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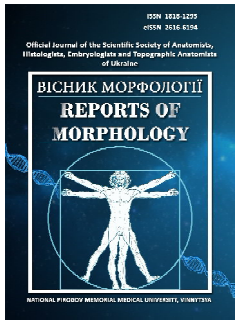

Modeling, based on discriminant analysis, the possibility of occurrence and features of the course of multiple sclerosis in Ukrainian women depending on the features of the structure and sizes of the body

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Considering the existence of different ways of the course of multiple sclerosis, the disability caused by this disease, modern medicine needs the creation of new, easy-to-use and cheap methods to solve this issue. Promising in this case may be the use of clinical anthropometry, which is already successfully used to predict the forms of development and severity of various diseases of various human organ systems. The objective of the study was to construct and analyze discriminant models predicting the likelihood and characteristics of multiple sclerosis progression in young Ukrainian women, based on anthropometric and somatotypological parameters. A clinical-laboratory and anthropo-somatotypological examination was conducted on 59 young Ukrainian women diagnosed with multiple sclerosis. Disability levels were assessed using the Expanded Disability Status Scale. The control group consisted of primary anthropometric and somatotypological data from 101 healthy Ukrainian women of the same age group (sourced from the database of the Scientific and Research Center of the National Pirogov Memorial Medical University, Vinnytsya). Discriminant models predicting the occurrence and progression of multiple sclerosis based on body anthropo-somatotypological parameters were constructed using the licensed "Statistica 6.0" software. The analysis revealed significant discrimination between healthy individuals and the general multiple sclerosis patient group, as evidenced by the discriminant equations (Wilks' Lambda=0.052, p<0.001). Key contributors to the discrimination models for distinguishing healthy women from those with multiple sclerosis included pelvic dimensions (37.50 %, contributing the most), body circumferences and head dimensions (25.0 % each), and the transverse lower thoracic diameter of the torso (12.5 %). Further analysis differentiated women with multiple sclerosis based on the severity of their symptoms mild, moderate, or moderately severe also demonstrated statistically significant differentiation (Wilks' Lambda=0.349, p<0.001). The most influential factors for mild, moderate, or moderately severe patients groups in these models were distal epiphyseal widths of long tubular bones in the extremities (33.33 %, contributing the most), pelvic conjugate diameter, maximum head length, the ectomorphic component of somatotype according to Heath-Carter, and the skeletal mass component according to Matiegka (each contributing 16.67 %). These findings underscore the importance of anthropometric and somatotypological parameters in predicting multiple sclerosis occurrence and progression severity in young Ukrainian women.

***Keywords**: nervous diseases, multiple sclerosis, anthropo-somatotypological body parameters, discriminant models, practically healthy and sick women.*

Introduction

Multiple sclerosis (MS) is a chronic, autoimmune, inflammatory and degenerative disease of the central nervous system, characterized by the destruction of the myelin sheath of neurons, the formation of sclerotic plaques and progressive damage to the nervous tissue. The disease is one of the leading causes of disability in

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young people in the world, as it most often affects people aged 20-40, a period of greatest social, professional and family activity. The pathology arises as a result of an autoimmune process in which the immune system attacks the myelin covering axons, causing nerve conduction disorders and causing numerous neurological symptoms. The symptoms of MS vary from moderate impairment of motor functions to severe disability, including loss of control over the limbs, impaired vision, speech, cognitive function and psychoemotional state, which significantly affects the quality of life of patients and their ability to social integration [6, 20].

MS has a wide geographical distribution, and the incidence of the disease varies depending on climatic, ethnic and socio-economic factors. In countries with a temperate climate, the incidence is much higher. For example, in Europe, the prevalence of MS ranges from 100 to 200 cases per 100,000 population, while in South Asia it is much lower 0.5-10 cases per 100,000 population [9, 12]. At the same time, in the Middle East and North Africa, the prevalence varies from 10 to 100 cases per 100,000 people, which confirms the influence of regional and genetic factors on the incidence of the disease [12]. Studies conducted in the United Kingdom demonstrate a steady increase in incidence, which may be associated with both improved diagnostic capabilities and an increase in the life expectancy of patients [16].

