



TURKISH JOURNAL OF PHYSIOTHERAPY AND REHABILITATION

TÜRK FİZİYOTERAPİ VE REHABİLİTASYON DERGİSİ

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Received: 20.10.2025 (Geliş Tarihi)

Accepted: 4.03.2026 (Kabul Tarihi)

Publication Date: 31.08.2026 (Yayınlanma Tarihi)

Cite this article as/Atif: Arsovski D, Chichevska-Jovanova N, Jankulovska A, Petkovska D, Etova R, Markova Y. When impairment is not always seen: invisible disabilities, daily functional challenges, and implications for rehabilitation in multiple sclerosis. Turk J Physiother Rehabil. 2026;37(2):136-144

WHEN IMPAIRMENT IS NOT ALWAYS SEEN: INVISIBLE DISABILITIES, DAILY FUNCTIONAL CHALLENGES, AND IMPLICATIONS FOR REHABILITATION IN MULTIPLE SCLEROSIS

ABSTRACT

Purpose: Multiple sclerosis is a chronic immunopathological condition of the central nervous system that is characterized not only by visible motor impairments, but also by invisible symptoms such as fatigue, cognitive dysfunction and emotional problems. These invisible disabilities are often overlooked despite their impact on quality of life and independence. The aim of this research was to characterize aspects of invisible disabilities in order to inform future rehabilitation and multidisciplinary management in multiple sclerosis.

Methods: A quantitative, cross-sectional design included 660 participants with a confirmed diagnosis of multiple sclerosis. Data were collected with structured and self-administered questionnaires that assessed demographic and clinical characteristics related to fatigue, cognitive function and emotional problems. Descriptive statistics presented prevalence and severity, while Spearman's correlation analyses and multiple linear regression analyses were used to examine associations with perceived disability.

Results: Fatigue was moderately correlated with cognitive difficulties ($r=0.49$, $p<0.001$) and emotional problems ($r=0.44$, $p<0.001$), while cognitive difficulties were moderately correlated with emotional problems ($r=0.39$, $p<0.001$). Regression analysis showed statistically significant independent associations of fatigue ($p=0.005$) and emotional problems ($p=0.014$) with perceived disability, whereas cognitive impairment was not independently associated ($p=0.603$).

Conclusion: Invisible symptoms, especially fatigue and emotional difficulties, cover key areas statistically associated with viewed disability in multiple sclerosis. These results show the necessity of rehabilitation that recognize invisible symptoms, serving as an initial step for developing comprehensive and multidisciplinary rehabilitation.

Keywords: Emotions, Fatigue, Invisible disabilities, Multiple sclerosis, Rehabilitation

YETERSİZLİĞİN HER ZAMAN GÖRÜNÜR OLMADIĞI DURUMLAR: MULTİPL SKLEROZDA GÖRÜNMEYEN ENGELLİLİKLER, GÜNLÜK FONKSİYONEL ZORLUKLAR VE REHABİLİTASYONA YÖNELİK ÇIKARIMLAR

ÖZ

Amaç: Multipl skleroz, yalnızca görünür motor bozukluklarla değil; aynı zamanda yorgunluk, bilişsel işlev bozuklukları ve duygusal sorunlar gibi görünmeyen semptomlarla da karakterize edilen kronik, immünopatolojik bir merkezi sinir sistemi hastalığıdır. Bu görünmeyen engeller, yaşam kalitesi, bağımsızlık ve toplumsal katılım üzerindeki belirgin etkilerine rağmen klinik uygulamada sıklıkla göz ardı edilmektedir. Bu çalışmanın amacı, multipl sklerozda görünmeyen engellilik alanlarını tanımlamak ve bu alanların rehabilitasyon planlaması açısından önemini ortaya koymaktır.

Yöntem: Bu çalışma, doğrulanmış multipl skleroz tanısı olan 660 katılımcıyı içeren kesitsel ve nicel bir araştırma olarak tasarlanmıştır. Veriler, yorgunluk, bilişsel güçlükler ve duygusal sorunlara ilişkin demografik ve klinik özellikleri değerlendiren yapılandırılmış, kendi kendine uygulanan anketler aracılığıyla toplanmıştır. Tanımlayıcı istatistikler semptomların yaygınlığını ve şiddetini ortaya koymak amacıyla kullanılmış; Spearman korelasyon analizleri ve çoklu doğrusal regresyon modelleri ise görünmeyen semptomların algılanan engellilik düzeyi ile ilişkisini incelemek için uygulanmıştır.

