ORIGINAL ARTICLE

CONTENTS

Sexual dysfunction in multiple sclerosis: Associations with disability, fatigue, affective symptoms and brainstem lesions

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ABSTRACT

Aim: To assess the prevalence and severity of sexual dysfunction in patients with multiple sclerosis and its associations with clinical, neuropsychological, and MRI-related factors, considering the primary, secondary, and tertiary components of sexual dysfunction.

Materials and Methods: This cross-sectional observational study included 109 patients with multiple sclerosis (80 women, 73.4%; 29 men, 26.6%). Sexual dysfunction was assessed using the Multiple Sclerosis Intimacy and Sexuality Questionnaire-19 (MSISQ-19), including total and subscale scores. Cognitive function, fatigue, depression, and anxiety were assessed using the Symbol Digit Modalities Test (SDMT), Modified Fatigue Impact Scale (MFIS), Beck Depression Inventory (BDI), and Hamilton Anxiety Rating Scale (HAM-A), respectively. Spearman's correlation analysis and the Mann–Whitney U test were used; $p < 0.05$ was considered statistically significant.

Results: Clinically relevant sexual dysfunction was identified in 60 patients (55.1%). The total MSISQ-19 score correlated positively with age ($\rho = 0.26$; $p = 0.016$), EDSS ($\rho = 0.40$; $p < 0.001$), BDI ($\rho = 0.36$; $p = 0.004$), HAM-A ($\rho = 0.57$; $p < 0.001$), and MFIS ($\rho = 0.64$; $p < 0.001$) score. Brainstem lesions on MRI were associated with higher primary sexual dysfunction subscale score (median 11.0 vs. 8.0; $p = 0.013$).

Conclusions: sexual dysfunction was common in patients with multiple sclerosis and was significantly associated with age, disability level, fatigue, depression, anxiety and brainstem lesions on MRI, supporting its multifactorial nature and the need for routine clinical assessment.

KEYWORDS: multiple sclerosis, sexual dysfunction, fatigue, anxiety, depression, brainstem lesions

Wiad Lek. 2026;79(9):2046-2052. doi: 10.36740/WLek/237513 DOI

INTRODUCTION

Multiple sclerosis (MS) is a chronic demyelinating disease of the central nervous system that leads to progressive neurological deficits and most commonly affects young people [1]. In addition to obvious physical symptoms, patients with multiple sclerosis may experience so-called "hidden symptoms," one of which is sexual dysfunction (SD) [2]. SD is one of the most common, often underestimated manifestations of the disease, that can be diagnosed at any stage of the disease, quite often at the early stages [3,5]. According to recent meta-analyses, the combined prevalence of this symptom is approximately 61% in women and 63% in men [4,5].

Sexual dysfunction in MS comprises three components: primary, secondary, and tertiary [6]. Primary dysfunction is associated with direct damage to the structures and neural pathways of the central nervous system involved in the regulation of sexual desire, sexual arousal, genital sensitivity, and orgasm. The secondary component is caused by the physical and functional consequences of the disease, which indirectly affect the patient's sex life. These include fatigue, weakness, spasticity, muscle spasms, impaired coordination and mobility, cognitive impairment, pain or sensory symptoms, adverse treatment effects, and pelvic organ dysfunction. The tertiary component of sexual dysfunction is associated with the psycho-emotional and sociocultural aspects of the condition. Its most common manifestations include low self-esteem, difficulties with emotional regulation, a negative body image, fear of rejection, and communication difficulties with a partner [7].

Despite growing interest in MS sexual dysfunction, this issue needs further investigation. Most studies have focused on assessing its prevalence, risk factors, and impact on quality of life, while associations with clinical disease characteristics, comorbid symptoms, neuroimaging data, and specific components of sexual dysfunction have been analyzed less frequently. Assessment of these aspects is important for a more complete understanding of the nature and clinical significance of sexual dysfunction in MS patients.

AIM

The aim of this study was to assess the prevalence and severity of sexual dysfunction in MS patients and to analyze its associations with age, sex, disease duration, neurological disability, cognitive function, fatigue, affective symptoms, and brainstem lesions on magnetic resonance imaging (MRI), with consideration of the primary, secondary, and tertiary components of sexual dysfunction.