MS is classified into several forms depending on the course of the disease. The most common form is the relapsing-remitting form, which accounts for up to 80 % of new cases and is characterized by alternating periods of exacerbation and remission. The primary-progressive form, which occurs in 10-15 % of patients, is characterized by a gradual progression of symptoms from the very beginning without pronounced remissions. The secondary-progressive form occurs in most patients over time against the background of a relapsing-remitting course and indicates a deterioration in functional status. Benign MS is defined as a form with minimal symptoms and a low level of disability even many years after diagnosis [17, 24].

The pathogenesis of the disease involves a complex interaction of genetic and environmental factors. The main triggers are Epstein-Barr virus infection, vitamin D deficiency, smoking, and disruption of the intestinal microbiota. Patients with MS exhibit chronic inflammation, which activates a cascade of processes leading to demyelination, neuronal degeneration, and the formation of sclerotic plaques [17]. These processes underlie many of the clinical manifestations of MS, including pain, coordination disorders, limb weakness, visual impairment, and cognitive impairment. Pain, as one of the main symptoms, is reported in 50-75 % of patients, significantly affecting their quality of life [8]. Cognitive impairments, such as decreased attention, memory, and processing speed, are a serious problem, especially for young patients, as they complicate their professional activities and social adaptation [13].

MS not only leads to serious disability, but also represents a significant economic burden on the health care system. In Europe, the average cost of treating a patient per year ranges from €22,000 to €57,500 depending on the severity of the disease, with the main costs related to treatment, rehabilitation and disability [18]. High-cost disease modifiers, such as interferons and monoclonal antibodies, are important in reducing disease activity, but they impose an additional financial burden on patients and the healthcare system [20]. The psychosocial impact of MS is also significant. According to meta-analyses, depression and anxiety disorders are observed in 30-50 % of patients, which complicates treatment and reduces their quality of life [23].

Thus, MS remains a complex multifactorial pathology with serious medical, social and economic consequences [30]. Therefore, the development of methods to predict the course and risk of MS is a priority area for research.

The purpose of the study construction and analysis of discriminant models of the possibility of occurrence and features of the course of multiple sclerosis in young Ukrainian women depending on the features of anthropo-somatotypological body parameters.

Material and methods

In 59 young Ukrainian women (aged 25-44 according to the WHO age classification, 2015) diagnosed with multiple sclerosis, a clinical-laboratory and anthropological examination was conducted based on the Bunak V. V. schemes as modified by Shaparenko P. P. [26], somatotypological assessment using the Heath-Carter method [4], determination of body composition components using the formulas of Matiegka J. [19], and assessment of muscle mass components according to the formulas of the American Institute of Nutrition [27]. This research was performed at the Department of Nervous Diseases of the National Pirogov Memorial Medical University, Vinnytsya, and the medical center “Salutem” (Vinnytsya). Committee on Bioethics of National Pirogov Memorial Medical University, Vinnytsya (protocol № 10 from 10.12.2021) found that the studies do not contradict the basic bioethical standards of the Declaration of Helsinki, the Council of Europe Convention on Human Rights and Biomedicine (1977), the relevant WHO regulations and laws of Ukraine.

The diagnosis of multiple sclerosis was established according to the 2017 McDonald criteria [29]. The degree of disability was assessed using the Expanded Disability Status Scale (EDSS). The group of patients with mild impairments (EDSS 2.0-3.0) included 26 women; those with moderate impairments (EDSS 3.5-4.5) comprised 24 women; and the group with moderately severe impairments (EDSS 5.0-6.5) consisted of 9 women.

As the control group, primary anthropo-somatotypological parameters of 101 practically healthy young Ukrainian women of the same age group were taken from the database of the Research Center at the National

Pirogov Memorial Medical University, Vinnytsya.