Bulgular: Katılımcıların çoğunluğu kadındı (%85,9) ve multipl skleroz tanısı aldıkları ortalama yaş 35,1 yıl olarak belirlenmiştir. Yorgunluk, katılımcıların %83,5'i tarafından bildirilen en yaygın semptom olup, %74,2'sinde sosyal veya mesleki yaşamı olumsuz etkilemiştir. Bilişsel ve duygusal sorunların da yaygın olduğu saptanmıştır. Yorgunluk ile bilişsel güçlükler ($r=0,49$, $p<0,001$) ve duygusal sorunlar ($r=0,44$, $p<0,001$) arasında orta düzeyde pozitif korelasyonlar belirlenmiştir. Bilişsel güçlükler ile duygusal sorunlar arasında da orta düzeyde pozitif korelasyon saptanmıştır ($r=0,39$, $p<0,001$). Regresyon analizi, yorgunluk ($p=0,005$) ve duygusal sorunların ($p=0,014$) algılanan engellilik düzeyi ile istatistiksel olarak anlamlı bağımsız ilişkiler gösterdiğini, bilişsel bozukluğun ise algılanan engellilik ile bağımsız olarak ilişkili olmadığını ortaya koymuştur ($p=0,603$).



ÖZ

Sonuç: Bu bulgular, multipl sklerozda görünmeyen semptomların, özellikle yorgunluk ve duygusal yükün, algılanan engellilik ile anlamlı biçimde ilişkili olduğunu göstermektedir. Sonuçlar, rehabilitasyon yaklaşımlarının yalnızca görünür motor bozukluklara değil, aynı zamanda görünmeyen semptomlara da odaklanması gerektiğini vurgulamakta ve multidisipliner, bireyselleştirilmiş rehabilitasyon modellerinin geliştirilmesi için bir temel sunmaktadır.

Anahtar Kelimeler: Duygular, Görünmeyen engellilikler, Multipl skleroz, Rehabilitasyon, Yorgunluk

INTRODUCTION

Multiple sclerosis is a chronic, immunopathological condition of the central nervous system detected by demyelination, axonal loss and progressive neurological impairment (1). While motor impairments and mobility limitations remain the most impactful and recognized effects of multiple sclerosis, a major subgroup of patients experience invisible disabilities (2). Those invisible disabilities include fatigue, cognitive dysfunction, psychological distress, chronic pain, sexual dysfunction and bladder or bowel impairments-symptoms that are not visible but affect quality of life, independence and social participation (3-8).

Invisible disabilities in this research are defined as self-reported functional impairments including fatigue, cognitive dysfunction and emotional problems. These categories were chosen based on their high prevalence in multiple sclerosis and their impact on daily functioning, in the absence of visible motor impairments. Invisible symptoms are among the most disabling and often described manifestations of this condition (9). Fatigue alone is estimated to affect up a large proportion of patients, often cited as the primary cause of unemployment and reduced participation in daily activities (10). Cognitive deficits mainly in attention, memory and executive functioning occur often in multiple sclerosis, weakening social and occupational performance (11,12). On the other hand, emotional conditions like depression and anxiety increase the impact of the condition, while pain, sexual dysfunction and urinary problems contribute to stigmatization, isolation and reduced well-being (13,14). Despite their prevalence and impact, these symptoms are neglected in practice, not fully recognized in rehabilitation and have yet to be fully explored in research (15, 16).

