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Relation between Stress Exposure and Relapse in Relapsing Remitting Multiple Sclerosis Patients

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Abstract

Background: Multiple sclerosis (MS) is a chronic autoimmune disorder characterized by demyelination and axonal damage within the central nervous system. Relapsing-remitting MS (RRMS) comprises 70–80% of cases, marked by episodic neurological deficits separated in time and space. Acute stressors have been implicated in precipitating MS relapses, yet the interplay between life stress and relapse risk remains incompletely understood. **Objectives:** To compare life stress index between RRMS patients during relapse and remission and to assess the predictive value of stress for relapse occurrence. **Methods:** In this cross-sectional comparative study, 60 RRMS patients (30 in relapse, 30 in remission) were assessed for Demographics, clinical history, neurological deficits, Expanded Disability Status Scale (EDSS), and life stress index. **Results:** 60 patients were divided equally into relapse and remission groups. Females and rural residents were significantly more prevalent in the relapse group (P = 0.004 and 0.018, respectively). The relapse group had a significantly elevated median EDSS score (4 vs. 1; $P < 0.001$). Psychiatric symptoms such as depression and anxiety were more frequent in the relapse group but not statistically significant. The life stress index was significantly elevated in the relapse group (median: 218 vs. 130; $P < 0.001$) and positively correlated with EDSS. Logistic regression identified life stress index as an independent predictor of relapse (OR: 1.8; $P < 0.001$). **Conclusions:** In our study, Life Stress index was significantly elevated in relapsing-remitting MS patients during relapses than remission. And it predicted relapse risk.

Keywords: Relapsing-remitting MS, Life Stress Index, Relapse Risk, Expanded Disability Status Scale

Introduction

Multiple sclerosis (MS) constitutes a persistent autoimmune condition in which the body's immune defenses mistakenly attack its own central nervous system (CNS), leading to myelin sheath degradation (demyelination) and axonal injury. MS represents a primary source of neurological disability in several populations [(1)]. Clinical signs vary depending on lesion location and disease subtype, commonly including visual disturbances, sensory anomalies (numbness, tingling), motor impairments (weakness, coordination deficits, balance issues, gait instability), and urinary dysfunction [(2)].

MS is classified according to disease trajectory, encompassing relapsing-remitting MS (RRMS), primary progressive MS (PPMS), secondary progressive MS (SPMS), clinically isolated syndrome (CIS), and radiologically isolated syndrome (RIS). RRMS is the most frequently encountered form, affecting roughly 70–80% of patients, and is characterized by episodic neurological relapses that may recover partially or fully over weeks or months [(3)]. Diagnosis of RRMS generally requires evidence of at least two distinct inflammatory events in the CNS. Although various diagnostic frameworks exist, the essential criterion involves demonstrating temporally and spatially separated episodes of demyelination [(4)].

Stress can manifest as physical, emotional, or environmental stimuli and is categorized by duration into acute or chronic types. Acute stress is a short-lived response to specific, impactful events, while chronic stress results from prolonged or repeated exposure, often eliciting adaptive physiological responses [(5)]. Research indicates that chronic stressors linked to illness do not significantly elevate relapse frequency in MS, whereas acute stressors may exert more pronounced effects due to their intensity [(6)].

Evidence suggests that MS exacerbation rates may increase when stress levels remain elevated. One mechanistic hypothesis involves rapid activation of CNS mast cells and increased blood–brain barrier (BBB) permeability, which may facilitate disease flares within days [(7)]. Acute stress may enhance susceptibility to relapses through corticotropin-releasing hormone–mediated mast-cell stimulation and release of vasoactive substances, including histamine and mast-cell–specific tryptase [(5–7)].

The exact biological pathways linking stress to inflammatory processes in MS remain incompletely defined. Stress responses appear to depend on the type, severity, and duration of the stressor, as well as individual psychological and physiological characteristics. Chronic stress exposure has been associated with reduced numbers and responsiveness of glucocorticoid receptors on immune cells, potentially altering immune regulation [(8)].