Discriminant models of the likelihood of occurrence and characteristics of multiple sclerosis progression depending on the body structure and size features of Ukrainian women were developed using the licensed software package “Statistica 6.0.”

Results

It has been established that when dividing Ukrainian women into practically healthy and the general group of those with multiple sclerosis, considering anthropometric, somatotypological parameters, and body composition indicators, the classification matrix encompasses 100 % of cases. The discriminant variables distinguishing practically healthy women from those with multiple sclerosis are the conjugate diameter (CONJ), forearm circumference in the lower part (OBPR2), intercristal distance (CRIS), lower thoracic transverse diameter of the trunk (PNG), interspinous distance (SPIN), sagittal arc of the head (SAG_DUG), calf circumference in the lower part (OBG2), and the maximum width of the head (B_SH_GL). Among these parameters, the conjugate diameter and intercristal distance of the pelvis contribute most significantly to the discrimination. The combination of all identified anthropometric variables demonstrates pronounced discrimination (Wilks’ Lambda statistic=0.052; p<0.001) between practically healthy women and the general group of those with multiple sclerosis.

The classification indicators (Df) identified in our study enable categorizing the obtained measurements as “typical” for either the group of practically healthy women or those with multiple sclerosis. Below, the determination of the Df value is presented in the form of equations, where a Df value close to 351.5 indicates belonging to the group of practically healthy Ukrainian women, while a Df value near 296.7 corresponds to Ukrainian women with multiple sclerosis:

– Df (*for practically healthy women*)= CONJ×3.827 + OBPR2×1.473 + CRIS×1.692 + PNG×1.016 + SPIN×0.569 + SAG_DUG×13.01 - OBG2×0.366 + B_SH_GL×9.332 - 351.5;
– Df (*for the general group of women with multiple sclerosis*)= -CONJ×0.046 + OBPR2×3.198 + CRIS×0.029 + PNG×2.521 + SPIN×1.398 + SAG_DUG×11.09 + OBG2×1.126 + B_SH_GL×7.276 - 296.7;

where (here and in the following), pelvic dimensions in cm; girth dimensions of the body in cm; transverse dimensions of the torso in cm; head dimensions in cm.

As can be seen from Table 1, the calculated χ^2 criterion with the removal of consecutive roots confirms the statistical significance of both discriminant functions.

When Ukrainian women were categorized into those with multiple sclerosis with mild (EDSS 2.0-3.0), moderate (EDSS 3.5-4.5), and moderately severe (EDSS 5.0-6.5) impairments, considering anthropometric, somatotypological parameters, and body composition indicators, the classification matrix accounted for 76.92 % of cases with EDSS 2.0-3.0, 79.17 % of cases with EDSS 3.5-4.5, and 55.56 % of cases with EDSS 5.0-6.5. Overall, the classification matrix covered 74.58 % of cases. The discriminant variables distinguishing women with mild, moderate, and moderately severe impairments were the width of the distal epiphysis of the forearm (EPPR), the width of the distal epiphysis of the upper arm (EPPL), the conjugate diameter (CONJ), the maximum length of the head (B_DL_GL), the ectomorphic component of the somatotype according to Heath-Carter (LX), and the bone component of body mass according to Matiegka (OM). Among these parameters, the widths of the distal epiphyses of the forearm and upper arm contributed the most to the discrimination. The combination of all identified anthropometric and somatotypological variables demonstrated moderate discrimination (Wilks’ Lambda statistic=0.349; p<0.001) among Ukrainian women with multiple sclerosis and varying degrees of impairments.

Table 1. Report of step-by-step analysis with the inclusion of the χ^2 criterion for practically healthy and multiple sclerosis patients Ukrainian women taking into account anthropo-somatotypological body parameters.