Rehabilitation provides the foundation for responding to invisible disabilities in multiple sclerosis (17,18). Rehabilitation have focused on physical limitations and mobility training, but increasing evidence show the need for integrative and multidisciplinary modalities that are focusing on invisible symptoms (19-22). Cognitive rehabilitation, programs for management of the fatigue, psychological interventions, pain management and lifestyle modifications such as kinesitherapy, nutrition and alternative medicine modalities have all shown potential to ease the unseen difficulties of multiple sclerosis (23-25). The main problem is how to integrate these approaches into personalized plans that acknowledge the interaction between physical, psychological and social dimensions of health (26, 27). It must be acknowledged that this research was theory based

in the biopsychosocial model of rehabilitation and consistent with the international classification of functioning, disability and health by World Health Organization (28). According to this model, disability results from the dynamic interaction between health conditions, body functions and contextual factors. Invisible disabilities such as fatigue, cognitive dysfunction and emotional problems indicate impairments in body functions that influence participation and activity, even in the absence of visible motor limitations (29).

Rather than testing a specific intervention, the aim of this research is to characterize the invisible symptoms that are most relevant for the design of rehabilitation programs and to found predictors that may inform the planning for individualized rehabilitation. Grounded in a biopsychosocial framework, the research paper aims to advance a more comprehensive rehabilitation perspective in multiple sclerosis by focusing on its clinical relevance of invisible disabilities and by pointing to future rehabilitation strategies that reach beyond visible impairments, with the ultimate goal of improving quality of life. Although the concept of invisible disabilities in multiple sclerosis includes many different symptoms including chronic pain, bladder and bowel dysfunction, sexual dysfunction and sensory disturbances, this research operationalized invisible disabilities through fatigue, cognitive dysfunction and emotional problems. This decision was guided by several considerations. First, these categories show some of the most prevalent and functionally disabling invisible symptoms reported by people with multiple sclerosis even in the absence of visible motor impairment. Second, fatigue, cognitive and emotional problems are frequently underrecognized in routine assessment and in the planning of rehabilitation despite their impact on participation, employment and quality of life. Third, these categories show a close association with the biopsychosocial model of disability and the International Classification of Functioning, Disability and Health as they reflect impairments in mental and emotional body functions that influence activity and participation. Finally, focusing on a limited number of key invisible categories enabled a coherent and interpretable analytical framework within the exploratory, cross-sectional design while acknowledging that other invisible symptoms are very important and call for more focused future research.

While fatigue, cognitive impairment and emotional distress in multiple sclerosis have been previously described in the literature, prior research papers have examined these categories

in isolation or in relation to specific interventions. The original contribution of this research lies in its integrative, rehabilitation perspective of invisible disabilities as interconnected categories and their combined association with perceived disability from the patients. By focusing on the subjective functional burden of the condition rather than neurological impairment assessed by clinicians, this research offers a different perspective on how invisible symptoms influence daily functioning, thereby providing an analytical foundation for personalized and multidisciplinary rehabilitation.

METHODS

Research Design

This research paper was designed as a cross-sectional, quantitative research with aim to assess invisible disabilities in persons with multiple sclerosis and to examine their associations with general disability. Rather than testing specific interventional hypotheses, the purpose of the research was to found some patterns and relationships between invisible symptoms and general disability within a large multinational sample. Accordingly, no a priori hypotheses were formulated, and the analyses were conducted with a descriptive and exploratory approach to provide a foundation for future research. Also, the focus of the investigation was placed on invisible symptoms that are not readily observable in routine clinical assessment, specifically fatigue, cognitive impairment and emotional problems in light of their recognized clinical and rehabilitative relevance. No a priori power calculation was performed, as the study was designed as an exploratory cross-sectional analysis without predefined hypothesis testing. The sample size was determined by participant availability through open online recruitment, and the resulting large sample was considered adequate for estimating associations among the variables under investigation.

Participants

A total of 660 patients with multiple sclerosis from USA, Canada, Mexico, France, Italy, Russia, North Macedonia, Germany, China, Croatia, Serbia, Spain with confirmed multiple sclerosis were included in this analysis. Participants were adults from 18 to 78 years at diagnosis with a prevalence of females (86 %) over males (14 %). Inclusion criteria required a diagnosis of multiple sclerosis and completion of demographic and questions focused on symptoms. For validity, participants were required to confirm that the diagnosis had been previously made by a neurologist, and they had to specify the type of multiple sclerosis. Cases with incomplete demographic data were excluded from final analyses to maintain consistency in the included statistical models. Missing data imputation procedures was not applied because the proportion of incomplete questionnaires was minimal (<5%) and the missingness appeared random across variables. Nevertheless,

we acknowledge that exclusion may bias results toward participants who were more motivated or engaged. To minimize cultural and linguistic variation, all items were translated into English language. The questionnaire relied on universally interpretable constructs such as fatigue, concentration, mood that have established validity in many cultural environments. Differences in healthcare system accessibility or national rehabilitation structures were not analyzed comparatively, as the aim of the present research was to find patterns of invisible symptoms rather than international differences.

