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Nutrition and multiple sclerosis severity: how diet and lifestyle choices shape disease course

In recent decades there is an interest in the effect of diet and lifestyle on Multiple Sclerosis (MS) symptoms and disease activity. Modulation of inflammation through modifiable factors, such as diet and lifestyle habits potentially related to the incidence of MS and its complications.

Objective — to explore the association of nutrition and lifestyle with the MS course and investigate dietary habits and meeting recommended dietary intake in patients with MS in Ukraine.

Materials and methods. A total of 28 patients diagnosed with MS, aged 18 years and older receiving inpatient and outpatient care in Kyiv City Clinical Hospital # 4, participated in this singlecenter crosssectional study. Data were collected from validated and adapted EPICNorfolk Food Frequency Questionnaire (FFQ) obtained from participants, medical records and neurological exam during November 2024 — January 2025. Nutrient data analysis was performed via the FETA software (developed by the MRC Epidemiology Unit, University of Cambridge). As a reference for recommended dietary intake, data from the Dietary Guidelines for Americans, 2020—2025, were used. The onesample ttest, ttest, Wilcoxon signedrank test for one sample were used to assess the differences between the sample and the reference data. Mann—Whitney tests were used for assessing differences between nutrient item and disability and severity score among MS patients. The chisquared test was used to analyse categorical data.

Results and discussion. The study encompassed a cohort of 28 patients with MS, consisting of 18 (64.3 %) women and 10 (35.7 %) men, median age — 34 (IQR 31.4—36.6).). This study demonstrates that the total energy value of the diet in the study group was lower from the recommended values based on age and level of physical activity ($p < 0.001$). The study showed that protein ((91.07 ± 51.56) g/day) intake among participants was significantly higher than the recommended, $p < 0.0001$. On micronutrient level, we also found that patients had significantly reduced dietary intake of vitamin D compared to recommended values $p < 0.0001$. Sodium intake among all participants ((2747.13 ± 1272.51) mg/day) was significantly higher than the recommended 2300 mg/day. Furthermore, a trend was observed suggesting that sweet consumption may influence disease severity (moderate effect size, $r = -0.32$, 95% CI (−0.65, 0.11)), and that smoking may be moderately associated with disability (effect size $r = -0.30$, 95 % CI (−0.63, 0.12)). However, neither trend reached statistical significance ($p = 0.14$ and $p = 0.12$), indicating the need for further research in larger cohorts to confirm these preliminary findings.

Conclusions. The study results indicate that the total dietary energy intake among MS patients was lower than the values recommended for their age and physical activity. We found that protein and sodium intakes in MS patients are significantly higher than recommended value and the consumption of vitamin D through food is below recommended standard.

Keywords: nutrition, multiple sclerosis, multiple sclerosis severity, Food Frequency Questionnaire, EDSS.

Multiple sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system that causes neurological impairment which mainly affects young adults [1]. The cause of MS remains so far unknown, but it has an immune-mediated basis and occurs in genetically susceptible individuals [4]. Other than genetic, various environmental factors seem to play a role in the development of MS. Microbial and

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viral infections, smoking, vitamin D, sun exposure, dietary habits may be relevant to its pathogenesis [12]. Several studies have reported that dietary factors influence the mechanisms of MS pathology, its development, and disease activity [12]. Modulation of milieu inflammation can be a protective factor against the occurrence, symptoms, and progression of MS [5]. As a modifiable factor, dietary patterns are closely related to the incidence of MS and its complications [6].

Physical exercise, assumed «healthy diet» and restoration of optimal concentrations of vitamin D have an anti-inflammatory effect and may ameliorate the course of many chronic inflammatory diseases, such as MS [7]. Smoking status is also a factor that has to be taken into the account. The epidemiological evidence reported to date suggests that smoking is probably associated with a greater risk of conversion from relapsing—remitting to secondary progressive MS [14].

Although the evaluation of nutritional status is important for all patients with chronic illnesses, the diet habits of patients with MS have not been adequately investigated [4]. Meta-analysis of epidemiological studies has demonstrated a relation between MS mortality and dietary fat, where intake of saturated fatty acids, mainly in animal fat products, correlates positively with MS mortality [2].

Although studies have shown the important role of nutrition in MS, the current therapy is not combined with any specific nutritional or lifestyle recommendation [13].

