

# Association between perceived level of stress, clinical characteristics and psychopathological symptoms in women with systemic lupus erythematosus

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## Abstract Objective

To evaluate psychopathological status and stress level from a sample with SLE; compare mental functioning and stress levels between women with SLE and healthy women; determine whether disease duration, disease activity, cumulative organ damage and stress have an influence on psychopathological symptoms in SLE patients; and evaluate whether perception of stress is related to SLE severity.

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## Methods

We conducted a cross-sectional study of 425 participants; 202 women with SLE, with an average age (SD) of 36.61 (10.15), and 223 healthy women, with age-matched controls. The assessment included the clinical characteristics (disease duration, SLE activity, cumulative organ damage, pharmacotherapy), the Symptom Checklist-90-Revised (SCL-90-R) and the Perceived Stress Scale. Descriptive, comparative, univariate and multivariate analysis were performed.

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## Results

SLE patients showed psychopathological alterations in the somatisation, obsessive-compulsive and positive discomfort subscales of SCL-90-R. Women with SLE reported significantly higher scores on the psychopathological dimensions and perceived stress compared to healthy women, except for paranoid ideation. Disease duration, SLE activity, cumulative organ damage, and perceived stress were shown to be significant predictors of psychopathological manifestations, explaining a range, between 20 and 43%, of variance across SCL-90-R dimensions. Moreover, perceived stress was related to SLE activity, after controlling for psychopathological dimensions.

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## Conclusion

The psychopathological manifestations in SLE appeared to be influenced by perceived stress, disease duration, disease activity and cumulative organ damage. In turn, perceived stress was associated with disease severity. This knowledge may contribute to a more comprehensive perspective of these manifestations in the SLE population in the clinical setting.

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## Key words

systemic lupus erythematosus, psychological stress, risk factors, psychopathology

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## Introduction

Systemic lupus erythematosus (SLE) is regarded as a chronic (long-term), multisystem, connective-tissue disease, characterised by an alteration in the immunological response (1-2). Its clinical course is usually unpredictable, with exacerbations and periods of remission (3). During the course of the disease, all tissues and organs may be potentially impaired, occasionally irreversibly (4). The SLE disease course presents a broad spectrum of clinical symptoms, a set of immunological alterations and specific anatomopathological characteristics (5). Common manifestations include inflammation, swelling (involving the skin and joints), pain, fatigue, rashes, arthritis, stiffness, lassitude, weight loss, hair loss, anemia and fever, appearing even in periods of disease latency (1, 6-8). Consequently, SLE may affect several aspects of patients' daily lives, leading to impairment of quality of life and patient functioning (3-4, 7). SLE clinical characteristics include psychopathological manifestations that can be present in almost 50% of the population during the disease course (9-10). These manifestations are even suggested to be an integral part of the SLE process (11). Symptoms of anxiety and depression have been shown to be related to poorer quality of life and work disability in these patients (12-13). However, the prevalence of psychopathological manifestations varies broadly in this population across the studies (14). This wide variation is mainly the result of methodological deficiencies. Research into this topic has usually employed poor comparison groups, or lacked them completely, has failed to use standardised measures, or has used small, unrepresentative and unbalanced samples (14-15). The literature has emphasised the importance of medical components in the disease course for SLE patients. However, although these are of considerable importance, psychological aspects, such as stress level or psychopathologic status, have been disregarded and neglected (6, 8, 16-17). Several studies highlight the relevance of psychological factors in autoimmune pathologies, and these factors have been considered

relatively independent from physical findings (18-20). Some investigations have reported that the stress level could cause a worsening of the disease course (6, 17, 21-22). Da Costa *et al.* (3) concluded that the stress level is the most important short-term factor of functional disability in SLE patients. On the other hand, some disease parameters, such as disease activity or cumulative organ damage, have been demonstrated to be independent components of health status among these patients (18). Several researchers have pointed out the need for additional studies, which may elucidate the critical variables for psychiatric symptoms in SLE patients (10-11). Nevertheless, although SLE patients seem to present psychopathological disorders, no studies have investigated the predictive factors of these manifestations in the SLE population. Furthermore, despite the clinical importance of the clinical characteristics and perceived stress on SLE, to our knowledge, the role of these factors regarding psychopathological manifestations remains uncertain.

Therefore, the objectives of the present study were: 1) to compare the psychopathological status and the stress levels between women with SLE and healthy women; 2) to determine whether disease duration, disease activity, cumulative organ damage and perceived stress have an influence on psychopathological levels in SLE patients; 3) to evaluate whether the perception of stress is related to SLE severity.