MATERIALS AND METHODS

STUDY DESIGN AND PARTICIPANTS

A cross-sectional observational study was conducted. The study included patients with multiple sclerosis diagnosed according to the McDonald (2017) diagnostic criteria [8]. Demographic, clinical, and questionnaire-based data were obtained during routine outpatient consultations with a neurologist at the State Scientific Institution "Center for Innovative Medical Technologies of the National Academy of Sciences of Ukraine" (Kyiv, Ukraine) from September 2024 to December 2025. The study included adults aged from 18 years or older who provided written informed consent and completed clinical and questionnaire-based data required for the analysis. Exclusion criteria were pregnancy, severe mental disorders, and clinically significant somatic comorbidities that could affect the assessed outcomes.

109 patients with MS were enrolled into the study including 80 (73.4%) women and 29 (26.6%) men. According to the presence of clinically relevant sexual dysfunction, patients were divided into two groups: the sexual dysfunction group (n = 60; 55.1%) and the comparison group of patients without sexual dysfunction (n = 49; 44.9%). The mean age of the patients at the time of study enrollment was 36.5 ± 10.2 years, and the mean duration of the disease was 5.5 ± 5.4 years. Based on the clinical course of the disease, 96 (88.1%) patients had relapsing-remitting MS. Progressive forms of multiple sclerosis (primary- and secondary-progressive) were identified in 13 (11.9%) patients. The level of disability, assessed using the EDSS scale, was characterized by a median value of 2.5 points (IQR 1.5–4.0).

CLINICAL AND PSYCHOMETRIC ASSESSMENT

The level of neurological deficit was assessed using the Expanded Disability Status Scale (EDSS) [9]. Sexual dysfunction was evaluated using the Multiple Sclerosis Intimacy and Sexuality Questionnaire-19 (MSISQ-19) [6] with analysis of the total score and the scores of the primary, secondary, and tertiary sexual dysfunction subscales. Cognitive function was determined using the Symbol Digit Modalities Test (SDMT) [10]. The level of depressive symptoms was assessed using the Beck Depression Inventory (BDI) [11], the level of anxiety was measured with the Hamilton Anxiety Rating Scale (HAM-A) [12]. The severity of fatigue was evaluated using the Modified Fatigue Impact Scale (MFIS) [13]. Fixed cutoff scores were used to interpret the results of the clinical and psychometric scales. Cognitive impairment was diagnosed when the SDMT score was < 40 points [10]. Sexual dysfunction was defined as a total MSISQ-19 score >30, in line with a previously used cut-off in MS research [14]. Clinically significant fatigue was defined as a total MFIS score ≥38 [13]. Clinically relevant depressive symptoms were defined as BDI score ≥10 [11], and clinically relevant anxiety symptoms as HAM-A score >15 [12].

STATISTICAL ANALYSIS

Statistical analysis was performed using nonparametric statistical methods. Quantitative variables were described as the median and interquartile range [Q1; Q3], while categorical variables were described as absolute numbers and percentages. Spearman's correlation analysis was used to assess the relationships between indicators. The Mann–Whitney U test was used to compare two independent groups. Data analysis was performed using GraphPad Prism 8 software.

ETHICS

The study was conducted in accordance with the principles of the Declaration of Helsinki. All patients were informed of the study's objectives and conditions and provided written informed consent to participate. Participants' personal data were anonymized and used exclusively for scientific purposes.

AI STATEMENT

The author states that no AI tools were used in writing this article.

RESULTS

Clinically relevant sexual dysfunction was present in 60 (55.1%) of MS patients. Among these patients, the median total MSISQ-19 score was 40.0 [35.0; 46.0]. Using the tertile-based approach, high levels of manifestations were observed in 30 patients (33.3%) for the primary, 31 patients (34.1%) for the secondary, and 30 patients (33.3%) for the tertiary MSISQ-19 subscales. Clinically significant sexual dysfunction was observed in 45 women (56.3%) and 15 men (51.7%). The total MSISQ-19

Table 1. Comparison of the main characteristics of patients with and without clinically significant sexual dysfunction