Given that stress is a recognized contributor to relapse risk, the present study aimed to compare stress levels between patients with relapsing and remitting MS, in order to investigate its influence on the occurrence and intensity of MS relapses.

Patients and methods

Study Design and Population

The study followed a cross-sectional, comparative design. It aimed to assess the differences between MS patients in relapses and remission phases, focusing on sociodemographic characteristics, neurological and psychiatric symptoms, life stress index. The research was conducted in a clinical setting at the Neuropsychiatric inpatient department and outpatient clinic in Benha University Hospital., over a period from May 2023 to July 2024.

Study Groups

The **Relapse group** included patients with RRMS who were experiencing an active relapse. The **Remission group** consisted of 30 RRMS patients who had not experienced a relapse for at least one month, with age and sex matched to the relapse cohort.

Eligibility Criteria

Inclusion criteria: Participants were adults aged >18 y of both sexes who met the Revised McDonald criteria for relapsing remitting MS (2017). The relapse group comprised those in relapse—defined as a focal neurological disturbance lasting for more than 24 hours, with 30 days of clinical stability prior to the onset of the neurological disturbance—whereas the remission group comprised those who were not in relapse [(9)].

Exclusion criteria: Those who were excluded were relapsing remitting MS patients (Revised McDonald criteria, 2017) in the opposite relapse status to their group (i.e., those not in relapse for the relapse group and those in relapse for the remission group), other types of multiple sclerosis including SPMS, PPMS, PRMS and clinically isolated syndrome, comorbid medical or neurological disease, other autoimmune diseases, pregnancy or lactation, MS patients who were not compliant on their regular treatment, and patients cognitive impairment or refuse to give consent [(9)].

Assessment Procedures

Those taking part in the study were assessed using four main domains. First, information was gathered about the patient's age, sex, place of residence, education, marital status, smoking habits, occupation, as well as details on MS (when it started, how long it has lasted, number of relapses), past and present treatments, psychiatric symptoms, hospitalizations, electroconvulsive therapy, current medications, adherence, and response. Next, the presence of MS in relatives, parental blood relations, similar disorders and neuropsychiatric problems,. Besides neuropsychiatric assessment, a thorough examination of the heart, abdomen, chest, and pelvis was done for each patient.

Instruments

1- **MRI brain with contrast**: It was done only for group 1 to confirm the relapse radiologically, and to assess the severity and number of new lesions.
2- **Life stress questionnaire:** Participants completed a 35-item life stress questionnaire, which includes a standardized scoring system. Scores ≤150 were considered within the normal range, 151–250 indicated a

potential risk for illness or accidents, 251–300 corresponded to approximately a 50% likelihood of adverse events, and scores >300 suggested a 75% probability of experiencing illness or accidents (10). The questionnaire was first translated into Arabic by two professors from the Faculty of Arts, English Department, and then back-translated into English by another pair of professors from the same department. The back-translated version was subsequently reviewed and compared with the original by two psychiatry professors to ensure conceptual and linguistic equivalence

3- **The Expanded Disability Status Scale (EDSS):** The EDSS is derived from the original Kurtzke Disability Status Scale (DSS) and evaluates eight functional systems (FSs): pyramidal, cerebellar, brainstem, sensory, visual, bowel and bladder, and cerebral functions [(10)].

Procedure

Eligible patients were identified during their outpatient visit or inpatient admission and were invited to participate in the study. After obtaining informed consent, a detailed medical history was taken and full general, medical and neurological examination were performed for each sing patient. Revised McDonald 2017 criteria for diagnosis of multiple sclerosis were used to select the patients under the study. The assessment tools were then administered in a face-to-face interview format by trained researchers. Each interview lasted approximately 60–75 minutes. Out of the randomly selected original sample size (70 patients), only 64 were responders and accepted to participate in the study. The remaining 6 (4 from group 1, 2 from group 2) were non- responders (8.7%) and were excluded from the study. Of those responders (64 students), only 60 (30 from group 1, and 30 from group 2) had fitted the inclusion criteria and the remaining 4 were excluded from the study

Sample Size Calculation

The sample size was calculated using STATA software (version 17) for conducting sample size analysis for cross sectional (or cohort) study. AlZahrani and co-authors exhibited that 47.9% stress had no effect on relapse, while Briones-Buixassa and co-authors exhibited that the odds of relapse in relapsing remitting multiple sclerosis patients after exposure to stress ranged from 1.1 to 3.1 [(11,12)].