	Eigen-value	Canonicl R	Wilks' Lambda	Chi-Sqr.	df	p-level
0	18.35	0.974	0.052	0.052	8	0.052

Notes: here and in the following table, Eigenvalue root value for each discriminant function; Canonicl R – canonical R value for different roots; Wilks` Lambda – Wilks` Lambda statistic; Chi-Sqr. – standard χ^2 test of consecutive roots; Df number of degrees of freedom; p-level p-level associated with the corresponding χ^2.

The determination of the Df value is presented below in the form of equations, where belonging to the group of Ukrainian women with multiple sclerosis and mild impairments is possible with a Df value close to 762.5; to the group with moderate impairments at a Df value close to 760.0; and to the group with moderately severe impairments at a Df value close to 794.3:

– Df (*for women with multiple sclerosis with mild impairments*)= -EPPR×46.50 + EPPL×180.9 - CONJ×1.908 + B_DL_GL×50.05 + LX×18.67 - OM×39.14 - 762.5;
– Df (*for women with multiple sclerosis with moderate impairments*)= -EPPR×37.53 + EPPL×179.0 - CONJ×1.560 + B_DL_GL×48.34 + LX×18.55 - OM×40.70 - 760.0;
– Df (*for women with multiple sclerosis with moderate to severe impairments*)= -EPPR×54.62 + EPPL×197.2 - CONJ×2.611 + B_DL_GL×50.25 + LX×19.78 - OM×42.05 - 794.3;

where, the width of the distal epiphyses of the long tubular bones of the limbs in cm; the components of the

somatotype in points; the indicators of the component composition of body weight in kg.

As can be seen from Table 2, the calculated χ^2 criterion with the removal of consecutive roots confirms the statistical significance of all discriminant functions.

Table 2. Report of a step-by-step analysis with the inclusion of the χ^2 criterion for Ukrainian women with multiple sclerosis with mild, moderate, and moderately severe disorders, taking into account anthropo-somatotypological body parameters.

	Eigen-value	Canonicl R	Wilks' Lambda	Chi-Sqr.	df	p-level
0	1.011	0.709	0.349	56.37	12	0.0000
1	0.426	0.547	0.701	19.00	5	0.0019

Notes: here and in the following table, Eigenvalue root value for each discriminant function; Canonicl R – canonical R value for different roots; Wilks` Lambda – Wilks` Lambda statistic; Chi-Sqr. – standard χ^2 test of consecutive roots; Df number of degrees of freedom; p-level p-level associated with the corresponding χ^2.

Discussion

Thus, in the classification of Ukrainian women into practically healthy and the general group of those with multiple sclerosis, the analysis of the obtained discriminant equations revealed statistically significant ($p<0.001$) and pronounced discrimination (Wilks' Lambda=0.052) based on the derived classification indicators (Df). The models distinguishing practically healthy women from the general group of those with multiple sclerosis include pelvic dimensions (37.50 %), body circumferences (25.00 %), head dimensions (25.00 %), and the transverse lower thoracic diameter of the torso (12.50 %). The greatest contribution to the discrimination between practically healthy women and the general group of those with multiple sclerosis was made by the conjugate diameter and the intercristal distance.

In the classification of Ukrainian women with multiple sclerosis into groups with mild, moderate, and moderately severe impairments, the analysis of the obtained discriminant equations revealed statistically significant ($p<0.001$) moderate discrimination (Wilks' Lambda=0.349) based on the derived classification indicators (Df). The models distinguishing women with mild, moderate, and moderately severe impairments included the widths of the distal epiphyses of long tubular bones of the limbs (33.33 %), the conjugate diameter, the maximum head length, the ectomorphic component of the somatotype according to Heath-Carter, and the bone component of body mass according to Matiegka (each at 16.67 %). The greatest contribution to the discrimination among women with mild, moderate, and moderately severe impairments was made by the widths of the distal epiphyses of the forearm and upper arm.

