NAR for each nutrient was the ratio of the patient's intake to the current recommended allowance for the individual's sex and age category based on Dietary Reference Intakes (DRIs). Its scale was considered from 0 to 1 and lower values illustrated insufficient intake of a nutrient. The overall evaluation of nutrient adequacy was obtained by mean adequacy ratio (MAR) that was computed from the sum of NAR divided by the number of nutrients (25). Dietary acid load indices were calculated using two methods of potential renal acid load (PRAL) (26, 27) and net endogenous acid production (NEAP) (28): PRAL (mEq/d)=(0.49×protein [g/d])+(0.037×phosphorous [mg/d])–(0.021×potassium [mg/d])–(0.013×calcium [mg/d])–(0.026×magnesium [mg/d]). NEAP (mEq/day)=(protein [g/d]×54.5/potassium [mEq/d])-10.2.

Data analysis was done using SPSS software (Version 23, Chicago, IL, USA). The quantitative data were presented as mean and standard deviation, while the qualitative data were presented as frequency and percentage. Data distribution normality was evaluated using the Kolmogorov–Smirnov test. The association between nutrient adequacy, fatigue and quality of life and dietary acid load indices were determined using partial correlation and Pearson correlation coefficient or the non-parametric Spearman's rank correlation coefficient. Statistical significance was specified at the level of $p<0.05$.

Results

The mean of MAR, NEAP, and PRAL was 0.9±0.18, 87.71±44.86, and 36.27±33.81, respectively. General and clinical characteristics of patients with MS were shown in Table 1. The mean age and weight of the participants were 38.34±9.95 years and 63.99±7.13 kg, respectively. Regarding the BMI category, 56.54% were in normal range and 87.63% were female. About half of the subjects (57.24%) were in undergraduate level of study. The duration of the disease was 6.27±3.35 years. Relapsing-remitting (81.27%) was the most common type of MS. According to EDSS, 87.63% of the patients were in the mild disability category. The MFIS score, PHC, and MHC were 49.31±8.57, 51.77±11.13, and 56.74±12.56, respectively.

Table 2 presents dietary intake of the patients with MS. The mean daily intake of energy, carbohydrate, protein, and fat was 2107.49±508.95 (Kcal), 284.50±78.85 (g), 50.28±12.57 (g), and 83.74±28.46 (g), respectively. The linear correlation between dietary acid load indices, nutrient adequacy, fatigue and quality of life was exhibited in Table 3. There was a significant, negative and very weak correlation between MAR and NEAP (p=0.006) and PRAL (p=0.028). However, MHC, PHC and MFIS had no significant correlation with dietary acid load indices. Table 4 demonstrates the partial correlation between dietary acid load indices, nutrient adequacy, fatigue and quality of life after adjusting for energy intake and gender variables. A significant, negative and very weak association was found between PHC and NEAP (p=0.003) and PRAL (p=0.007). However, the association between

Table 1: General and clinical characteristics of the patients with multiple sclerosis.

Variable	Frequency (percentage)/ Mean±SD
Age (year)	38.34±9.95§
Weight (kg)	63.99±7.13
BMI (kg/m^2)	24.877±2.77
BMI category	
Underweight (<18.5 kg/m^2)	1 (0.35)*
Normal (18.5-24.9 kg/m^2)	160 (56.54)
Overweight (25-29.9 kg/m^2)	108 (38.16)
Obese (>30 kg/m^2)	14 (4.95)
Gender	
Female	248 (87.63)
Male	35 (12.37)
Education	
Undergraduate	162 (57.24)
Bachelor of Science	106 (37.46)
Master of Science	15 (5.30)
Duration of disease (year)	6.27±3.35
Type of MS	
Relapsing-remitting	230 (81.27)
Clinically isolated syndrome	29 (10.25)
Primary progressive	21 (7.42)
Secondary progressive	3 (1.06)
EDSS	
0-4	248 (87.63)
4.5-5.5	27 (9.54)
6-10	8 (2.83)
MFIS	49.31±8.57
Physical subscale	23.08±5.82
Cognitive subscale	23.23±5.57
Psychosocial subscale	3.01±1.56
MSQoL-54	
PHC	51.77±11.13
MHC	56.74±12.56

EDSS: expanded disability status scale; MFIS: modified fatigue impact scale; MHC: mental health composite; MS: multiple sclerosis; MSQoL-54: multiple sclerosis quality of life-54; PHC: physical health composite; SD: standard deviation; §: Mean±SD; *: Frequency (percentage).