Considering OR of 2.5, the sample size will be 27 per group, at a power of 80% and alpha error of 5%. They were increased to 30 in each group to compensate for differences between populations.

Data Management and Statistical Analysis

Data were managed and analyzed using SPSS version 28 (IBM, Armonk, NY, USA). Quantitative variables were assessed for distribution normality using the Shapiro-Wilk test and visual inspection. Depending on normality, continuous data were presented as mean ± standard deviation (SD) or median with range. Categorical variables were expressed as counts and percentages. Comparisons of quantitative variables between groups were performed using the independent t-test for normally distributed data or the Mann-Whitney U test for non-

normal data. Categorical variables were compared using the Chi-square test or Fisher's exact test, as appropriate. Associations between continuous variables were evaluated using Pearson's or Spearman's correlation coefficients. The measured indices were further compared across different parameters using independent t-tests or Mann-Whitney U tests. Multivariate logistic regression was conducted to identify predictors of relapse, with results exhibited as odds ratios (ORs) and 95% confidence intervals (CIs). Additionally, multivariate linear regression was performed to predict EDSS scores, with regression coefficients (β) and 95% CIs exhibited. All tests were two-tailed, and a $P < 0.05$ was considered statistically significant.

Ethical Approval

Ethical clearance was obtained from the Research Ethics Committee, Faculty of Medicine, Benha University, Approval code: (MS 19-3-2023) in accordance with the principles of the Declaration of Helsinki. All participants received comprehensive explanations regarding the study objectives, procedures, and their rights. Written informed consent was obtained prior to enrollment, and participant confidentiality and anonymity were strictly maintained throughout the study.

Statistical Design

Data management and statistical analysis were done using SPSS version 28 (IBM, Armonk, New York, United States). Quantitative data were assessed for normality using the Shapiro-Wilk test and direct data visualization methods. According to normality, quantitative data were summarized as means and standard deviations or medians and ranges. Categorical data were summarized as numbers and percentages. Quantitative data were compared between the studied groups using the independent t-test or Mann-Whitney U test for normally and non-normally distributed quantitative variables, respectively. Categorical data were compared using the Chi-square or Fisher's exact test. Correlations were done using Pearson's or Spearman's correlation. The indices studied were compared according to different parameters using the independent t-test or Mann-Whitney U test. Multivariate logistic regression analyses were done to predict relapse. The odds ratios with 95% confidence intervals were calculated. A multivariate linear regression analysis was done to predict EDSS. Regression coefficients with 95% confidence intervals were calculated. All statistical tests were two-sided. P values less than 0.05 were considered significant.

Results

This research included 60 patients with MS recruited from both inpatient wards and the outpatient clinic at Benha University Hospitals, between May 2023 and July 2024. Participants were categorized into a **Relapse group** (n = 30) and a **Remission group** (n = 30).

Gender distribution differed significantly between groups: males predominated in the remission cohort (43.3%), whereas females were more frequent in the relapse cohort (90.0%) (P = 0.004). Place of residence also demonstrated a significant association with

disease status; a greater proportion of relapse patients resided in rural areas (56.7%), while most remission patients were urban dwellers (73.3%) (P = 0.018). Age, occupation, marital status, and number of offspring exhibited comparability between the group. **Table 1**.