Variable	Patients with SD (n=60)	Patients without SD (n=49)	p-value
Age, years	36.0 [29.0; 42.5]	32.5 [26.75; 38.5]	0.124
EDSS score, points	3.0 [2.0; 4.1]	2.0 [1.5; 3.0]	0.0026
Disease duration, years	4.0 [2.0; 10.0]	3.0 [1.0; 5.5]	0.081
SDMT score, points	47,5 [35,0; 57,0]	51.5 [45.5; 60.25]	0.077
MFIS score, points	38,0 [26,5; 47,5]	18.0 [10.0; 25.75]	<0.0001
BDI score, points	13.0 [7.0; 17.25]	6.0 [3.0; 10.5]	0.0002
HAM-A score, points	16.0 [10.0; 25.0]	8.0 [6.0; 15.25]	<0.0001

Source: compiled by the authors of this study

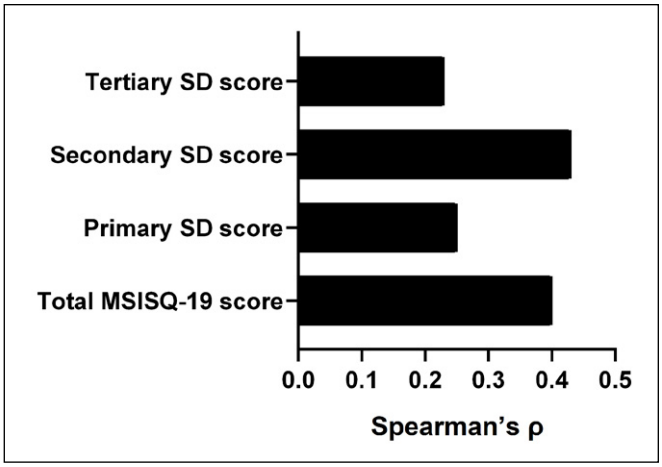


Fig. 1. Correlations between EDSS score and total and subscale MSISQ-19 score
Picture taken by the authors

score did not differ significantly between women and men (p = 0.335). No significant sex-related differences were found for the primary or secondary MSISQ-19 subscales (p = 0.137 and p = 0.958, respectively). At the same time, tertiary subscale scores were significantly higher in women than in men (median 8.0 vs. 6.5; p = 0.032). Disease duration was not significantly associated with sexual dysfunction measures. Specifically, multiple sclerosis duration did not correlate with the total MSISQ-19 score (ρ = 0.11; p = 0.308), as well as with the primary (ρ = 0.01; p = 0.901), secondary (ρ = 0.12; p = 0.257), and tertiary subscale scores (ρ = 0.07; p = 0.512). Moderate positive correlation between patient`s age and the total MSISQ-19 score (ρ = 0.26, p = 0.016) was found. Analysis of the MSISQ-19 subscales revealed that the strongest association was observed between patient`s age and secondary SD scores (ρ = 0.37, p < 0.001). A weak but statistically significant correlation was also found between patient`s age and the level of tertiary SD (ρ = 0.24, p = 0.029). At the same time, the association between age and primary sexual dysfunction was weak and statistically insignificant (ρ = 0.04, p = 0.69). Correlation analysis revealed a statistically significant positive association between the level of disability according to the EDSS score and the total MSISQ-19 score (ρ = 0.40, p < 0.001). Analysis of individual MSISQ-19 subscales revealed that the strongest correlation was found between the EDSS score and the secondary sexual dysfunction subscale score (ρ = 0.43, p < 0.001). Less pronounced but statistically significant correlations were found between the EDSS score and the scores of the primary (ρ = 0.25, p = 0.023) and tertiary (ρ = 0.23, p = 0.034) subscales (Fig. 1). A comparative analysis between patients with relapsing-remitting MS and those with progressive forms of the disease revealed no statistically significant differences in the total MSISQ-19 score (median 34.0 vs. 38.0; p = 0.211). Similarly, scores on the primary (p = 0.399) and tertiary subscales (p = 0.968) did not differ between groups. At the same time, for the secondary subscale of sexual dysfunction, there was a trend toward higher scores in patients with progressive forms of multiple sclerosis (median 20.0 vs. 15.0), which did not reach statistical significance (p = 0.080). Correlation between the SDMT score and the total MSISQ-19 score did not reach statistical significance (ρ = –0.20, p = 0.072). At the same time, a weak inverse correlation was found between SDMT scores and the parameters of the MSISQ-19 subscales. Thus, lower SDMT scores were associated with higher scores on the subscales assessing the severity of primary (ρ = –0.22, p = 0.046) and secondary sexual dysfunction (ρ = –0.22, p = 0.047). The association between SDMT scores and the parameters of the tertiary subscale was weak and statistically insignificant (ρ = –0.13, p = 0.237). Depressive and anxiety symptoms were notably associated with the severity of sexual dysfunction in patients with MS. In particular, the BDI score had a moderate positive correlation with the total MSISQ-19 score (ρ = 0.36, p = 0.004) (Fig.2). An analysis of the MSISQ-19 subscales revealed a statistically significant correlation between BDI score and on all three subscales score: tertiary (ρ = 0.39, p = 0.002), primary (ρ = 0.28, p = 0.031), and secondary (ρ = 0.34, p = 0.008). A strong positive correlation was found between the HAM-A score and the total MSISQ-19 score (ρ = 0.57, p < 0.001). Analysis

