Lupus
2024, Vol. 33(10) 1139–1144
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DOI: 10.1177/09612033241266987
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Psychological impact of life events in systemic lupus erythematosus patients – Differences between flares and remission

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Abstract

Background: Stress has been linked to worsening symptoms and increased disease activity in patients with Systemic lupus erythematosus (SLE). Life-events are individual stress points, and there is conflicting evidence regarding their role in SLE activity and disease perception.

Methods: Adult SLE patients were recruited for the study. Clinical and laboratory features of SLE were recorded, and previous diagnosis of anxiety or depression were retrieved from patients' electronic charts. Flares were defined by the Systemic Lupus Erythematosus Disease Activity (SLEDAI) flare Index, and flares during the previous year were documented. During a routine visit, they completed validated Portuguese translations of the 10-item Perceived Stress Scale (PSS-10), Hospital Anxiety and Depression Scale (HADS) and Life Experience Survey (LES) for the previous year.

Results: A total of 47 female SLE patients were recruited. Ten patients (21.3%) had experienced recent flares. Patients with recent flares reported fewer life events, with lower positive, negative, and total weightings sums compared to those without recent flares. Although 42.2% of patients perceived pathological levels of stress in the previous month, 48.9% had anxiety symptoms, and 34% were at high risk for an anxiety disorder, these psychometric measures did not differ significantly between the recent flare and no-flare groups.

Conclusions: There is a high prevalence of pathological levels of stress among SLE patients. SLE patients with recent flares report less psychological impact from life events, both positive and negative, independent of other psychological or pharmacological factors.

Keywords

Psychological impact, life-events, stress, systemic lupus erythematosus, flare

Date received: 21 January 2024; accepted: 20 June 2024

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Introduction

Systemic lupus erythematosus (SLE) is a chronic and debilitating systemic autoimmune disease characterized by significant clinical heterogeneity. This heterogeneity encompasses a wide range of physical and laboratory findings as well as psychological, emotional, and social repercussions. Stressful life events have been linked to the development,[1] severity, and progression of both mental and physical health conditions, including autoimmune diseases.[2] Stress is known to exacerbate symptoms and is associated with increased lupus activity.[3,4] However, the relationship between SLE disease activity and the impact of life events remains controversial, with conflicting data reported.[3,4]

This study aimed to explore the relationship between SLE disease activity and the psychological impact of life events and perceived stress.

Methods

Participants

Adult female SLE patients were consecutively recruited from the Autoimmune Patients Clinic at Unidade de Imunologia Clínica – Centro Hospitalar Universitário de Santo António. All patients who agreed to participate were interviewed and completed the questionnaires. They all met the modified American College of Rheumatology (ACR) 1997 and SLICC classification criteria for SLE. Recruitment began in March 2017 and was halted due to the COVID-19 pandemic lockdown in mid-March 2020. Patients with other concomitant systemic autoimmune diseases (e.g.: Sjogren's syndrome, Antiphospholipid Syndrome) were excluded. Sociodemographic characteristics were collected during the interview.

Psychiatric history and psychometric measures

Previous diagnosis of depression or anxiety was retrieved from the patients' clinical records. During a routine visit, patients completed validated Portuguese translations of the 10-item Perceived Stress Scale (PSS-10),[5] Hospital Anxiety and Depression Scale (HADS)[6] and Life Experience Survey (LES) for the previous year.[7]

HADS-A screens anxiety, and HADS-D screens for depressive symptoms. Scores above 8 points are considered borderline abnormal, and scores above 11 are considered abnormally high.[8] The PSS-10 assesses the degree to which an individual perceived their life as unpredictable, uncontrollable, and overloading over the previous month. Individuals are considered to have pathological levels of stress if their PSS-10 scores are 22 or above.[5] The LES is a 57-item instrument that asks respondents to report the occurrence of significant life events (such as losing a loved one, getting married, being fired, etc.) during the last six months or year[9]; the Portuguese validation uses only the rates for the previous year.[7] If a patient has experienced an event, they must then rank it from very negative to very positive in impact. The LES results in five composite scores: total number of life events, sum of negative weightings, sum of positive weightings, total (absolute) positive and negative weightings sum, and balance (arithmetic sum) of positive and negative weightings.