Data Collection

Data were collected with structured, self-administered questionnaires including validated and standardized instruments. The multiple sclerosis quality of life questionnaire (MS-QoL)-54 was administered as a main measure. Disability, used as the dependent variable in the regression analyses was assessed as a self-reported measure of viewed functional disability. A global disability score was obtained from selected MS-QoL-54 items indicating limitations in daily activities, functioning and the perceived impact of multiple sclerosis on everyday life. This score was treated as a continuous variable with higher values that indicate greater perceived disability. This operationalization was chosen to found the subjective experience of disability rather than neurological impairment assessed by clinicians.

Participants were recruited through open invitations via online platforms dedicated to multiple sclerosis communities including patient support groups, organizational pages and rehabilitation forums. Participation was entirely voluntary, and no compensation was provided. As recruitment relied on open electronic dissemination rather than a defined sampling frame, the denominator population and response rate could not be determined. After exclusion of incomplete submissions, the final analytic sample included 660 fully completed questionnaires. Fatigue was assessed with the Fatigue assessment scale-FAS measuring both physical and mental aspects of fatigue on a five-point Likert scale. Total scores range from 10 to 50, with higher scores showing greater fatigue severity. The FAS has showed strong internal consistency (Cronbach's $\alpha \approx 0.90$) and validity in neurological and chronic disease populations (30). Cognitive difficulties were evaluated with three self-reported items assessing concentration, attention, and memory, based on categories from the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) framework (31). Emotional disturbances were assessed with items focusing on low mood, frustration, discouragement and worries about their health.

Ethical Considerations

This research paper was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics

Committee of the Higher Medical School - Bitola, University "St. Kliment Ohridski" Bitola, North Macedonia (approval no: 03-472/1, date: 07.10.2025). All participants provided electronic informed consent prior to participation. Participation was voluntary and anonymous and respondents were informed of their right to withdraw at any time before submission without providing a reason. No personal identifiers, medical records or sensitive clinical data were collected. Given the anonymized, non-interventional nature of the online data collection, no additional institutional consent or risk assessment was required.

Statistical Analysis

Data were analyzed with descriptive and inferential statistical methods. Descriptive analyses included frequencies and percentages for categorical variables as well as means, standard deviations, medians and ranges for continuous variables. Age was also categorized into 10-year intervals to ease the descriptive comparisons. Symptom prevalence analyses were conducted for fatigue, cognitive problems and emotional problems with results presented in tables and figures. Associations between invisible symptoms were examined with Spearman's rank correlation coefficients. To investigate their relationship with disability, multiple linear regression analysis was used with viewed disability as the dependent variable and fatigue, cognitive and emotional problem scores as independent variables. The analysis was intentionally limited to invisible symptom categories in order to examine their associations with the viewed disability within an exploratory framework. Regression results were reported as unstandardized coefficients (B), standard errors, t values, p-values, 95% confidence intervals, and model fit indices (R^2). Predictors with $p < 0.05$ were considered statistically significant.

The assumptions of linear regression were evaluated prior to analysis. Data were inspected with histograms and normal Q-Q plots and residuals were examined for linearity and homoscedasticity. No deviations from normality were found. Although the variables of this research were measured with five-point Likert scales, their approximately continuous distribution and the large sample size (660) supported the use of parametric regression techniques. Ordinal logistic regression was considered, but given the approximately normal distribution of the dependent variable and satisfactory model fit diagnostics, multiple linear regression was retained to improve the interpretability and comparability with previous studies. It is important to address that the regression analyses were intended to identify statistical associations rather than causal relationships. Owing to the cross-sectional design, causal inferences cannot be drawn and the term predictors is used only to denote variables statistically connected with higher viewed disability scores. In that matter, the disability outcome represents patient-reported perceived functional burden

from MS-QoL-54 functional impact items and does not show objective neurological disability or disease severity.