Table 2: Daily dietary intake of patients with multiple sclerosis.

Daily dietary intakes	Mean±SD
Energy intake (kcal)	2107.49±508.95
Carbohydrate (gr)	284.50±78.85
Protein (gr)	50.28±12.57
Fat (gr)	83.74±28.46
Vitamin A (µg RE/day)	400.32±231.60
Vitamin E (mg/day)	8.60±3.86
Vitamin D* (µg/day)	11.63±6.39
Vitamin C (mg/day)	86.83±49.81
Folate (µg/day)	261.21±113.98
Calcium (mg/day)	633.44±216.19
Phosphorus(mg/day)	869.88±195.26
Zinc (mg/day)	7.55±2.47
Magnesium (mg/day)	235.94±97.10
Iron (mg/day)	11.14±3.69
Copper (µg/day)	1216.5±342.02
Selenium (µg/day)	78.45±31.44
Potassium (mg/day)	1950.34±323.12
Sodium (mg/day)	2324.98±1048.87

*Vitamin D intake is the sum of dietary vitamin D and vitamin D supplement prescribed by the physician; RE: retinol equivalent; SD: standard deviation.

MAR and NEAP (*p*=0.003) remained significant, but not between MAR and PRAL. No significant association was found between MFIS and NEAP and PRAL.

Discussion

In the present study, we found a significant, negative, and very weak association between NEAP and PRAL and PHC. No other study was available to evaluate the relationship between dietary acid load indices and quality of life in MS patients. However, in a study carried out on elderly Japanese women, the higher dietary acid load was associated with higher incidence of weakness and low physical activity. In this study, the short-form 36-item health survey (SF-36) was used to evaluate the weakness and metabolic equivalent-hours score per day based on several activities (12). A study conducted on a large sample of MS patients, dietary habits including the use of vegetables, fruits, dairy, and meat intake were assessed online. The results showed a significant positive association between high intake of vegetables and fruits with physical and mental aspects of health-related quality of life (HRQOL). In addition, a higher score of PHC and MHC was found in patients who did not receive any dairy product or meat (7). Other studies found a positive relationship between dietary acid load and the inflammatory process due to the development of metabolic acidosis (29, 30). In MS disease, intake of fruits and vegetables could affect the inflammation process (31), in addition to the fact that these food compounds were base producing and help balance the acid base through the exchange of hydrogen ions in the nephrons and neutralization of electrons (32).

On the other hand, previous studies have illustrated increasing body fat mass to be associated with physical disability (33-35). In a cross-sectional study of physical education students aged 18–25 years, dietary acid load was evaluated based on

Table 3: The relationship between fatigue, quality of life, nutrient adequacy and dietary acid load indices of patients with multiple sclerosis.

Variable	NEAP		PRAL	
	r	*P* value	r	*P* value
MFIS	0.010	0.870	0.024	0.692
PHC	-0.104	0.081	-0.112	0.060
MHC	-0.033	0.580	-0.026	0.663
MAR	-0.162	0.006*	-0.131	0.028*

**P* value <0.05; Linear correlation; NEAP: net endogenous acid production; MFIS: modified fatigue impact scale; MHC: mental health composite; PHC: physical health composite; MAR: Mean Adequacy Ratio; PRAL: potential renal acid load; r: correlation coefficient.

Table 4: The relationship between fatigue, quality of life, nutrient adequacy and dietary acid load indices of patients with multiple sclerosis$.

Variable	NEAP		PRAL	
	r	*P* value	r	*P* value
MFIS	0.050	0.408	0.067	0.261
PHC	-0.178	0.003*	-0.160	0.007*
MHC	-0.017	0.775	-0.009	0.887
MAR	-0.174	0.003*	-0.117	0.050

**P* value <0.05; Partial correlation; NEAP: net endogenous acid production; MFIS: modified fatigue impact scale; MHC: mental health composite; PHC: physical health composite; MAR: Mean Adequacy Ratio; PRAL: potential renal acid load; r: correlation coefficient. $Adjusted variables for energy intake and gender.