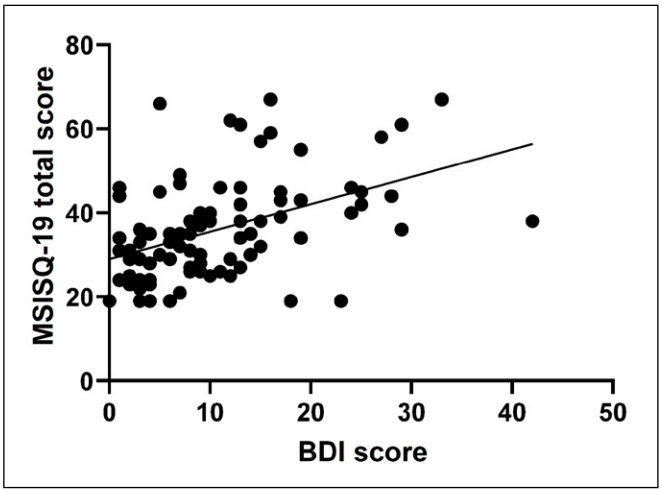


Fig. 2. Association between BDI score and total MSISQ-19 score
Picture taken by the authors

of the subscales also revealed statistically significant positive correlations between HAM-A score and the subscale score characterizing primary ($\rho = 0.46$, $p < 0.001$), secondary ($\rho = 0.42$, $p < 0.001$), and tertiary SD ($\rho = 0.42$, $p < 0.001$). Strong positive correlations were found between fatigue severity and parameteres of sexual dysfunction. In particular, the total MFIS score had a strong, statistically significant association with the total MSISQ-19 score ($\rho = 0.64$, $p < 0.001$). Analysis of individual MSISQ-19 subscales revealed that MFIS scores were significantly correlated with all the components of sexual dysfunction. The strongest correlation was observed for secondary sexual dysfunction ($\rho = 0.52$, $p < 0.001$), whereas for primary ($\rho = 0.46$, $p < 0.001$) and tertiary ($\rho = 0.47$, $p < 0.001$) dysfunction, the correlations were moderate but also statistically significant.

Our study also included a comparative analysis of the main characteristics between both groups of patients with sexual dysfunction (n=60) and those without it (n=49). Patients with sexual dysfunction had significantly higher EDSS, MFIS, BDI, and HAM-A scores than those in the comparison group (Table 1, Fig. 3). No significant difference was observed in age, disease duration, or SDMT score between both groups of patients (Table 1).

To assess the probable association between brainstem lesions and presence of sexual dysfunction, MSISQ-19 scores were compared between patients with and without brainstem lesions on MRI. Patients with brainstem lesions had significantly higher primary sexual dysfunction subscale scores than those without such lesions (median 11.0 vs. 8.0; $p = 0.013$). In contorary, between-group differences in the total MSISQ-19 score (median 35.0 vs. 31.0; $p = 0.072$), as well as secondary (median 15.5 vs. 15.0; $p = 0.522$) or tertiary MSISQ-19 subscale scores (median 8.0 vs. 7.0; $p = 0.068$) did not reach statistical significance.