RESULTS

Table 1A shows the demographic data of participants in this research. Most participants were women (85.9%), with men showing 14.1% of the cohort. The mean age at diagnosis was 35.1 years with standard deviation = 10.3, aged from 18 to 78 years.

Table 1B shows the distribution of the types of multiple sclerosis among the participants. Relapsing-remitting type of multiple sclerosis was the most common type (68.5%), followed by primary progressive type (13.9%) and secondary progressive type of multiple sclerosis (12.7%). A small number of participants were classified as clinically isolated syndrome (2.1%). For 18 participants (2.7%), data on the type of multiple sclerosis were not reported.

Table 1C shows the age of the participants, divided into age groups. The majority of the participants were diagnosed

Table 1A. Demographic characteristics of the participants

Characteristic	Value
Gender	Female: 567 (85.9%) Male: 93 (14.1%)
Age at diagnosed multiple sclerosis	Mean $\pm$ standard deviation: 35.1 $\pm$ 10.3 Median (IQR): 35 (27-42) Range: 18-78
IQR: Interquartile Range.	

Table 1B. Clinical characteristics of participants by type of multiple sclerosis

Type of multiple sclerosis	n	Percent
Relapsing-remitting type	452	68.5
Primary progressive type	92	13.9
Secondary progressive type	84	12.7
Clinically isolated syndrome	14	2.1
Not reported	18	2.7

Table 1C. Age at diagnosis of multiple sclerosis among the participants

Age	n	Percent
10-19	35	5.3
20-29	189	28.6
30-39	225	34.1
40-49	148	22.4
50-59	52	7.9
60-69	10	1.5
70-79	1	0.2

between 20-39 years, accounting for more than 60% of the cohort. Smaller proportions were diagnosed in adolescence (10-19 years, 5.3%) or later adult-hood (≥ 50 years, 9.6%).

Table 2 shows the prevalence of symptoms related to fatigue. Almost all participants (94.7%) showed that their motivation decreases when tired, while 83.5% confirmed that they become easily fatigued. Approximately three-quarters of the respondents reported that fatigue interferes with physical functioning (79.7%), daily activities (74.2%) and social or occupational participation. A smaller, but significant proportion (64.5%) stated that fatigue prevents them from fulfilling responsibilities.

Figure 1 shows how responses are distributed among five categories for each cognitive function. A large number of participants reported cognitive problems at least some time with the highest frequencies found for difficulties in concentration (73%) and memory (74%). One third of the participants answered that these issues occurred most of the time or all the time showing their cumulative effect. Reports also confirmed the presence of deficit in concentration and attention. These results show that cognitive dysfunction is a significant invisible disability in multiple sclerosis. Its high prevalence among many categories shows that cognitive impairment is not an isolated issue but rather a persistent problem that affects quality of life, social participation and functional independence.

Table 3A shows how emotional and psychological problems are experienced by participants. More than three-quarters reported at least occasional low mood, discouragement, frustration or worry about their health. Some of them (20-30%) indicated that these problems occurred most of the time or all the time, pointing to a considerable psychological problem. These results show the relevance of invisible emotional problems in

multiple sclerosis which are often underestimated compared to visible physical impairments. The high prevalence of discouragement, frustration and persistent worry confirms the need for systematic psychological support and individualized rehabilitation.

As shown in Table 3B, fatigue showed a moderate positive correlation with cognitive difficulties ($r=0.49$, $p<0.001$) and emotional problems ($r=0.44$, $p<0.001$). Cognitive difficulties were also moderately positively correlated with emotional problems ($r=0.39$, $p<0.001$). These findings indicate that fatigue, cognitive difficulties, and emotional problems were significantly interrelated within the study sample.

Table 4 shows the results of the multiple linear regression analysis that examines predictors of perceived disability. Fatigue and emotional problems showed statistically significant independent associations with perceived disability, whereas cognitive problems did not show a statistically significant independent association. The regression model explained approximately 27% of the variance in perceived disability ($R^2=0.27$).