The substantially higher percentage of pelvic, torso, and head dimensions included in the discriminant models distinguishing healthy women from the general group of those with multiple sclerosis (75.00 % of all variables) and the percentage of the widths of distal epiphyses of long tubular bones of the limbs, pelvic dimensions, head dimensions, the ectomorphic component of the somatotype, and the bone component of body mass included in the discriminant models distinguishing women with mild, moderate, and moderately severe impairments (100 % of all variables), which according to the literature are highly genetically determined indicators [10], suggest a predominant genetic predisposition to both the development and progression of this multifactorial disease.

The relationship between multiple MS and anthropometric parameters is a complex and multifaceted issue that is at the center of current research. Anthropometric parameters, such as body mass index (BMI), fat distribution, and physical activity levels, have been shown to have a significant impact on the risk of developing MS, the course of the disease, and its clinical outcomes. One of the most important factors determining the relationship between MS and anthropometric parameters is BMI. A high BMI before the manifestation of MS can significantly increase the risk of developing this disease. In a large cohort study conducted by Cortese M. et al. [7], it was found that an increased BMI in adolescence is associated with a higher probability of MS in adulthood (relative risk is 2.0 for obese individuals compared with normal weight). Similar results were obtained in the study by Guerrero-Garcна J. D. J. et al. [11], where it was found that obesity contributes to systemic inflammation and increased levels of pro-inflammatory cytokines, which can activate autoimmune processes characteristic of MS.

On the other hand, excess weight also affects the course of the disease. A study by Stampanoni Bassi M. et al. [28] demonstrated that obesity enhances central inflammation and increases the risk of disability progression. High BMI was correlated with more severe clinical manifestations of MS, including a higher number of relapses and accelerated progression of the secondary progressive form of the disease. Similarly, Castro K. et al. [5] demonstrated that obesity modulates metabolic pathways, in particular through changes in ceramide metabolism, which may affect DNA methylation and the course of the disease.

The level of physical activity is also an important factor that can modify the risk of developing MS. According to a study by Sääksjärvi K. et al. [25], regular physical activity is associated with a reduced risk of MS, which is also supported by the study by Cortese M. et al. [7]. The authors emphasize that an active lifestyle can reduce systemic inflammation and improve immune regulation, which are key mechanisms of protection against autoimmune diseases.

The role of genetic and epigenetic factors in the association between anthropometry and MS remains an

important question. The work of Olsson T. et al. [22] emphasizes that genetic predisposition to obesity can interact with environmental factors, such as diet and physical activity, to influence the risk of MS. For example, the study of Amato M. P. et al. [1] suggested that vitamin D deficiency, characteristic of individuals with high BMI, may be a key mediator in the pathogenesis of MS.

In addition, some anthropometric changes may be secondary to MS. The study of Vikdahl M. et al. [31] reported a significant increase in central obesity in patients with early-stage MS, which may be a consequence of the disease-induced decrease in physical activity. Similarly, McKay K. A. et al. [21] noted that weight changes may be the result of both systemic inflammation and the side effects of glucocorticosteroids, which are often used to treat MS flare-ups.

The use of predictive models to examine the relationship between anthropometry and MS progression has also become an important area of research. As Brown F. S. et al. [3] noted, incorporating BMI and other anthropometric measures into predictive models can more accurately predict the risk of disability and relapse in patients with MS. F. B. Briggs et al. [2] noted that such approaches may contribute to the individualization of therapeutic strategies aimed at weight control and improving the physical condition of patients.

Overall, current evidence supports the important role of anthropometric factors in the pathogenesis, clinical course, and prognosis of MS [14, 15]. Future studies should focus on unraveling the precise mechanisms of these relationships, which will allow for improved preventive and therapeutic strategies for patients with MS.

Conclusions

1. Based on the specific anthropo-somatotypological body parameters, reliable discriminant models have been developed that allow for high-probability prediction of the risk of developing multiple sclerosis in young Ukrainian women (the classification matrix covers 100 % of cases, Wilks' Lambda=0.052; p<0.001) and moderate-probability assessment of disease progression characteristics (the classification matrix covers 74.58 % of cases, Wilks' Lambda=0.349; p<0.001).