Systemic lupus erythematosus measures

Clinical and laboratory cumulative and current manifestations were retrieved from the patients' clinical records. Disease activity was measured using Systemic Lupus Erythematosus Disease Activity Index (SLEDAI-2k; the score ranges from 0 (no activity) to 105 (maximal activity))[10]; a flare was defined by the SLEDAI flare index.[11] A flare was considered recent if patients had flare according to SLEDAI flare index at any visit during the previous year (up to, and including, the recruitment visit). Damage was assessed by the Systemic Lupus International Collaborating Clinics/ ACR (SLICC/ACR) damage index (SDI), with scores ranging from 0 (no damage accrual) to 45 (maximal damage).[12]

Statistical analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) software version 27. T-tests were used to compare means in homogeneous variables, Mann-Whitney tests for non-parametric comparisons, Chi-square tests for categorical variables, Pearson correlation tests for homogeneous continuous variables correlations, and Spearman correlation tests for non-homogeneous ones. p values <0.05 were considered significant.

The study was approved by the institution's Research Ethics Committee (Internal code: 212/2014; 182-CES) and all participants gave written informed consent.

Results

Demographics

Forty-seven patients agreed to participate and completed the questionnaires. The sociodemographic, clinical, and psychometric characterization of the participants are summarized in Table 1. All participants were Caucasian women with a mean age of 44.5 years. Most patients had at least 12 years of education (68.1%) and were employed (83.0%). Nearly half of the participants (44.7%) were married.

Table 1. Demographic and Clinical Characterization of subgroups of patients with and without Recent Flares.

	Recent flare subgroup (*n* = 10)	No recent flare subgroup (*n* = 37)	
	Mean ± SD or *n* (%)		*p* value
Demographics			
Current age, years	43.70 ± 8.38	44.65 ± 9.82	0.782
Age at diagnosis, years	29.70 ± 10.41	30.89 ± 10.41	0.750
Disease duration, years	13.50 ± 7.56	13.38 ± 7.05	0.962
Cumulative SLE organ involvement			
Constitutional	21 (44.7%)		
Mucocutaneous	45 (95.7%)		
Musculoskeletal	42 (89.4%)		
Renal	16 (34.0%)		
Neuropsychiatric	6 (12.8%)		
Haematological	38 (80.9%)		
Current SLEDAI	**6.00 ± 6.41**	**1.22 ± 1.90**	**<0.001**
Type of recent organ involvement			
Constitutional	1 (10.0%)		
Mucocutaneous	5 (50.0%)		
Musculoskeletal	5 (50.0%)		
Renal	3 (30.0%)		
Neuropsychiatric	1 (10.0%)		
Haematological	8 (80.0%)		
Pericarditis	1 (10.0%)		
Damage accrual	1 (10.0%)	14 (37.8%)	0.094
SDI score (if accrual)	1.00 ± 0.00	1.50 ± 0.94	0.552
Current oral corticosteroids (Yes)	5 (50.0%)	17 (45.9%)	0.820
Daily corticosteroids dosage (mg)	5.00 ± 1.77	4.67 ± 1.80	0.792
Current antimalarial use (Yes)	9 (90.0%)	29 (78.4%)	0.407
Current immunosuppressant use (Yes)	4 (40.0%)	13 (35.1%)	0.776
Current antidepressant use (Yes)	3 (30.0%)	12 (32.4%)	0.884
Current benzodiazepine use (Yes)	1 (10.0%)	10 (27.0%)	0.259

SD – standard deviation; SDI – Systemic Lupus International Collaborating Clinics Damage Index; SLE – Systemic Lupus Erythematosus; SLEDAI – Systemic Lupus Erythematosus Disease Activity Index. p value is significant <0.05. Bold indicates significant p differences ($p < 0.05$).