## Materials and methods

### Study population and design

This is an observational, cross-sectional study. The total sample consisted of 425 women, living in Andalusia (Spain), with an average age of 36.20 years (SD=10.62) in an age range between 18 and 78 years. Participants were divided into two groups, people with SLE (SLE patients group, n=202) and healthy people (healthy control group, n=223). All participants with SLE were patients at the Systemic Autoimmune Disease Units, from two Public Health Service hospitals in the Autonomous Community of Andalusia (Spain). The healthy control group was recruited in a con-

secutive manner from relatives of SLE patients and workers from the hospital and university, so they tend to share a similar socioeconomic environment. The inclusion criteria for both groups were: being a woman and having a level of education higher than elementary. The SLE group also had to meet at least four of the American College of Rheumatology criteria for SLE (23). Exclusion criteria were: having a severe cardiovascular disease, having a history of another autoimmune disease, having severe neurological damage and abusing alcohol or other drugs. All participants gave their signed informed consent to participate in this study. Procedures followed standards from the responsible Human Bioethics committee and the Helsinki Declaration.

#### *Information collected*

A specific demographic questionnaire (age, education, civil status) was created for this study. Clinical data of SLE such as disease duration (years), the SLE activity, cumulative organ damage and pharmacotherapy (corticosteroid therapy dose, corticotherapy, antimalarial agents, psychotropic and immunosuppressant drugs) were collected. Psychopathological manifestations (mental functioning) and perceived stress level were evaluated for both groups by using the Symptom Checklist-90-Revised and Perceived Stress Scale, respectively. All measures were validated instruments for the Spanish population.

#### *The SLE Disease Activity Index (SLEDAI)*

The total SLEDAI score shows the level of activity of the disease over the last ten days, ranging from 0 (no activity) to 105 points (maximum activity) (24-25).

#### *Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index*

The SLICC/ACR evaluates cumulative organ damage caused by the disease itself or complications after therapy interventions. The total score ranges from 0 (no damage) to 48 points (maximum damage) (26-27).

#### *The Symptom Checklist-90-Revised (SCL-90-R)*

The SCL-90-R is a 90-item self-report symptom inventory that evaluates mental functioning/psychological distress. This instrument comprises nine primary symptom dimensions and three summary scores, determined as global scores. The principal symptom dimensions are categorised as somatisation, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism. The global measures result in the global severity index (GSI), the positive symptom distress index (PSDI) and the positive symptom total (PST). The total score ranges from 0 (not at all) to 4 points (extremely), considering how patients feel or how the specific problem has bothered them in the last week (28-29).

#### *Perceived Stress Scale (PSS)*

This tool is a self-report questionnaire that assesses the perceived stress level over the last four weeks. This scale has fourteen items with a five-point frequency response scale, ranging between 0 (never) to 4 points (very often). Higher scores are interpreted as a higher level of perceived stress. The PSS has demonstrated adequate reliability (internal consistency with a Cronbach alpha of 0.81), and good concurrent validity and sensitivity in the Spanish population (30).

#### *Procedure*

The procedure for collecting all the study information was similar to what was published previously by Peralta-Ramírez *et al.* (16). The first contact was with the internist at the outpatient clinic for autoimmune disease. Potential participants that met the inclusion-exclusion criteria were recruited. All these patients were informed about the study objectives and they were invited to participate (response rate of 89%). In the first session, full details on the study were provided and participants were asked to sign the written consent form. Then, investigators collected the demographic and clinical information, and the psychopathological and stress evaluation was completed. The study

was conducted between March 2013 and January 2016. The healthy (control) group was recruited in a consecutive manner. This study was approved by the Human Bioethics Committee – Hospital Virgen de las Nieves (Granada, Spain).

#### *Statistical analysis*

The analyses for this study were performed using SPSS software, v. 20.0. The total sample was divided into two groups (SLE and control group). A descriptive analysis was performed and a normal distribution of variables was confirmed with the Kolmogorov Smirnov test. The Box-Cox transformation was performed for non-normal distributed variables. The Levene's test was used to evaluate the equality of variances. Independent *t*-tests and  $\chi^2$  tests were used to assess differences between the SLE group and the control group. We performed twelve multiple regression analyses to evaluate which disease and psychological outcomes best explain the scores on the SCL-90-R for SLE patients. The dependent variables were the scores on each of the subscales of the SCL-90-R inventory. The independent variables were stress scores, disease duration, SLEDAI and SLICC. A Multivariate analysis of covariance (MANCOVA) was performed to evaluate whether the level of perceived stress and SLE severity were related, while correcting for the psychopathological variables. The MANCOVA was carried out using the level of perceived stress (perception of stress vs. no perception of stress) as independent variables, and SLEDAI and SLICC (disease severity) as dependent variables. The SLE sample was divided into two groups of perceived stress, taking the mean for the Spanish population (25 points on PSS scale). All psychopathological dimensions that were found to be clinically significant in the SLE patients group were introduced as covariates.

## **Results**

### *Description of demographics and clinical data, psychopathological symptoms, and perceived stress of the SLE group*

The average age of the subjects in the SLE sample is 36.61 (SD=10.15) years.