From our previous research there were found that a great portion of patients with MS are uncertain about dietary advice, they are unsatisfactory with nutrition recommendations both from the internet and from the doctors that is why didn't receive proper evidence-based dietary guidance [9].

According to the identified needs assessment of diet and nutrient intake is an approach that has been used to evaluate diet-disease association [13] in order to identify whether nutrients play a role in MS in the Ukrainian population.

Objective — to explore the association of nutrition and lifestyle with the multiple sclerosis course and investigate dietary habits and meeting recommended dietary intake in patients with multiple sclerosis in Ukraine.

Materials and methods

Design and Recruitment

A single-center, non-interventional cross-sectional study was conducted to assess and analyze the association between dietary and environmental habits and MS severity in the Ukrainian population. The study included a total of 28 patients undergoing inpatient and outpatient treatment from June 2024 to January 2025 at the Partners Multiple Sclerosis Department of Kyiv City Clinical Hospital #4, Kyiv, Ukraine.

All 28 patients were previously enrolled in our microbiome research project. The inclusion criteria were as follows: a diagnosis of MS according to the McDonald criteria (2017), gender: male/female, age: 20—40 years, consent to participate in the Food Frequency Questionnaire (FFQ)-survey, ability to maintain consistent contact and ability to use digital type of survey, signed informed consent after a full explanation of the research method. Significant cognitive-cooperative impairment and lack of compliance were considered exclusion criteria.

All the participants provided sociodemographic and other clinical data, which included age, sex, body mass index (BMI). Dietary intake was assessed using a validated semi-quantitative EPIC-Norfolk FFQ in Ukrainian language. Physical activity and smoking habits were also investigated. To evaluate the role of Ultra-processed food (UPF) in MS severity, the NOVA classification was applied for grouping FFQ food items. Patients were classified in two groups based on MS severity: mild to moderate and severe.

The study was conducted in accordance with the Declaration of Helsinki, and the protocol for this study received prior approval from the Bioethics and Research Ethics Committee of Bogomolets National Medical University during its meeting on November 07, 2018, as documented in Protocol No. 115, and informed consent was obtained from each subject.

Data collection

Anthropometric measures were conducted during the visit and BMI was calculated as weight (kg): $height^2/(m^2)$ and then patients were classified as under-weight patients, normal-weight, overweight, and obese.

Neurological assessment

Neurological examination was conducted by researchers during the hospital visits. The neurological disability of MS patients was quantified by the Expanded Disability Status Scale (EDSS), which rates seven neurological domains (Visual, Brainstem, Pyramidal (motor), Cerebellar (coordination), Sensory, Cerebral, and Bowel/bladder) in the context of a standard neurological examination. For MSSS calculation retrospective analysis of medical records was performed. We used a severity score categorized as «mild to moderate» if EDSS level is < 4 and «severe» if EDSS level is ≥ 4. EDSS >3.0 is used as a threshold to classify patients according to their disability status, where EDSS < 3.0 classified as no disability and ≥ 3.5 is disability.

Data about smoking habits, physical activity were collected through FFQ-survey. Physical activity level categorized as four domains: (I) low-activity (routine tasks: housework, shopping, etc.), (II) light activity (routine tasks + 30—60 minutes of moderate activity/day, e. g., walking 3—5 km/h, gymnastics, stretching, slow swimming, light cycling, etc.), (III) active (routine tasks + ≥ 60 minutes of moderate activity/day, e. g., walking 3—5 km/h, gymnastics, stretching, slow

swimming, light cycling, etc.), (IV) very active (active life-style + an additional 120 minutes of moderate activity/day + 60 minutes of intense activity, e. g., chopping wood, rock climbing, intense running, etc.). Smoking status was classified as: (I) non-smoker, (II) hookah-smoker, (III) cigarette smoker, (IV) e-cigarette use.