The most common deficit in the relapse group was pyramidal involvement, affecting 56.7% of patients, while sensory deficits and bladder or bowel dysfunction were each observed in 6.7% of patients of the relapse group. Residual symptoms were assessed in both relapse and remission groups. Pyramidal symptoms were the most common residual deficit, observed in 36.7% of patients in the relapse group compared to 26.7% in the remission group (p = 0.405). The median EDSS score was very highly significant in

the relapse group (4, range: 1–6) compared to the remission group (1, range: 0–6), with a P of <0.001. **Table 2**

The studied groups exhibited comparability regarding clinical psychiatric findings (p>0.05). Depressive symptoms were present in 36.7% of relapse group compared with 16.7% of remission group, while anxiety symptoms were present in 33.3% of relapse group compared with 20.0% of remission group. **Table 3**

The median life stress index was significantly elevated in the relapse group (218, range: 55–420) compared to the remission group (130, range: 35–270), with a P of <0.001. Moreover, the highest percentage of relapse group had possibility of experiencing illness and accidents (46.7%), however the highest proportion of remission group were normal (73.3%) and the relation was of very high significance (P<0.001). **Figure 1**

In both groups, the life stress index was significantly positively correlated with EDSS, in relapse group r = 0.680, P < 0.001, in remission group r = 0.634, P < 0.001.While age number of rwlapses before and after treatment did not show significant correlations **Table 4**

To examine factors associated with relapse in MS, both univariate and multivariate logistic regression analyses were conducted. Variables suspected to influence relapse risk were initially assessed individually using univariate regression. This analysis identified that elevated life stress scores, female sex, rural residence, elevated EDSS, and the presence of depressive or anxiety symptoms were each linked to an increased probability of relapse. Subsequently, these variables were incorporated into a multivariate model to determine independent predictors. In this analysis, only elevated life stress scores remained a significant independent predictor of relapse **(Table 5).**

Table 1: Sociodemographic data of the studied groups of patients with multiple sclerosis.

Variables	Relapse (n = 30) n (%)	Remission (n = 30) n (%)	P
Age (years)			0.143
< 20	6 (20.0)	2 (6.7)	
20 – 40	22 (73.3)	22 (73.3)	
> 40	2 (6.7)	6 (20.0)	
Sex			**0.004****
Males	3 (10)	13 (43.3)	
Females	27 (90)	17 (56.7)	
Occupation			0.408
Manual worker	5 (16.7)	4 (13.3)	
High performance	4 (13.3)	4 (13.3)	
Student	8 (26.7)	14 (46.7)	
Unemployed	13 (43.3)	8 (26.7)	
Residence			**0.018***
Rural	17 (56.7)	8 (26.7)	
Urban	13 (43.3)	22 (73.3)	
Marital status			0.185
Single	18 (60.0)	11 (36.7)	
Married	8 (26.7)	16 (53.3)	
Divorced	2 (6.7)	2 (6.7)	
Widow	2 (6.7)	1 (3.3)	
Active smoking	0 (0)	3 (10)	0.237
Number of offspring			0.573
≤ 2	20 (66.7)	22 (73.3)	
> 2	10 (33.3)	8 (26.7)	

*Significant P-value; ** Highly significant P-value; SD: Standard deviation; n: Number.

Table 2: Neurological symptoms of the studied groups of patients with multiple sclerosis.

Variables	Relapse (n = 30)	Remission (n = 30)	P
	n (%)	n (%)	
New relapse deficit			
Pyramidal	17 (56.7)	-	-
Ambulation	9 (30)	-	-
Cerebellar	4 (13.3)	-	-
Visual	12 (40)	-	-
Sensory	2 (6.7)	-	-
Bladder or bowel	2 (6.7)	-	-
Residual symptoms			
Pyramidal	11 (36.7)	8 (26.7)	0.424
Ambulation	2 (6.7)	1 (3.3)	
Cerebellar	2 (6.7)	5 (16.7)	
Visual	2 (6.7)	3 (10)	
Sensory	3 (10)	2 (6.7)	
EDSS	**Median (range)**	**Median (range)**	**<0.001*** **
	4 (1 - 6)	1 (0 - 6)	

*Significant P-value; *** Very highly significant P-value; n: Number; DMF: Dimethyl fumarate

Table 3: Clinical psychiatric findings of the studied groups of multiple sclerosis patients.