From this sample, 80.6% of patients scored 0 points on the SLICC index, showing no cumulative organ damage. Specifically, five SLE patients suffered from neuropsychiatric SLE, three from renal damage and fifteen from neurological damage. They reported scores above 70 points in the subscales of somatisation (M=71.21), obsessive-compulsive (M=72.04) and positive symptom total index (M=71.98), indicating clinical psychopathology in these dimensions. From the SLE sample, 64.9% presented clinical somatisation, 65.7% obsession-compulsion, 48.5% interpersonal sensitivity, 45.3% depression, 54.5% anxiety, 47.5% hostility, 34.7% phobic anxiety, 45.5% paranoid ideation and 55.4% psychoticism. In addition, 18% showed a clinical alteration in the global severity index, 32.7% in the positive symptom distress index and 64.9% in the positive symptom total. The mean score of perceived stress was 26.37 (SD=9.31) points. The remaining descriptive information is shown in Tables I–III.

#### *Differences between the SLE group and the healthy control group for sociodemographic variables*

In the comparison between groups (SLE/control group) for the main sociodemographic variables, there were no differences between groups, except for level of education. The healthy women's control group demonstrated a higher educational level than the SLE group. Means, SD and percentages of sociodemographic variables, and between-group comparisons are shown in Table I.

#### *Differences between the SLE group and the healthy control group for psychopathological dimensions and perceived level of stress*

In contrast to SLE patients, healthy participants showed significantly lower scores across all dimensions of the SCL-90-R, except for the paranoid ideation subscale. There were also significant differences between groups for the perceived stress scale. Table III shows the mean psychopathological and perceived stress in the SLE sample compared with the control group.

**Table I.** Mean (SD), percentages and level of significance of differences between SLE and healthy control group for sociodemographic variables (n=423).

Characteristics	LES group (n=202)	Control group (n=223)	T/Chi-square	p-value
	Mean (SD)/ Percentage (%)	Mean (SD)/ Percentage (%)		
Age	36.61 (10.15)	35.82 (11.05)	0.768	0.443
Educational level				
Primary school	33.5 %	11.4 %	38.50	0.001
Secondary school	40.1 %	31.3 %		
Associate's degree	26.4 %	57.3 %		
Civil status				
Single	30.8 %	41.7%	4.99	0.082
Married	61.5 %	44.4 %		
Widowed/ separated/ divorced	7.7 %	13.9 %		

**Table II.** Clinical outcomes of SLE group (n=202).

Clinical outcomes	Mean (SD)	Percentage (%)
Disease duration	10.15 (8.34)	
SLEDAI	2.28 (2.78)	
SLICC. Range (0 – 6)	0.34 (0.91)	
SLICC = 0		80.60%
SLICC > 0		19.40%
Pharmacotherapy		
Dose corticosteroid therapy	3.66 (3.68)	
Corticotherapy		53.44 %
Antimalarial agents		12.87 %
Psychotropic drugs		5.45 %
Immunosuppressive agents		18.81 %

SLE: systemic lupus erythematosus; SLEDAI: SLE Disease Activity Index; SLICC: Systemic Lupus International Collaborating Clinics.

A comparison between the two groups for the psychopathological profile is also depicted in Figure 1.

#### *Effect of disease parameters and perceived level of stress on psychopathological dimensions in SLE patients*

The results revealed that the disease duration, disease activity, cumulative organ damage and perceived stress scores were significant predictors of all dimensions from the SCL-90-R inventory in the SLE sample. The disease duration, PSS and SLEDAI scores were associated with somatisation, predicting almost 25% of the total variance in this dimension. The same clinical and psychological variables were also associated with the obsessive-compulsive and interpersonal sensitivity dimensions, and a positive discomfort index score, predicting 32%, 20% and 37% of the total variance, respectively. The PSS and SLEDAI scores predicted almost 42%

of the variance for depression and 16% for the global severity index; the PSS and disease duration scores explained 27% of anxiety, 22% of psychoticism and 27% of the positive symptom total; the PSS and SLICC scores explained 22% of hostility; and the PSS predicted 8% of phobic anxiety. In general, the perceived level of stress was a partial predictor for all dimensions of the SCL-90-R inventory (see Table IV).