DISCUSSION

Clinically significant sexual dysfunction was common in our cohort of patients with multiple sclerosis. These findings are consistent with recent studies showing that sexual dysfunction remains highly prevalent in MS. Thus, in a study by Dehghaniathar R. et al. [15], sexual dysfunction was reported in 40–80% of women and 50–90% of men with multiple sclerosis, depending on the age group and the assessment tool used. In a large cohort study by Totuk O. et al. [16], sexual dysfunction was found in 69.0% of patients, specifically in 73.9% of women and 57.6% of men. Previous studies have reported heterogeneous findings regarding sex-related differences in sexual dysfunction among patients with multiple sclerosis [15,16]. In our cohort, no statistically significant differences between men and women were found in the total MSISQ-19 score or in the primary and secondary sexual dysfunction subscales. However, sex-related differences were more apparent in the tertiary MSISQ-19 subscale, with higher scores observed in women than in men. In contrast, a study by Celik D. et al. [17], in which patients were also classified according to the

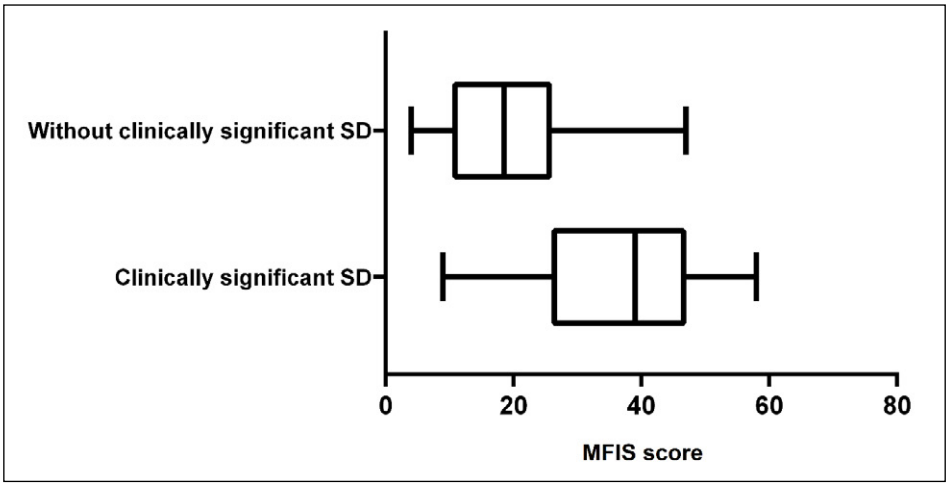


Fig. 3. Comparison of MFIS score between patients with and without clinically significant sexual dysfunction ($p < 0.0001$)
Picture taken by the authors

three subscales of the MSISQ-19, showed that women had higher total MSISQ-19 scores and reported more severe symptoms of secondary sexual dysfunction compared to men. At the same time, the study by Matusik E et al. [18] showed that male gender was associated with indicators of sexual dysfunction; however, this association pertained only to the primary component of the MSISQ-19. According to the results of our study, the duration of the disease was not significantly associated with sexual dysfunction. The available data on this issue are inconsistent. In contrast to our findings, a systematic review and meta-analysis by Yazdan Panah M. et al. [19] found an association between disease duration and sexual dysfunction in multiple sclerosis. Similar results were obtained in a study by Yeni K. et al. [20] among women with MS. Meanwhile, the results of a number of studies indicate that there is no independent association between disease duration and sexual dysfunction, which is consistent with the findings of our study. In particular, a large cohort study by Totuk O. et al. [16] found no statistically significant association between the presence of sexual dysfunction and disease duration. Similar results were obtained in the multicenter study by Petracca M. et al. [14] and the study by Altmann P. et al. [21], where the duration of MS was not associated with sexual dysfunction. In addition, these scientific publications identified patient age as one of the factors associated with sexual dysfunction. A similar pattern was observed in our cohort, where older age was positively correlated with increased severity of sexual dysfunction. This finding is also consistent with the study by Matusik E. et al. [18].

Our study found a statistically significant moderate positive correlation between the level of disability on the EDSS scale and the total MSISQ-19 score, as well as all of its subscales. The strongest association was observed for secondary sexual dysfunction. Similar results were obtained in the study by Mohammadi K. et al. [22], which also demonstrated significant associations between EDSS and both the total MSISQ-19 score and individual subscales, with the strongest correlation noted specifically for the secondary component. The results obtained are also consistent with the studies mentioned above [14, 16, 19–21], in which the level of disability as measured by the EDSS scale is considered one of the key factors associated with the severity of sexual dysfunction in multiple sclerosis.