Variables	Relapse (n = 30)	Remission (n = 30)	P
	n (%)	n (%)	
Depressive symptoms	11 (36.7)	5 (16.7)	0.08
Anxiety symptoms	10 (33.3)	6 (20)	0.243
Mixed anxiety & depression	2 (6.7)	0 (0.0)	0.492
Obsessive symptoms	6 (20)	5 (16.7)	0.739
Phobia	8 (26.7)	3 (10)	0.095
Mania symptoms	0 (0)	0 (0)	-
Psychosis symptoms	1 (3.3)	0 (0)	1.0
Suicidal ideation	2 (6.7)	0 (0)	0.492
Substance abuse disorder	0 (0)	0 (0)	-
Psychiatric family history	2 (6.7)	2 (6.7)	1.0

n: Number

Table 4: Correlation between life stress scale and other parameters of studied groups of the studied groups of patients with multiple sclerosis**.**

Variables	Life stress index			
	Relapse		Remission	
	r	P	r	P
Age (years)	0.027	0.887	-0.146	0.442
EDSS	.680	**<0.001*** **	.634	**<0.001*** **
Number of relapses before treatment	0.142	0.210	0.161	0.432
Number of relapses after treatment	0.064	0.742	-0.306	0.128

*Significant P ** Highly significant P-value; *** Very highly significant P-value; EDSS: Expanded Disability Status Scale; r: Correlation coefficient

Table 5: Univariate and multivariate logistic regression analyses for predicting MS relapse.

Variables	Univariate		Multivariate	
	OR (95% CI)	P	OR (95% CI)	P
Life stress index	1.0 (1.0-1.2)	**<0.001*** **	1.8 (1.7-1.9)	**<0.001*** **
Age	1.0 (0.9-1.1)	0.902	1.4 (0.8-3.0)	0.248
Sex	6.9 (1.7 - 27.8)	**0.007****	1.0 (0.0-6.7)	0.219
Residence	0.3 (0.09) - 0.8)	**0.021***	3.0 (0.0-4.1)	0.252
Marital status	1.3 (0.9-2.0)	0.180	3.2 (0.9-4.3)	0.229
Duration of illness	0.6 (0.3-1.2)	0.178	0.0 (0.0-1.0)	0.246
EDSS	3.0 (1.8-5.2)	**0.001*** **	5.2 (0.4-64.4)	0.199
Depression symptoms	10.3 (2.6-41.4)	**0.001*** **	7.1 (0.1-9.2)	0.231
Anxiety symptoms	10.7 (2.1-53.3)	**0.004*** **	5.3 (0.6-7.7)	0.221

*Significant P-value; **highly significant P-value; *** Very highly significant P-value; OR: Odds ratio; 95% CI: 95% Confidence interval.