#### *Relationship between perceived level of stress and lupus severity while controlling for psychopathology in SLE patients*

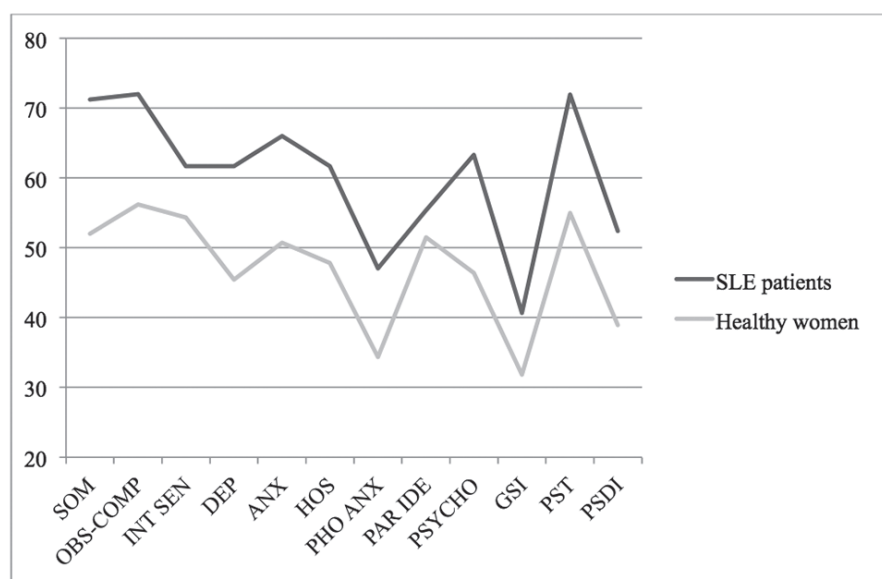
The results from the MANCOVA analyses, controlling for psychopathological dimensions, indicate that stressed SLE patients and non-stressed SLE patients differ significantly regarding disease activity (SLEDAI) (F=4.628, p=0.011). After introducing the psychopathological dimensions as covariates, the subgroup of SLE patients reporting



**Table III.** Mean (SD) and level of significance of differences between SLE and healthy control group for mental functioning (SCL-90-R) and stress level (PSS) (n=423).

Outcomes	SLE group (n=202)		Control group (n=223)		T	p-value
	Mean	SD	Mean	SD		
Mental functioning						
Somatisation	71.22 <sup>a</sup>	26.27	52	23.3	7.92	0.001
Obsessive-compulsive	72.04 <sup>a</sup>	26.06	56.20	26.51	6.17	0.001
Interpersonal sensitivity	61.72	30.48	54.32	27.65	2.60	0.010
Depression	61.72	28.69	45.42	25.66	6.12	0.001
Anxiety	66.01	25.83	50.76	25.78	6.06	0.001
Hostility	61.69	28.05	47.83	25.01	5.34	0.001
Phobic anxiety	47.04	36.12	34.36	29.49	3.93	0.001
Paranoid ideation	55.38	33.96	51.51	28.70	1.26	0.210
Psychoticism	63.29	33.79	46.38	30.96	5.45	0.001
GSI	40.66	28.11	31.84	24.95	3.38	0.001
PST	71.98 <sup>a</sup>	28.09	54.97	23.88	5.30	0.001
PSDI	52.43	27.31	38.91	28.24	6.28	0.001
Level of stress						
PSS	26.37	9.31	20.95	7.75	6.40	0.001

SLE: systemic lupus erythematosus; GSI: Global Severity Index; PST: Positive Symptom Total; PSDI: Positive Score Discomfort Index; PSS: Perceived Stress Scale. <sup>a</sup>Standard T scores for subscales of the SCL-90-R higher than 70 points. Statistical significance  $p < 0.05$ .



**Fig. 1.** Mean scores for the psychopathological dimensions (SCL-90- R) and comparison between groups (SLE patients/healthy control group).

SOM: somatization; OBS-COMP: obsessive-compulsive; INT SEN: interpersonal sensitivity; DEP: depression; ANX: anxiety; HOS: hostility; PHO ANX: phobic anxiety; PAR IDE: paranoid ideation; PSYCHO: psychoticism; GSI: global severity index; PST: positive symptom total; PSDI: positive symptom distress index.

stress had significantly higher levels of disease activity if compared with SLE patients not reporting stress (M=2.44 vs. M=2.01, respectively). However, there was no multivariate difference for cumulative organ damage between the two groups; both groups revealed similar levels of cumulative organ damage (SLICC).

**Discussion**

The objectives of this research were to compare mental functioning and stress levels between women with SLE and healthy women, to determine whether several disease parameters and perceived stress have an influence on psychopathological levels in SLE patients, as well as evaluating whether stress and

disease severity are related. The results have shown that the SLE sample from this study seems to show a specific psychopathological profile, characterised by manifestations of somatisation, obsessive-compulsive symptoms and high scores on the positive symptom total index. This profile indicates that SLE subjects could be at clinical risk of suffering alterations for these dimensions. When SLE patients and healthy participants were compared, the SLE sample showed significantly higher levels for the variables of somatisation, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, psychoticism and perceived stress. Several disease parameters and the level of perceived stress were associated with the psychopathological status of SLE patients. In turn, perception of stress and activity disease were related (while controlling for psychopathology), with higher disease severity scores among SLE patients that reported stress.