In our study, the severity of sexual dysfunction was not associated with the clinical course of multiple sclerosis. In particular, no statistically significant differences in MSISQ-19 scores were found between patients with different clinical types of the disease, that is compatiable with data from recent studies [14, 16].

No statistically significant association was found between the total MSISQ-19 score and the SDMT score depicting cognitive functions state, that was consistent with other scientific data and pointed out that cognitive impairment was not among the leading factors contributing to sexual dysfunction in multiple sclerosis [14]. At the same time, our study revealed weak correlations between SDMT and primary and secondary subscales score. However, the available data were limited on a detailed analysis of the relationship between cognitive functions and the MSISQ-19 subscales. In this context, in the study by Marinetto S. et al. [23] executive functions were associated with greater severity of sexual dysfunction, mainly due to the tertiary component.

Taking into consideration obtained results, positive correlations between MSISQ-19 scores and levels of depression and anxiety measured by the BDI and HAM-A scales were observed. The most pronounced associations were found between parameters of BDI and HAM-A scales and MSISQ-19 secondary and tertiary SD subscales, which is partially consistent with the conceptual structure of tertiary SD subscale that mainly reflects psychoemotional and social aspects related to sexual function [6]. The association with the secondary subscale score and the BDI and HAM-A scales score identified in our study may reflect the role of the physical manifestations of the disease, which are potentially linked to the development of psychoemotional disorders. The results obtained in our study are partially consistent with those reported by Domingo S. et al. [24], who showed that patients with sexual dysfunction had higher depression severity; however, no statistically significant difference was found between level of depression and all the sexual dysfunction subscales score. Similar results were highlited in the study by Sari Y. et al. [25], in which higher depression and anxiety score were associated with more pronaunced sexual dysfunction severity. However, the current clinical data are inconsistent, in particular Altmann P. et al. [21] found no association between depression and anxiety and sexual dysfunction in patients with MS.

Our study identified moderate positive correlations between fatigue severity scale score and sexual dysfunction level according to the total and MSISQ-19 subscales score. This is consistent with the current studies, which indicated fatigue as one of the key factors associated with sexual dysfunction in MS. Systematic review and meta-analysis by Yazdan Panah M. et al. [19] showed that in women with MS, decreased sexual function was associated with higher fatigue severity. According to findings reported by Dourou P. et al. [26], the level of fatigue severity in women with MS notably correlated with both the total MSISQ-19 score and the subscale scores describing primary, secondary, and tertiary sexual dysfunction. Similar associations were found in the studis of both sex patient cohorts with MS; specifically, the international study by Marck C. et al. [27] showed that sexual dysfunction and dissatisfaction

with sexual function were associated with presence of fatigue, along with other clinical and psychoemotional factors. Additionally, in a 6-year prospective study by Kisic-Tepavcevic D. et al. [28], fatigue was identified as an independent prognostic factor for the deterioration of sexual function.

According to the our data, the presence of brainstem lesions on MRI was associated with higher primary sexual dysfunction MSISQ-19 scale score. This findings can be explained by the brainstem role in the regulation of the autonomic, sensory, and motor mechanisms involved in sexual function [29]. The available data regarding associations of the MRI lesions and SD in MS remain inconsistent. Thus, our results are partially coherent with the findings of previous studies. Ramezani M. et al. [30], in their systematic review, suggested that the localization of demyelinating lesions can be relevant to sexual dysfunction, particularly in cases involving the brainstem. They also noted a possible link between orgasmic dysfunction and pons involvement. In contrast, Seyman E. et al. [31] found no statistically significant association between quantitative MRI measures of the brain and spinal cord and the severity of sexual dysfunction.

CONCLUSIONS

Sexual dysfunction in MS patients is a common symptom, and is mainly associated with fatigue, affective symptoms, and the level of neurological disability. The strongest associations were observed for the secondary component of sexual dysfunction, whereas the tertiary component was more closely related to affective manifestations. Cognitive impairment did not show a statistically significant association with the overall level of sexual dysfunction; however, it was weakly associated with its individual components. The presence of brainstem lesions on MRI was associated with greater severity of primary sexual dysfunction. Our results support multifactorial nature of SD in MS and emphysize the need for its routine clinical assessment.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article

RECEIVED: 16.04.2026
ACCEPTED: 30.08.2026

CREATIVE COMMONS 4.0