As illustrated in Figure 2, the 95% confidence intervals for the regression coefficients did not cross zero for fatigue and emotional problems, whereas the confidence interval for cognitive problems included zero. Accordingly, fatigue and emotional problems showed statistically significant independent associations with perceived disability, while cognitive problems did not show a statistically significant independent association. These findings should be interpreted as statistical associations within the cross-sectional model rather than as evidence of causal relationships.

Table 2. Prevalence of fatigue-related symptoms among participants

Questions associated with fatigue	% of agreement of participants with the statement
My motivation is reduced when I am tired	94.7
I get tired easily	83.5
Fatigue interferes with my physical functioning	79.7
Exercise makes me tired	76.8
Fatigue is one of the three worst symptoms	75.2
Fatigue affects my work, family or social life	74.2
Fatigue causes frequent problems for me	69.8
Fatigue prevents me from fulfilling my responsibilities	64.5

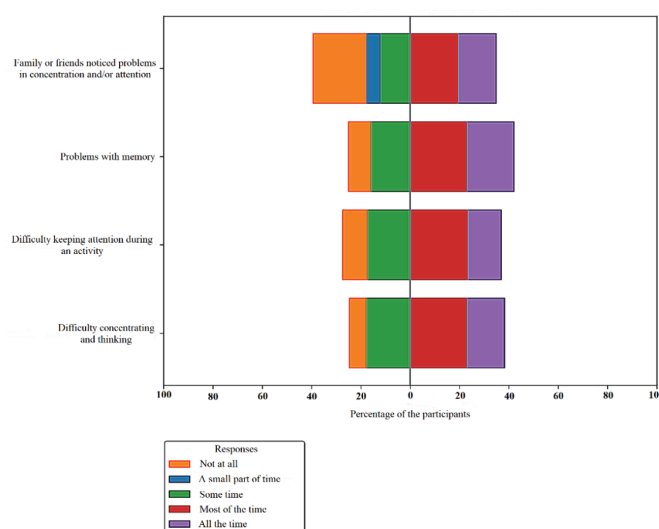


Figure 1. Distribution of cognitive problems.

DISCUSSION

These results define the clinical relevance of invisible symptoms in multiple sclerosis with fatigue and emotional problems showing associations with perceived disability. Although the proportion of explained variance in the regression model was moderate, the results suggest that invisible symptoms may contribute to disability through cumulative and interactive mechanisms rather than through strong individual effects. This pattern connects with the many-sided nature of disability in multiple sclerosis in which subjective functional problems

appear to arise from the convergence of fatigue, emotional distress and cognitive strain rather than from isolated symptom categories. Although fatigue and emotional problems showed statistically significant associations with perceived disability severity, the magnitude of the regression coefficients indicates small to moderate effects at the individual level. These results should therefore be interpreted as indicators of relative contribution rather than as evidence of clinical causation or disability progression. Given the cross-sectional design of our research, causal pathways cannot be established, and the term predictor is used strictly in a statistical sense. The clinical relevance of these associations lies in their cumulative and interactive impact, which may become meaningful at the population level or within rehabilitation planning rather than as direct determinants of individual disease outcomes.

The marked overrepresentation of women in the research shows the established epidemiology of multiple sclerosis, which disproportionately affects females. Nevertheless, this imbalance may have implications for the generalizability of the results. Gender related differences have been reported in the experience, perception and reporting of invisible symptoms such as fatigue, emotional distress and cognitive complaints potentially influencing self-reported disability outcomes. Consequently, the associations observed in this research

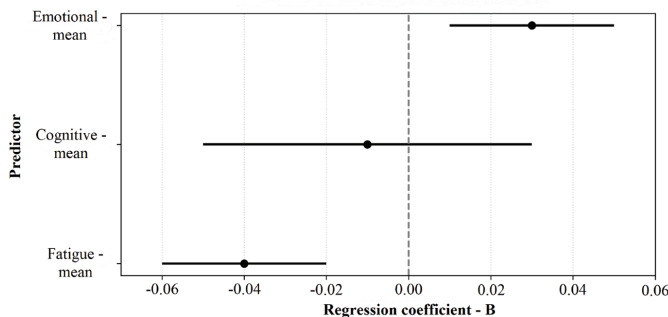


Figure 2. Regression coefficients and 95% confidence intervals for the associations between invisible symptom categories and perceived disability.