Dietary assessment

Each patient received instructions from the researcher on the rules about survey participation. We used a consistent explanation for survey completion. Dietary intake was assessed using the Ukrainian version of the food frequency questionnaire «the EPIC-Norfolk FFQ», which was previously adapted and validated for Ukrainian adults by [10]. This version consists of 124 food items and items that are not available or not commonly consumed in Ukraine, such as marmite, watercress, quiche, Horlicks and some kinds of margarine were removed. Median time duration for the questionnaire compilation was 35 min. Frequency options for each item were «never or less than once/month», «1—3 per month», «2—4 per week», «5—6 per week», «once a day», «2—3 per day», «4—5 per day», «≥ 6 per day»). For each food item of the FFQ, we indicated the medium serving size. The average food consumption was calculated (in g) by following the standard portion sizes and frequency indication calculated per day additionally. Energy, macro and micro-nutrient intakes were obtained using an open source FFQ EPIC Tool for Analysis (FETA). Additionally selected food items such as fast-foods, confectioneries, salty snacks, soft drinks, breakfast cereals, ultra processed meet, ultra processed fish, ultra processed dairy products, sauces and ice cream were group according to the NOVA classification into group UPF.

Each survey took approximately 30—55 minutes to complete. Some patients asked the researchers for clarification, and all confusion regarding questions was resolved. Strict confidentiality measures were observed throughout the study to protect participant privacy. All collected data was anonymized and securely stored.

We set recommended dietary calorie needs based on age, sex and physical activity levels of each participant and intake for macro- and micronutrients was assessed based on the Dietary Reference Intakes (U. S. Department of Agriculture and the U. S. Department of Health and Human Services, Dietary Guidelines for Americans).

Analysis

Descriptive statistics were used to summarize the demographic and clinical characteristics of the study population. Continuous variables were reported as mean (SD) or median (IQR), while categorical variables were presented as frequencies and percentages. The findings were presented in the form of diagrams, charts, and tables, allowing for an objective representative of results.

Wilcoxon signed-rank test (for non-normally distributed data) and one-sample t-test (for normally distributed data) were used to assess the differences between daily nutrients intake, physical activity level, smoke habits and MS severity categories.

Initially clinical data were entered into the RedCap and data obtained from the FFQ encoded in Excel sheets, then analyzed via FETA software to calculate nutrient data [8]. A p-value < 0.05 was considered statistically significant. Data analysis was conducted in R (v4.0.5, r-project.org).

Results

Study population

The study encompassed a cohort of 28 patients with MS, consisting of 18 (64.3 %) women and 10 (35.7 %) men, median age — 34 years old (IQR — 5.25). The majority of patients were diagnosed with relapsing-remitting MS, accounting for 92.9 % (n = 26) of the sample, while 6.9 % (n = 2) with primary-progressive MS. Based on the distribution of disease severity in the study sample, participants were categorized as «mild-moderate» (EDSS level is < 4; n = 17), and «severe» MS (EDSS level is ≥ 4; n = 11). EDSS median = 3; IQR = 2. Dietary restrictions were reported by 17.9 % of individuals in the sample (n = 5). The median BMI was 23.0 kg/m² (IQR = 7.0). 57.1 % (n = 16) participants constantly or very often took dietary supplements, 17.9 % (n = 5) used supplements inconsistently and 17.9 % (n = 5) didn't take supplements. Table 1 outlines the principal socio-demographic and clinical features of the study population.

Difference between daily macronutrients and micronutrients intake

In order to investigate the balance of patients' nutrition and their compliance to recommended norms of macro- and micronutrient intake for maintaining health, we compared actual consumption levels of proteins, sodium, fats, carbohydrates, vitamin D. Additionally, we assessed the difference in total food calories intake according to the recommended norms. The whole data is shown in Table 2.

The total energy value of the diet in the study group was significantly different from the recommended values according to age and level of physical activity p = 0.002 (women: (1983.58 ± 1166.67) kcal/day; men: (2055.97 ± 782.88) kcal/day) using Wilcoxon Signed-Rank Test.

When analyzed at the macronutrient level, a statistically significant difference was observed in protein consumption and no deviations were found in fat and total carbohydrate consumption. Protein intake among participants in both male and female groups ((91.07 ± 51.56) g/day) was significantly higher than the recommended (p < 0.0001). There is no statistically significant difference in total carbohydrate intake between males ((234.67 ± 106.02) g) and females

T a b l e 1

Baseline demographic and clinical features of the study group

Characteristics	Value
Total patients	28
Female	64.3 % (n = 18)
Male	35.7 % (n = 10)
Age, years (Me (IQR))	34, 5.25
BMI, kg/m² (Me (IQR))	23.0, 7.0
Relapsing-remitting MS	92.9 % (n = 26)
Primary-progressive MS	6.9 % (n = 2)
Severity	
• Mild to moderate (EDSS level is < 4)	17
• Severe (EDSS level is ≥ 4)	11
• Disability	
• EDSS < 3	12
• EDSS ≥ 3.5	16
Physical activity	
• low	10
• light	9
• active	8
• very active	1
BMI categories:	
• underweight (< 18.5 kg/m²)	8
• normal (18.5—24.9 kg/m²)	15
• overweight (25.0—29.9 kg/m²)	3
• obese (≥ 30.0 kg/m²)	2
Smoking:	
• non-smoker	14
• hookah-smoker	1
• cigarette smoker	7
• e-cigarette use	6