PRAL and NEAP that was positively correlated with fat mass, after adjusting for confounders (36). Recently, it has been reported that patients with MS had higher fat mass which was related to a higher disability and a lower HRQOL (37). This issue may be due to the effects of excess fat mass on biological mechanisms such as inflammation and psychological functions (37). Some studies have reported that increasing body fat can be associated with pain intensity, and this association has been shown in MS patients (38, 39). Another cross-sectional study conducted on diabetic patients also revealed a positive significant relationship between PRAL and fat mass (40).

Another finding of the current study was a significant, negative, and very weak correlation between MAR and NEAP and PRAL in a crude model. An investigation on obese women displayed that greater dietary acid load indices were associated with a decrease in MAR (13). As previously mentioned, MAR was calculated based on 14 micronutrients. Some components of MAR, including phosphorus, calcium, magnesium and potassium can directly affect acid load indices; however, other components might indirectly determine acid load indices, which indicate the amount of protein, vegetable, and fruit consumption (13).

No significant association was observed between fatigue score and dietary acid load indices. In line with our study, a recent research that investigated long-term dietary acid load correlation with fatigue in MS patients found no relationship (14). The main strength of this study was the large sample size. However, the present study had some limitations, such as not investigating the relationship between food groups and the dietary acid load, as well as the cross-sectional design of the study, which does not express the causal relationship between the indicators. Additionally, the calculation of acid load indices based on FFQ can overestimate or underestimate the levels.

Conclusion

The result of the current study indicated that an increase in the dietary acid load could reduce the quality of life in a physical dimension. In addition, a significant relationship was found between the nutrient adequacy ratio and dietary acid load indices. Nevertheless, prospective studies are necessary to clarify these findings.

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Authors' Contribution

ZMSF: data collection, research idea, writing and drafting the manuscript. ZM: supervised the study, study design, research idea, critical revision of the manuscript and editing. SI: data collection, revision of the manuscript. MF: study design, data analysis and interpretation. All authors read and approved final manuscript.

Conflict of Interest

None declared.

References

1 Mazloum Z, Razmjouei N, Hejazi N, et al. Food Insecurity in Patients with Multiple Sclerosis and Its Association with Anthropometric Measurements. *Int J Nutr Sci.* 2017;2:80-84.

2 Walton C, King R, Rechtman L, et al. Rising prevalence of multiple sclerosis worldwide: Insights from the Atlas of MS, third edition. *Mult Scler.* 2020;26:1816-21. DOI: 10.1177/1352458520970841. PMID: 33174475.

3 Mehrabani G, Gross DP, Aminian S, et al. Comparison of fitbit one and activPAL3TM in adults with multiple sclerosis in a free-living environment. *J Meas Phys Behav.* 2021;4:257-65. doi: 10.1123/jmpb.2020-0066.

4 Mehrabani G, Aminian S, Norton S, et al. Preliminary efficacy of the "SitLess with MS" intervention for changing sedentary behaviour, symptoms, and physical performance in multiple sclerosis. *Disabil Rehabil.* 2022;44:6374-6381. doi: 10.1080/09638288.2021.1966520. PMID: 34433359.

5 Manns PJ, Mehrabani G, Norton S, et al. The SitLess With MS Program: Intervention Feasibility and Change in Sedentary Behavior. *Arch Rehabil Res Clin Transl.* 2020;2:100083. doi: 10.1016/j.arrct.2020.100083. PMID: 33543106.

6 Mehrabani G, Aminian S, Mehrabani G, et al. Dietetic Plans within the Multiple Sclerosis Community: A Review. *Int J Nutr Sci.* 2019;4:14-22. doi: 10.30476/IJNS.2019.81531.1007.

7 Hadgkiss EJ, Jelinek GA, Weiland TJ, et al. The association of diet with quality of life, disability, and relapse rate in an international sample of people with multiple sclerosis. *Nutr Neurosci.* 2015;18:125-36. DOI: 10.1179/1476830514Y.0000000117. PMID: 24628020.