Table 3A. Emotional and psychological problems of the participants

Type of emotional issue	Not at all	A small part of the time	Some time	Most of the time	All the time
Low mood, nothing can lift spirits	23.5%	30.3%	27.1%	13.2%	5.9%
Discouraged by health problems	21.8%	25.7%	28.8%	16.6%	7.1%
Frustrated about health	19.2%	28.4%	29.3%	15.0%	8.1%
Frequently worried about health	18.6%	26.5%	30.0%	16.8%	8.1%
Feeling tired of health-related limitations	17.9%	28.1%	31.2%	15.4%	7.4%

Table 3B. Correlations between fatigue, cognitive, and emotional problems

Variable	Fatigue	Cognitive	Emotional
Fatigue	1.00	0.49***	0.44***
Cognitive	0.49***	1.00	0.39***
Emotional	0.44***	0.39***	1.00

*Values are presented as Spearman's rank correlation coefficients (r). ***p<0.001 indicates a statistically significant correlation.

Table 4. Multiple linear regression analysis of the associations between fatigue, cognitive, emotional problems, and perceived disability

Predictor	B	SE	t	p-value
Constant	1.00	0.00	/	<0.001
Fatigue-mean	-0.04	0.01	-2.82	0.005
Cognitive-mean	-0.01	0.02	-0.52	0.603
Emotional problems-mean	+0.03	0.01	2.46	0.014

may be more representative of the female multiple sclerosis population. Future research with gender stratified analyses is needed to determine whether patterns of invisible disability differ between women and men.

Our results are consistent with recent results from one research which showed that addressing fatigue, cognitive and emotional problems through psychoeducational and cognitive-behavioral rehabilitation improved the psychological well-being of the patients and acceptance of multiple sclerosis as condition (32). Another research reviewed the application of cognitive behavioral therapy for fatigue and depression in multiple sclerosis, showing its efficacy in reducing symptom problems and supporting its role as part of a multidisciplinary treatment approach (33).

Fatigue and emotional problems showed as statistically independent factors associated with higher perceived severity of disability within the analyzed model. Fatigue and emotional problems may intensify viewed disability by limiting engagement in daily tasks. These pathways coexist and strengthen each other, showing the necessity of longitudinal research papers to determine temporal order and causative mechanisms. In line with these results, one research showed that improving quality of life should be a goal in the management of multiple sclerosis and that non-pharmacological interventions including exercise cognitive behavioral therapy and cognitive rehabilitation are effective in treating the invisible symptoms (34). Our research showed that invisible symptoms such as fatigue and emotional problems are commonly observed in multiple sclerosis and act as independent predictors of the severity of disability and these results show the importance of broadening rehabilitation beyond visible motor impairments. This perspective is consistent with one review which showed that modern neurorehabilitation must target both motor and non-motor symptoms such as fatigue, spasticity, dysphagia and bladder dysfunction through various interventions like exercise, cognitive rehabilitation and physical therapy (35).

Another recent work on stigma and concealment in multiple sclerosis showed that invisible or less visible symptoms are often stigmatized and lead to concealment, isolation and reduced self-efficacy (36). This research and our research show that the problems of invisible symptoms reach beyond physical impairment, and they are influencing psychosocial wellbeing and social participation among the patients that may cause stigmatization. One research complements recent evidence on the social dimensions of hidden disability in multiple sclerosis (37), where patients described exclusion, misunderstanding and even accusations of faking symptoms due to the invisibility of their condition. Taken together, our research and this research show that invisible disabilities in multiple sclerosis are a dual challenge, medical and social. Addressing them requires not

only rehabilitation but also broader societal awareness and recognition to reduce stigma and improve the participation in daily life among the patients with multiple sclerosis.