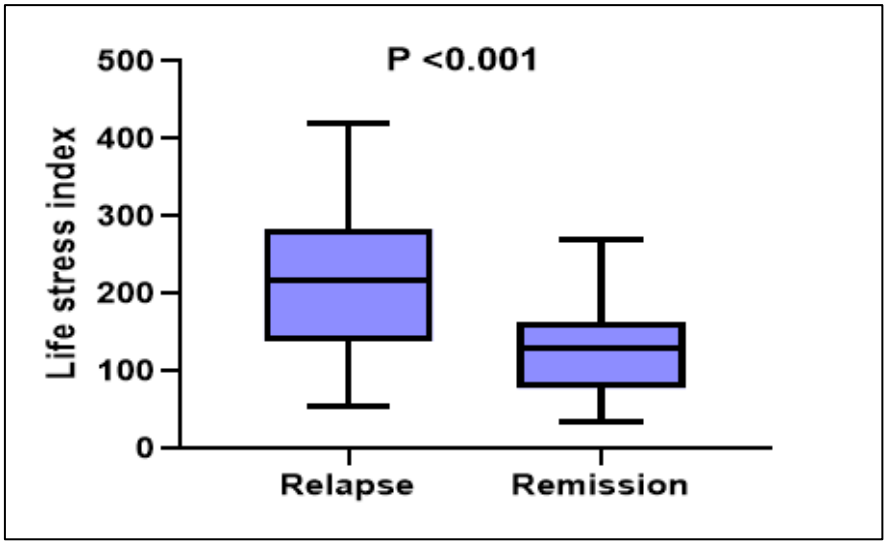

Figure 1: life stress index in the studied groups

Discussion:

MS represents a prevalent neurological disorder and a leading cause of disability among young adults. Effective stress management in individuals with MS may contribute to improvements in both physical health and psychological well-being [3]. The present research examined the relationship between life stress levels and disease activity in patients with relapsing-remitting MS, comparing those experiencing an active relapse with patients in remission.

While age distribution did not differ significantly between groups, sex showed a highly significant disparity ($p = 0.004$), with females predominating in the relapse group (90%) and males being more common in the remission group (43.3%). This was supported extensively in previous literatures [13,14].

This reflects known epidemiological patterns, as MS disproportionately affects females, who are also more susceptible to autoimmune reactivation and stress-related relapses due to hormonal and immunological differences. Moreover, estrogen fluctuations can influence disease activity, possibly explaining the female predominance in active disease [15]. However, Christianson and co-authors claimed that low estrogen states such as menopause and the postpartum period favor exacerbations of multiple sclerosis in women with the disease [16].

Pyramidal involvement was the most common acute deficit in the relapse group (56.7%), reflecting typical corticospinal tract inflammation. Ambulation, cerebellar, and visual deficits followed. These findings align with the multifocal demyelination hallmark of MS. The persistence of residual pyramidal symptoms in both groups also illustrates incomplete recovery after relapses, which can contribute to accumulating disability.

This aligns with the findings of Zhang and co-authors who also exhibited motor dysfunction as the most common presenting symptom during MS relapses [17]. The high prevalence in our study may be explained by the anatomical susceptibility of long tract systems like the corticospinal tract to demyelination, which is a hallmark of MS pathology.

Visual symptoms were exhibited in 40% of relapse patients, consistent with previous studies (Ford, 2020; Nazish and co-authors 2018) which highlighted optic neuritis as one of the earliest and most common manifestations of Relapsing remittent MS. Other deficits like ambulation (30%), cerebellar (13.3%), sensory (6.7%), and bowel/bladder dysfunction (6.7%) were less frequently exhibited. These variations in symptom prevalence may be attributed to lesion location, severity of immune activity, and inter-individual neuroanatomical differences [18,19].

Residual pyramidal symptoms were observed in both groups in this current study, with 36.7% in the relapse group and 26.7% in remission. However, the difference was not statistically significant ($p = 0.405$). This suggests that while some deficits improve with treatment, a significant portion of patients may not fully recover, possibly due to irreversible axonal damage. Comparable findings were exhibited by Hosny and co-authors who emphasized that residual deficits are

common even in early RRMS and are predictive of long-term disability [20].

In the same line with our study, in a prospective, longitudinal, actively treated, single-center cohort study, that recruited patients that were being followed-up for almost 14 years, showed that relapses were associated with a transient increase in disability over 1-year intervals [21]. Elevated EDSS scores during relapses are expected, as relapses involve new or worsening neurological symptoms. The EDSS is a widely used scale to quantify disability in MS, and scores typically increase during relapse periods [20,21].

In our study, Psychiatric symptoms, particularly depression and anxiety, were more prevalent in the relapse group and were associated with elevated stress indices. Depression was present in 36.7% of the relapse group, compared to 16.7% in remission. These findings align with those of Chwastiak and Ehde (2007), who exhibited that psychiatric comorbidities are common in MS and may modulate the impact of stress on disease activity [22].