Psychiatric history and psychometric measures

Seventeen patients (36.2%) had a previous diagnosis of anxiety, and 20 (42.8%) had a diagnosis of depression. At the time of the study, almost half (48.9%) of the patients had anxiety symptoms (HADS-A), and 16 (34%) were at high risk for an anxiety disorder. Around one-fourth (25.5%) of the patients had depressive symptoms (HADS-D), with 12.8% at high risk for depression. Nineteen patients (42.2%) perceived pathological levels of stress in the previous month (PSS-10).

Patients with higher levels of perceived stress also had more anxiety (Pearson's r = 0.759, $p < .001$) and depression symptoms (Pearson's r = 0.660, $p < .001$). On the LES scale for the previous year, patients reported experiencing an average of 3.40 (±2.79) major life events, with only 4 (8.5%) not reporting any event. The negative weighting sum was on average higher than the positive weighting sum (−5.02 vs 1.98). Negative weighting of life events was higher in patients reporting higher perceived stress in the previous month (Pearson's r = −0.450, $p = .002$). There was no association between the negative weighting of life events and previous diagnosis of depression or anxiety, current anxiety or depressive symptoms, or the use of antidepressants or anxiolytic.

The positive weighting sum of life events was lower in patients previously diagnosed with depression (0.90 vs 2.78 points, $p = .040$) and in those with anxiety symptoms (Spearman's r = −0.324, $p = .027$). There was no association between the positive weighting sum and perceived stress, antidepressants use, or anxiolytic drug use.

Clinical SLE features

The mean disease duration was 13.4 years (SD 7.08), with a range from 1 to 27 years. Previous organ involvement is described in Table 1. Twenty-eight patients (59.6%) never had neuropsychiatric, renal, or other major involvement. At the time of the study, mean SLEDAI-2k score was 2.15 (SD 3.76) points, ranging from 0 to 23. Five patients (10.6%) were experiencing a flare, and 31 (66.7%) were in DORIS 2021 remission.[13] Ten patients (21.3%) had experienced flares in the year prior to or at the time of the study visit.

The mean damage SDI score was 0.47 (±0.86 points), with a range from 0 to 4, and 15 patients (31.9%) had accrued damage, primarily ocular and skin damage. At the time of the study, 38 patients (80.9%) were on hydroxychloroquine, 22 (46.8%) were on steroids with mean prednisolone dose of 4.7 mg/day (maximum 7.5 mg/day), and 17 (36.2%) were on other immunosuppressants. Fifteen patients (31.9%) were on antidepressants, and 11 (23.4%) were on benzodiazepines.

Association between clinical and psychological features

Patients with recent flares reported a lower number of life events, with lower positive, negative, and total weightings sums compared to those who had no recent flares (Table 2). To account for the possible effect of a lower reported number of life events, we also calculated the ratio of positive, negative, and total weightings per event. Although not statistically significant, the same differential tendency was observed (Table 2). There was no difference in previous depression diagnosis or current depressive or anxiety symptoms between the two subgroups. However, there was a tendency for more previous anxiety diagnoses in the no recent flare subgroup.

No other clinical parameter (disease duration, number of classification criteria, organ involvement, current activity index, damage accrual, or medication) was associated with a diagnosis of anxiety or depression or any other psychological scale parameters.

Discussion

In our study, SLE patients with recent flares reported experiencing fewer life events and attributed less positive, negative, and overall impact to these events compared to patients with no recent flares. Assessing the positive and negative impact of recent life events is a useful mental health evaluation tool, as it considers both the exposure to a stressor and the individual's response, which depends on their psychological burden and the balance between protective and aggravating factors.

Several factors can potentially modulate the impact of life events, including psychological factors (perceived stress, anxiety, and depression)[9,14] and pharmacological exposure (antidepressants,[15] benzodiazepines[16] or glucocorticoid dosage[17]). In our study, there were no major differences between groups in terms of the most relevant sociodemographic and psychological factors. While perceived stress, anxiety, and depressive symptoms were high in our patients compared with

Table 2. Demographic and Psychometric Differences between of subgroups of patients with and without Recent Flares.