$((233.73 \pm 143.43)$ g; $p = 0.985)$, and the intake levels in both groups are within the recommended range. Mean fat intake was (84.54 ± 44.79) g/day which means that consumption levels are within the norms. On micronutrient level, we also found that patients had significantly reduced dietary intake of vitamin D compared to recommended values $(p < 0.0001.)$ The average intake of vitamin D in the sample was (3.46 ± 2.76) µg, which corresponds to approximately (138 ± 110) IU, well below the recommended 600 IU per day. Sodium intake among participants $((2747.13 \pm 1272.51)$ mg/day) was significantly higher than the recommended 2300 mg/day, $p = 0.026)$.

BMI among MS patients and severity score

The comparison of BMI between patients with mild-moderate and severe disease severity revealed no statistically significant difference. The median BMI was 21.00 in the mild-moderate group and 23.00 in the severe group, with a Wilcoxon signed-rank test of $W = 75.50$; $p = 0.41$, and a small effect size $r = -0.19$. Although a slightly higher BMI was observed in the severe group, the difference was neither statistically nor clinically meaningful in this sample.

Consumption of confections and severity score among MS patients

We previously calculated the consumption of each product based on the data on the amount of consumption and standard portions after filling out the questionnaire and looked at whether there was a relationship between the consumption of fast food, sauces, sweets, ultra-processed meat, fish and dairy products with the severity of MS. The analysis of dietary intake revealed that patients with severe disease reported higher consumption of confections compared to those with mild to moderate disease. The median intake was 14.80 g per day in the mild-moderate group and 70.30 g per day in the severe group. This difference was not statistically significant $(p = 0.17)$. However, the size effect is moderate $r = -0.32$; 95 % CI $[-0.65; 0.11]$. These findings imply

T a b l e 2

Mean nutrient intake among study participants

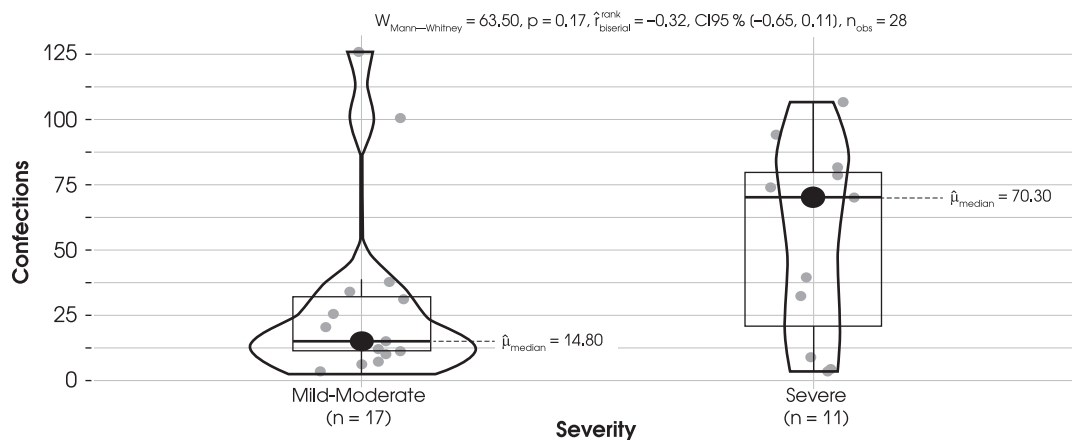| Characteristics	Male		Female		Total
	Mean intake	Recommended dietary intake mean	Mean intake	Recommended dietary intake mean	Mean intake
Total energy, kkal	2055.97 ± 782.88	2400.00	1983.58 ± 1166.67	2161.11	2025.81±1076.40
Total fat, g	93.19 ± 41.11	80.00	79.72 ± 47.14	70.00	84.54 ± 44.79
Total protein, g	82.05 ± 25.63	56.00	96.08 ± 61.64	46.00	91.07 ± 51.56
Total carbohydrates, g	234.66 ± 106.02	283.00	233.73 ± 143.43	273.00	234.06 ± 129.23
Vitamin D, µg	3.79 ± 2.81	15.00	3.27 ± 2.80	15.00	3.46 ± 2.76
Sodium, mg	3032.74 ± 1410.44	2300.00	2588.45 ± 1201.65	2300.00	2747.13 ± 1272.51