2. The constructed models distinguishing practically healthy women from those with multiple sclerosis most frequently include pelvic dimensions (37.50 %), while the models differentiating women with mild, moderate, and moderately severe impairments due to multiple sclerosis most commonly incorporate the widths of the distal epiphyses of long tubular bones of the limbs (33.33 %).

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МОДЕЛЮВАННЯ, НА ОСНОВІ ДИСКРИМІНАНТНОГО АНАЛІЗУ, МОЖЛИВОСТІ ВИНИКНЕННЯ ТА ОСОБЛИВОСТЕЙ ПЕРЕБІГУ МНОЖИННОГО СКЛЕРОЗУ В УКРАЇНСЬКИХ ЖІНОК У ЗАЛЕЖНОСТІ ВІД ОСОБЛИВОСТЕЙ БУДОВИ ТА РОЗМІРІВ ТІЛА

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Зважаючи на існування різних шляхів перебігу множинного склерозу, інвалідизацію, що викликає дане захворювання, сучасна медицина потребує створення нових, простих у застосуванні і дешевих методик для вирішення даного питання. Перспективним у даному випадку може бути застосування клінічної антропометрії, що вже успішно застосовується для передбачення форм розвитку та тяжкості різноманітних захворювань різних систем органів людини. Мета дослідження – побудова та аналіз дискримінантних моделей можливості виникнення та особливостей перебігу множинного склерозу в українських жінок молодого віку в залежності від особливостей антропо-соматотипологічних параметрів тіла. Проведено клініко-лабораторне та антропо-соматотипологічне обстеження 59 українських жінок молодого віку, хворих на множинний склероз. Оцінка ступеня інвалідизації проводилася за допомогою шкали Expanded Disability Status Scale. В якості контрольної групи використані первинні антропо-соматотипологічні показники 101 практично здорової української жінки аналогічної вікової групи (взяті з банку даних науково-дослідного центру Вінницького національного медичного університету ім. М. І. Пирогова). Дискримінантні моделі можливості виникнення та особливостей перебігу множинного склерозу в залежності від антропо-соматотипологічних параметрів тіла побудовані в ліцензійному пакеті «Statistica 6.0». Встановлено, що при розподілі українських жінок на практично здорових та загальну групу хворих на множинний склероз, при аналізі отриманих дискримінантних рівнянь можлива достовірна виражена дискримінація (Wilks' Lambda=0,052, p<0,001) отриманих показників класифікації. До складу моделей між практично здоровими та загальною групою хворих на множинний склероз жінок входять розміри таза (37,50 %, вносять найбільший внесок у дискримінацію), обхватні розміри тіла та розміри голови (по 25,0 %), а також поперечний нижньогрудний діаметр тулуба (12,5 %). При розподілі українських жінок на хворих на множинний склероз з легкими, помірними та помірно-тяжкими порушеннями, при аналізі отриманих дискримінантних рівнянь також можлива достовірна середня дискримінація (Wilks' Lambda=0,349, p<0,001) отриманих показників класифікації. До складу моделей між хворими на множинний склероз із легкими, помірними та помірно-тяжкими порушеннями жінками входять ширина дистальних епіфізів довгих трубчастих кісток кінцівок (33,33 %, вносять найбільший внесок у дискримінацію), зрвнішня кон`югата, найбільша довжина голови, ектоморфний компонент соматотипу за Хіт-Картер та кістковий

компонент маси тіла за Матейко (по 16,67 %). Ці дані підкреслюють важливість антропометричних і соматотипологічних параметрів у прогнозуванні виникнення та тяжкості прогресування розсіяного склерозу у молодих українських жінок.
***Ключові слова**: нервові захворювання, множинний склероз, антропо-соматотипологічні параметри тіла, дискримінантні моделі, практично здорові та хворі жінки.*

Author's contribution

Gunas M. M. – conceptualization, formal analysis and validation, research, review writing and editing, methodology and writing of the original draft.
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