8 Simpson-Yap S, Nag N, Probst Y, et al. Prospective associations of better quality of the diet with improved quality of life over 7.5 years in people with multiple sclerosis. *Mult Scler Relat Disord*. 2022;60:103710. DOI: 10.1016/j.msard.2022.103710. PMID: 35219239.
9 Kirkland H, Campbell J, Reece J, et al. Higher diet quality is associated with short and long-term benefits on SF-6D health state utilities: a 5-year cohort study in an international sample of people with multiple sclerosis. *Qual Life Res*. 2023;32:1883-96. DOI: 10.1007/s11136-023-03361-w. PMID: 36821020.
10 Rodrigues Neto Angéloco L, Arces de Souza GC, Almeida Romão E, et al. Alkaline Diet and Metabolic Acidosis: Practical Approaches to the Nutritional Management of Chronic Kidney Disease. *J Ren Nutr*. 2018;28:215-20. DOI: 10.1053/j.jrn.2017.10.006. PMID: 29221627.
11 Williams RS, Heilbronn LK, Chen DL, et al. Dietary acid load, metabolic acidosis and insulin resistance - Lessons from cross-sectional and overfeeding studies in humans. *Clin Nutr*. 2016;35:1084-90. DOI: 10.1016/j.clnu.2015.08.002. PMID: 26299332.
12 Kataya Y, Murakami K, Kobayashi S, et al. Higher dietary acid load is associated with a higher prevalence of frailty, particularly slowness/weakness and low physical activity, in elderly Japanese women. *Eur J Nutr*. 2018;57:1-12. DOI: 10.1007/s00394-017-1449-4. PMID: 28405820.
13 Fatahi S, Qorbani M, P JS, et al. Associations between dietary acid load and obesity among Iranian women. *J Cardiovasc Thorac Res*. 2021;13:285-97. DOI: 10.34172/jcvtr.2021.44. PMID: 35047133.
14 Saul A, Taylor BV, Blizzard L, et al. Long-term dietary acid load is associated with depression in multiple sclerosis, but less evidence was found with fatigue and anxiety. *Mult Scler Relat Disord*. 2023;69:104415. DOI: 10.1016/j.msard.2022.104415. PMID: 36434910.
15 Polman CH, Reingold SC, Banwell B, et al. Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. *Ann Neurol*. 2011;69:292-302. DOI: 10.1002/ana.22366. PMID: 21387374.
16 Cambil-Martín J, Galiano-Castillo N, Muñoz-Hellín E, et al. Influence of body mass index on psychological and functional outcomes in patients with multiple sclerosis: a cross-sectional study. *Nutr Neurosci*. 2016;19:79-85. DOI: 10.1179/1476830514Y.0000000156. PMID: 25225836.
17 Fisk JD, Pontefract A, Ritvo PG, et al. The impact of fatigue on patients with multiple sclerosis. *Can J Neurol Sci*. 1994;21:9-14. PMID: 8180914.
18 Harirchian MH, Nasergivechi S, Maddah M, et al. Evaluation of the Persian version of modified fatigue impact scale in Iranian patients with multiple sclerosis. *Iran J Neurol*. 2013;12:32-4. PMID: 24250896.
19 Vickrey BG, Hays RD, Harooni R, et al. A health-related quality of life measure for multiple sclerosis. *Qual Life Res*. 1995;4:187-206. DOI: 10.1007/BF02260859. PMID: 7613530.
20 Ghaem H, Borhani Haghighi A, Jafari P, et al. Validity and reliability of the Persian version of the multiple sclerosis quality of life questionnaire. *Neurol India*. 2007;55:369-75. DOI: 10.4103/0028-3886.33316. PMID: 18040110.
21 Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology*. 1983;33:1444-52. DOI: 10.1212/wnl.33.11.1444. PMID: 6685237.
22 Kamali-Sarvestani E, Nikseresht A, Aflaki E, et al. TNF-alpha, TNF-beta and IL-4 gene polymorphisms in Iranian patients with multiple sclerosis. *Acta Neurol Scand*. 2007;115:161-6. DOI: 10.1111/j.1600-0404.2006.00743.x. PMID: 17295710.
23 Mirmiran P, Esfahani FH, Mehrabi Y, et al. Reliability and relative validity of an FFQ for nutrients in the Tehran lipid and glucose study. *Public Health Nutr*. 2010;13:654-62. DOI: 10.1017/S1368980009991698. PMID: 19807937.
24 Guthrie HA, Scheer JC. Validity of a dietary score for assessing nutrient adequacy. *J Am Diet Assoc*. 1981;78:240-5. PMID: 7217578.
25 Hatløy A, Torheim LE, Oshaug A. Food variety--a good indicator of nutritional adequacy of the diet? A case study from an urban area in Mali, West Africa. *Eur J Clin Nutr*. 1998;52:891-8. DOI: 10.1038/sj.ejcn.1600662. PMID: 9881884.
26 Remer T, Manz F. Estimation of the renal net acid excretion by adults consuming diets containing variable amounts of protein. *Am J Clin Nutr*. 1994;59:1356-61. DOI: 10.1093/ajcn/59.6.1356. PMID: 8198060.
27 Remer T, Dimitriou T, Manz F. Dietary potential renal acid load and renal net acid excretion in healthy, free-living children and adolescents. *Am J Clin Nutr*. 2003;77:1255-60. DOI: 10.1093/ajcn/77.5.1255. PMID: 12716680.
28 Frassetto LA, Todd KM, Morris RC, et al. Estimation of net endogenous noncarbonic acid production in humans from diet potassium and protein contents. *Am J Clin Nutr*. 1998;68:576-83. DOI: 10.1093/ajcn/68.3.576. PMID: 9734733.