Fig. 1. Comparison of Confections Intake Across Disease Severity Groups

a possible trend but do not provide sufficient evidence to confirm a meaningful association between disease severity and confection consumption. A trend toward higher confection consumption among participants with severe disease course is shown in Fig. 1.

No statistical changes were found for other groups of UPF products (Ultra-processed fish p = 0.87, Ultra-processed meat p = 0.10, sources p = 0.24, fast food p = 0.92, ice cream p = 0.17, cereals p = 0.23, diary p = 0.07)

*Influence of smoking behavior
on severity score among MS patients*

A comparison of smoking behavior between individuals with and without disability was conducted using the Wilcoxon signed-rank test. The median smoking score was 1.00 in the no disability group (n = 13) and 3.00 in the disability group (n = 15). Although the p-value indicates a non-significant difference, the effect size (r = −0.30; 95 % CI [−0.63; 0.12] suggests a moderate association between smoking and disability. However, the wide confidence interval indicates uncertainty about the direction and magnitude of the association.

Discussion

In this study we investigated the difference between daily nutrient intake in MS patients in Ukraine compared to the recommended guidelines for healthy diet and influence of smoking behavior as part of recommendations for maintaining a healthy lifestyle. We found that protein, sodium and vitamin D intake have significantly changed in MS patients' diets. Study showed that patients with MS have increased levels of protein and sodium. High levels of protein intake and sodium correlate with our previous study, in which we found that MS patients were more likely to have enterotype 1, which is associated with high levels of animal protein, fast food, and sweets, compared to standard recommendations.

Our study found no significant difference between total fat, total carbohydrate intake and the

recommended value. Despite the fact that many studies have examined the role of fats, the results of case-control studies still remain inconsistent and debatable. Our results align with those of S.M. Zhang et al., 2000 study that did not support relations between intakes of total fat or major specific types of fat and the risk of MS [15].

The total energy value of the diet in the study group was significantly different from the recommended based on age and level of physical activity p < 0.001 (women: (1983.58 ± 1166.67) kcal/day; men: (2055.97 ± 782.88) kcal/day). Findings from M. Habek et al. [4] suggest that many patients suffer from various forms of malnutrition. In patients with MS malnutrition has been connected to impairment of the immune system, mental function, respiratory muscle strength and increased risk of specific nutrient deficiencies. Our results can be explained by several factors. First, according to our previous study on the assessment of the level of satisfaction with nutritional recommendations, patients are lost in unproven advice and may restrict their diet unjustifiably, including in the amount of calories [9]. On the other hand, the questionnaire assessment method involves recall and self-reporting biases. Despite the data obtained, the overall body mass index is not associated with the degree of disability in our study.

The decreased consumption of vitamin D through the diet is consistent with numerous studies about the role of vitamin D in MS pathogenesis. Data from research made by D. Eyles et al. [3] showing that vitamin D regulates myelin production by the oligo- dendrocytes as well as other neuronal processes. In our sample, more than half of the patients take vitamin D supplements as prescribed by their doctor consistently. However, our findings can be used in clinical practice to provide more precise recommendations for this category of patients who do not take vitamin D or taken irregularly, with further investigation of serum vitamin D levels.

Consistent with other studies about environment influence on autoimmune diseases, we detected

possible relationship between smoking and disability with moderate size effects (biserial rank = −0.32), indicating that smoking may affect the progression of the MS. Given the detrimental effects of smoking on overall health, patients should be informed about its possible influence on their general and neurological condition.

As for our knowledge, we first in Ukraine analyzed nutrition and dietary nutrients intake with validated EPIC-FFQ among MS patients.

Although our study provides new insights into the role of diet in MS patients, it is not without limitations. The observed trend between confections and severity of MS duration groups suggests no significance correlation but with moderate size effect and may warrant further investigation with a larger sample size. Also, the epidemiological distribution of this disease coincides with our group, but further studies should include more participants with progressive forms of the course.