The added value of our research lies not in identifying the presence of invisible symptoms per se, but in showing their relative and cumulative contribution to perceived disability within a large, multinational sample. Unlike prior research that has focused on isolated symptom categories or intervention outcomes, these results contextualize fatigue, cognitive difficulties and emotional problems within a unified, rehabilitation framework. This integrative perspective supports a shift from symptom-specific management toward comprehensive assessment strategies that more accurately shows the lived experience of disability in multiple sclerosis. From a rehabilitation perspective, these results show the importance of addressing invisible symptoms alongside physical impairments. The observed associations between fatigue, emotional problems and perceived disability support the integration of patient outcome measures into routine rehabilitation assessment, even among individuals with relatively preserved motor function. Rather than prioritizing single symptom interventions, the results call for comprehensive, multidisciplinary rehabilitation that incorporate fatigue management, psychological support and cognitive interventions as the most important components of individualized rehabilitation.

Limitations

Despite the large sample size and the inclusion of participants from multiple countries, several methodological and limitations related to the sampling should be acknowledged. First, recruitment through online platforms and multiple sclerosis patient communities may have introduced self-selection bias in favor for persons who are more digitally engaged, motivated or higher functioning. Consequently, the results may underrepresent persons with more severe disability, limited access to digital tools, or lower engagement with online health resources. Second, the substantial overrepresentation of women shows the known epidemiology of multiple sclerosis, but this imbalance may limit the generalizability of the results, especially with regard to potential gender specific differences in the experience and reporting of invisible symptoms. Although participants were recruited from various geographical regions, country differences in healthcare systems, access to rehabilitation services and sociocultural contexts were not examined. The absence of such analyses limits interpretation of how structural and contextual factors may influence the experience and impact of invisible disabilities in multiple sclerosis. Future studies with stratified or registry sampling approaches and various country analyses are needed to better define these determinants.

The absence of an a priori power calculation is an additional methodological limitation. However, given the exploratory nature of the analyses and the large sample size, this research was sufficiently powered to detect small to moderate associations. Nevertheless, statistical significance should be interpreted with effect sizes and clinical relevance rather than p-values alone. Another limitation relates to the exclusive use of digitally administered and self-reported questionnaires. Data collection through online formats may have excluded persons with limited digital access, lower digital literacy, or more pronounced cognitive impairment. In addition, other clinically relevant invisible symptoms such as pain, bladder and bowel dysfunction and sexual dysfunction were not included in the research. The exclusion of these categories may underestimate the general problem of invisible disability in multiple sclerosis.

Also, information about the engagement in rehabilitation of the participants at the time of data collection or prior to participation was not available. Rehabilitation interventions, especially those that focus on fatigue, psychological well-being and functional capacity are known to influence symptom severity. The broad age range of participants (from 18 to 78 years) is a further limitation. Fatigue, cognitive functioning and emotional state are influenced by biological, psychological, and social factors that may differ across the adult lifespan. Although age distributions were reported, age analyses were not conducted.

CONCLUSION

Invisible symptoms such as fatigue, cognitive problems, and emotional problems are prevalent in people with multiple sclerosis and contribute to the general disability. Among them, fatigue and emotional problems showed as independent predictors of disability severity, showing their role in daily functioning. These results inform current multiple sclerosis rehabilitation by showing fatigue and emotional problems as priority focus for assessment and intervention, supporting a greater focus on patient-centered care and multidisciplinary rehabilitation. Although no rehabilitation intervention was implemented in this research, the associations show that addressing fatigue and emotional problems could improve individualized rehabilitation. Future interventional studies are required to verify whether integrating these categories into rehabilitation leads to measurable improvements in independence, participation and quality of life.

Ethics: This research paper was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the Higher Medical School - Bitola, University "St. Kliment Ohridski" Bitola, North Macedonia (approval no: 03-472/1, date: 07.10.2025).

Informed Consent: All participants provided electronic informed consent prior to participation.

Sources of Support: The authors received no financial support for this study.

Conflict of Interest: The authors declare that they have no conflict of interest.

Author Contributions: Concept- DA, NCJ; Design- DA, YM, AJ; Supervision- NCJ, RE; Materials- DA, NCJ, RE; Data Collection and/or Processing- DA; Analysis and/or Interpretation- AJ, DP, RE; Literature Research- DA, NCJ, YM; Writing Manuscript- DA, AJ, DP; Critical Review- RE, NCJ, YM.

Explanations: None.

Acknowledgements: None.

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