On the other hand, the level of cumulative organ damage was low in the SLE sample, probably because the SLICC is an index of organ damage, even when there are activity outbreaks. Close follow-up and monitoring of patients allows an early therapeutic approach to prevent involvement or impairment of the vital organs. Classically renal (and neurological) involvement conditioned disease prognosis. However, current therapeutic options can contain this. The most superior treatments include the use of corticosteroids. These drugs are a classic treatment but their use has been modified over the years, with greater control over doses and how long they are used to avoid long-term side effects on classic cardiovascular risk factors (diabetes, hypertension, hypercholesterolaemia, abdominal obesity), among others. Furthermore, immunosuppressants are also used early on to decrease the doses of corticosteroids and to help control the activity. All this can help reduce functional alterations in the organs due to persistent SLE activity. To our knowledge, this is the first study evaluating the association between the disease parameters, perceived stress, and psychopathological status of SLE

**Table IV.** Final lineal multiple regression model of predictive associated factor to mental functioning (SCL-90-R) in women with SLE (n=202).

Dependent V	Predictor V	R <sup>2</sup>	R <sup>2</sup> corrected	Beta	T	p-value
Somatisation	Disease duration	0.254	0.235	-0.189	-2.680	0.008
	PSS			0.403	5.638	0.001
	SLEDAI			-0.139	-0.139	0.044
Obsessive-compulsive	Disease duration	0.339	0.322	-0.198	-2.987	0.003
	PSS			0.479	7.134	0.001
	SLEDAI			-0.130	-2.002	0.047
Interpersonal sensitivity	Disease duration	0.218	0.198	-0.264	-3.658	0.001
	PSS			-0.277	2.794	0.001
	SLEDAI			0.171	2.375	0.019
Depression	PSS	0.429	0.415	0.607	9.725	0.001
	SLEDAI			-0.129	-2.143	0.034
Anxiety	Disease duration	.291	.273	-0.201	-2.929	0.004
	PSS			0.442	6.344	0.001
Hostility	PSS	0.239	0.220	0.418	5.799	0.001
	SLICC			0.160	2.261	0.025
Phobic anxiety	PSS	0.099	0.077	0.215	2.737	0.007
Psychoticism	Disease duration	0.239	0.220	-0.214	-3.012	0.003
	PSS			0.384	5.332	0.001
GSI	PSS	0.181	0.160	0.312	4.168	0.001
	SLEDAI			0.250	3.474	0.001
PST	Disease duration	0.268	0.268	-0.166	4.168	0.017
	PSS			-2.413	3.474	0.001
PSDI	Disease duration	0.386	0.371	-0.233	-3.643	0.001
	SLEDAI			-0.139	-2.222	0.028
	PSS			0.504	7.790	0.001

V: variable; SLE: systemic lupus erythematosus; GSI: Global Severity Index; PST: Positive Symptom Total; PSDI: Positive Score Discomfort Index; PSS: Perceived Stress Scale; SLEDAI: SLE Disease Activity Index; SLICC: Systemic Lupus International Collaborating Clinics.

patients. The higher levels of psychological alteration in the SLE group could be explained by the uncertainty of the disease course, medical symptoms, therapy, pain, and the loss of function and personal autonomy. These results contrast with other investigations, reporting that SLE patients seem to have the same level of depression, perceived stress, tension or anger as the subjects from the control groups (11, 21, 31). These findings also show that PSS, SLEDAI and SLICC scores, as well as the disease duration of SLE patients, have a significant influence on the psychopathological manifestation of patients with SLE. These variables explained more than 20% of the variance of somatisation, interpersonal sensitivity, anxiety, hostility, psychoticism and positive symptom total; more than 30% of the obsessive-compulsive and positive discomfort index score variances; and 42% for depression.

However, the associations were cross-sectional; hence, we cannot determine the cause and the effect.

Specifically, the perceived level of stress appeared to be associated with all of the psychopathological dimensions in patients with SLE. Therefore, perceived stress could have an impact on psychopathological manifestations or vice versa. Although the mechanisms involved in these associations cannot be determined from this study, some speculation is possible. The chronic and unpredictable nature of the disease could lead patients to live with a possible and sudden disruption of independency, autonomy and health. Paralleling this explanation, Peralta-Ramírez *et al.* (16) reported that daily stress is also a cognitive functioning predictor. They claim that stress may impair visual memory, fluency and attention-related resources. Impairment of these cognitive functions

could influence brain interpretations and general mental functioning. Other authors report that stress, evaluated by registering major life events, such as a job loss or a divorce, and hassles such as time pressure or financial worries, contributes to psychopathological status (15). However, contrary to this assumption, other findings point to psychopathology, which affects the perception of stress. In the study conducted by Palagini *et al.* (32), these authors included an anxiety and depressive symptoms evaluation, assessing its influence on perceived stress, using the same scale as the present study. This research concluded that insomnia, stress and psychopathology (especially depression) were related.