	Recent flare subgroup (*n* = 10)	No recent flare subgroup (*n* = 37)	
	Mean ± SD or *n* (%)		*p* value
Years in education	14.34 ± 3.94	12.31 ± 4.73	0.149
Depression			
Previous diagnosis	4 (40.0%)	16 (43.2%)	0.854
HADS-D	5.00 ± 5.19	5.54 ± 4.15	0.731
Anxiety			
Previous diagnosis	1 (10.0%)	16 (43.2%)	0.052
HADS-A	8.10 ± 3.98	8.51 ± 5.10	0.814
Perceived stress scale	18.44 ± 7.26	18.92 ± 7.82	0.870
Life experience survey (1 year)			
Number of events/patient	**2.00 ± 2.54**	**3.78 ± 2.77**	**0.016**
Positive weightings sum	**0.10 ± 0.32**	**2.49 ± 3.98**	**0.027**
Positive weightings sum per event	0.13 ± 0.35	0.53 ± 0.70	0.082
Negative weightings sum	**−4.00 ± 6.39**	**−5.30 ± 3.99**	**0.037**
Negative weightings sum per event	−1.53 ± 1.22	−1.58 ± 0.95	0.963
Total weightings sum	**4.10 ± 6.33**	**7.78 ± 5.95**	**0.014**
Total weightings sum per event	1.66 ± 0.97	2.11 ± 0.73	0.198
Balance positive and negative weightings	−3.90 ± 6.47	−2.81 ± 5.30	0.585

HADS-A – Hospital Anxiety and Depression Scale - anxiety; HADS-D - Hospital Anxiety and Depression Scale - depression; SD – standard deviation. p value is significant ($p < 0.05$). Bold indicates significant p differences ($p < 0.05$).

the Portuguese population,[5,6] these factors and pharmacological exposure were not significantly different between the Recent Flare and No Recent Flare subgroups. This suggests that SLE flares might somehow modulate the impact of life events on the individual.

One possible explanation for our findings is that patients with recent flares experienced fewer life events, which had less impact. However, this alone seems unlikely to be the only reason. An interesting additional explanation is recall bias[18]: patients with recent flares might not remember events or their impact accurately, as their memory accuracy and volume could be influenced by having had an SLE flare. This "diversion of attention" could result from concerns about their illness or an inability to feel the life events and their impact.

Recent studies[19] have revealed interesting findings regarding the Default Mode Network (DMN) and pre-frontal cortex metabolism in SLE patients during non-neurological flares versus inactive SLE patients. The DMN region is partly responsible for intrinsic awareness. These studies concluded that flaring SLE patients were less able to suppress DMN regions during a working memory task, potentially leading to emotional interference during cognitive tasks. This mechanism suggests that both recall bias and diversion of attention are potential, non-mutually exclusive explanations for the results seen in our study. Flaring patients might not only be less aware of events, but they also might not register these events in working memory, and thus, they might not be recorded in long-term memory. This points to the possibility of both cognitive and emotional "Lupus Fog", which we consider a likely explanation for our study results.

This study was limited by its small sample size and exclusive inclusion of Caucasian female patients. Larger patient cohorts are needed to confirm these results. Further studies that record concomitant psychological impact, apathy scales, cognitive tests, and functional neuroimaging are required to validate the association between hypofunction in specific brain areas and cognitive and emotional "Lupus Fog" during flares. Exploring the contribution of these mechanisms to the well-being and quality of life of SLE patients, particularly those who have experienced recent flares, is also particularly important.

In summary, we demonstrated a difference in the quantification and reported impact of recent life events between two groups of SLE patients – those with and those without flares in the past year. This finding may shed light on the emotional component of "Lupus Fog" that should be assessed during SLE flares.

Acknowledgments

Joana Ferreira, Ana Tavares, Denis Sousa, Márcia Cravo and Cláudia Ferrão for study logistic support.

Author contributions

RF, CV and MFB conceived the study design; RF, DGO executed and acquired data; RF, DGO, RA, CV, and MFM analysed and interpreted the data; RF, DGO, CV and MFB wrote the draft; all authors substantially and critically reviewed the article.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: DGO work is funded by a doctoral research grant from FCT – Foundation for Science and Technology (UI/BD/150742/2020); UMIB (UIDB/00215/2020; UIDP/00215/2020); ITR (LA/P/0064/2020).

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