29 Giugliano D, Ceriello A, Esposito K. The effects of diet on inflammation: emphasis on the metabolic syndrome. *J Am Coll Cardiol*. 2006;48:677-85. DOI: 10.1016/j.jacc.2006.03.052. PMID: 16904534.

30 Wu T, Seaver P, Lemus H, et al. Associations between Dietary Acid Load and Biomarkers of Inflammation and Hyperglycemia in Breast Cancer Survivors. *Nutrients*. 2019;11:1913. DOI: 10.3390/nu11081913. PMID: 31443226.

31 Riccio P, Rossano R, Liuzzi GM. May diet and dietary supplements improve the wellness of multiple sclerosis patients? A molecular approach. *Autoimmune Dis*. 2011;2010:249842. DOI: 10.4061/2010/249842. PMID: 21461338.

32 Osuna-Padilla IA, Leal-Escobar G, Garza-García CA, et al. Dietary Acid Load: mechanisms and evidence of its health repercussions. *Nefrologia (Engl Ed)*. 2019;39:343-54. DOI: 10.1016/j.nefro.2018.10.005. PMID: 30737117.

33 Sipilä S, Koskinen SO, Taaffe DR, et al. Determinants of lower-body muscle power in early postmenopausal women. *J Am Geriatr Soc*. 2004;52:939-44. DOI: 10.1111/j.1532-5415.2004.52261.x. PMID: 15161458.

34 Visser M, Harris TB, Langlois J, et al. Body fat and skeletal muscle mass in relation to physical disability in very old men and women of the Framingham Heart Study. *J Gerontol A Biol Sci Med Sci*. 1998;53:M214-21. DOI: 10.1093/gerona/53a.3.m214. PMID: 9597054.

35 Visser M, Langlois J, Guralnik JM, et al. High body fatness, but not low fat-free mass, predicts disability in older men and women: the Cardiovascular Health Study12. *Ame J Clin Nutri*. 1998;68:584-90. DOI: 10.1093/ajcn/68.3.584. PMID: 9734734.

36 Mansordehghan M, Daneshzad E, Basirat V, et al. The association between dietary acid load and body composition in physical education students aged 18-25 years. *J Health Popul Nutr*. 2022;41:58. DOI: 10.1186/s41043-022-00340-8. PMID: 36529754.

37 Pilutti LA, Motl RW. Body composition and disability in people with multiple sclerosis: A dual-energy x-ray absorptiometry study. *Mult Scler Relat Disord*. 2019;29:41-7. DOI: 10.1016/j.msard.2019.01.009. PMID: 30658263.

38 Marck CH, De Livera AM, Weiland TJ, et al. Pain in People with Multiple Sclerosis: Associations with Modifiable Lifestyle Factors, Fatigue, Depression, Anxiety, and Mental Health Quality of Life. *Front Neurol*. 2017;8:461. DOI: 10.3389/fneur.2017.00461. PMID: 28928713.

39 Janke EA, Collins A, Kozak AT. Overview of the relationship between pain and obesity: What do we know? Where do we go next? *J Rehabil Res Dev*. 2007;44:245-62. DOI: 10.1682/jrrd.2006.06.0060. PMID: 17551876.

40 Kord Varkaneh H, Fatahi S, Rahmani J, et al. Association of dietary acid load with body composition and inflammatory biomarkers in patients with type 2 diabetes. *Qom Univ Med Sci J*. 2018;12:63-72. (In Persian)