Moreover, SLE patients that reported stress showed significantly higher levels of disease activity (when psychopathology was controlled), highlighting the importance of the perceived level of stress on disease severity (3, 6, 17, 33). In the literature, stress is revealed to be a modifiable risk factor that is involved in the onset, the course and the exacerbation of several chronic diseases. In fact, many SLE patients report that stressful life events are linked to exacerbations of SLE symptoms (3). Furthermore, a high percentage of SLE patients seem to perceive a worsening in their clinical symptomatology caused by the effects of daily stress (6). Several researchers such as Peralta-Ramírez *et al.* (6), Adams *et al.* (22) and Pawlack *et al.* (17) have shown that daily stress, and not stressful life events, may worsen the subjective clinical symptomatology of SLE. Therefore, perceived stress plays a central role in contributing to a more comprehensive perspective of SLE symptoms.

It was shown that disease duration was related to the somatisation, obsessive-compulsive, interpersonal sensitivity, anxiety, psychoticism, positive symptom total dimensions, and the positive symptom total index. This can be interpreted as: the higher the number of years with the disease, the lower the psychopathological manifestation scores, probably because SLE patients present an emotional adaptation to chronic disease when they must cope

with the daily symptoms (18, 34). In the research carried out by Purandare *et al.* (10), the SLE sample with psychopathological manifestations was similar to those who presented no psychiatric disorders regardless of the disease duration and the disease activity. However, these authors explained that these findings were due to the small sample size and low statistical power (10).

The disease activity also seems to predict the psychopathological status for dimensions such as interpersonal sensitivity, somatisation, obsessive-compulsive, depression, positive symptom total, and global severity index. Along this line, prior research suggests that disease activity may influence psychological status in the acute phase, causing mild psychiatric disorders (14). In contrast, some findings exploring the link between depressive symptoms and SLE patients' disease activity have been inconclusive (18, 35). Seguí *et al.*'s study (14) and other researchers have claimed that the psychopathological symptoms are similar to what would be expected in other populations coping with similar stress (14, 31, 36). Our results show that specific SLE course factors, such as disease duration or disease activity were associated with psychopathological manifestations. However, in turn, disease severity seems to be related to perceived stress, as previously discussed. Moreover, these results also showed that cumulative organ damage only explained part of the variability of the hostility dimension, probably indicating frustration and feelings caused after becoming aware of impairment to vital functions. Conversely, the study performed by Baker *et al.* (37) found no statistical correlation between psychopathology and the severity of SLE or the degree of renal damage.

Finally, it should be discussed that the major difficulty regarding the evaluation of neuropsychiatric symptoms lies in their attribution to the underlying disease activity or to a concomitant psychopathology secondary to the chronic disease or even to a primary comorbidity, especially for mild psychiatric symptoms. The attribution of these symptoms to the SLE disease (termed primary neuropsychiatric SLE)

or to comorbidities/therapy complications, remains challenging because of multiple problems regarding the available diagnostic tests. Hence, to facilitate physicians' evaluation of these symptoms, several models have been proposed, such as SLICC or the Italian Study Group on neuropsychiatric SLE. The study by Fanouriakis *et al.* (38) evaluated these models and compared them against the clinical judgment of physicians with experience in SLE. These authors concluded that using the SLICC model as a "standard" may lead to problems. This instrument only seems to attribute a small number of neuropsychiatric symptoms to SLE. For these reasons, the judgment of an experienced physician should also be considered. However, this judgment should not be relied upon solely, due to possible subjectivity and different levels of expertise among physician (38). In our study, the investigator that administered the SLICC tool was a physician with 20 years of experience in evaluating and monitoring SLE patients.

When considering the findings of the present study, there are some limitations. Firstly, the cross-sectional nature of this study makes it difficult to obtain conclusive results regarding the directionality of the relationships. It is possible that psychopathological problems are the cause of the impairment in the disease parameters and of the higher levels of perceived stress, or vice versa. Secondly, groups from this study were not statistically equal at an educational level. This difference could introduce a bias; therefore, the results should be interpreted with caution. Thirdly, psychopathological aspects were related to an increase in stress perception but we have not controlled for coping strategies. These strategies should be included in future studies, considering the effect that they might have on the relationship between stress and psychopathological symptoms in SLE patients.

In conclusion, the findings highlight that the SLE sample is at risk of suffering psychopathological alterations, especially in dimensions such as somatisation, obsessive-compulsive and positive symptoms. Comparisons between

SLE patients and the healthy control group show statistical differences in the psychopathological status, with the SLE group reporting lower scores. In turn, psychopathological manifestations seem to be partially influenced by the perceived stress, disease duration, disease activity and cumulative organ damage, and disease severity by perceived stress. In general, these findings may contribute to a more comprehensive understanding of the risk factors of psychopathological alterations in SLE patients. These results also draw attention to the need for clinicians to include psychological components as part of more comprehensive patient monitoring. This information would improve the understanding of medical and psychological components involved in SLE disease. Interventions from the health professional teams could lead to adequate levels of stress and decreased psychopathological symptomatology.