Conclusions

This is the first nutritional assessment study among patients with MS in Ukraine. We conducted an analysis of nutritional intakes and compared findings with recommended standards. Additionally, we investigated the role of smoking behaviour and UPF consumption in MS patients using validated EPIC-FFQ.

This study demonstrates that protein intakes in MS patients are higher from recommended values. Sodium intake is also a concern. It has been established that the consumption of vitamin D with foods is below standard and therefore it is important to draw patients' attention to the importance of taking it as a supplement.

Preliminary trends suggest that smoking may be associated with disability and higher sweet intake with increased disease severity. Further studies with larger cohorts are needed to validate these findings.

Patient education on healthy balanced diet and smoking cessation may be a valuable component of disease management and should be considered in clinical practice.

Perspectives for further research include larger cohorts and longitudinal collection of samples, which will be required to investigate these clinical associations, including subjects with progressive forms of the disease.

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Вплив дієти та способу життя на тяжкість перебігу розсіяного склерозу

Протягом останніх десятиліть спостерігається зростання інтересу до вивчення впливу дієти та способу життя на перебіг розсіяного склерозу (РС). Ці чинники потенційно можуть модулювати запальну відповідь, а відтак пов'язані із захворюваністю на РС та його прогресуванням.

Мета роботи — вивчити зв'язок харчування та способу життя з тяжкістю перебігу розсіяного склерозу, а також харчові звички та дотримання рекомендованих норм споживання нутрієнтів у пацієнтів із розсіяним склерозом в Україні.

Матеріали та методи. В одноцентровому поперечному дослідженні взяли участь 28 пацієнтів віком понад 18 років із діагнозом РС, які отримували стаціонарну або амбулаторну допомогу в Київській міській клінічній лікарні № 4 у період із листопада 2024 р. до січня 2025 р. Проаналізовано відповіді на валідований і адаптований опитувальник щодо частоти прийому їжі (FFQ) EPIC-Norfolk, дані медичної документації та результати неврологічного огляду. Аналіз даних про поживні речовини проводили за допомогою програмного забезпечення FETA (розробленого відділом епідеміології Кембриджського університету). Як стандарт для оцінки відповідності харчування рекомендованому дієтичному споживанню використано дані з Дієтичних рекомендацій для американської популяції (2020—2025). Для оцінки відмінностей між вибіркою та еталонними даними застосовували t-критерій Стьюдента для незалежних вибірок, тест Вілкоксона для однієї вибірки, непараметричний тест Манна—Вітні.

Результати та обговорення. У досліджуваній когорті було 18 (64,3 %) жінок і 10 (35,7 %) чоловіків, середній вік — 34 (31.4—36.6) роки (міжквартильний розмах — 5,25). Установлено, що загальна енергетична цінність раціону була нижчою від рекомендованих значень з урахуванням віку та рівня фізичної активності ($p < 0,001$). Споживання білка (($91,07 \pm 51,56$) г/день) серед учасників було значно вищим за рекомендоване ($p < 0,0001$). Виявлено, що пацієнти значно менше споживали вітаміну D з їжею порівняно з рекомендованими значеннями ($p < 0,0001$), тоді як споживання натрію (($2747,13 \pm 1272,51$) мг/день) значно перевищувало рекомендовані 2300 мг/день. Зареєстровано тенденцію, яка свідчила про те, що споживання солодкого може впливати на тяжкість захворювання ($r = -0,32$; 95 % ДІ ($-0,65$; $-0,11$)), а куріння може бути помірно пов'язане з інвалідністю ($r = -0,30$; 95 % ДІ ($-0,63$; $-0,12$)). Однак обидві тенденції не мали статистичної значущості ($p = 0,14$ і $p = 0,12$), що вказує на необхідність проведення досліджень у більших когортах для підтвердження попередніх результатів.

Висновки. Результати дослідження свідчили про те, що енергетична цінність раціону хворих на РС була нижчою, порівняно із показниками, рекомендованими для відповідного віку та фізичної активності. Виявлено, що загальне споживання білка та натрію у хворих на РС значно перевищувало рекомендовані значення, а споживання вітаміну D з їжею було нижчим за показники здорового харчування.

Ключові слова: харчування, розсіяний склероз, перебіг розсіяного склерозу, анкета FFQ, EDSS.

ДЛЯ ЦИТУВАННЯ

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