In a recent study conducted by Moss and co-authors declared that Mental health disorders are prevalent among patients with MS and can substantially compromise overall well-being and daily functioning. Despite their significant impact, these psychiatric conditions frequently remain underrecognized and undertreated in this population [23].

Furthermore, Paykel demonstrated that partial remission, characterized by lingering residual symptoms, represents a significant outcome in major depression. This condition likely reflects a milder persistence of the initial disorder and serves as a strong predictor of elevated relapse risk [24].

Relapsed patients also had significantly elevated life stress scores (median = 218) than those in remission (median = 130), again with $p < 0.001$. Nearly half (46.7%) of the relapse group were classified as having a significant risk of illness or accident. Stressful life events, particularly chronic social or occupational strain, have been linked to MS relapses in prior cohort studies.

Evidence from a systematic review indicates that the link between stress and the development of multiple sclerosis is variable and not consistently observed. Furthermore, the period during which stress occurs, whether in childhood or adulthood, seems to have little impact on either the initial onset of MS or the likelihood of subsequent relapses [25].

On the other hand, Nielsen and co-authors failed to prove any relation between MS onset and relapse [26].

On contrary, another systematic review exhibit a strong heterogeneity between studies, so no secure conclusions could be drawn [27].

Moreover, Briones-Buixassa et al. exhibit that research about the effects of stress on multiple sclerosis has yielded contradictory results [28].

The life stress index was also significantly correlated with EDSS in both groups (relapse: $r = 0.680$, remission: $r = 0.634$, both $P < 0.001$).

These findings are consistent with previous literatures that exhibited that

stressful life events were associated with increased neurological symptoms and new brain lesions in MS patients. Similarly, a longitudinal study by Ackerman et al, exhibit that high perceived stress was significantly associated with increased lesion load and relapses [(29)].

However, against our current study, Kotas et al. claimed that there was no significant relationships were exhibit between stress or coping and MS relapse severity [(30)]. The strong correlation in both relapse and remission groups suggests that stress might not only be a trigger for relapse but also play a role in sustaining disease activity or subclinical inflammation even during remission.

Logistic regression analyses in our study revealed that the life stress index were significant predictors of MS relapse. In the multivariate model, the odds ratios (OR) for the life stress indices were 1.9 and 1.8, respectively ($P < 0.001$ for both), indicating that elevated stress levels significantly increase the risk of relapse.

These findings are in line with the stress-as-a-trigger hypothesis. The landmark study by Ackerman showed that stressful life events preceded MS relapses in a significant proportion of patients [(29)]. More recent work by Yamout et al. also supports this, linking stress to clinical and radiological disease activity [(31)].

Recent evidence indicates that stress may contribute to the risk and activity of MS. A meta-analysis of three studies examining clinically diagnosed stress disorders found that such conditions were associated with nearly a twofold increase in MS risk (OR 1.87, 95% CI 1.061–3.429). The role of stress in triggering MS relapses has been assessed across 19 diverse studies. In particular, analyses from two separate military cohorts exposed to the same conflict demonstrated a threefold higher relapse rate during periods of war (relapse rate: 3.0; 95% CI 1.56–5.81). Additional research has linked stressful life events to heightened MRI activity, and several studies suggest that exposure to stressors may modestly influence overall disease progression in MS [(32)].

In the univariate regression, depression and anxiety symptoms were highly significant predictors of relapse (OR for depression = 10.3, anxiety = 10.7; both $P < 0.01$). However, in the multivariate model, they lost significance, possibly due to collinearity with stress indices.

This supports the notion that stress, depression, and anxiety are interlinked constructs, and their combined influence may be more meaningful than their independent effects. This is also supported by the biopsychosocial model, which posits that psychological states can influence disease processes through neuroendocrine and immune pathways [(32)].

Conclusions

In our study, life stress index was significantly elevated in relapsing-remitting MS patients during relapses than remission, it also predicted relapse risk. These findings emphasize stress management as a critical component of MS relapse prevention.

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Declaration of interest statement: None to be declared.

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