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#### References

1. LUPUS. <http://www.rheumatology.org/I-Am-A/Patient-Caregiver/Diseases-Conditions/Lupus> (2017, accessed 12 January 2017).
2. NISHIMURA K, OMORI M, KATSUMATA Y *et al.*: Psychological distress in corticosteroid-naive patients with systemic lupus erythematosus: A prospective cross-sectional study. *Lupus* 2015; 25: 463-71.
3. DA COSTA D, DOBKIN PL, PINARD L *et al.*: The role of stress in functional disability among women with systemic lupus erythematosus: a prospective study. *Arthritis Care Res* 1999;12: 112-19.
4. GARCÍA-MORALES M, CALLEJAS RUBIO JI, PERALTA-RAMÍREZ MI *et al.*: Impaired sexual function in women with systemic lupus erythematosus: A cross-sectional study. *Lupus* 2013; 22: 987-95.
5. COÍN-MEJÍAS MA, PERALTA-RAMÍREZ MI, SANTIAGO-RAMAJO S *et al.*: Alterations in episodic memory in patients with systemic lupus erythematosus. *Arch Clin Neuropsychol* 2008; 23: 157-64.
6. PERALTA-RAMÍREZ MI, JIMÉNEZ-ALONSO J, GODOY-GARCÍA JF, PÉREZ-GARCÍA M: The effects of daily stress and stressful life events on the clinical symptomatology of patients with lupus erythematosus. *Psychosom Med* 2004; 66: 788-94.
7. NAVARRETE-NAVARRETE N, JIMENEZ-ALONSO J, SABIO JM, PERALTA-RAMÍREZ MI: Pain and psychological distress in patients with systemic lupus erythematosus:

- Comment on the article by Somers *et al.* *Arthritis Care Res* 2013; 65: 1204.
8. BARBOSA F, MOTA C, PATRÍCIO P, ALCÁNTARA C, FERREIRA C, BARBOSA A: The relationship between alexithymia and psychological factors in systemic lupus erythematosus. *Compr Psychiatry* 2011; 52: 754-62.
  9. YU CH, LEE MB, TSENG MMC, LIAO SC: Obsessive-compulsive symptoms as a manifestation of neuropsychiatric systemic lupus erythematosus. *J Formos Med Assoc* 2008; 107: 68-72.
  10. PURANDARE KN, WAGLE AC, PARKER SR: Psychiatric morbidity in patients with systemic lupus erythematosus. *QJM* 1999; 92: 283-6.
  11. IVERSON G, MCCRACKEN L: Attributing psychopathology to systemic lupus erythematosus: some methodological considerations. *Ann Rheum Dis* 1992; 51: 134-5.
  12. YILMAZ-ONER S, ONER C, DOGUKAN FM *et al.*: Anxiety and depression predict quality of life in Turkish patients with systemic lupus erythematosus. *Clin Exp Rheumatol* 2015; 33: 360-5.
  13. MOK C, CHAN K, HO L: Association of depressive/anxiety symptoms with quality of life and work ability in patients with systemic lupus erythematosus. *Clin Exp Rheumatol* 2016; 34: 389-95.
  14. SEGUÍ J, RAMOS-CASALS M, GARCIA-CARRASCO M *et al.*: Psychiatric and psychosocial disorders in patients with systemic lupus erythematosus: a longitudinal study of active and inactive stages of the disease. *Lupus* 2000; 9: 584-8.
  15. DOBKIN PL, FORTIN PR, JOSEPH L, ESDAILE JM, DANOFF DS, CLARKE AE: Psychosocial contributors to mental and physical health in patients with systemic lupus erythematosus. *Arthritis Care Res* 1998; 11: 23-31.
  16. PERALTA-RAMÍREZ MI, COÍN-MEJÍAS MA, JIMÉNEZ-ALONSO J *et al.*: Stress as a predictor of cognitive functioning in lupus. *Lupus* 2006; 15: 858-64.
  17. PAWLACK CR, WITTE T, HEIKEN H *et al.*: Flares in patients with systemic lupus erythematosus are associated with daily psychological stress. *Psychother Psychosom* 2003; 72: 159-65.
  18. BARBASIO C, VAGELLI R, MARENGO D *et al.*: Illness perception in systemic lupus erythematosus patients: The roles of alexithymia and depression. *Compr Psychiatry* 2015; 63: 88-95.
  19. SHARPE L, SENSKYT, ALLARD S: The course of depression in recent onset rheumatoid arthritis: the predictive role of disability, illness perceptions, pain and coping. *J Psychosom Res* 2001; 51: 713-9.
  20. KOJIMA M, KOJIMA T, SUZUKI S *et al.*: Alexithymia, depression, inflammation and pain in patients with rheumatoid arthritis. *Arthritis Care Res* 2014; 66: 679-86.
  21. JUNG JY, NAM JY, KIM HA, SUH CH: Elevated salivary alpha-amylase level, association between depression and disease activity, and stress as a predictor of disease flare in systemic lupus erythematosus: a prospective case-control study. *Med July* 2015; 94: e1184.
  22. ADAMS SG, DAMMERS PM, SAIA TL, BRANTLEY PJ, GAYDOS GR: Stress, depression and anxiety predict average symptom severity and daily symptom fluctuation in systemic lupus erythematosus. *J Behav Med* 1994; 17: 459-77.
  23. ACR-ENDORSED CRITERIA FOR RHEUMATIC DISEASES. SYSTEMIC LUPUS ERYTHEMATOSUS: <http://www.rheumatology.org/Practice-Quality/Clinical-Support/Criteria/ACR-Endorsed-Criteria> (2017, accessed 12 January 2017).
  24. BOMBARDIER C, GLADMAN DD, UROWITZ MB, CARON D, CHANG CH: The development and validation of the SLE Disease Activity Index (SLEDAI). *Arthritis Rheum* 1992; 35: 630-40.
  25. MINIÑO M: Índice de actividad lupídica y tratamiento del Lupus Eritematoso en dermatología. *Dermatol Rev Mex* 2008; 52: 20-8.
  26. GLADMAN D, UROWITZ MB, GOLDSMITH C, FORTIN P, GINZLER E, GORDON C: The reliability of the SLICC/ACR damage index in patients with SLE. *Arthritis Rheum* 1997; 40: 809-13.
  27. STOLL T, SEIFERT B, ISENBERG DA: SLICC/ACR Damage Index is valid, and renal and pulmonary organ scores are predictors of severe outcome in patients with systemic lupus erythematosus. *Br J Rheumatol* 1996; 35: 248-54.
  28. DE LAS CUEVAS C, GONZÁLEZ DE RIVERA JL, HENRY-BENÍTEZ M, MONTERREY AL, RODRÍGUEZ-PULIDO F, GRACIA MARCO R: Análisis factorial de la versión española del SCL-90-R en la población general. *Anales de Psiquiatría* 1991; 7: 93-6.
  29. DEROGATIS LR: SCL-90: Administration, scoring and procedures manual I for the revised version. Baltimore: John Hopkins University School of Medicine, Clinical Psychometrics Research Unit; 1977.
  30. REMOR E: Psychometric Properties of a European Spanish Version of the Perceived Stress Scale (PSS). *Span J Psychol* 2006; 9: 86-93.
  31. ALLEN TW, GLICKSMAN M: Psychologic involvement in systemic lupus erythematosus: A psychometric approach. *Clin Rheumatol Practice* 1986; 64-70.
  32. PALAGINI L, MAURI M, FARAGUNA U *et al.*: Insomnia symptoms, perceived stress and coping strategies in patients with systemic lupus erythematosus. *Lupus* 2016; 25 (9):988-96.
  33. PERALTA-RAMÍREZ MI, JIMÉNEZ-ALONSO J, PÉREZ-GARCÍA M: Which stressors are responsible for the worsening in the clinical symptomatology of lupus?. *Health* 2009; 1 (04): 313-9.
  34. TANI C, TRIESTE L, LORENZONI V, CANNIZZO S, TURCHETTI G, MOSCA M: Health information technologies in systemic lupus erythematosus: focus on patient assessment. *Clin Exp Rheumatol* 2016; 34 (Suppl. 101): 54-6.
  35. PALAGINI L, MOSCA M, TANI C, GEMINGNANIA, MAURI M, BOMBARDIERI S: Depression and systemic lupus erythematosus: a systematic review. *Lupus* 2013; 22: 409-16.
  36. WEKKING EM: Psychiatric symptoms in systemic lupus erythematosus: an update. *Psychosom Med* 1993; 55: 219-28.
  37. BAKER M, HADLER NM, WHITAKER JN, DUNNER DL, GERWIN RD, DECKER JL: Psychopathology in systemic lupus erythematosus. II. Relation to clinical observations, corticosteroid administration, cerebrospinal fluid CP. *Seminars Arthritis Rheum* 1973; 3: 34-51.
  38. FANOURIAKIS A, PAMFIL C, REDNIC S, SIDIROPOULOS P, BERTSIAS G, BOUMPAS DT: Is it primary neuropsychiatric systemic lupus erythematosus? Performance of existing attribution models using physician judgment as the gold standard. *Clin Exp Rheumatol* 2016; 34: 910-7.